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AIOS- COL.RANGACHARI AWARD WINNER

Proteomics-Based Approach For Differential Diagnosis Of Age-Related Macular Degeneration Subtypes

Dr. Pukhraj Rishi, Dr. Ekta Rishi, Dr. Muna Bhende, Dr. Dhanashree Ratra
PRESIDENTIAL ADDRESS

Prof. (Dr.) Mahipal S. Sachdev
Awarded Padmashree by President of India
Chairman, Medical Director & Senior Consultant Ophthalmology. Centre for Sight Group of Eye Hospital
Email: president@aios.org

Respected Chief Guest Shri. Amitabh Kant, Guest of Honour Shri. Sudhir Singla, Prof. Harminder Dua, Prof. Chee Soon Phaik, other dignitaries on the Dias, my esteemed Senior Colleagues, brothers and sisters from the Ophthalmic Community.

It is one of the most important days of my life today, as I stand here in front of you. It is not every day and for everyone to have the proud privilege of addressing the gathering of top Ophthalmic minds in the Country and abroad, including one’s mentors, colleagues and students. This honour that has been bestowed on me is wholly and completely due to the support, faith and encouragement I have received in abundance from each one of you. I thank you all for giving me this opportunity to put in my best for the ultimate glory of Indian Ophthalmology.

It is my proud privilege to welcome amongst us, the Chief Guest for today’s event, Mr. Amitabh Kant, a Career Bureaucrat. Mr. Amitabh Kant is an IAS officer of the 1980 batch. As of June 2019, he is the CEO of NITI Aayog. An alumni of Alliance Manchester Business School, Jawaharlal Nehru University, St Stephens College and Modern School; his passion for the upliftment of his cadre state, Kerala was instrumental in making it “God’s Own Country. “Make in India” and “Stand up India” initiatives would have lost their momentum, had it not been for his passion and zeal to achieve the impossible. With his expertise, experience and efficiency, he is the right torch-bearer as the present government moves towards the target of a 5 Trillion US dollar economy. He has been the catalyst for a lot of positive steps this government has
taken towards promoting entrepreneurs, business and industry. It is only apt, that his presence here today should work as an elixir for us, as we at AIOS stand poised to step on the gas. On behalf of the All India Ophthalmological Society, I extend a warm welcome to Mr. Amitabh Kant, and am sure his presence will leave us richer for ideas and strategy; at the same time giving us an opportunity to acquaint him with the challenges faced by the Ophthalmic Community in India.

I also welcome our Guest of Honour, the beloved leader of BJP and MLA from Gurugram Shri. Sudhir Singla for being with us.

The best way to move forward is to get our bearings by looking at the past. The last couple of years have been filled with a lot of new initiatives, renewed vigor, consolidation of the old activities and innovative projects which were focused on maximum participation from the members of AIOS. It has been in no small measure due to the efforts of Dr. Natarajan, that AIOS has made it a mission to screen all diabetics of India for Retinopathy through the use of Community Outreach, Artificial Intelligence and Mega camps. This unique initiative, with the help of the present government will take us miles ahead in eradicating preventable blindness from the face of this country. The last year saw us at AIOS holding a record number of webinars, CMEs and surgical skill enhancement capsules, with the idea that the physical location of an Ophthalmologist in a remote area should not come in the way of learning and acquiring the latest skills and knowledge.

Last year also saw us making concerted efforts to make our voices heard in the corridors of power as regards the contentious issues plaguing the medical fraternity in general and the Ophthalmic Community in particular. This saw us challenging the applicability of the PNDT act on Ultrasonic Biometry Machines, the irrational rules of the insurance agencies in respect to health insurance packages or payouts and the complex issue of pricing of surgeries in various panels and government
schemes. We also contested the harassment of Ophthalmic Community by GST officers in various states on the issue of laser vision correction surgeries.

But then this is just a pitstop. I will be failing in my duties, if I don’t layout before you today, the path on which I see AIOS moving in the coming year.

Today, the medical care provider has become a convenient and populist target for any folly or shortcoming in the healthcare industry. A case of cluster Endophthalmitis sees the Ophthalmologist being taken to task, even if subsequent investigation proves beyond doubt that the fault lay in the irrigating fluid or some other factor, not in direct control of the treating ophthalmologist. This “shoot the messenger” mentality is further fanned by an overzealous media and individuals out for cheap and quick popularity. The impact it has on the healthcare provider not only results in personal turmoil for him, but also effects his treatment strategy, where the best interest of the patient is diluted by his apprehension about personal safety. We need to impress upon the appropriate authorities the need to have a logical, level headed approach to such events guided by principles of natural justice.

We at AIOS will repeatedly and continually approach all those who matter to make legal framework to safeguard the eye care-provider from physical, financial and emotional distress, when the fault lies somewhere else. This would also include all efforts to insulate doctors from impulsive, violent and abusive behavior at the hands of the patients and relatives.

Closely related to this subject is the status and importance accorded to professional societies like AIOS by government agencies. AIOS is the Ophthalmic Society having the largest number of life members in the world and has members with rich, vast and varied clinical and administrative experience. It is not difficult to envisage the value addition which can be accrued by tapping this talent pool for formulating policies and regulation concerning ophthalmic practice. Unfortunately, till date such symbiotic initiatives have been few and far between. It will be our intention at AIOS to make
the government of the day aware of the substantial benefit to the nation which can be gained by involving national professional societies in formulating policies.

Ophthalmic Practice is unique from the other branches of medical practice, in being equipment intensive and fairly non-dependent on external investigative modalities like laboratory and radiological inputs. This has resulted in ophthalmology being largely practiced in a single specialty clinic or hospital. Irrespective of the size, most of the eyecare facilities are stand-alone, clean, focused day care facilities. This trend is not geographically limited to India, but can be seen in the practice patterns all across the world. Unfortunately, the present regulations do not have any special head under which rules for such day-care centres are formulated. These day-care centres are weighed in the same scale as multispecialty hospitals, resulting in lot of infructuous and illogical requirements being asked to be met by the regulatory authorities. The criteria of infrastructure status being accorded to healthcare facilities relies heavily on the number of in-patients, availability of emergency facilities and such parameters which unjustly exclude eye care centres from being eligible for funding and taxation benefits which accompany the label. This aberration needs rectification, and we at AIOS will ensure that we make the right noises in the right offices, including that of our Chief Guest!!!!

We all daily keep hearing about the ease of doing business, and the way India is climbing the charts of this parameter vis-à-vis other countries. No doubt things are moving in the right direction in this respect, but a few sticky points need to be pondered over.

A medico, after finishing his education, (though a medico’s learning phase never ends), finds himself shackled by various bonds of rural service in sub-optimal facilities. Having done his bit for the country or community, which by the way, no other professional graduate like an engineer or lawyer passing out from the highly subsidized government colleges is required to do, he still finds his right to earn a decent living
clamped by abysmally low financial payout. This is an indirect fallout of the squeeze applied on the rates of health care unilaterally decided by the agencies responsible. A survey by one of the most reputed audit agencies pegged the input cost of a cataract surgery by the currently practiced techniques at Rs 24,000. The rate being offered for a similar surgery under Ayushman Bharat is Rs 7500.

The rates of surgeries offered by government panels like CGHS, DGHS have not been revised at least for a decade. This pill is made even more bitter by the fact that the renumeration offered by health insurance agencies have seen a downward revision, which with the rising human resource and material costs is sounding the death knell for Ophthalmic Care in the country. You can’t realistically offer ridiculously low rates and ask for state-of-the-art care. This is making the practice of Ophthalmology a daunting and unenviable proposition.

Looking inwards, we also have ambitious plans of strengthening our society, making it more effective, vibrant and productive. AIOS has an unmatched pool of human resource skills. More than many of our members are sought after faculty on international podiums and are called to help in tackling complex cases. What is surprising is that despite being a society with a rich heritage, glorious past and an energetic present, we have not been able to garner eyeballs globally. Our International Membership is one way to spread the good work of the society and stamp its relevance on the global stage.

Towards this end, we will initiate ways and means to encourage Foreign Ophthalmologists to become members of the society, increasing our international footprints.

Ophthalmology is rapidly moving towards super-specialization. These special branches of Ophthalmology need to be supported by providing them the right environment to mature. We at AIOS plan to set up specialty groups in coordination with the
national sub-specialty associations to amalgamate and synchronize the efforts towards scientific advancement and growth.

AIOs in the coming year will also try to get a grip on the issue of accreditation. Though substantial progress has been made in this field in the past year by getting special parameters laid out for eye care organizations, much still needs to be done to get all on the same platform. We need to make the requirements more realistic, achievable and driven by practical realities rather than paper filling exercises.

A lot of our young Ophthalmologists are taking the cue from the prevailing startup scenario in the country and venturing out to start their individual/group practices after acquiring reasonable skills. Astute clinicians, these young friends sometimes lack in business acumen. We plan to set up an SOS cell (Support for Ophthalmology Startup) which will hand-hold these entrepreneurs through the whole process of setting up an eye care facility and be a meeting ground for the industry and the practitioner.

Along the same lines, every Ophthalmic Practice requires an HIMS to function. With increasing importance being placed on the record maintenance each passing day, having a standardized and robust Ophthalmic Practice management software becomes an essentiality. We at AIOs envisage developing an HMIS suited to ophthalmology practice and plan to make it available to AIOs members at a nominal per user charge. This will not only reduce the cost of procuring such software, but will also standardize record keeping, thus making transfer, exchange and collation of data easier and effective. As a consequence, this will be the first step in setting up a National Ophthalmology database providing an accurate, exhaustive and one-stop solution for research and training.

On the anvil is a path breaking government resolution, expected to be enforced by April, which will remove the geographical restrictions placed on an Ethics Committee in respect to the projects it can approve. This will open the way for AIOs to have its
own in-house ethics committee to review and approve Ophthalmic Research Projects, thus giving a further impetus to research and clinical trials.

In our country we are blessed with the excellent quality of the best research minds and the abundant quantity of patient data at our disposal. With the easy availability of the ethics committee, I am sure our long-term goal of promoting research will be fulfilled.

Friends, our biggest strength is our unity, and numbers. This strength of numbers empowers us with the power to negotiate from a position of strength. These negotiation skills will be put to use in our dealings with Health Insurance Agencies for including all Ophthalmologists in their eligibility for reimbursement and offering near uniform rates. This will also help us drive a hard bargain with the industry, forcing them to offer reasonable rates and effective after-sales service.

A penny saved is penny earned. These are hard times for eyecare facilities, with input costs rising, regulators tightening the noose and the financial renumeration dwindling. Make in India is something, which is the need of the hour. This indigenous production of material and consumables will help each Ophthalmic setup save some funds, which will be critical in today’s scenario. We at AIOS will walk the extra mile to encourage industry, institutes and individuals in inventing and improvising by providing them with all the support required.

Friends, we, the office bearers at AIOS have set ambitious targets for the society. All of this will remain a dream and a fairy tale on paper, unless we all join hands and resolve to make this a success. It is my humble request to each one of you to help me take this wonderful organization of ours to its rightful place at the top. I am a firm believer of teams being bigger than an individual. Towards this end, I have made it a point to ensure my availability and easy accessibility in whatever post I have held in the past. The same would be my endeavor as President, AIOS. I would be honored to receive your inputs, feedback, suggestions and constructive criticism.
by phone, mail or any other medium, because this will make my job of doing my best for AIOS that much easier.

Before I conclude, I bow in reverence to the lord almighty, who has always been very kind to me. I would like to convey my gratitude to my colleagues in the AIOS OBSC specially Prof. Natrajan, Dr. Barun Nayak, Dr. Ajit Babu Majji, Dr. Lalit Verma, Dr. Namrata Sharma, Dr. Santosh Honavar, Dr. Rajesh Sinha, Governing Council, Managing Committee, the LOC, Haryana Ophthalmological Society, and all others who have worked tirelessly and relentlessly to make my being here possible today. The silent workers at the AIOS Headquarters including Mr. Kripal and Ms. Rakhi need a special mention for their relentless pursuit in meeting deadlines. I am also indebted to my wife, Dr. Alka and my family whose support was the backbone for my being able to dedicate myself single-mindedly to this cause. My second family, each and every member of team Centre for Sight; my special thanks to you for believing in me, and being my strength each and every day. Last but not the least, this journey would not have taken off, had it not been for my Alma Mater, R P Centre for Ophthalmic Sciences.

Once again, thank you all for giving me this responsibility.

Have a fabulous conference and may we progress, prosper and flourish together, making 2020 a year to remember at AIOS.

**Prof. (Dr.) Mahipal S. Sachdev**

Awarded Padamshree by President of India
President, All India Ophthalmological Society
Chairman, Medical Director & Senior Consultant Ophthalmology
Centre For Sight Group of Eye Hospitals
Dear Esteemed Colleagues,

Greetings from the Desk of Editor Proceedings (EP) AIOS. It was great meeting many of you at the Gurugram AIOC 2020. I would like to thank you for re-electing me to the post of Editor Proceedings for the second term (2020 to 2022). We are all moving through difficult times due to the COVID-19 global pandemic and we are coping with the reality of getting used to the New Normal in all facets of our existence. This has also brought about a few changes in the functioning of the wing.

We, at the EP office, have been busy with our proceedings work right from the memorable AIOS meeting in Gurugram and in this address I plan to apprise you of the activities of the EP Wing of AIOS.

**Proceedings Website**

As you know, the Proceedings Website has taken on a new format and become more vibrant from the last term onward. It contains all Invited Talks, Instruction Courses, the Pre-conference Sessions, the Free paper Sessions, the Video Session, and all the Non-Podium presentations including the E-Posters and Videos. The submitted texts of the free papers are also uploaded in the proceedings website.

It gives me great pleasure to inform you that the Proceedings team was active in the background as the Scientific Sessions were happening simultaneously in as many as 18 Halls in Gurugram. A double camera recording facility (which enables a picture-in-picture format in the recording) was in place in most of the larger halls with 300 plus sitting capacity. The rest of the smaller rooms had a single camera recording feature and we have captured the power-points which will have synchronised audio. I had already prepared a list of do’s and do not’s and a check-list to enhance the video capture quality which has been shared...
and meticulously discussed with the audio visual team. But I’m sure that the AIOS appointed A-V team should perform even better in the years to come. About 22 TB of videos were processed and 2986 videos were uploaded into YouTube.

Our IT team has done a commendable job on the raw footage received to enhance the audio and the video quality.

With a strong and robust process in place, we have been able to upload all the available conference videos within two months from the last date of the conference and this was achieved despite numerous restrictions in operations due the COVID 19 pandemic.

We continue to use Word Press as a platform for the AIOS proceedings website. Like in 2019 we have uploaded High-Resolution videos which provide more clarity for viewers. The content has been segmented into ICs, FPs, E-Posters, Physical Posters, Film Festival, Invited talks, Hyde Park and Pre-Conference Sessions. For the convenience of the members, speaker wise videos have been uploaded. The viewers have the option of viewing only a particular topic of interest. Speaker wise filters are available for easy access. Predictive search/autosuggest has been implemented. We have worked on auto-generated tag cloud and related search term. The Proceedings team is looking into new ways to provide scientific value to the members of AIOS.

The Proceedings Website also includes the AIOC 2019 scientific contents as well as the archived contents of 2018 and 2017. These meeting contents are available for you to view and learn.

Many of you have communicated to me appreciating our efforts - Thank you very much.

**Mass E-mail Campaign**

Mass e-mail campaigns with each e-mail highlighting a segment of the AIOC scientific presentations have been a continuation of a new and innovative concept introduced by the Proceedings wing during the previous term (2017-2019). This
has enabled even those who were unable to attend the AIOC meeting to access the rich information presented through their Smart phones and Tablet Devices when they are free or in transit.

Many members have communicated their appreciation for this continued effort from our side.

This has given us enough zeal to work harder and in 2020, we were able to initiate our communications with the AIOS members within a week from the last day of the conference and we intend to disseminate relevant information throughout the year. We have decided to increase the frequency of the e-mails to a biweekly format. In fact, you would already have received more than 80 bi-weekly capsules (as of preparing this report) - including the top selected videos, the Col Rangachari award paper and the BPOSs.

Opening rate of the E-mails ranges from 25% to 60% which is a very impressive number. So I think we have been able to make AIOS Annual Conference Contents reach out to majority of the AIOS Membership.

**AIOS Proceedings Book 2020 (Best Papers)**

It has been a pleasure to put together the best free papers (PDF format) of the Gurugram AIOC conducted between February 13th and 16th, 2020 in the form of the AIOS Proceedings Book (Best Papers) - 2020. This includes an intense effort trying to collect the un-submitted texts at the annual meeting as well as the missing images and tables in the text. All BPOS texts are proofread by proofreaders and I would like to thank all the section editors who are tried their best to help us get the proceedings book ready. This book contains all of the 39 Best Papers of the Sessions (BPOS) this year. All the sections were evaluated by 39 evaluators.

In deference to instructions from the President and Honorary Secretary AIOS, no hard copies of the Proceedings book will be available for the AIOC 2020. This decision was also approved by the Governing Council and the Office bearers of AIOS in line with the AIOS “Go Green” drive, members’ preference for digital
resources, need to share resources with other wings of the society and paucity of funds. The soft copy of the AIOS Proceedings book (BPOS) will be available to all AIOS members on the AIOS Website. The texts of the rest of the free papers presented in AIOC 2020 will be available in the website under appropriate category headings adding great value to the post meeting resource content.

I would like to thank the AIOS Governing Council, Office Bearers & Managing Committee Members, the AIOS Secretarial staff and staff from Numerotech for their cooperation and help provided enabling me to do a highly enjoyable and successful job. My thanks are also due to the highly cooperative team of AIOS members who did proof reading of the BPOS texts. Thanks are also due to the staff of Chakrabarti Eye Care Centre for helping me out at different points in time.

I would also request you to add editorproceedings@gmail.com to your address book so that the educational mails from the Editor Proceedings land up directly to your inbox and not to the promotional or spam category. May I also request you to update your current address, e-mail and cell phone number with AIOS by e-mailing to aiosoffice@aios.org. I would also encourage you to pass on this information to your friends and colleagues.

I will be getting in touch with you at frequent intervals for updates.

Please don’t hesitate to contact me for any queries. Let us all work together to take AIOS to greater heights.

Best wishes
Yours Sincerely
Dr. Arup Chakrabarti
editorproceedings@aios.org
Best Free Paper Awardees

AIOS- Sante Vision Award (Cataract) - Dr. Amar Pujari (P19120) - Delhi Ophthalmological Society:- The “Magic” of Macro Lens

AIOS- Sante Vision Award (Cataract) - Dr. Prabhakar G V (G18472) - PCO Ring – A Novel Device to Prevent Posterior Capsule Opacification and Enhance ToricIOL Stability

AIOS- J S Mahashabde Award - Dr. Karishma Goyal (S17505) - Retinopathy of Prematurity-Epidemiology & Treatment Outcome of Anti-VEGF& Laser Photocoagulation

AIOS- APOS K. Vengala Rao Award - Dr. Santosh Mahapatra (M10205) - Multi Piece PCIOL As Suture Less, Glue Less SFIOL

AIOS- Cornea Award - Dr. Anushri Agrawal (A18605) - Looking Beyond: Sutting Technique in DALK For Patients with Keratoconus for A Better Visual Outcome

AIOS-Rema Mohan Award - Dr. Rajesh Ramanjulu (R14072) - Photo – Biomodulation (PBM) in Diabetic Macular Edema (DME) Resistant to Standard Treatment

AIOS-APOS Pradeep Swarup Award - Dr. Raksha Rao (R17558) - Outcomes of Ruthenium – 106 (Ru106) Plaque Brachytherapy in OSSN With Scleral Invasion

AIOS-D B Chandra Disha Award - Dr. Pratheeba Devi Nivean, [N13366] - Comparative Study on Effects Dorzolamide Vs Timolol On Ocular Bloodflow In Normal Tension Glaucoma

AIOS- APOS Santosh Honavar Award - Dr. Birendra Prasad Kashyap (K02624) - Make Your Own Punctal Plug for Punctal Occlusion

AIOS- S D Athawale Award - Dr. Anita Ambastha (A08530) - Status of Aqp4 – Ab Antibody in Optic Neuritis in A Tertiary Eye Center And Its Implications
AIOS- Ocular Pathology / Ocular Oncology and Tumors Award - Dr. Gagan Dudeja (D08805) - Targeted Retinoblastoma Therapy: Specific Tumor Killing by Cationic Peptides (Caps)

AIOS- Optics/ Refraction / Contact Lens - Dr. Mihir Trilok Kothari (K08617) - Dynamic Ophthalmoscopy (Do): A Novel Objective Technique for Estimation of Accommodation In Children

AIOS- Sujatha Savitri Rao Award - Dr. Amrita Sawhney (S17593) - Case Series of Immunoglobulin G4 – Related Ophthalmic Inflammation: An Emerging Disease

AIOS-Hanumantha Reddy Award - Dr. Simar Rajan Singh (S16917) - Outcomes of an All-Nasal Approach to Lens Sparing Vitrectomy in Stage 4b Retinopathy of Prematurity

AIOS- Shiv Prasad Hardia Award - Dr. Shreyas Ramamurthy (R14399) - Analysis of Visual Outcomes Following Cyclotorsion Compensation Versus None in Smile for Astigmatism

AIOS- Prem Prakash Disha Award - Dr. Siddharth Baindur (B21593) - Surgical Outcomes of Plication Versus Resection in Intermittent Exotropia: A Comparative Study

AIOS- Rakesh Sharma Memorial Award - Prof. Tariq Syed Qureshi (T07159) - Clinical Profile and Visual Outcome of Pellet Gun Related Ocular Trauma

AIOS- Rakesh Sharma Memorial Award - Dr. Moreker Sunil Ratilal (M09512) - Clinical Audit of Ocular Trauma Across Six Tertiary Centers Over 10 Years

AIOS- Narsinga Rao Award - Dr. Murthy Somasheila (M09092) - Utility of Anterior Segment Optical Coherence Tomography (AS–OCT) In Diagnosis of Anterior Scleritis

AIOS- S Natarajan Award - Dr. Pukhraj Rishi (R08659) - Proteomics – Based Approach for Differential Diagnosis of Age – Related Macular Degeneration Subtypes
BEST FREE PAPERS
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The Magic of Macro Lens (Best paper of DOS)
Dr. Amar Pujari, Prof. Namrata Sharma

ABSTRACT
Smart phone-based ocular imaging is an evolving speciality, where, innovative techniques using simple optical instruments can be very fruitful. A commercially available clip lens called “macro lens” is used for high magnification smart phone photography, it is a 10 x magnifying lens. After clipping it along the smart phone camera, high definition Anterior Segment Photography, iris torsional changes, posterior segment retinal photography with added 90 D lens, central corneal thickness and anterior chamber depth quantification can be performed. The imaging technique is easy and inexpensive; therefore, it can be incorporated into routine practices to ease clinical documentation and diagnosis.

KEYWORDS
Smart phone ophthalmic imaging, Macro lens, Smart phones in Ocular Imaging, Iris Torsion, Clinical Photographs, Smart phone optic nerve head assessment, Toric IOL smart phone assessment.

INTRODUCTION
Smart phones have become indispensable in our daily lives as we approach towards the end of the second decade of this millennium. In this regard, Ophthalmology has not been untouched by this massive revolution. Smart phones are convenient tools which can be used to educate, test, document, review and present in clinics and outside, therefore, clinically useful innovations using these devices will have immense benefits across the
Ophthalmic Community.1,2,3 A simple commercially available lens called Macro lens can be attached to any smartphone camera to acquire ocular images for various purposes. The methodology, clinical utility and its significance have been highlighted here.

**MATERIALS AND METHODS**

Commercially available macro lens, which is available online for less than 100 rupees, was used in our observations. The lens is available online at all online stores, manufactured by various manufacturers. The readers can buy any lens and perform these exercises. We do not have any financial interest in any of the products discussed here.

The macro lens comes with a customized clip, and its length can vary.

![Figure 1: Commercially available macro lens with a customized clip mounted/clipped along the smartphone camera](image)

In smartphones where the camera is in its periphery, a small clip can be purchased and when the camera is in the centre of the smartphone, a longer clip can be purchased. Here, in our observations, we preferred an iPhone 6 (Apple Inc. California, USA) and a shorter clip. The lens is clipped to the camera and the following observations were made.
First, the subject is made to sit in front of the slit lamp biomicroscope (Model BQ900; Haag-Streit USA Inc., Mason, OH) on a chair and requested to place his/her chin on the chin rest. Examiner projects a slit or diffuse light on ocular tissues, after which the viewing system of slit lamp biomicroscope is moved away. The observer now slowly moves the smartphone which has been clipped with the lens, usually at a distance of 3 cm to 5 cm from the tissue of interest, a clear image can be seen on the smartphone screen. If required any part of the screen can be manually tapped to focus clearly on any structure, meanwhile the second observer should make sure that both his elbows are perfectly rested on the table surface.

OBSERVATIONS AND RESULTS

High definition Adnexal Imaging: Using the smartphone and macro lens combination, eyelid and other periocular structures can be imaged with great ease.

Anterior chamber Depth and Central Corneal Thickness Quantification: By using the macro lens and smartphone combination Anterior Segment Structures are photographed after projecting a thin slit light of the slit lamp biomicroscope from a perpendicular direction. The images are obtained from the temporal side at an angle of 30 degrees. These images are then transferred on to an image J software and after setting a scale, anterior chamber depth and central corneal thickness is quantified.
Figure 3: Quantification of central aqueous depth

Figure 4: Quantification of central corneal thickness

High definition imaging of the anterior segment structures: By following the steps described above, anterior segment structures, that is Cornea, Anterior Chamber, Iris, Lens, Intraocular Lens and The Posterior Capsule can be imaged clearly and comfortably.
Figure 5 High definition Anterior Segment Images acquired from the front after projecting a diffuse slit lamp light along the Ocular Surface

Figure 6 : Example of Acquired Anterior Segment Photograph

Posterior Pole Retinal Imaging: In addition to the above method, a 90 D lens is held between the smartphone and eye to acquire images of the Posterior Pole Retina. These are clinically useful in various diseases affecting the macula. Here the light source is from the smartphone and the pupil needs to be dilated before imaging.

Torsional changes Quantification of Anterior Segment Structures: In this exercise, a 360 degree protractor camera application is downloaded from the app store. After clipping the lens, the camera application is opened via the downloaded app which
projects a 360 degree protractor on the smart phone screen continuously. Now the same procedure of anterior segment image acquisition is followed and the centre of the protractor is aligned with the centre of the pupil. The iris structures or the iris markings are prominently appreciated, this procedure is repeated pre and post-operatively in strabismus patients who have either oblique muscle overaction or under action. Later by identifying a common iris crypt, change in the torsion can be approximately quantified.

**Figure 7:** Iris images are captured by opening the camera application under a protractor application. Pre and post-surgery images are captured to assess the change in torsion

Punctal dimension quantification: After everting the eyelid, punctal pictures are obtained and pictures are transferred to ImageJ software. After setting a scale, serial monitoring of the punctal dimension can be performed.

**Figure 8:** Quantification of punctal dimensions after transferring the images into ImageJ software
Anterior Chamber Cell Movement Documentation: To document, assess and teach the anterior chamber cell movement in anterior uveitis, endophthalmitis and other conditions with this technique.

![Figure 9: Standstill image of the anterior segment showing anterior chamber cells](image)

**DISCUSSION**

Digital documentation of anterior segment structures can be augmented by the smartphones, as the existing routine tools are expensive, bulky and immobile.

Amongst the smart phone-based Ophthalmic Techniques, Optic Nerve Head Imaging and Retinal Imaging have been explored extensively.\(^1\)\(^-\)\(^5\) Recently Gunasekera et al described unaided or direct Optic Disc Imaging using an iPhone X, however, the description was genuine but the quality of images obtained were not of good quality for diagnosis and/or documentation.\(^5\) We explored this role further\(^6\) and we described good quality disc video documentation,\(^7\) comparisons with standard tools for teaching purposes\(^8\) and also to create retinal montage image in cases of retinoblastoma and other diseases.\(^9\) Our work continues to evolve in this subsection, where, retinal imaging should be more easy, inexpensive and reliable.\(^10\) The other modes of customized adapter based smartphone clips are always appreciated from an innovation point of view, however, when it comes to actual clinical applicability, these may prove less fruitful, because the adapters may not be available to everyone and everywhere, especially in our continent. Therefore, the iPhone X based optic disc and retinal imaging, video documentation and montage creation appears to be more fruitful with less technical difficulties.
The advantages of these simple techniques are

1) Only a small, portable and inexpensive attachment is required for high quality image acquisition.

2) These smartphone-macro lens observations have been compared and contrasted with the existing gold standard tools, and have been found to be reasonably accurate.

3) This simple magnifying lens can be used under various subspecialties to acquire images, therefore, serves a multipurpose role in a larger subset of practitioners.

Limitations of this technique are

1) as the quality of images is dependent upon the camera resolution; the users may not get the same clarity of images with various smart phones.

2) Customized clips for each smartphone are not available at present, therefore manual adjustments in the existing instruments are necessary.

3) The skills of this technique needs to be mastered with repeated practices.

CONCLUSION

To conclude, by simply using the macro lens and free smartphone applications, anterior segment and posterior segment clinical imaging, torsional changes, Anterior Chamber Depth and Central Corneal Thickness quantification, Anterior Chamber Cell Movement documentation and punctal morphological changes can be imaged easily and quite accurately in routine clinical practices.

REFERENCES


Refining the Art of Phacoemulsification – A Radical New Design of Angled Chopper and Dialor (FP 73)

Dr. Gaurav Kapoor

DESIGN CONCEPT OF ANGLED CHOPPER AND DIALER

Cataract Surgery using phacoemulsification is one of the most commonly performed surgeries worldwide and is widely accepted as the preferred method of cataract extraction. However, the move for surgeons from Extra Capsular Cataract Extraction (ECCE) or Small Incision Cataract Surgery (SICS) to phacoemulsification has a very steep learning curve but is essential if they have to meet the aspirations of an increasingly demanding and educated clientele.

The move to phacoemulsification is fraught with complications ranging from capsular tears, leaky wounds to the most dreaded nucleus drop. The Chopper and Dialer are two instruments which are indispensable for the phaco surgeon and are used in all cases. Having performed well over 8000 cataract surgeries over the years using Phacoemulsification, it was evident that the design of the conventional chopper and dialer was fraught with certain problems especially for beginners and even for experienced surgeons as below:-

a) Straight vertical tip leaves very little safety margin for preventing an iatrogenic Posterior Capsular Tear (Figure 1)
b) The straight vertical tip has a reduced peripheral reach (Figure 1)

![Diagram showing Normal Chopper/Dialor and Angled Chopper/Dialor with labels: Safety margin less for beginners, 110 degree forward angulation, Improved safety margin, Better reach to periphery.]

Fig 1

For surgeons using primary incisions at 10 o’clock and 2 o’clock, chopping the nucleus requires sideways movement which causes a lot of wound distortion and reduces the efficiency of chopping. (Figure 2)

![Diagram showing Normal Chopper and Angled Chopper with labels: Normal Chopper: Direction of chopper and Phaco probe misaligned reducing efficacy of chopping, Angled Chopper: 20 degree sideways angulation of tip, More effective chopping without wound distortion.]

Fig 2

Keeping these problems in mind, the design concept of an angled chopper and dialer has been developed to improve the safety profile, reduce risk of complications and increase the efficacy and efficiency of chopping the nucleus during phacoemulsification. Two simple design changes have been incorporated to achieve this.
a) 110 degree forward angulation with sharper ultrafine chopper tip and blunt tip in dialer for Soft Cataracts (figure 1)

b) 20 degree sideway angulation to increase efficiency of chopping and reduce wound distortion. (Figure 2)

These simple design changes are going to be greatly useful in reducing the complications associated with phacoemulsification and improve the efficacy and efficiency of the technique of chopping in phacoemulsification with vastly improved surgical and visual outcomes, especially for the beginners and even intermediate phaco surgeons looking to perfect their technique of chopping in phacoemulsification.
Occupational Radiation Exposure and Cataractogenesis in a Tertiary Care Hospital (Best paper of Odisha State Ophthalmological Society)

DR. SHRUTAKIRTY PARIDA

ABSTRACT

OBJECTIVES

a) To determine the incidence & type of cataract found in occupationally exposed medical personnel and to compare it with non-exposed age & sex matched controls (medical personnel)

b) To find out the Post-Cataract Surgery visual prognosis & compare it with BCVA at presentation in the study subjects and

c) To establish the preventive role of protective eye shields in the exposed group.

METHODS

This is a hospital based case-control study conducted in Regional Institute of Ophthalmology SCB medical college & Hospital, Cuttack from September 2016-August 2018. 223 subjects (Age :20 - 60 years) were selected of which 155 subjects (78 cases and 77 controls) were included, as per the inclusion criteria. All the
selected participants completed a questionnaire regarding detail occupational history after giving written informed consent. A complete ophthalmological evaluation was done including BCVA, IOP, LPI, Dilated Fundus Examination. Lens opacity grading was done with slit lamp biomicroscopy (Haag streit), and graded as Nuclear, Posterior Subcapsular (PSC), and Cortical Opacity by the Lens Opacities Classification System III (LOCS III) system.

RESULTS

Incidence of Cataract in test Vs control group- 24.8% vs 10% with a p-value < 0.0001, which is statistically significant type of cataract in test vs control group- PSC (19%) vs nuclear Cataract (6.3%). Effectiveness of protective eye wears on incidence of cataract is well evidenced with a R.R of 0.387. M:F ratio is 1.48:1, with a earlier onset of cataract in test (40 - 50 yrs) vs control (50 - 60 yrs) group.

CONCLUSION

Radiation Induced Cataractogenesis occurs at lower doses than expected. Frequent failure of use of protective leaded eye wears explains the crucial need for radiation monitoring and risk assessment for medical staff. Long-term follow-up studies are needed to analyze the risk of cataract formation over extended time periods following low-dose ionizing radiation.

INTRODUCTION:

Use of ionizing radiation has led to advances in medical diagnosis and treatment. Exponential growth in the use of fluoroscopy for diagnosis and procedure guidance has enhanced our growing concern regarding occupational radiation exposure. Coronary interventions like coronary angiography, coronary angioplasty & cardiac catheterisation are the most common fluoroscopy guided procedures performed by the interventional cardiologists which makes them most highly exposed of all medical personnels (because of their exposure to scattered X-rays). Failure to use protective leaded eye wears is the major contributory factor.
Crystalline lens is one of the most radiosensitive tissues. Ocular ionizing radiation exposure produces characteristic dose related, progressive lens changes leading to cataractogenesis. Cataractogenesis associated with ionizing radiation is well known from experimental studies and has been demonstrated in humans by studies among survivors of the Hiroshima and Nagasaki atomic bombs.

1. Over the past three plus decades, the International Commission on Radiological Protection (ICRP) has classified radiation effects into tissue reactions (previously called non-stochastic or deterministic effects) and stochastic effects.

2. By definition, tissue reactions result from injury to populations of cells, and are characterized by a threshold below which no effect would occur. Typical examples are cataracts and non-cancer skin changes, the severity of which increases with dose. Deterministic effects occur with a dose threshold depending on the rate of dose delivery (acute, fractionated/protracted, or chronic).

3. UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation) 2008 Report considers radiation induced cataractogenesis as a stochastic effect (non-threshold effect). The latest revision took place in 2012 when the ICRP Seoul Statement on tissue reactions lowered the chronic threshold for VIC (Vision Impairing Cataract) from >8 Gy to 0.5 Gy and the occupational equivalent dose limit for the lens from 150 mSv/year to 20 mSv/year (100 mSv in defined 5 years with no single year exceeding 50 mSv).

PATHOGENESIS OF RADIATION INDUCED CATARACT (E. A. AINSBURY ETAL):

Ionizing radiation is associated with posterior sub-capsular, and sometimes cortical opacities. The damage begins at the anterior surface, where dividing cells normally form a clear crystalline protein fibre that migrates towards the posterior pole of the lens in the PSC region. This differentiation is altered by exposure to ionizing radiations. The fibre cells elongate and align with each other prematurely causing loss of lens fibres\(\frac{1}{4}\) transparency. On a molecular level, the cyclin-dependent kinase inhibitor (CDKN1A) gene, that regulates the cell cycles and DNA synthesis are vulnerable...
to radiation crystallins (lens proteins). It is well known that ionising radiation causes double strand breaks (DSBs) in DNA. Damage to central zone & dividing cells of lens epithelium and impaired DNA damage repair mechanisms in addition to dysregulation of lens cell morphology all contribute to the pathogenetic process.

**AIMS AND OBJECTIVES:**

This study aims at

a) Determining the incidence & type of cataract found in occupationally exposed medical personnel & to compare it with non-exposed age & sex matched controls (medical personnel)

b) To find out the Post-Cataract Surgery visual prognosis & compare it with BCVA at presentation in the study subjects

c) To establish the preventive role of protective eye shields in the exposed group and

d) To create awareness regarding regular and appropriate use of protective equipments, so as to prevent early cataract formation.

**MATERIALS AND METHODS:**

This is a hospital based case-control study conducted in Regional Institute of Ophthalmology SCB Medical College & Hospital, Cuttack from September 2016-August 2018. 223 subjects (Age : 20 - 60 years) were selected of which 155 subjects (78 cases and 77 controls) were included, as per the inclusion criteria (Duration of occupational exposure with dose monitoring > 5 years and Cumulative recorded radiation dose >10 msv /year). The rest participants were excluded (those with history of any cataract or prior Cataract Surgery, Ocular Trauma, Radiation Therapy for any head & Neck Malignancy, any ocular disease, Congenital or Developmental Cataract, Metabolic Diseases that may produce Cataract or prolonged use of systemic & Topical Steroids). Cases included interventional Cardiologists, Interventional Cardiology Staff, Radiologists, Orthopaedicians, Electrophysiology Lab Technicians and Nurses, while the controls
included the same number of unexposed medical personnel of the same age and sex cohort. All the selected participants completed a questionnaire regarding detailed occupational H/o after giving written informed consent. The questionnaire enquired about start & duration of radiation exposure, dose per exposure, average number of weekly procedures, cumulative radiation dose exposure, history of associated risk factors for cataract development, including smoking, use of Steroids, Diabetes Mellitus, Alcohol Consumption. The recorded doses were based on film dosimeter worn outside the lead apron. No separate dose estimates were done for ocular structures, including lens. The participants were enquired about regular use of protective eye shields.

A complete Ophthalmological evaluation was done including BCVA, IOP, LPI, Dilated Fundus Examination. Lens opacity grading was done with slit lamp biomicroscopy (Haag streit), and graded as Nuclear, Posterior Subcapsular (PSC), and cortical opacity by the Lens Opacities Classification System III (LOCS III) system. Statistical analyses were performed with SPSS software. P values less than 0.05 were considered statistically significant. Data is expressed as mean +/- SD for continuous and as percentage for discrete variables. Chi-square test was used for statistical analysis of categorical variables. Risk ratio (Relative risk) was calculated. Biometry was done to calculate IOL Power in patients planned for Cataract Surgery.

RESULTS:

<table>
<thead>
<tr>
<th>AGE RANGE</th>
<th>NO OF EYES WITH CATARACT IN MALES</th>
<th>NO OF EYES WITH CATARACT IN FEMALES</th>
<th>TOTAL NO OF EYES WITH CATARACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 - 40 YRS</td>
<td>06</td>
<td>04</td>
<td>10 (3.2%)</td>
</tr>
<tr>
<td>40 - 50 YRS</td>
<td>29</td>
<td>20</td>
<td>49 (10.9%)</td>
</tr>
<tr>
<td>50 - 60 YRS</td>
<td>11</td>
<td>07</td>
<td>18 (5.8%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>46 (14.8%)</td>
<td>31 (10%)</td>
<td>77 (24.8%)</td>
</tr>
</tbody>
</table>
Table 1. Demographic data in test group

<table>
<thead>
<tr>
<th>AGE GROUP</th>
<th>TEST GROUP (NO OF EYES)</th>
<th>CONTROL GROUP (NO OF EYES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 - 40 YRS</td>
<td>10 (3.2 %)</td>
<td>NIL</td>
</tr>
<tr>
<td>40 - 50 YRS</td>
<td>49 (10.9 %)</td>
<td>04 (1.3 %)</td>
</tr>
<tr>
<td>50 - 60 YRS</td>
<td>18 (5.8%)</td>
<td>27 (8.7%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>77 (24.8 %)</td>
<td>31 (10%)</td>
</tr>
</tbody>
</table>

Table 2. Demographic distribution of cataract in test vs control group:

<table>
<thead>
<tr>
<th>OCCUPATION</th>
<th>MEAN AGE OF ONSET OF CATARACT</th>
<th>NO OF EYES WITH CATARACT (MALES)</th>
<th>NO OF EYES WITH CATARACT (FEMALES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERVENTIONAL CARDIOLOGISTS</td>
<td>45 ± 3</td>
<td>17</td>
<td>02</td>
</tr>
<tr>
<td>INTERVENTIONAL CARDIOLOGY STAFF</td>
<td>48 ± 5</td>
<td>10</td>
<td>01</td>
</tr>
<tr>
<td>NURSES</td>
<td>52 ± 5</td>
<td>00</td>
<td>09</td>
</tr>
<tr>
<td>RADIOLOGISTS</td>
<td>47 ± 4</td>
<td>07</td>
<td>00</td>
</tr>
<tr>
<td>ORTHOPAEDICANS</td>
<td>51 ± 5</td>
<td>05</td>
<td>00</td>
</tr>
<tr>
<td>ELECTROPHYSIOLOGY LAB TECHNICIANS</td>
<td>48 ± 2</td>
<td>03</td>
<td>01</td>
</tr>
</tbody>
</table>

Table 3. Occupational variability of cataract among study subjects:
<table>
<thead>
<tr>
<th>PARTICIPANTS</th>
<th>RADIATION EXPOSURE (YEARS)</th>
<th>AVG NO OF WEEKLY PROCEDURES</th>
<th>AVG NO OF FLUROSCOPY GUIDED PROCEDURES PER WEEK</th>
<th>LENS EQUIVALENT DOSE (IN MSV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERVENTIONAL CARDIOLOGISTS</td>
<td>11 ± 4.5</td>
<td>7 ± 3</td>
<td>5 ± 2</td>
<td>13 ± 8.5</td>
</tr>
<tr>
<td>INTERVENTIONAL CARDIOLOGY STAFF</td>
<td>9 ± 2.5</td>
<td>5 ± 2</td>
<td>3 ± 1</td>
<td>9.6 ± 7.8</td>
</tr>
<tr>
<td>NURSES</td>
<td>10 ± 2.7</td>
<td>3 ± 1</td>
<td>2 ± 1</td>
<td>4.5 ± 2.7</td>
</tr>
<tr>
<td>RADIOLOGISTS</td>
<td>10 ± 2.5</td>
<td>7 ± 2</td>
<td>3 ± 2</td>
<td>8 ± 5.5</td>
</tr>
<tr>
<td>ORTHOPAEDICIANS</td>
<td>9 ± 2.5</td>
<td>3 ± 2</td>
<td>2 ± 1</td>
<td>5.4 ± 2.2</td>
</tr>
<tr>
<td>ELECTRO-PHYSIOLOGY LAB TECHNICIANS</td>
<td>8 ± 3.2</td>
<td>5 ± 3</td>
<td>2 ± 1</td>
<td>9 ± 5.4</td>
</tr>
</tbody>
</table>

Table 4. Radiation characteristics of test subjects:

<table>
<thead>
<tr>
<th>LOCS CATARACT TYPE</th>
<th>TEST GROUP (NO OF EYES)</th>
<th>CONTROL GROUP (NO OF EYES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NUCLEAR</td>
<td>2 (0.64%)</td>
<td>19 (6.3%)</td>
</tr>
<tr>
<td>CORTICAL</td>
<td>16 (5.16%)</td>
<td>10 (3.2%)</td>
</tr>
<tr>
<td>POSTERIOR SUB-CAPSULAR</td>
<td>53 (19%)</td>
<td>3 (0.97%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>77 (24.8%)</td>
<td>31 (10%)</td>
</tr>
</tbody>
</table>
Table 5: LOCS grading of cataract in test vs control:

<table>
<thead>
<tr>
<th>OCCUPATION</th>
<th>NUCLEAR OPACITIES</th>
<th>CORTICAL OPACITIES</th>
<th>PSC</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTERVENTIONAL CARDIOLOGISTS</td>
<td>NIL</td>
<td>03</td>
<td>19</td>
</tr>
<tr>
<td>INTERVENTIONAL CARDIOLOGY STAFF</td>
<td>NIL</td>
<td>04</td>
<td>11</td>
</tr>
<tr>
<td>NURSES</td>
<td>01</td>
<td>03</td>
<td>09</td>
</tr>
<tr>
<td>RADIOLOGISTS</td>
<td>NIL</td>
<td>03</td>
<td>08</td>
</tr>
<tr>
<td>ORTHOPAEDICIANS</td>
<td>NIL</td>
<td>01</td>
<td>05</td>
</tr>
<tr>
<td>ELECTRO-PHYSIOLOGY LAB TECHNICIANS</td>
<td>01</td>
<td>02</td>
<td>07</td>
</tr>
<tr>
<td>TOTAL</td>
<td>02 (0.64%)</td>
<td>16 (5.2%)</td>
<td>59 (19%)</td>
</tr>
</tbody>
</table>
Table 6: Occupation wise cataract distribution:

<table>
<thead>
<tr>
<th>BCVA RANGE</th>
<th>BCVA AT PRESENTATION (NO OF EYES)</th>
<th>1 WEEK POST CATARACT SURGERY (NO OF EYES)</th>
<th>6 WKS POST CATARACT SURGERY (NO OF EYES)</th>
<th>6 MONTH POST SURGERY (NO OF EYES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/6 - 6/18</td>
<td>17</td>
<td>22</td>
<td>35</td>
<td>51</td>
</tr>
<tr>
<td>6/18 - 6/60</td>
<td>35</td>
<td>29</td>
<td>23</td>
<td>15</td>
</tr>
<tr>
<td>6/60 - 3/60</td>
<td>20</td>
<td>20</td>
<td>16</td>
<td>09</td>
</tr>
<tr>
<td>&lt; 3/60</td>
<td>05</td>
<td>03</td>
<td>03</td>
<td>02</td>
</tr>
<tr>
<td>TOTAL</td>
<td>77</td>
<td>77</td>
<td>77</td>
<td>77</td>
</tr>
</tbody>
</table>
Table 7: Visual prognosis in test subjects:

OBSERVATION AND DISCUSSION:

Incidence of cataract in test vs control group- 24.8% vs 10% with a (p-value < 0.0001), which is statistically significant type of cataract in test vs control group - PSC (19%) vs Nuclear Cataract (6.3%). Effectiveness of protective eye wears on incidence of cataract is well evidenced with a R.R of 0.387. M:F ratio is 1.48:1, with an earlier onset of Cataract in test (40 - 50 yrs) vs control (50 - 60 yrs) group. Our study is in accordance with French Society of Cardiology’s O’CLOC study (Occupational Cataracts and Lens Opacities in Interventional Cardiology) which shows increased risk of cataracts among exposed interventional cardiologists compared with a control group. 5. A Study by Junk A et al (2004) showed higher frequency of posterior subcapsular cataracts in 22 out of 59 participants (37.3%). 6. European Society of Cardiology congress study (2009) also revealed significant difference in frequency of lens opacities (37.9% vs. 12%, p < 0.005) between test & control groups. 7. Higher radiation doses have a greater cataract incidence, but the shape of the dose response curve (especially at low doses) is not clear from the available data. Blue Mountains Eye Study shows no association between CT scans of the head and cataract Whereas Beaver Dam Eye Study shows that exposure to CT scans are significantly associated with PSC. 8. Out of 155 subjects – 85 (170 eyes) gave H/o of regular use of protective eye wears for the entire working period. 29 of the 170 eyes (0.17%) of these 85 subjects developed cataract whereas 31 subjects with irregular use of protective eye wears, of which
12 eyes (3.9%) developed cataract. Rest 39 subjects didn't use protective eye shields, of which 63 eyes (20.3%) developed cataract. Relative risk calculated was 0.387 (s/o protective effect).

CONCLUSION:

Radiation induced cataractogenesis occurs at lower doses than expected. Several epidemiological studies strongly suggest a non-threshold effect. It has an earlier onset than senile cataracts. Frequent failure of use of protective leaded eye wears explains the crucial need for radiation monitoring and risk assessment for medical staff. This study will provide some evidence about the risk of radiation-induced cataracts and will help improve the medical personnel’s awareness of the importance of radiation protection. Long-term follow-up studies are needed to analyze the risk of cataract formation over extended time periods following low-dose ionizing radiation.

REFERENCES:


5. (O’CLOC) group (2013) Jacob et al. investigated the risk of cataract in French interventional cardiologists and electrophysiologists & found a mean exposure of 423 mSv was found for a mean working time of 22 years, with an OR of 3.8 (95% confidence interval, 1.3–11.4) for the development of PSCCs in exposed medical personnel compared with non exposed controls.

7. A study presented at the European Society of Cardiology congress in 2009 did use both an exposed and a control group and found a significant difference in the frequency of lens opacities (37.9% vs. 12%, p < 0.005).


Correlation of Quality of Vision, Lens Density and Dysfunctional Lens Index in Presbyopes (FP 1377)

Dr. Rohan Mehra, Dr. Rohit Shetty, Dr. Prajakta Paritekar, Dr. Luci Kaweri

INTRODUCTION

Dysfunctional lens syndrome (DLS) is the term for describing ageing of crystalline lens. [1] This ageing process happens in 3 stages. 2 Stage 1 correlates with presbyopia, starting from 40 years, is associated with loss of accommodation and restricted scattering of light. Stage 2 starting from 50 years, is linked with increase in light scatter and early lens changes may be noticed. Stage 3 is usually seen in 65 years or older and is analogous with obvious lens changes. [2] However this division is not fixed and there is an overlay of symptoms in each stage. [3].

There are patients who complain of decreased visual quality despite having normal visual acuity quantitatively. [4] Also the patients who had corneal laser vision correction surgery in the past may complain that their visual acuity has decreased over time. [5] One of the causes for this could be the increased internal higher order aberrations due to dysfunctional lens. Tools used to assess dysfunctional lens comprise of subjectively studying lens density changes using LOCS III classification, objectively by Scheimpflug Densitometry changes and objective scatter index of optical quality assessment system (OQAS HD analyser). [1] However there were issues due to inter and intraobserver variations in LOCS III and OQAS cannot differentiate whether
the scatter is from cornea or lens. So the cases with dysfunctional lens but no obvious density changes were difficult to be diagnosed.

The iTrace Visual Function Analyzer (Tracey Technologies, Houston, TX) is a Ray-Tracing Aberrometry system that provides several parameters, including the Dysfunctional Lens Index (DLI). [6] A previous study demonstrated a relationship between the DLI and other methods of cataract assessment, such as Scheimpflug-based lens density and the LOCS III grading score. [7] The aim of the current study was to describe the Dysfunctional Lens Index (DLI) in presbyopic patients and to study its correlation with quality of vision metrics and lens density changes based on LOCS III and the Scheimpflug Densitometry on Pentacam HR. (Oculus Optikgeräte, GmbH, Wetzlar, Germany)

METHODS

The prospective, observational, cross sectional study was approved by the institutional research and ethics committee of Narayana Nethralaya Multispecialty hospital, India and conducted in accordance with the tenets of Declaration of Helsinki. Written informed consent was obtained from the patients.

STUDY POPULATION:

Inclusion criteria were patients between 40 to 70 years of age with best Corrected Distance Visual Acuity (CDVA) of 20/20, best Corrected Near Visual Acuity (CNVA) of N6 with clear crystalline lens or early lens colour changes. Exclusion criteria included presence of Corneal Opacity, Posterior Subcapsular Cataract, Obvious Lenticular changes requiring cataract surgery, Posterior Segment Pathologies or any systemic issues limiting the visual potential.

STUDY DESIGN:

Patients underwent a complete eye examination, which included manifest refraction, IOP measurement, slit-lamp examination and dilated fundoscopy. Lens density was graded by two independent masked observers using lens opacity classification system (LOCS III). Objective assessment of lens density was performed with the Pentacam-
HR Scheimpflug camera (Oculus Optikgeräte GmbH, Wetzlar, Germany). Ray Tracing aberrometry (iTrace Visual Function Analyzer) was used to assess the internal aberrations, quality of vision metrics and dysfunctional lens index.

**STATISTICAL ANALYSIS:**

All continuous variables were reported as mean ± standard error of the mean (SEM) after confirming normality of distribution with the Kolmogorov-Smirnov test. The variables analyzed were subjective grading of cataract as clear or early lens changes, maximum and average lens density on Pentacam, Pentacam nuclear staging and Dysfunctional Lens Index (DLI). The quality of vision was assessed by modulation transfer function as area under the curve (MTFAUC), Strehl ratio and Internal Aberrations. For further analysis subjects were divided into three groups based on DLI values (Group I- DLI >7, Group II- DLI 5 - 7, Group III- DLI <5).

**RESULTS**

A total of 166 eyes of 83 patients were included in the study. The study population consisted of 79 men and 87 women. Mean age was 57.92 years (range: 40 - 70 years). Table 1 shows average values of DLI, SR, MTF AUC and Internal HOA.

Of the 76 eyes that were graded clear lens in subjective grading, 51 had grade 1 and 1 had grade 2 Pentacam nuclear staging. And of the 82 eyes that were labelled as early lens changes clinically, 18 cases were graded as PNS 0. (Likelihood ratio 0.005)

**DISCUSSION**

There is increasing awareness among patients about various modalities of spectacle independence. Extensive work has been done on cornea based refractive procedures due to availability of objective parameters. On the other hand, objective parameters for lenticular vision quality assessment are not very popular. Dysfunctional Lens Index is one such objective tool that helps the surgeon to counsel their patients that where exactly is the origin of their problems. This index is provided by wavefront sensor in the iTrace and calculated based on internal HOAs, pupil size and contrast sensitivity. It is ranked as zero (very poor) to 10 (excellent).
The representation of DLI on the iTrace is simple and patient friendly. It uses Snellen’s E-chart to showcase the quality of vision. Poor DLI score is represented by blurred and distorted ‘E’ which becomes well defined and clear as the DLI score improves. This makes it easy for the surgeon to educate and counsel the patient regarding the dysfunctional lens inspite of BCVA being 20/20.

Earlier studies on DLI were done in cataractous eyes. But the real purpose of this tool is to find those cases where the lens behaves as cataract despite the fact that clinical cataract has not become obvious. In our study we found that 16 cases (out of 76), who had dysfunctional lens but were graded clear lens clinically. Which means 21% of cases were sent without clearly explaining them of their situation. With the availability of the current tool, the counselling part would be much easier.

We found a significant positive correlation of DLI with MTF AUC and SR and negative with Internal HOAs, which means that DLI is also an indicator of the quality of vision. Since DLI correlated with average density of Pentacam but not with maximum density and PNS grading, it means we should be looking more at average density in presbyopic patients. Results similar to our study were also found by Fernando et al. They also showed that reduction in CDVA was strongly correlated to DLI than LOCS or Pentacam grading. This emphasizes the fact that DLI is a reliable quality performance indicator of the crystalline lens.

Pentacam gives the objective lens densitometry compared to LOCS grading which may vary from observer to observer. Hence Pentacam densitometry was used to correlate with DLI. Similarly ray tracing aberrometer was selected because of its known advantages over Hartmann Shack aberrometers.

The demand of refractive cataract surgery is on the rise. The era of evidence-based medicine requires objective metrics to quantify the nuclear opalescence. Due to subjective nature of LOCS III and lack of qualitative analysis in Scheimpflug imaging, DLI can be one of the objective indicators for refractive lens surgery. It can also be used for monitoring the progression of cataract over subsequent visits.
Another study conducted by Fernando et al. also showed that patients with poor DLI score turned out to have high CDE score at the end of phacoemulsification surgery. They thus claim the utility of DLI to predict phacodynamics and intra operative events to make the surgeon thoroughly prepared beforehand.

DLI, thus helps the Ophthalmologists to consider lens dysfunction as an important cause of patient discomfort. It postulates preference of lens based procedures over cornea based to alleviate visual quality symptoms of young patients inspite of having clear lens. It is a breakthrough for surgeons to treat presbyopia by doing RLE in cases having poor DLI. It is also a simple educational tool to convince the patient regarding the need for early surgery.

Authors strongly recommend use of this novel objective tool to deliver promising outcomes in modern cataract refractive practices.

REFERENCES:


PCO RING - A Novel Device to Prevent Posterior Capsule Opacification and Enhance Toric IOL Stability. (FP1110)

Dr. Prabhakar G V, Dr. K S Siddharthan, Dr. Jagadeesh Kumar Reddy

METHODS:

50 patients with bilateral grade 2 nuclear cataract were included in the study. Both eyes phacoemulsification was done 1 week apart by same surgeon. One eye was implanted with PCO RING after IOL (hydrophobic) implantation and other was implanted with same IOL without PCO RING. At 3 years post op, patients were valued for PCO. 30 eyes with toric IOL implantation with PCO RING compared with 30 eyes without PCO RING for rotational stability.

RESULTS:

At 3 years, 11 (22%) eyes without PCO RING developed PCO where as only 1 eye (0.5%) developed PCO in which PCO RING was implanted. Mean rotation of Toric IOL at 3 m postoperatively was 2.85 ± 1.54° in eyes with PCO RING and 5.02 ± 1.06° in eyes without PCO RING. Stastically significant in both studies.
CONCLUSIONS:

Insertion of PCO ring along with IOL is effective in both controlling the PCO occurrences thus ensuring long term visual quality and enhances the rotational stability of TORIC IOL enhancing refractive outcomes.

INTRODUCTION:

Opacification of the posterior capsule caused by postoperative proliferation of cells in the capsular bag remains the most frequent complication of Cataract Intraocular Lens (IOL) surgery. 1,2 In addition to classic Posterior Capsule Opacification (PCO, secondary cataract, after cataract), postoperative lens epithelial cell (LEC) proliferation is also involved in the pathogenesis of Anterior Capsule Opacification/Fibrosis (ACO) and Inter-Lenticular Opacification (ILO). 3-6 Secondary Cataract (PCO) has been recognised since the origin of Extracapsular Cataract Surgery (ECCE) and was noted by Sir Harold Ridley in his first IOL implantations.7,8 It was particularly common and severe in the early days of IOL surgery (in the late 1970s and early 1980s) when the importance of cortical cleanup was less appreciated. Through the 1980s and early 1990s, the incidence of PCO ranged between 25-50%.9 PCO is a major problem in Paediatric Cataract Surgery where the incidence approaches 100%. 10-12 One of the crowning achievements of modern Cataract Surgery has been a gradual, almost unnoticed decrease in the incidence of this complication. Our data at present show that with modern techniques and IOLs, the expected rate of PCO and the subsequent Neodymium: Yttrium Aluminium Garnet (Nd: YAG) laser posterior capsulotomy rate is decreasing to a single digit (less than 10%).13,14

Six Factors to Reduce PCO Surgery-Related Factors (“Capsular” Surgery)

1. Hydrodissection-enhanced cortical clean-up

2. In-the-bag fixation

3. Small CCC with edge on IOL surface IOL-Related Factors (“Ideal” IOL)
1. Biocompatible IOL to reduce stimulation of cellular proliferation
2. Maximal IOL optic- posterior capsule contact, angulated haptic, “adhesive” biomaterial to create a “shrink wrap”
3. IOL Optic Geometry Square, Truncated Edge

In spite of taking all the precautions and using latest IOL technology, incidence of PCO at 5 years is as high as 11.9% 15

Considering this unpredictability, for better control on PCO, we designed a new device made of hydrophobic material in the shape of ring which has to be implanted in the bag after IOL implantation. This device is called PCO ring. It works in two ways, one acting as a barrier at the equator preventing migration of epithelial cells, two by pushing IOL optic against posterior capsule thereby eliminating the space for epithelial cells to migrate on to posterior capsule. The same concept applies to enhancing toric IOL stability.

METHODS:

50 patients with bilateral grade 2 nuclear cataract were included in the study. Both eyes phacoemulsification was done 1 week apart by same surgeon. One eye was implanted with PCO RING after IOL (hydrophobic) implantation and other was implanted with same IOL without PCO RING. At 3 years post op, patients were evaluated for PCO. 30 eyes with toric IOL implantation with PCO RING compared with 30 eyes without PCO RING for rotational stability.

RESULTS

At 3 years, 11 (22%) eyes without PCO RING developed PCO where as only 1 eye (0.5%) developed PCO in which PCO RING was implanted. Mean rotation of toric IOL at 3 m postoperatively was 2.85 ± 1.54° in eyes with PCO Ring and 5.02 ± 1.06° in eyes without PCO RING. Statistically significant in both studies.
DISCUSSION

The results of our study suggest that implantation of an PCO ring device has the potential to significantly reduce PCO formation after uneventful cataract surgery. The impact of these findings could be considerable because PCO is still a common event and one that constitutes a burden to the patient, the treating Ophthalmologist,
and the medical system, especially in the setting of premium IOLs. The many approaches that have been tried in the attempt to prevent PCO include pharmacological agents, such as catalin, methotrexate, and mitomycin; they were effective in preventing PCO, but they were toxic to the corneal endothelial cells, iris, ciliary body, and retina.

The mechanism(s) by which PCO is prevented by our device is by acting as a barrier for epithelial cell migration to posterior capsule and by pressing the optic on to the posterior capsule thus eliminating space between optic and posterior capsule for the cells to migrate.

**CONCLUSIONS**

Insertion of PCO ring along with IOL is effective in both controlling the PCO occurrence thus ensuring long term visual quality and enhances the rotational stability of TORIC IOL enhancing refractive outcomes.

**REFERENCES:**


ABSTRACT:

BACKGROUND:

Children with visual disability need augmentation with assistive technology for their academic and non-academic activities. The aim of present study was to assess availability of assistive technology for education and non-education purpose and its trainers in schools for the blind in Delhi.

METHODS:

This cross-sectional study was conducted in ten schools for the blind in Delhi involving a face to face interview with the principals or head teachers. The questionnaire consisted of fifty-one assistive technologies for visual impairment that were divided into writing, reading, math, sciences, games, mobility and daily living devices. Information on availability of special educators or trainers were also collected. Data were analysed descriptively and presented with numerical as well as percentages. Confidentiality of school data per se was maintained.
RESULTS:

Total ten principals were interviewed from ten of the twenty-four schools for the blind in Delhi. Of the 51 assistive technologies, only six devices were available in all schools, and four devices in nine schools, two in eight schools. The remaining technologies had poor availability in these schools. Most of available assistive technologies were haptic or sound based. Availability of visual based devices which would benefit to low vision students was poor. Five mobility trainers were available in these ten schools, whereas 38 teachers for reading and writing training were available.

CONCLUSION:

There were a huge shortage of assistive technology for visual impairment and mobility trainers in schools for the blind in Delhi.

KEYWORDS:

Students with visual disability, Schools for the blind, Assistive technology, Delhi

INTRODUCTION

In India, students with visual disability can study either in special schools for the blind or mainstream schools (inclusive or integrated) for their education. The schools for the blind are designed based on the assumption that children with visual impairment require some special additional resources for academic learning that could not be met in the mainstream or regular schools. [1], [2] Integrated schools are schools that provide few settings with adaptation and resources for students with disabilities, but on condition that disabled student with special educational needs can fit in with pre-existing structures, attitudes and an unaltered environment of the school. Inclusive schools are the mainstream schools where there is a provision to removing all kind of barriers, including attitudinal, to ensure the full participation of everyone irrespective of child’s condition. Such school provides a conducive learning and teaching environments for all children regardless of their physical, intellectual, social, emotional, socio-economic status, religion and ethnicity.[1],[3],[4] Schools are the place where
children learn and develop many academic activities, improve their self-esteem and cognitive function. The fact is that in India, many children with disability do not enroll to schools. Such children are usually ignored and inherently neglected from going to schools due to many reasons. The World Bank reported that children with disability in India are five times more ignored from going to school than children without disability.[5] Further, it is shown that illiteracy rate among children with visual loss is around 80% in India. Another study from developing nations reported showed that the literacy rate among blind and visual impairment was low (3%).[6] It is true that children with visual impairment suffer a severe compromise in educational activities with respect to reading, writing and playing compared to children with good vision. These children need assistive technology either in the form of vision enhancement or vision substitutions or replacement for their educational learning and skills development. There are substantial number assistive technologies available which can enhance and facilitate students in their both academic and non-academic gains. In the educational perspectives, students with low vision up-to 1/60 (Best Corrected Vision Acuity) would likely benefit with visual based assistive technology (VATs) like large print books, magnifiers, electronic magnifiers etcWhereas students with best corrected vision acuity of less than 1/60 would benefit with tactile and sound based assistive technology (TATs) for their education learning, for example, Braille books, audio format materials etc. [7], [8] Children need to learn using these assistive technologies to maximize their academic learning according to vision status. Empirical evidences are available across the world that shows using assistive technologies improve and enhance academic skills in terms of fine and gross motor, reading and writing capacity, mathematics and sciences knowledge and problem-solving skills among children with visual disabilities. [9], [10] Studies also reported about improvement in non-academic performance mobility, social interaction, self-esteem, autonomy and independence in daily living activities.[11] Special schools are the responsible for making accessible and supply of these assistive technologies for visual impairment for their teaching as well as learning. There is a limited or no data available about assistive technology available in schools for the blind in national capital, Delhi. It is also unknown which types of assistive technology predominately
present in these schools for reading and writing to students with visual impairment. Therefore, the purpose of the study is to assess the availability of assistive technology for visual impairment for education and non-education purpose, in schools for the blind in Delhi. To the best of our knowledge, present study is first of its kind in India.

MATERIALS AND METHODS

A cross-sectional descriptive study was conducted in ten schools for the blind of the twenty-four in Delhi during month of June and July 2018. The principal or headteacher of each school was interviewed in the study about availability of assistive technology as well as trained human resources. A study tool consisting of fifty-one assistive technologies was developed for the study. It was further sub-categorized into seven different domains as “Reading”, “Writing”, “Maths”, “Sciences”, “Games & Sports”, “Mobility” and “Activities of Daily Living”. Further, assistive technology in each domain was divided based on body sense use in learning as Visual Based Assistive Technologies (VAT): based on visual skills e.g. large print books, typoscope, magnifiers (Figure 1) etc.

[Figure 1: Magnifiers (near and distance)]
These are assistive technologies that could benefit students with binocular best corrected visual acuity less than < 6/18 to 1/60. Tactile and sound ATs (TAT): based on visual substitution skills e.g. Braille books, DAISY books (Figure 2), walking cane (Figure 3) etc. These assistive technologies could benefit students with binocular BCVA less than 1/60 to no light perception.

Figure 2: DAISY books

Figure 3: Various type mobility canes
A colour pictorial booklet of assistive technologies was also prepared along with the study tool to avoid any confusion about terminologies of the assistive technologies during the interview. In addition to this, information on availability for trainers was also obtained. A team with experience in field work consisted of an optometrist and one medical social worker and principal of each selected school on pre-decided day.

We used the definition of assistive technology as defined by World Health Organization (WHO 2011) - Any piece of equipment, or product, tool whether it is acquired commercially, modified, or customized, that is used to increase, maintain, or improve the functional capabilities of individuals with disabilities. [12][13] The term ‘availability’ in this study defines as any AT being present as well as usable at the time of visits to the schools by researcher. The broken ATs were not included in the category. Ethical approval was obtained from the institute ethics committee. Permission and written consent were taken from respective principal before the interview.

Data management and analysis was done in STATA 14 (StataCorp 2015, Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). Data was analysed descriptively. Confidentiality of data was maintained throughout study period. Anonymity of data for school, including the availability of trained human resources, per se was maintained throughout study period.

RESULTS

A total of ten principals were interviewed from ten schools for the blind, selected conveniently from 24 schools for the blind in Delhi, using a standard questionnaire which consists of fifty-one assistive technologies (Table 1). Of the fifty-one assistive technologies (ATs), only six assistive technologies were available in all schools as shown in table 1. From the remaining ATs, four assistive technologies in nine schools, two ATs in 8 schools and 3 ATs in seven schools were available. All these ATs except audible ball were tactile and sound based (TATs). The remaining ATs were reported as a poor available or less accessible among these schools.
Table 1: Assistive technology in schools for the blind in Delhi

<table>
<thead>
<tr>
<th>Assistive Device</th>
<th>AT type</th>
<th>Schools: 10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Yes (%)</td>
</tr>
<tr>
<td><strong>Reading</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large Print Book</td>
<td>VAT</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Optical Magnifier</td>
<td>VAT</td>
<td>3 (30)</td>
</tr>
<tr>
<td>Braille Reading Books</td>
<td>TAT</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Electronic Magnifiers Aids</td>
<td>VAT</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Audio Format Materials</td>
<td>TAT</td>
<td>9 (90)</td>
</tr>
<tr>
<td>Refreshable Braille Displays</td>
<td>TAT</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Braille Translator Software (Braille 2000)</td>
<td>TAT</td>
<td>5 (50)</td>
</tr>
<tr>
<td>Mobile App for Reading</td>
<td>VAT</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Typoscope (single window)</td>
<td>VAT</td>
<td>1 (10)</td>
</tr>
<tr>
<td><strong>Writing</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Braille Slate and Stylus</td>
<td>TAT</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Braille Type Writer</td>
<td>TAT</td>
<td>9 (90)</td>
</tr>
<tr>
<td>Large Computer Key Board</td>
<td>VAT</td>
<td>3 (30)</td>
</tr>
<tr>
<td>Adaptive Paper</td>
<td>TAT</td>
<td>8 (80)</td>
</tr>
<tr>
<td>Handheld Pen Magnifiers</td>
<td>VAT</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Handheld Held Audio Recorder</td>
<td>TAT</td>
<td>7 (70)</td>
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<td>Walking (Long) Canes</td>
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<td>Children’s Canes (60 to 85 cm)</td>
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<td>Smart Cane</td>
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<td>Talking Watch</td>
<td>TAT</td>
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<td>Simplified Mobile Phone</td>
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</tr>
<tr>
<td>Audio Labeller</td>
<td>TAT</td>
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</tr>
</tbody>
</table>

VAT: Visual Based Assistive Technology, TAT: Tactile & Sound Based Assistive Technology
READING

Of the total nine reading ATs, Braille reading books were possessed by all schools, followed by audio format digital recorders in nine schools. Two of ten schools owned for large print books, electronic magnifiers, and Refreshable Braille Display, whereas three schools had optical magnifiers.

WRITING

Braille slate with stylus and Taylor frame were available in all schools. Braille typewriter was possessed by nine schools and adaptive paper by 8, digital audio recorder by 7 schools. Screen readers like NVDA and Braille notetaker each were available in one of the ten schools.

MATHEMATICS & SCIENCES

Abacus was available in all schools. Seven schools had tactile geometric kit, whereas braille cube and ruler each were owned by 6 schools, followed Braille compass by 5 schools and talking calculator by 4 schools. The assistive technology for sciences learning, tactile map was owned by 7 schools whereas 3D model learning was available in only 2 schools.

MOBILITY

Six mobility canes were included in the list. All schools had at least one or more mobility canes. Of the six canes, walking long cane was owned by nine out of ten schools and smart cane in 8 schools. Other remaining canes (children mobility canes and Guide and symbol cane) were available in two schools.

GAMES AND SPORT

Braille chess and audible balls were present in all schools, whereas large print play cards in 6 schools, tactile dice in five schools, and large print card with braille in two schools.

DAILY LIVING ACTIVITIES

Nine schools of the ten had talking watch (Figure 4), followed by five for simplified mobile phone. The rest of ATs for daily living was available in limited number in schools e.g. color detector and liquid sensor.
Figure 4: Talking watch

TRAINERS

Only five orientation & mobility trainers are available in these ten schools. Nine special teachers or trainers to teach maths and seven for sciences were available in these schools whereas a total 38 teachers were present for reading and writing rehabilitation.

DISCUSSION

Blindness and visual impairment are the conditions that severely affect educational activities amongst children who suffer from it. The schools for the blind are special schools that help children with visual loss for their academic and non-academic development e.g. social interaction, cognitive function. Assistive technology is one of the very important ways to improve such skills and maximize the students’ potential in learning educational exercise. Studies already have proved about the enhancement and improvement in these activities with help of ATs.[14],[9], [15] Schools for the blind must have a wide range of ATs from low cost, low tech to high cost, high tech ATs for children’s education. It is very important to ensure children accessible, but not limited low tech, even high, advanced ATs which can facilitate and maximize education gains.

The present study reports the poor availability of assistive technologies for visual impairment in these schools for the blind. The most frequently available ATs are
TATs, i.e. nine of the ten ATs, only one belongs to VATs. This indicates that the visual based assistive technologies e.g. magnifiers, large print books etc. which would benefit low vision students are not present in most of the schools. This implies that students with Best Corrected Vision Acuity (BCVA) less than 6/18 to 1/60 will have a limited access to VATs in the schools. This group of students constitutes around 14% to 28% of the total students as reported in few studies conducted in these schools in Delhi. [7], [16]

On the contrary, Braille materials like books, slate with stylus are widely present in these schools for reading, writing and training. This shows that students do not have many choices for reading and writing rehabilitation in their schools. They have to learn Braille irrespective of their vision status.

A study conducted on awareness and utilization about assistive technologies among students in schools for the blind in Delhi reported that majority of students irrespective vision status use Braille materials for reading and writing. [17], [18] In India visual disability percentage of 40% or more (BCVA <6/18 or worse in the better eye) can seek for admission in these schools. [19] This shows that students who are not completely blind are also beneficiaries for such schools’ facilities. [20] Therefore, it is an important that this group of students would be able to access VATs for their education.

The poor availability of other visual and tactile & sound based assistive technologies will hinder students in further learning or delay in cognitive development skills in the related disciplines, for example, maths or sciences or games etc. A lack of availability for children walking canes and mobility trainers will hamper students to participate and commute to other school’s indoors and outdoors environments, for example, classroom, library, refectory etc. Few probable reasons for poor availability of ATs are due a lack of awareness among teachers, unable to afford for the ATs, or lack of productions at local etc. However, further study is required to assess factors or reasons for poor availability of ATs in these schools.

The study also shows that there is a huge shortage of trained human resources especially for orientation & mobility, sciences and maths in these schools. This may be linked with the widespread lack of ATs in the schools, resulting less demands for ATs for
visual impairment. Limited special teachers will affect the effective application or adoption of relevant assistive technology in special education training since very often students need one to one or small groups training session.

Few limitations of the study, firstly, the results may not be generalizable since schools are chosen conveniently, secondly, there may be a response bias from headteacher, teachers might like to show that they have a particular AT. We don’t present about the information on awareness and use of ATs among students since it was published in a separate paper.

CONCLUSION:

Children with visual disability not only need assistive technology for their educational activities but also for their future empowerment and employment. There is a widespread of lack of ATs (VATs and TATs) in the schools for the blind in Delhi. This is true that the students with usable vision function for education activities are not able to access the visual based assistive technologies. Further, lack of orientation and mobility trainers in these schools will make students difficult to manage daily movement and accessing schools’ facilities independently.

CONFLICT OF INTEREST:

There are no conflicts of interest.

FUNDING:

No financial disclosure.

REFERENCES


18. Senjam Suraj FA. Situation analysis on the awareness, utilization and barriers to access of assistive technology among children with visual impairment in schools for the blind Delhi [Master’s thesis]. International Centre for Eye Health; London School of Hygiene & Tropical.


Rainbow – A Gift of Vision on Wheels’ – A School Outreach Programme with A Fully Equipped Bus. (FP1190)

Dr. Parul Priyambada, Dr. Ranjini H, Dr. Rajlaxmi Wasnik, Dr. Rajesh Prabu

ABSTRACT

PURPOSE

Rainbow is a comprehensive eye care programme by a tertiary eye care hospital to detect, treat and prevent low vision and permanent visual loss in Coimbatore district with a fully equipped Rainbow bus visiting schools.

METHOD

In Rainbow programme, teacher volunteers who are trained at the base hospital help identify children with visual ailments when the bus visits their school on a scheduled date. The bus which is run by Optometrist and Paramedical Staff, is equipped with Autorefractometer, Noncontact Tonometer, Slitlamp, Ophthalmic Chair Unit, Refraction Facilities, Telemedicine facilities to access doctors and provide real time data at base hospital. Students needing further management visit the base hospital where investigations and surgeries are done free of cost.
RESULTS
To date 2,13,810 students have been screened. 10,631 have been given free spectacles, 2044 students have been seen at base hospital, 122 free surgeries have been performed.

CONCLUSION
Rainbow is a gift of vision to children with undetected untreated visual ailments.

TEXT
INTRODUCTION
Visual defects amongst children are common. This may range from a simple refractive error to various pathologies like Cataract, Ptosis, Strabismus, Corneal Scars, Keratoconus and Retinal Lesions. Around 4% of school children have some form of visual ailment that the children and their parents are unaware of. 40% of childhood blindness is due to preventable/curable causes. The prevention or an early cure of visual ailments in a child not only improves his quality of life and learning but also prevents long term irreversible problem like amblyopia. An effective screening programme helps detect visual ailments early. The Rainbow programme is a Comprehensive Paediatric Eye Care Programme that aims to provide preventive and curative eye care to school children. The rainbow bus is a fully equipped bus with Autorefractometer, Noncontact Tonometer, Slitlamp, Ophthalmic Chair Unit, Refraction Facilities, Opticals and Telemedicine.

MATERIALS AND METHOD
The concept of screening of school children was initiated by Sankara Eye Hospital, Coimbatore in the early 1990s and this was perfected year after year. This programme has now developed into a Comprehensive Paediatric Eye Care Programme that aims to provide preventive and curative eye care to school children. Its motto is to screen school going children and cure visual ailments as early as possible to prevent long term permanent defects like amblyopia. Unique to this programme is the ‘Rainbow
Bus’. First of its kind in the country, the Rainbow bus is an air conditioned fully equipped bus which has various ophthalmic diagnostic equipment like autorefractometer, non contact tonometer, slit lamp, ophthalmic chair unit, refraction unit and an optical counter.

The entire programme is conducted in a phased manner with initial involvement of teacher volunteers. The teacher volunteers are trained at the base hospital to screen children for visual ailments. On a scheduled date the Rainbow bus visits the school. The children are then screened in the Rainbow bus by Paramedical Staff and trained Optometrist. The bus is equipped with telemedicine facilities which help the optometrist, teachers and children to communicate with the doctors in the base hospital. The Doctors have access to real time data from the bus and are able to provide expert opinion. Retinoscopy and refraction is done by the optometrists in the bus. The students who are screened to be normal are given a ‘Green card’ and are educated about the importance of regular eye checkup. The students detected with visual ailments are given a ‘Red card’ and are referred to the base hospital. At the base hospital all investigations and further treatment which may range from glasses to surgeries are done free of cost. The rainbow bus works 5 days a week from 9 am to 5 pm and travels to various schools in and around Coimbatore.

RESULTS

A total of 2,13,810 children (1,01,672 boys and 1,12,138 girls) have been screened to date. Ocular defects have been identified in 21,858 children (10.22 % ) which included Refractive errors, Cataract, Ptosis, Squint and Keratoconus. Out of these, 8111 children have been referred to the base hospital for further management.
10.22% of the screened children had ocular defects.

1,01,672 boys and 1,12,138 girls were screened.
REFRACTIVE ERRORS

Out of 21,858 ocular defects, the most common was refractive errors seen in 12,472 children. These include children with undetected refractive errors as well as those with detected refractive error using glasses where a repeat test was done to detect any change in power.

Refractive errors were seen more commonly in females than males.

Out of 12472 Refractive Errors, 7466 were Females and 5006 were Males.

Refractive errors were more commonly seen in the rural population compared to urban.
79% of Refractive Errors detected were from Rural Population.

To this date, 10661 children have been given glass prescription. 10632 glasses have been given for free. 3086 children were advised to continue the same glasses.

58% of all Ocular Defects detected were due to Refractive Errors.
SQUINT

Squint was seen in 477 children (214 males and 263 females) screened

![Graph showing squint prevalence](image)

*Fig: 6*

Squint was seen more commonly in the rural community 41 children have been benefited from free squint surgery under the rainbow programme.

*Fig: 7*
PTOSIS

Ptosis (drooping of eye) was detected in 66 children, out of which 46 were males.

![Fig: 8](image)

Ptosis was seen more commonly in rural population. The patients were referred to base hospitals. 4 children have benefited from ptosis correction surgeries.

CATARACT IN CHILDREN

Cataract was seen in 28 cases, out of which 13 were Males and 15 were Females.

![Fig: 9](image)

26 cataract surgeries have been done under the Rainbow programme.
KERATOCONUS

Keratoconus is caused by abnormal corneal curvature. This worsens with time and can lead to permanent defective vision. If left untreated, in later stages they might need Corneal Transplantation from the donor to restore the vision. Early detection helps in the prevention of the corneal changes from worsening.

17 patients have benefited from Corneal Collagen Crosslinking (C3R) a procedure that prevents further worsening of keratoconus.

1 patient with very advanced form of keratoconus was detected by the Rainbow Programme and underwent Deep Anterior Lamellar Keratoplasty. Cornea from a donor eye was transplanted and vision was restored for the child.

SURGERIES

A total of 122 surgeries have been done to this date. 63 Males and 59 Females have been operated under rainbow programme

Fig: 10
The Rainbow Programme is an ongoing programme. Data to the present date shows that despite of available facilities and growing awareness, many preventable visual ailments remain undetected.

It is noteworthy that Refractive Error, which is most easily and effectively correctable with glasses remains the most undetectable cause of visual defects in children. This largely affects the child’s learning and development. Furthermore, negligence in wearing glasses at the correct age may lead to amblyopia which may not be reversible after a particular age. Our constant efforts continue to screen this as early as possible and ensure that children benefit with glasses. To add to this, children and parents are constantly counseled and encouraged to use glasses.

Significant number of students were seen to have squint. It is seen that parents are often aware of squint amongst their children but are ignorant to the visual impacts of squint. Even educated parents see squinting as a symbol of luck that can be corrected at a later stage of life, without realizing the fact that it can cause permanent blindness if not treated early. Rainbow ensures these children are referred to the base hospital. After analyzing all parameters, parents are counseled and advised for surgery. An early squint surgery preserves good vision and binocularity and prevents permanent loss of vision.

Amongst parents, it’s a misconception that cataract is a disease of the old. Blinded by this misconception, Cataract is a neglected but significant cause of blindness amongst children. It can be Congenital, Developmental or followed by other causes like trauma. Detecting and treating these cataracts is one of the major success stories of Rainbow.

Similarly, it was seen that parents were unaware of conditions like Keratoconus. Such patients are often detected in school screening and have benefited from collagen cross linking ensuring vision and preventing need for Corneal Transplant later.

Other conditions like ptosis have also been surgically corrected.
CONCLUSION

In conclusion, it is seen that a comprehensive programme like Rainbow not only ensures an early screening of children and detecting visual ailments but also ensures that these patients are followed up and referred to the base hospital where thorough examination and appropriate management is done. This prevents long term effects of poor vision like amblyopia. It is seen that despite the available advancements in eye care, many children lack timely intervention because of negligence and unaffordability on part of parents. Rainbow is a gift of vision to such children. Numerous underprivileged children have benefited from the Rainbow programme.
Retinopathy of Prematurity- Epidemiology & Treatment Outcome of Anti-VEGF & Laser Photocoagulation (FP47)

Dr. Karishma Goyal, Dr. Kamlesh Khilnani, Dr. Ritika Gaur

INTRODUCTION

Retinopathy of prematurity (ROP) is a significant cause of preventable childhood blindness across the world. The continuous rise in the incidence of ROP is mainly because of the recent advancements in neonatal health care and so, an increase in survival rate of low birth weight infants [1]. Globally, 50,000 infants are affected by ROP every year. In India, annual blindness from ROP is around 500 children [2]. A well planned and effective screening strategy combined with early treatment is the most important diagnostic and prognostic factor for ROP management program. This also decreases the incidence of the blinding advance stage of ROP. [3]. The retina of premature infants have poorly developed vascularization, may lead to the abnormal neovascular development. These abnormal new blood vessels are fragile and are prone to leak or bleed. This may cause fibrovascular proliferation and finally retinal detachment in late stages, that is the main cause of visual impairment in ROP. [4]. According to the literature, there is significant and consistent association of three factors with ROP: low gestational age, low birth weight and prolonged exposure of oxygen following delivery. [5]
Intervention options for ROP mainly consist of Laser ablation and anti VEGF intraocular injections. Till now there is no general consensus regarding their use but all studies have shown improved outcome with their use. [6,7,8]

This study aimed to determine the prevalence of ROP in a tertiary center in North-West India and associated risk factors promoting development and progression of ROP. Our research also aimed to contribute to the existing knowledge of ROP in the Indian population. It will help to develop an unified screening guidelines. This study also included the treatment outcome of the identified infants with ROP, using two different modalities of treatment.

MATERIAL & METHODS

The institute ethical committee approved this prospective interventional trial. The study was conducted in the Department of Ophthalmology, in a tertiary center of North-west India in the year 2017. As per the screening guidelines, 200 consecutive newborns who were referred from the Pediatrics Department & those who attended Ophthalmology OPD were included in the study. All the relevant perinatal data including gestational age, post conceptional age and risk factors like exposure to oxygen, sepsis, anemia and blood transfusion, acidosis, total parenteral nutrition, intraventricular hemorrhage, were documented. Prenatal variables were gestational age, birth weight, sex and mode of delivery. Postnatal variables were respiratory distress syndrome, oxygen therapy, sepsis, intraventricular hemorrhage (cranial ultrasound) and blood transfusion.

SCREENING

Screening guidelines were according to national neonatology forum (NNF) of India. Screening for ROP was performed in all preterm neonates who were born < 34 weeks gestation and/or < 1750 grams birth weight; as well as in newborns 34-36 weeks gestation or 1750 - 2000 grams birth weight if they had risk factors for ROP. The first retinal examination was performed not later than 4 weeks of age or 30 days of life in infants born e” 28 weeks of gestational age. Infants born < 28 weeks
or < 1200 grams birth weight were screened early, by 2 - 3 weeks of age, to enable early identification of Aggressive Posterior Retinopathy of Prematurity (AP-ROP).

International classification of ROP (ICROP) was taken as the standard for classification of ROP in 3 zones and 5 stages. [9]. Schedule for follow up was according to the recommendation of AAO, AAP, and AAPO. [10].

Screening was performed by a single retina specialist using an Indirect Binocular Ophthalmoscope with a + 20 diopter lens with all aseptic precautions.

The stage of ROP at the time of diagnosis, treatment intervention, and treatment outcomes, Gestational Age, Birth Weight, the current age of the patient and risk factors were documented.

Treatment was given under ETROP guidelines. Type 1 ROP with Zone 1, posterior zone 2 and plus disease in any zone were treated with Ranibizumab 0.2 mg injection each eye. All other Type 1 were treated with Laser ablation under topical anaesthesia. Type 2 ROP were kept under close observation.

The success of treatment was measured by regression of neovascularization and absence of recurrence. Secondary outcome was measured by complication rate and structural outcome of retina measured by occurrence of myopia at 9 months.

Follow up for Type 2 ROP was done weekly for 1 month or until complete vascularization of retina. Thereafter once a month for one year.

Type 1 ROP were followed twice weekly for 4 weeks after adequate intervention as per the guidelines. Thereafter they were followed similarly as Type 2 ROP. If reoccurrence noted, treatment was given as and when required and follow up was done accordingly.

**STATISTICAL ANALYSIS**

Data was analyzed by software IBM SPSS 19.0. The prevalence rate of ROP was described in simple proportion. Group comparisons were done by the Chi-squared test or Fisher’s exact test for categorical variables. A probability of less than 0.05 was considered significant.
RESULTS

200 consecutive newborns who fulfilled the inclusion (screening) criteria were considered in our study. There were 112 (56%) males and 88 (44%) females. Out of the 200 newborns, 59 (29.5%) developed ROP.

The birth weight of ROP newborns ranged from 700-1800 grams with a mean weight of 1220 ± 270 gm, while that of non-ROP newborns ranged from 820-1900 gm, with a mean weight of 1430 ± 340 grams. The gestational age of ROP newborns ranged from 22-34 weeks with a mean gestational age of 28.83 ± 1.96 weeks; while that of non-ROP newborns ranged from 24 - 38 weeks with a mean age of 31.50 ± 2.88 weeks. The difference of mean weights between two groups was statistically significant with a p-value of 0.0001 (p< 0.05). Also, the difference of mean gestational age between the two groups was significant with a p-value of 0.0001 (p< 0.05).

FIGURE 1-

Scatter plot showing the distribution of cases according to gestational age and birth weight.

Various risk factors were evaluated in our study including sex, mode of delivery [vaginal (55%) or cesarean (45%)], respiratory distress syndrome (RDS) (32.5%), sepsis (62.5%), oxygen therapy (71%), intraventricular hemorrhage (5.5%) and blood transfusion (34%). Table 1 shows the relationship between ROP and risk factors. Statistically, significant relationship had been shown between the occurrence of ROP and oxygen therapy (p = 0.0337), sepsis (p = 0.0094) and blood transfusions (p = 0.0085). No significant relationship was found with sex (p = 0.5249), mode of delivery (p = 0.4462), RDS (p = 0.9549) and intraventricular hemorrhage (p = 0.8684). Mean duration of oxygen therapy required was 6 days (range 2-46 days).
<table>
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</thead>
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<td>31, 28</td>
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<tr>
<td>Mode of delivery</td>
<td>Vaginal 110, Cesarean 90</td>
<td>30, 29</td>
<td>0.4462</td>
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<td>Respiratory distress syndrome</td>
<td>65</td>
<td>19</td>
<td>0.9549</td>
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<tr>
<td>Sepsis</td>
<td>125</td>
<td>45</td>
<td>0.0094</td>
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<tr>
<td>Oxygen therapy</td>
<td>142</td>
<td>48</td>
<td>0.0337</td>
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<tr>
<td>Intraventricular hemorrhage</td>
<td>11</td>
<td>3</td>
<td>0.8684</td>
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<tr>
<td>Blood transfusion</td>
<td>68</td>
<td>12</td>
<td>0.0085</td>
</tr>
</tbody>
</table>
Out of 59 ROP positive newborns, 6 had stage 4 or 5 disease for which they underwent 23G parsplana vitrectomy and 43 newborns underwent interventions in form of LASER or AntiVEGF.

Newborn with advanced disease presented late with no birth record. Mean birth weight that required intervention was 1200 ± 299 grams and mean gestation age was 28.902.09 weeks.

Other 10 cases regressed spontaneously without any intervention. All the 43 newborns, who required intervention, had history of oxygen therapy for an average period of 10 days. Out of these 43 newborn, 28 had sepsis, 4 had respiratory distress syndrome, and 10 had required blood transfusion.

32 eyes were treated with Anti VEGF injection. Out of these reoccurrence was seen in 8 eyes with 4 to 6 weeks and a repeat injection of Anti VEGF was given. Even after second injection, progression didn’t stop in 6 eyes and required Laser ablation. Among complications in this group, 9 had subconjunctival hemorrhage, which resolved by their own and 2 had partial retinal detachment who were treated with pars plana vitrectomy.

Rest 44 eyes were treated with Laser ablation. Out of these 44 eyes, reoccurrence was noted in 10 eyes. These 10 eyes further required Laser treatment. 6 eyes still went into retinal detachment (4 partial and 2 total).

Better structural outcome was recognized with Anti VEGF group than Laser ablation group at 9 months follow up measured by Indirect Ophthalmoscopy. Mean myopia in Anti VEGF group was -1 D and -4 D in Laser group. This stated overall less myopia in Anti VEGF group.

**DISCUSSION**

Due to the betterment of healthcare facilities in Paediatric Neonatal ICUs, there is better survival of high-risk newborns and hence increasing ROP incidence. It is one of the major and serious blinding issue in this age group. Severe ROP, if left untreated, leads to permanent visual loss and thus hampers the quality of life of an individual [11]. In India, the incidence of ROP is reported between 24% and 47%.[12]
In 2004, Gupta et al. (Indian study), reported the incidence of 21.7% [13]. In our study, the incidence of ROP among preterm infants in a tertiary care hospital is 29.5%.

All infants who developed ROP in our study, weighed < 1,800 gram at birth. The majority of the infants had a birth weight between 1,000 & 1,499 gram (69%). The second most common range was < 1000 gram (18.64%). This low rate of cases less than 1000 gram in the current study could be explained by the inadequate and poor nursery and health care systems for premature infants resulting in greater mortality of infants < 1,000 gram. Also due to the lack of proper education on the necessity of visual examination and parents skip follow up. Lastly, due to low presentation rate because of poor referral system. The percentage of ROP positive infants were higher in group with birth weight < 1000 gram (76 %, 25 positive out of 33) where as in group with birth weight between 1,000 - 1,500 gram, it was 55% (64 positive out of 115). This clearly explains the increased ROP association with decreased birth weight.

ROP being a multifactorial disease, poses a necessity to study various risk factors. The most significant risk factors for the development of ROP in our study are low birth weight and low gestational age as also shown in many studies [14,15]. Shah et al [16] and Fortes et al [17] also had similar results. It is because of the increased susceptibility to oxidative damage due to poorly developed vascularization. In our study, the other significant risk factors were oxygen therapy, sepsis, and blood transfusion. [18]

Sepsis causes secretion of endotoxins that effects retinal blood vessels and this may lead to ROP. This significant effect of sepsis on ROP occurrence was also proved by Shah et al. [16], Vinekar et al [19] and Chaudhari et al. [20]

Shah et al [16] and Weinberger et al [21] proved the significant relationship between ROP and oxygen therapy. We also found significant association between the two. According to some studies, duration of oxygen therapy > 7 days was a significant risk factor for the development of ROP [16]. But, like Dutta et al. [22], it was insignificant in our study.
In our study, we found significant association between development of ROP and blood transfusion. Similar findings were reported by Deepak et al.[23] and Dutta et al.[22]. They found that the frequency of blood transfusions was an independent risk factor for the development of ROP. This can be explained as, transfused adult RBCs are rich in 2, 3 DPG and adult hemoglobin, which have less affinity for oxygen, thus release excess oxygen to the retinal tissue. While Hirano et al.[24] stated that iron overload is a major culprit in the development of ROP due to repeated blood transfusion.

Other risk factors including respiratory distress syndrome and intraventricular hemorrhage, showed an insignificant relationship with the occurrence of ROP. Taqui et al.,[25] reported the insignificant relation between ROP and intraventricular hemorrhage, but according to them systemic hypoxia results in Retinal Hypoxia and more need for oxygen therapy and thus there is a significant relationship between the development of ROP and respiratory distress syndrome.

Laser photocoagulation was found to be very effective in regressing ROP. In agreement with Coats et al [1], there was a regression of neovascularization of the retina with regular follow up, following Laser Photocoagulation, supporting the need for rapid treatment intervention to preserve vision. Laser is now considered more effective and precise than cryotherapy to treat severe forms of ROP.[26]

We used Anti VEGF in 32 eyes with Type 1 ROP in zone 1 mainly. 25 % of patients had reoccurrence and 6 % had retinal detachment. Laser was used in 44 eyes. 23% of patients had reoccurrence and 13% had partial or total retinal detachment. Landmark studies done over treatment of ROP are ETROP, BEAT ROP and RAINBOW study. [6,7,8]. They have got similar results. But they include comparison between the groups which our study doesn’t.

Like other studies, this study also has its own limitations. A larger sample size would have authenticated the results more. Genetic, social, economic, nutritional factors should be the focus of future studies in view of developing incidence of ROP. Further study should compare the intervention methods and the efficacy of the results in
large sample with heterogeneous population after proper randomization with a longer followup.

**CONCLUSION**

Gestational age and birth weight are the well-documented risk factors for the development of ROP. But there is a strong need to identify the other risk factors to decrease the burden of this blinding disease. Our study outlines the prevalence of pre and postnatal risk factors for the development of ROP. Thus highlights the need to strategize the screening guidelines for Indian population for better assess. Early recognition and treatment with either Anti VEGF or laser ablation can significantly improve results.

**REFERENCES**


Multi Piece PCIOLAs Suture Less, Glue Less SFIOL (FP557)

Dr. Santosh Mahapatra, Dr. Anuja Mohanty, Dr. Uttam Prakash, Dr. Navya Mannem

ABSTRACT

PURPOSE

To report the outcomes of sutureless, glueless Multi Piece Posterior Chamber Intraocular Lens (PCIOL) as Scleral Fixated Intraocular Lens (SFIOL) Implantation in patients with poor or no posterior capsular support.

MATERIAL AND METHODS

Medical records of 45 eyes of 42 patients who underwent SFIOL implantation where no suture or glue was used to fixate IOL to the sclera from November 2016 to October 2017, with minimum 18 months of follow up were retrospectively analyzed. The Best-Corrected Visual Acuity (BCVA), indication of surgery, other significant Eye Examination Findings, and complications were analyzed.

RESULTS

Out of 42 patients 62% were males and 38% were females. Mean age of subjects was 48.5 ± 16.5 yrs (range 13 - 79 yrs). Mean pre-operative and post-op visual acuity was 1.48 ± 0.6 log MAR units and 0.6 ± 0.3 log MAR units respectively.
Most common complication was vitreous hemorrhage 6 eyes (13.3%) followed by post-operative hypotony in 5 eyes (11.11%). Other complications like Transient Post-Op IOP rise, Hyphema, Tilted IOL, Cystoid Macular Edema, Retinal Detachment were also noted.

CONCLUSION

Multi piece PCIOL used as SFIOL without any sutures and glue is a viable, cost effective method of IOL implantation in eyes with aphakia following surgical complication or trauma, with comparable outcome to other techniques of SFIOL implantation.

KEYWORDS

Multi Piece PCIOL, SFIOL, sutureless, glueless.

INTRODUCTION

Cataract surgery is one of the most commonly performed intraocular surgeries. Presence of weak zonules, inadequate capsular support and optical aphakia (secondary to surgery or posterior lens dislocation) makes the conventional placement of Posterior Chamber Intraocular Lens (PCIOL) in the Capsular Bag or the Ciliary Sulcus difficult or impossible. Such cases can be surgically managed by an Anterior Chamber IOL (ACIOL), iris fixated lens, iris claw lens or sclera fixated IOL (SFIOL). Both ACIOL and Iris fixated/Iris claw lens are associated with pigment dispersion and Intraocular Inflammation. Also, ACIOL and Iris Claw IOLs demand an intact Iris Diaphragm which may not be so in all cases of Traumatic Aphakia.

SFIOL behaves as a PCIOL implanted in sulcus, the position being near the nodal point of eye; hence advantageous. [1] SFIOL though a safer option for Optical Rehabilitation in cases with Inadequate Capsular/Zonular Support is associated with suture related complications. [1] This had led to several modifications in techniques for SFIOL implantation that include glued IOL, suture less, flapless SFIOL. Here we describe a technique of suture less, glueless SFIOL using a three piece PCIOL and analyze the complications associated with this procedure.
METHODS

The records of 45 eyes of 42 patients who had undergone suture less, glue less SFIOL between November 2016 and October 2017 were studied retrospectively. All surgeries were performed by a single surgeon. The study protocol was approved by the institutional ethics committee.

The following details were recorded: age, gender, pre- and postoperative Best-Corrected Visual Acuity (BCVA), indication for surgery, detailed Slit-lamp and Fundus Examination, pre/post operative Intraocular Pressure (IOP) and complications (if any). The patients were followed up postoperatively at 1 week, 1 month, 3 months, 6 months, 12 months and 18 months. The main outcome measures were postoperative BCVA, IOP and intraoperative/postoperative complications.

OPERATIVE PROCEDURE

The surgery was performed under peribulbar anaesthesia. A 270 degrees peritomy was done from 4 to 8 O’clock. 23G 3-port PPV was done in all cases (including those who had undergone primary vitreoretinal surgery). Two partial thickness sclera flaps (4 x 2 mm) were fashioned 180 degrees apart at 3 O’clock and 9 O’clock. A 6 mm sclera corneal tunnel centred at 12 O’clock meridian was made which was used for IOL explantation / lens extraction (in cases of IOL drop/posterior dislocation of lens/ subluxated lens) and IOL insertion. Sclerotomy ports parallel to the iris were made beneath the sclera flaps about 1.5 mm behind the limbus with a 22G MVR blade. A three-piece IOL [polymethyl methacrylate (PMMA) optic and prolene haptics, Aurolens (Aurolab, model number B3602 India) of 6 mm optic diameter, overall size 13.5 mm, A constant 118.5, modified C loops haptics] was preferred (no financial interest) as it is very economic and affordable to the patients. The 3-piece IOL was inserted with McPherson’s forceps through the sclero-corneal tunnel. A 23 G end gripping forceps was introduced through the sclerotomy beneath the scleral flap to grasp the tip of the leading haptic and externalize it. The same technique was again repeated 180º opposite to externalize the trailing haptic.
26 G needle (bent to 60° about 1mm from the hub) fixed to a 2 ml syringe containing trypan blue dye was used to create a stained intra scleral tract on either side to tuck the haptics. The trocars were removed at the end and integrity of the incisions ensured. Conjunctiva was apposed with 8 - 0 vicryl sutures. Subconjunctival injection of Dexamethasone and Gentamicin was given. The eye was padded following antibiotic ointment application. Post operative medications included antibiotic-steroid eye drops in tapering schedule and atropine 1% eye drops. Some patients with post operative hypotony needed a short course of oral steroids.

RESULTS

The study comprised of 45 eyes of 42 patients who underwent PPV with suture less, glue less SFIOL. The mean age of subjects was 48.5 ± 16.5 yrs (range 13-79 yrs). Out of 42 patients 26 were males (62%) and 16 were females (38%).

SFIOL was performed for aphakia following complicated Cataract Surgery in 20 eyes (44.4%). Of these 12 cases (60%) had large posterior capsular rent (PCR), 4 cases (20%) had nucleus drop and 4 cases (20%) had IOL drop. SFIOL was performed for traumatic aphakia in 11 cases (24.4%) – 4 cases (36.36%) had posterior IOL dislocation and 7 cases (63.63%) had Anterior/Posterior Lens Subluxation/Dislocation. Of the total, 7 eyes (15.5%) were operated for aphakia following surgery done elsewhere and 5 eyes (11.11%) underwent SFIOL as a secondary procedure following primary vitreoretinal surgery. One patient (2 eyes) with Marfan's syndrome underwent SFIOL implantation for bilateral subluxated lens.

The mean pre-operative visual acuity was 1.48 ± 0.6 log MAR units. The mean post-operative BCVA was 0.6 ± 0.3 log MAR units at 1month, 0.8 ± 0.2 log MAR units at 3 months, which was maintained till 18months of follow up.

Mean pre-operative IOP was 17.3 ± 6.2 mmHg. Post-operative IOP rise (mean 20.2 + 8.3 mm Hg) was noted in 2 eyes (4.4%) at 1week which returned to normal levels (13.7 + 4.2 mm Hg) at 1month follow-up without any anti-glaucoma medications suggesting inflammation as the cause. Post-operative hypotony (mean IOP 3.2 ± 0.9 mmHg) was noted in 5 eyes (11.11%) but it returned to normal following a short
course of oral steroids. Most common complication was mild vitreous hemorrhage (VH) in 6 eyes (13.3%) which resolved on its own in 1 week. Other complications included cystoid macular edema (CME) in 2 eyes (4.4%), IOL tilt in 3 eyes (6.6%), SFIOL haptic disinsertion in 1 eye (2.2%) and retinal detachment (RD) in 1 eye (2.2%). The RD was noted at 3 months post op when the patient reported sudden diminution of vision. It was a case operated for Traumatic Posterior Lens Dislocation and RD was caused by an anterior break near the ora that was missed.

DISCUSSION

The placement of IOL in the capsular bag is anatomically the most preferable following Cataract Extraction as it provides stable fixation and is closest to the nodal point of eye. In eyes with inadequate or no capsular support there are various IOL implantation or fixation techniques, SFIOL being the most popular and safe. To avoid the suture related complications, Gabor and Pavlidis developed a suture less SFIOL technique where the exteriorized haptics of a PCIOL were fixated into sclera tunnel parallel to the limbus.[2] A standard 3-piece PCIOL with an overall length of 12.5 - 14 mm ensures a stable fixation in the posterior chamber behind the iris.[3] The large optic diameter of 6 mm reduces the risk of significant postoperative decentration.[4] In addition, the longer haptics when exteriorized along its curvature stabilizes the axial positioning of the IOL and thus, reduces IOL tilt.[5]

Minor issues like haptic kinking (occurs if the haptic is not grasped at its tip with the forceps while exteriorizing it) and mild hyphema (due to injury to the iris root/ciliary body) is common with beginners. Other complications were comparable to previously described techniques of SFIOL fixation (Table 1).[6] There was excellent visual recovery at the end of 1 month, which was maintained throughout the 18 months of follow-up.

CONCLUSION

This method of IOL implantation is appropriate for eyes with deficient or absent posterior capsule that can be easily performed with available IOL designs, instruments, and less surgical time. This technique is also safer than other IOL implantation methods.
in cases with inadequate capsular support. Also in cases with deficient iris tissue this method of fixation ensures IOL stability in the absence of iris diaphragm. Our experience with this technique of sutureless, glueless SFIOL with adequate sample and longer duration of follow-up suggests the stability of this surgical technique and its potential in surgical correction of aphakia.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Scharioth et al.[7][sutureless SFIOL, n=63]</th>
<th>Kumar et al.[8][glued SFIOL, n=53]</th>
<th>Yamane et al.[9][flanged SFIOL, n=100]</th>
<th>Our study (sutureless, flapless SFIOL, n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP rise</td>
<td>2 (3.2%)</td>
<td>0</td>
<td>2 (2%)</td>
<td>2 (4.4%)</td>
</tr>
<tr>
<td>Hypotony</td>
<td>1 (1.6%)</td>
<td></td>
<td>2 (2%)</td>
<td>5 (11.11%)</td>
</tr>
<tr>
<td>CME</td>
<td>1 (1.6%)</td>
<td>4 (7.5%)</td>
<td>1 (1%)</td>
<td>2 (4.4%)</td>
</tr>
<tr>
<td>VH</td>
<td>2 (3.17%)</td>
<td>0</td>
<td>5 (8%)</td>
<td>6 (13.3%) - mild VH</td>
</tr>
<tr>
<td>IOL tilt /decentration</td>
<td>3 (5.6%) [decentration]</td>
<td></td>
<td></td>
<td>3 (6.6%) [tilt]</td>
</tr>
<tr>
<td>Others</td>
<td>Spontaneous IOL dislocation - 2 (3.17%)</td>
<td>Hyphema - 2 (3.7%)</td>
<td>SFIOL Haptic disinsertion - 1 (2.2%), RD - 1 (2.2%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Comparison of complication rates with other techniques of sutureless SFIOL
REFERENCES


Our Experience of Pythium Keratitis – A Clinical Diagnostic Dilemma and Challenges in Management. (FP1680)

Dr. Bharat Gurnani, Dr. Shivananda Narayana, Dr. Josephine Christy

ABSTRACT

PURPOSE
To study the demographic profile, clinical diagnostic features, challenges in management, treatment outcomes and ocular morbidity of microbiologically culture proven Pythium keratitis in a Tertiary Eye Care Hospital in South India.

METHODS
Retrospective analysis of microbiologically proven Pythium keratitis patients was performed at a Tertiary Eye Center from October 2017 to October 2019. Demographic details, risk factors, microbiology investigations, clinical course, and visual outcome were analyzed.

RESULTS
Twenty-eight patients were analyzed. Mean age was 43.1±17.2 years. History of injury was present in 61.9% and no history of injury in 28.5%. Visual
acuity at baseline was 6/9 to perception of light (PL). Five (23.8%) patients improved with medical treatment alone and 19 patients underwent Therapeutic Keratoplasty (TPK). Seven had graft reinfection, and 3 developed Endophthalmitis. Final visual acuity was hand movement and positive perception of light in 18 patients, 1/60-6/60 in 4 patients, 6/60 or better in 6 patients and phthisis in 3 patients.

CONCLUSION

Prompt diagnosis, clinical awareness and specific treatment options are needed for managing successfully this devastating corneal disease

INTRODUCTION

Pythium Insidiosum is an Oomycete, otherwise called parafungus since it causes keratitis in eye that closely resembles fungal ulcer. It has gained importance in recent years owing to rare presentation, difficult diagnosis by routine microbiological methods and poor visual prognosis due to absence of response to the conventional anti fungals. Incidence of systemic pythiosis dates back to 1884, whereas ocular infection was primarily reported in Thailand, Australia, USA and Israel in 2009. It is believed that many of the infections in India, might have been unrecognized due to lack of awareness about identification techniques. Reports from South India have started since 2014, paving way to increased knowledge about diagnosing techniques like Zoospore demonstration and DNA sequencing. Medical treatment with anti-bacterials including Tigecycline, Macrolides, Tetracyclines and Linezolid have been studied with susceptibility in animal studies. However, the results are not consistent with good visual outcome in real time scenarios.

This study aims at reporting our experience of Pythium keratitis, the clinical diagnostic dilemmas and challenges faced in management.

STUDY TYPE

Retrospective observational study
STUDY PERIOD
October 2017 – October 2019

METHODS

Case records of all twenty eight patients who were diagnosed as Pythium keratitis at our Centre, were taken and analyzed for demographic profile, clinical features, response to medical and surgical treatment and visual outcome.

RESULTS

There were 28 patients in total over a period of 24 months. One patient had co-existing acanthamoeba cysts with Pythium and was treated for mixed infection. Mean age of the patients was 43.1 years and it ranged from 9 – 70 years. Male: Female ratio was 17:11. There were 13 farmers, 7 housewives, 8 students and software professional. Risk factors were history of injury in 61.9%, bathing in pond in 1 patient and no history of injury in 28.5%. Average time taken from onset of symptoms to presentation was 11.9 days. Visual acuity at presentation ranged from 6/9 to PL+. Clinical features were patchy dot like stromal infiltrates in 3 patients, stromal infiltrate with feathery margins in 10 patients, subtotal infiltrate with peripheral furrowing in 4 patients, tentacular projection in 3, thick endothelial and anterior chamber exudates in 13 patients and total corneal melt in 3 patients. Hypopyon was present in 46.5%. Healing margins were present in 7 out of 28 patients. Characteristic ‘finger-like’ projections were seen in 3 patients.

All patients were positive for fungal filaments on first direct microscopic examination were. 71% had positive Pythium in corneal scraping, 2 patients in repeat corneal scraping and 4 patients were identified late in their clinical course when the corneal button removed for keratoplasty was positive for Pythium. Pythium was confirmed by Zoospore formation in incubated carnation leaf. Five patients healed with medical management. Before culture results 14 out of 28 patients were treated with Natamycin and Voriconazole hourly eye drops and 7 patients were treated with Natamycin eye drop and Itraconazole ointment. After culture results all patients were treated with Linezolid and 18 patients were treated with Azithromycin eye drops. Five patients
healed with medical treatment and 19 patients underwent therapeutic keratoplasty (TPK). Four patients were lost to follow up. Among the healed and TPK group, average time taken for presentation was 4.6 days in the former and 14.18 days in the latter. Also the average infiltrate size at presentation was smaller 14.4mm² in the healed group and 40.12mm² in the TPK group.

Recurrence was seen in 7 patients who required repeat keratoplasty. Adjunctive measures like Tarsorrhaphy was done for recurrent graft melt in 4 patients and cyanoacrylate glue in 4 patients. Endophthalmitis was noted in 3 patients. Final visual acuity was perception of hand movements and positive Perception of light in 18 patients, 1/60 - 6/60 in 4 patients, 6/60 or better in 6 patients and phthisis bulbi in 3 patients. None of the patients required evisceration.

DISCUSSION

Similar to existing reports on Pythium keratitis, the clinical features closely resemble fungal keratitis. Most of the corneal infiltrates in our study were stromal with feathery margins. Like previously described characteristic features of Pythium keratitis, dot like infiltrates, peripheral furrowing and tentacle-like infiltrate margins were found in 8 patients. Other common features noted in our study were, early in the presentation it presents like patchy scattered stromal infiltrates, with tendency to spread towards limbus and a trace hypopyon. During the clinical course, healing margins were seen in 7 out of 28 patients, thereby highlighting success of medical treatment with linezolid and azithromycin. Thick endothelial and anterior chamber exudates were noted in advanced cases confirming the virulent nature and fast progression of the organism.

Four patients who were treated with Azithromycin and Linezolid eye drops and three patients who were treated with Natamycin and Itraconazole ointment attained healing with medical treatment alone. Early presentation with smaller infiltrate size was associated with better outcome. Among the patients who underwent TPK, 40% required a repeat TPK for recurrence of infection and among them 4 patients underwent tarsorrhaphy for repeat graft melt. Cyanoacrylate glue was also used to stabilize the corneal melt in 4 patients. Though Endophthalmitis is a grave complication
in pythiosis, but our study has only 3 cases which were less compared to other studies. Moreover our globe salvage rate was 75% which was comparatively higher than the published literature.

Though the organism in KOH is very difficult to be differentiated from Pythium with its sparsely septate fungal filaments, the characteristic flat feathery edged colorless to light brown growth in a blood agar can be a remarkable clue for change in line of treatment. Culture is mandatory before labeling the case as Pythium Keratitis. The average time taken for this growth can be approximately 3-5 days. Increased awareness among microbiologists about these growth morphologies can improve early diagnosis. Early diagnosis and treatment with upcoming antibiotics like Azithromycin and Linezolid can definitely improve outcomes. If the response seen is not significant in the first week, immediate therapeutic keratoplasty, before the formation of thick anterior chamber (AC) exudates can fasten the recovery. The AC exudates in the angle can remain as a constant source of infection even after a successful clearance of corneal infiltrate during therapeutic keratoplasty.

CONCLUSION

So in a nutshell Pythium keratitis is more prevalent in younger patients < 50 years of age majority being students and software engineers). Most common clinical findings were stromal infiltrate with hyphated edges with or without limbal involvement. Around 70 % patients needed TPK. Majority had poor response to medical therapy. Globe Salvage was around 75%. Since the organism mimics fungus and is highly virulent, still no specific treatment can eradicate it completely. Large scale randomized trials are needed to exactly pinpoint the medical treatment.
Stromal Infiltrate with Tentacular Projections in Periphery

Stromal Infiltrate with Peripheral Furrowing and Trace Hypopyon
Full thickness Infiltrate with thick Endothelial plaque

Graft Re-infection
Innovative Technique of Stromal Lenticule Addition Keratoplasty For Advanced Keratoconus (FP1528)

Dr. Bhupesh Singh, Dr. Neha Bharti, Dr. Sudhank Bharti

INTRODUCTION

Keratoconus is a bilateral, progressive, non-inflammatory eye condition in which there is a thinning and steepening of the cornea occurs.

OPTIONS IN KERATOCONUS MANAGEMENT:

- RGP Trial
- Collagen cross linking
- Intra stromal ring segment
- DALK
- PKP

THE CULPRIT

- Decrease in corneal thickness
- Decrease in corneal biomechanics
- Leads to corneal steepening
- Hydrops

RESEARCH IDEA

To increase the corneal thickness along with corneal stiffness
**ADDITION KERATOPLASTY**

In this procedure a corneal pocket is created into anterior stroma with the help of femtosecond laser.

Donar lenticule harvested from patients who underwent refractive surgery (SMILE) were placed in the lamellar corneal pocket and collagen crosslinking was done.

This in turn increases the corneal thickness of advance keratoconus patients in which epi- off cross linking was not possible.

**SURGICAL VIDEO**

**POST OP OCT AND EPITHELIAL MAP:**
PURPOSE
To know the outcomes of lenticule addition Keratoplasty for advanced Keratoconus.

METHODOLOGY
Prospective interventional study.
12 eyes of 12 patients with advance keratoconus were included in the study.
Eyes with thinnest pachymetry between 350 and 400 micron were included in the study.
Preoperative complete ocular examination and pentacam was done.
Stromal lenticule removed from patients eye of known thickness were used.
Follow up was done at 1 st day, 1 st week, 1 st month, 6 th month and 1 st year.

RESULTS
Corneal Pachymetry-Corneal pachymetry was increased in all cases depending upon the thickness of stromal tissue added.

![Graph showing corneal pachymetry over time](image)

Pre op 3 month 6 months 1 year

Keratometry-Keratometry reading showed significant decrease. Average decrease in keratometry reading was 3 Diopters.
RESULTS

BCVA-Comparison of preoperative and 1st year postoperative UDVA (uncorrected distant visual acuity) and CDVA (corrected distant visual acuity) showed statistically significant improvements (P = 0.022 and 0.006, respectively) from 1.69 ± 0.29 to 1.32 ± 0.28 and from 1.05 ± 0.16 to 0.60 ± 0.31 logMAR respectively. All eyes showed an improvement in UDVA (P < .001).
COMPLICATIONS:

• No complications were reported in any of the eyes.
• No eyes had graft rejection or infection at 1 year follow up.

DISCUSSION:

• This technique holds significant potential for treating advanced cases of keratoconus.
• Rate of doing DALK/PKP in keratoconus eyes can be reduced with this procedure.

CONCLUSION

• Surgical technique is easy to learn and perform.
• Limitations in the availability of laser lenticule extraction system.
• Addition keratoplasty is an innovative procedure with good outcomes.

Long term results will further establish this technique as a treatment modality for keratoconus.
Blindspot In Ultrasound Central Corneal Thickness (CCT) Measurement. CCT Of Apex Vs CCT Of Vertex (FP1425)

Dr. R. Prasanna Venkatesh, Dr. Abhinay A, Dr. Sathyan Parthasarathi

ABSTRACT

INTRODUCTION

Corneal Thickness is an important and sensitive indicator of corneal health. It is useful in monitoring corneal diseases such as Corneal edema and Keratoconus; and selecting patients for Refractive Surgery. Central Corneal Thickness (CCT) is a risk factor for Primary Open Angle Glaucoma (POAG) and an important pre-operative parameter for refractive surgeries.

AIM

To compare CCT using ultrasound pachymetry (CCT apex) and Specular Microscopy (CCT vertex), and also to find out the intra-reading variability between readings produced by the same instrument.
MATERIALS AND METHODS

This prospective study was conducted on 12 patients (24 eyes) aged 20 to 50, with clinically non-pathological corneas. The patients underwent CCT measurements by both ultrasound pachymetry and specular microscopy. Both the eyes were analysed. Eight measurements by Specular Microscopy and eight measurements by ultrasound pachymetry were taken by two different observers on day one, followed by repeating the same on day two. Each observer was masked of the values from the other.

STATISTICAL ANALYSIS

The readings were averaged and compared by paired t-test. SPSS software was used for statistical analysis. Variability between the eight readings produced by the same instrument was calculated and coefficient of variation was plotted. Inter-examiner variability and intra-examiner variability of the two modalities were also studied, and it was considered statistically significant if the p value was less than 0.05.

RESULTS

The mean CCT by ultrasound pachymetry was 522.7 μm and the mean CCT by specular microscopy was 519.4 μm. The mean CCT by two machines varied by 3.3 μm. However the coefficient of variation of the 8 readings varied significantly between the machines. On an average, the coefficient of variation was 0.4% compared to 0.8% in Specular Microscopy and ultrasound pachymetry respectively. 1% of variation would indicate a 5.2 μm from the mean CCT, if mean CCT was 520 μm, on both sides (standard deviation).

CONCLUSION

The CCT measurement by ultrasound pachymetry gives slightly higher values compared to Specular Microscopy measurement. The intra-reading variability of ultrasound CCT is twice as that compared to the intra-reading variability.
INTRODUCTION

Corneal thickness is an important and sensitive indicator of corneal health [1]. It is useful in evaluating corneal barrier and endothelial pump function, monitoring corneal diseases such as corneal oedema and keratoconus, and selecting patients for refractive surgery [2,3]. In clinical practice, it is useful in the evaluation of Contact Lens Wear and Dry Eye Therapy [4,5]. Also, CCT is a significant risk factor for progression of ocular hypertension to POAG, thus an important parameter in the risk profiling of ocular hypertensives and glaucoma patients [6,7]. CCT is also a predictive factor for glaucoma progression in patients with higher baseline intraocular pressure (IOP). Since IOP measurement by applanation tonometry is influenced by CCT, it is important to obtain the reliable Corneal Pachymetry for each patient with glaucoma and adjust the IOP for the measured CCT [1,8].

There are numerous methods available to measure CCT. The two different centres of the cornea (the corneal apex and the corneal vertex as shown in Figure 1) are measured by using two different techniques. The corneal apex CCT is measured by using the pupillary centre (optical axis) as a landmark. Whereas the corneal vertex CCT is measured by using a fixation target and aligning the corneal vertex with the visual axis, by Purkinje image method.

Currently, ultrasound pachymetry is viewed as the gold standard because it is very easy, fast and convenient to repeat several measurements to minimise error [7]. It also has a high degree of intra-operator, inter-operator and inter-instrument reproducibility [9]. Ultrasound pachymetry is a contact procedure which measures CCT from apex. It
requires contact with the cornea and uses the Doppler Effect to determine thickness [4].

Figure 1. Centres of the cornea - Corneal apex and Corneal vertex

Literature reveals there is a potential blindspot in the methodology of the studies involving ultrasound pachymetry, on how the CCT from the apex was measured. In majority of the studies, the identification of the centre of the cornea was not mentioned properly, there is no proper description regarding the orientation or placement of the probe, and some studies even ended up citing a previous study for their methodology without proper scientific back up. [10,11,12]

A significant yet thought provoking point was that the investigator seemed to visually locate the centre for placing the probe during CCT measurement from the corneal apex, which can lead to bias as shown in Figure 2,3.

Whereas specular microscopy is an automated procedure where the investigator has very minimal role to play. Non-contact Specular Microscopy with Nidek CEM 530 (NIDEK CO., LTD., Japan) specular microscope, is a new non-contact optical instrument that provides pachymetry measurements from the vertex (CCT vertex) and Specular Microscopic examination simultaneously as shown in Figure 4. Measurement of corneal thickness by Specular Microscopy requires differential focusing on the epithelial and endothelial cell density.
Figure 2. Probe positioning on the cornea.

Figure 3. Orientation of the probe in relation to the cornea.
Therefore, in this prospective study, CCT measurements of Specular Microscopy (CCT vertex) were compared with CCT measurements of Conventional Ultrasonic Pachymetry (CCT apex). This study has also evaluated CCT measurements made with Specular Microscopy and Ultrasound Pachymetry between two different observers on same day (Inter-examiner variability) and between same observer on two different days (Intra-examiner variability). Intra-reading variation among the 8 readings taken from the two different machines were also tested. To our knowledge, this is the first study to test the intra-reading variability.

MATERIALS AND METHODS INCLUSION CRITERIA

- Non-pathological eye with virgin corneas
- Age of 20-50 years

EXCLUSION CRITERIA

- Any previous Refractive procedures
- Any previous Corneal procedures
- Uncontrolled Diabetes mellitus
- Any previous Glaucoma surgeries
- Corneal pathologies like Dystrophies, Degeneration, Micro-Cornea, Irido Corneal Endothelial Syndrome

**DAY-1 EXAMINATION**

- Specular readings by examiner A for both eyes (8 readings)
- Specular readings by examiner B for both eyes (8 readings)
- Apply proparacaine (0.5%) eye drops to both eyes and wait for 5 minutes
- Ultrasound Pachymetry by examiner A for both eyes while asking the patient to fixate on a target (8 readings)
- Ultrasound Pachymetry by examiner B for both eyes while asking the patient to fixate on the same target (8 readings)

**DAY-2 EXAMINATION**

- Repeat specular readings by examiner A for both eyes (8 readings)
- Repeat specular readings by examiner B for both eyes (8 readings)
- Apply proparacaine (0.5%) eye drops to both eyes and wait for 5 minutes
- Repeat ultrasound pachymetry by examiner A for both eyes (8 readings)
- Repeat ultrasound pachymetry by examiner B for both eyes (8 readings)

**ULTRASOUND PACHYMETRY**

Ultrasound pachymetry was determined using A-scan (DGH technology, Inc, Pachette 2, USA). Prior to taking the measurement, the ultrasound pachymeter was calibrated according to the manufacturer’s instruction manual. A-scan velocity was set at 1640 m/s for all the measurements and then tested with an appropriate test block [13]. Topical anaesthesia used was proparacaine hydrochloride 0.5% eye drops. The patient was made to sit upright and was asked to look straight ahead. The hand held probe was placed perpendicularly on the centre of the cornea, which was visually located by the investigator. All measurements of ultrasound pachymetry in the study were performed by the same investigator. Eight
readings were obtained. Values with Standard Deviation (SD) of 5 μm or less were considered suitable for inclusion [8]. The probe was sterilised with alcohol after using for each patient.

**SPECULAR MICROSCOPY**

A Non-Contact Specular Microscope (CEM-530; NIDEK CO., LTD., Japan) was used to obtain the CCT measurement. The participant’s head was positioned against the head band and chin rest. They were instructed to look straight ahead at the fixation target. Images of the central corneal area were captured after proper positioning of the alignment dot circle bar, on the screen, with the Purkinje image method of the cornea. CCT analyses were carried out automatically with the retraceing method using the manufacturer’s built in image analysis software.

**STATISTICAL ANALYSIS**

The readings were averaged and compared by paired t-test. SPSS software was used for statistical analysis. Variability between the eight readings produced by the same instrument was calculated and coefficient of variation was plotted. Inter-examiner variability and intra-examiner variability of the two modalities were also studied, and it was considered statistically significant if the p value was less than 0.05.

**RESULTS**

Among the 12 patients, 24 eyes were examined totally four times (two times by investigator A and two times by investigator B). So in total there were 96 data set from 24 eyes to be analysed. The mean CCT by Ultrasound Pachymetry is 522.7 μm and the mean CCT by specular microscopy is 519.4 μm. The mean CCT by two machines varied by 3.3 μm.

However the coefficient of variation of the 8 readings varied significantly between the machines. On an average the coefficient of variation was 0.4% compared to 0.8% in specular microscopy and ultrasound pachymetry respectively as shown in Figure 5,6. 1% of variation would indicate a 5.2 μm from the mean CCT, if mean CCT is 520 μm, on both sides (standard deviation).
DISCUSSION

CCT is a frequently measured parameter in clinical practice. Though the indications vary, ultrasound pachymetry has been the gold standard for measurement of CCT. Development of newer modalities like Orbscan, Pentacam, Anterior Segment-Optical Coherence Tomography (AS-OCT) and Specular microscopy has widened the options and introduced further accuracy.
In this study, the CCT measurements of ultrasound pachymetry (CCT apex) and specular microscopy (CCT vertex) were compared. The CCT measured by ultrasound pachymetry is slightly higher than the CCT measured by specular microscopy. The possible reason may be due to the influence of local anaesthetic agent or the unlikely human error in placement of the probe while performing CCT with ultrasound pachymetry.

The corneal vertex (which intersects the visual axis) is slightly nasal compared to the corneal apex (which intersects the optical axis) as shown in Figure 7,8,9,10. Difference between CCT measured between the two centres in our study was 3.3 µm. Other studies revealed that they can be as minimal as less than 1 µm [14]. In non-pathological eyes, the corneal vertex and the apex are very close to each other. Therefore the CCT values can be taken from any one of the centres.

Figure 7. Corneal vertex versus corneal apex

Corneal vertex (2) is slightly nasal to the corneal apex (1)
Figure 8. Corneal apex

Figure 9. Corneal vertex
However the variability of one reading over another with the same instrument was twice with CCT by ultrasound, compared to the intra-reading variability of CCT by Specular Microscopy. According to our knowledge, this is the first paper to highlight on this variability (intra-reading variability). Previously there were papers on intra-session, inter-session, intra-observer, inter-observer variability of CCT but none on the intra-reading variability. So far this has somehow fallen in our blind spot.

INTER-EXAMINER VARIABILITY

There is a statistically significant difference between examiner A and B for ultrasound CCT on day one. There is no statistical significance between examiner A and B for ultrasound CCT on day two. This can be explained by the difficulty in reproducibility of ultrasound pachymetry, as it is depend on the examiner for the manual placement of the probe. There is no statistical significance between examiner A and B for specular CCT on day one and two respectively. This can be explained by the automated reading taken with the help of an internal fixation target focusing the purkinje image consistently on the same spot on the corneal vertex, for performing the test.

INTRA-EXAMINER VARIABILITY

There is statistically no significant difference between Specular and Ultrasound CCT by examiner A on day one. There is a statistically significant significance between specular and ultrasound CCT by examiner A on day two. Similarly there is a statistically significant difference between the specular and ultrasound CCT by examiner B on
day one. And there is no statistical significance between specular and ultrasound CCT by examiner B on day two. Intra examiner variability is inconsistent owing to more variability of ultrasound CCT readings compared to the specular CCT readings.

Studies have also shown that the repeatability of Specular Microscope is comparable to ultrasound pachymetry for CCT measurement and highly reliable [15].

CONCLUSION

The CCT measurement by Ultrasound Pachymetry gives slightly higher values compared to Specular Microscope measurement. However both instruments are comparable to each other with good reliability and can be used interchangeably.

The intra-reading variability of ultrasound CCT is twice as that compared to the intra-reading variability of specular microscopy. Though statistically significant, it may only have mild clinical relevance. However the clinical relevance of the spread is still important in routine practice.

REFERENCES


Looking Beyond: Suturing Technique in DALK For Patients with Keratoconus for A Better Visual Outcome. (FP1452)

Dr. Anushri Agrawal, Dr. Jagadeesh Kumar Reddy K, Dr. K S Siddharthan

ABSTRACT

This prospective study was done to assess a new donor trimming and suturing technique with the change in keratometry over time following DALK in patients with advanced keratoconus. 70 consecutive patients who underwent DALK for advanced keratoconus from period of January 2013 to December 2016 were followed up for a period of over 2 years. Initially at the time of surgery, tight sutures were put and keratometry readings were noted at every follow up visit. Gradual steepening of cornea was seen in successive follow-up visits bringing the eye from immediate hyperopic state to emmetropic state over time. The technique of use of tight sutures at the time of DALK surgery helps in favourable visual outcome in course of time due to later steeping effect on the cornea.

INTRODUCTION

Keratoconus is a degenerative, non-inflammatory corneal disorder characterized by progressive stromal thinning and ectasia. Its management depends on the severity of ectasia. Early to moderate cases can be effectively managed with rigid gas permeable contact lenses, providing satisfactory visual rehabilitation. However, more advanced cases, especially those with apical scarring, need surgical intervention. Traditionally,
Penetrating Keratoplasty (PKP) has been commonly performed for such cases. However over the last decade, Deep Anterior Lamellar Keratoplasty (DALK) has increasingly been advocated as a reliable alternative to PKP for the treatment of keratoconus. DALK removes and replaces the pathologic corneal stroma while preserving host healthy endothelium. The advantages of DALK over PKP have been well documented including the mitigation of endothelial rejection, the reduced duration of postoperative immunosuppressive agents, and earlier suture removal.

Despite the advantages of DALK over PKP, the potential for reduced visual outcome can be a significant drawback. Here we attempt to maximise visual outcome in patients with advanced keratoconus after DALK using a new donor trimming and suturing technique.

**METHODS**

This prospective study was done to assess 70 consecutive patients who underwent DALK for advanced keratoconus from period of Jan 2013 to December 2016 at Sankara Eye Hospital, Coimbatore. All patients were followed up for a period of over 2 years.

Preoperative slitlamp examination was done for all patients. Uncorrected Visual Acuity (UCVA), Best Corrected Visual Acuity (BCVA) with refractive correction was documented for all patients. Corneal topography with Pentacam was done for all patients and keratometry readings were documented.

All surgeries were done under general anaesthesia. The big-bubble technique introduced by Anwar and Teichmann was performed in all patients for exposure of Descemet membrane (DM) by the injection of air deep into the stroma. Approximately 80% of corneal thickness was trephined and a 27 or 30 gauge needle (bevel facing downward), attached to a 5cc syringe was inserted into the deep stroma aiming toward the center of the cornea. Air was gently injected into the deep stroma until a round, well-demarcated big-bubble was formed extending to the borders of trephination. After big-bubble formation, debulking of the anterior two-thirds of the corneal stroma was performed with a crescent blade. This was followed by a peripheral paracentesis and excision of the remaining stroma using blunt scissors. Following host dissection, the graft tissue
was prepared. Donor corneas were trephined to a final size 0.25 mm larger than the recipient’s button. DM was scrolled out after staining with Trypan blue. Graft was held and posterior edge of graft was trimmed in a slant so as to provide better approximation and adherence at the graft host junction. Donor tissue was then put with tight suturing using 10-0 nylon sutures. The knots of all sutures were tightened so as to provide little flattening of the graft in the immediate postoperative period.

**POSTSURGICAL CARE AND FOLLOW-UP**

The eyes were patched for 24 hours after surgery. Postoperative medications consisted of topical dexamethasone 0.1% every 6 hours tapered over 5 to 6 months along with lubricating and cycloplegic eye drops. Follow-up examinations at 6 months, 1 year and 2 years consisted of slitlamp biomicroscopic examination, UCVA, BCVA, refractive correction and keratometry readings from Pentacam. UCVA and Best Spectacle Corrected Visual Acuity (BSCVA) were recorded in logMAR notation for statistical comparison. Mean refractive spherical equivalent preoperatively and at each follow up visit was also compared.

**RESULTS**

The mean UCVA L = logMAR value was 1.219 ± 0.203 preoperatively. It improved to 0.625 ± 0.224 after 6 months. After 1 year, the value was 0.518 ± 0.221. After 2 years UCVA further improved to 0.394 ± 0.188. The mean spherical equivalent value was -8.473 ± 4.475 preoperatively. It became positive in immediate post operative period and then was reduced to 0.038 ± 2.226 after 6 months. After 1 year, the value reduced to -0.618 ± 2.204. After 2 years it reduced further to -1.145 ± 1.796 and started to stabilise. Average K value was 60.236 ± 6.652 preoperatively. It reduced to 43.289 ± 2.071 after 6 months. After 1 year, the value reduced to 44.104 ± 1.873. After 2 years it reduced further to 44.576 ± 1.7786.

**DISCUSSION**

DALK appears to be an acceptable alternative to PKP in stromal corneal diseases because it retains the advantages of both lamellar and full-thickness corneal transplantation and eliminates the drawbacks of the interface created during conventional
lamellar keratoplasty. However, there are still some aspects of DALK that require further study. More extensive studies with longer follow-up periods are required to understand the advantages and disadvantages of DALK. Suturing techniques have varied from interrupted, continuous, or a combination of both in DALK surgery. No significant differences in refractive outcome have been noted between the techniques. In this study, we have tried to device a novel graft trimming and suturing technique which helps in improving postoperative visual outcomes. We believe that trimming the posterior edge of graft tissue increases the area of contact and also helps in better opposition at the graft host junction. In a recent retrospective study analysing various techniques of DALK surgery, mean BSCVA was noted to be 20/25 (range 20/30-20/20) at last follow up. In our study, we have incorporated the use of tight sutures intraoperatively, so as to flatten the graft in immediate post-operative period. On successive follow-ups, we observed that the cornea progressed from a hypermetropic state towards a more emmetropic state due to progressive steepening effect from the peripheral ectatic host rim. We found the mean BCVA to be 0.125 ± 0.099 (range 6/6 - 6/12) at the end of 2 years.

In conclusion, we believe this novel technique of donor trimming and suturing can be an effective measure of improving post-operative visual outcomes for DALK in advanced keratoconus patients.


Photo-Biomodulation (PBM) In Diabetic Macular Edema (DME) Resistant to Standard Treatment (FP352)

Dr. Rajesh Ramanjulu, Dr. Aditya Barigali, Dr. Divyansh Mishra, Dr. Mahesh Shanmugam P

ABSTRACT

Photo-Biomodulation (PBM) for recalcitrant / resistant diabetic macular edema (DME).

INTRODUCTION

Diabetic retinopathy (DR) is one of the major causes of legal blindness in adults of working age worldwide. Diabetic Macular Edema (DME) is a leading cause of central vision impairment. The risk for developing DME is associated with longer duration of diabetes and elevated levels of glycosylated hemoglobin (HbA1c). The global prevalence of DME is estimated to be 7.5%, affecting approximately 21 million individuals. As the prevalence of diabetes is steadily increasing and expected to rise by more than 50% globally from 2000 to 2030, with the number of diabetes cases estimated to reach 366 million worldwide by 2030, DME will therefore causes a tremendous medical burden globally.

Although the pathogenesis of DME has not yet been completely clarified, elevated vitreous levels of vascular endothelial growth factor (VEGF) with increasing vascular permeability is known to play a role in the development of DME. In addition, intravitreal
anti-VEGF therapy has shown promising results for treating DME in several large randomized clinical trials recently\textsuperscript{6-10}. Although intravitreal injection of anti-VEGF agents has become the first-line treatment for patients with DME some studies have shown that there are still some patients who respond poorly to anti-VEGF therapies.\textsuperscript{11-14}

Thus, the purpose of this study is to assess the safety and efficacy of Photo-Biomodulation (PBM) in eyes with resistant macular edema secondary to diabetic retinopathy.

**METHODS**

11 eyes with macular edema secondary to diabetic retinopathy either refractory or recalcitrant to standard care were treated with PBM and were followed up (range: 6 - 24 months).

PBM was done by asking the patients to see sunlight for cumulative 5 minutes using a yellow narrow band filter which allowed light of wavelength 570 nm to pass through it.

**The time duration of exposure was calculated as follows:**

The light intensity at a particular area was measured in Lux.

Standard Sunlight Intensity = 15,000 Lux.

Already established luminous efficacy of sun = Lumens per Watt – 93lm/w

Surface area of Macula = 1094 mm\(^2\)

Net power delivered is 0.1764 W.

Total energy = \(W \times T = 0.1764 \times 180 = 31.752\) J/cm

The primary end point evaluation was the V/A and change in the CMT/ retinal edema. The secondary end point was to look into the functional aspect of the retina exposed to sunlight.
Patients were assessed pre and post-treatment with SS-OCT, visual acuity, HVF 10-2 SITA standard and MfERG.

Eyes with macular edema refractory to anti-VEGF and Ozurdex implant were included. Fellow eyes were taken as control. None of the eyes underwent any other form of therapy during the study period.

RESULTS

Mean macular thickness at baseline was 442.5 µ. Response was divided into 3 categories based upon the reduction in CMT

Very good (CMT reduction > 100 µ): 40% of eyes

Response (50 < CMT reduction < 100 µ): 30% of eyes

Minimal/no response: 30% of the eyes.

None of the study eyes had progressive increase in CMT from baseline while all the fellow eyes had increase in CMT at the end of the study. Most of the patients either maintained or had a betterment on HVF 10-2 or responses on MfERG. None of the patients had detrimental effects.

To further strengthen our hypothesis 2 patients (2 eyes) were asked to stop the PBM which resulted in reversal in the reduction of CMT.

CONCLUSION

Photo-biomodulation is a safe and effective treatment modality for refractory and recalcitrant diabetic macular edema.

BIBLIOGRAPHY


Suprachoroidal Injection of Triamcinolone With 30 Gauge Needle Using A Novel Injection Device.(FP2411)

Dr. Ajay Aurora, Dr. Ritu Aurora, Dr. Khushboo Srivastav, Dr. Charu Malik

PURPOSE:
Evaluate safety & efficacy of Suprachoroidal Injection of Triamcinolone Acetonide (SCITA) using a novel Suprachoroidal Injection Device (SCID) in patients with Macular Edema due to diverse retinal conditions.

METHODS:
SCITA 0.1 ml/4 mg was given in 44 eyes of 40 patients with 30 G needle, bevel down 4mm from limbus using novel SCID in eyes with recalcitrant macularedema. BCVA, IOP and central subfield thickness (CST/SDOCT) measured on day (D) 1, 7, 30, 60 & 90.

RESULTS:
SCITA was pain free, well tolerated and no eye developed Retinal/Choroidal Injury. Mean baseline CST (475.60µ) decreased to normal
range (256 μ) at D7; was maintained at 229.3μ/ D30 & 318.3 μ/ D90. Edema resolution occurred in 62.5% at D30 & 50% eyes remained edema free at D90. BCVA improved 1 line in 50% & 3 lines in 30% at D30. No eye had increased IOP.

CONCLUSIONS:

SCITA using the novel SCID is cheap, safe, effective, well tolerated and devoid of adverse ocular event. It may be used as an alternative to Ozurdex.

Drugs can be delivered to the eye by drops, systemically, periocular injections and Intravitreal injections. Intravitreal injections deliver drugs into the vitreous cavity when the target tissue is not vitreous but retina. Suprachoroidal injections are emerging as preferred methods of delivering drugs to the posterior segment. Pharmacokinetic studies following administration of Triamcinolone (TA) into the Suprachoroidal space in rabbits, demonstrate 12-fold higher amounts of drug in the retina and sclera-choroid and relatively minimal amounts (ranging from trace to 3%) of drug in the lens and anterior segment compared with exposure of TA following intravitreal injection.

Most drugs that at present are being given Intravitreally can be administered in the suprachoroidal space (SCS). The SCS is bound by the ciliary body anteriorly, Optic Nerve posteriorly, choroid internally and Sclera externally. It is a potential space that can expand with the introduction of drug formulation. Hence fewer ocular side effects are expected due to dose sparing and also because drugs are compartmentalized away from non-target tissues (e.g., lens causing cataract and Trabecular meshwork producing glaucoma).

Triamcinolone acetonide is a synthetic corticosteroid that has been used for the treatment of various inflammatory conditions in the body for over five decades.¹ and has a long history of use for treatment of a variety of ocular inflammatory diseases. TA quietens inflamed eye, reduces macular edema and improves visual outcomes.² It is, therefore, a good candidate to evaluate in a new route of ocular administration.
To achieve Suprachoroidal Injection, a specialized micro needle matching the scleral thickness has been constructed ³ (Fig1). To demonstrate the safety and tolerability of TA in the SCS, it was injected in the SCS in a phase I/II clinical trial (NCT01789320) to treat noninfectious posterior uveitis.

Clearside Biomedical are actively pursuing Suprachoroidal delivery of triamcinolone for diverse indications using a specially made injector, with preloaded triamcinolone and a special micro needle which is available in two lengths: 900 µm and 1100 µm. With the Clearside Biomedical device the injection is made perpendicular to the sclera. The decision to use a 900 µm or an 1110 µm needle is arbitrary. At this time, the Clearside Biomedical Triamcinolone (CLS -TA) is not available commercially but when launched is expected to be expensive. It is also being projected that the triamcinolone acetonide, (CLS-TA / Zuprata), being used by Clearside is specially formulated to allow delivery through a 30 G needle.

**FIGURE 1.** Microneedle for SCS injection. Low-magnification view of Microneedle at the end of a syringe (A) and high-magnification comparison of a microneedle (left) to the tip of a 30-gauge hypodermic needle (right). Scale bars: 5 mm (A) and 500 µm (B)
The standard 30 Gauge needle has a bevel length of 1.5 mm. Hence, cannot be used for Suprachoroidal Injection perpendicularly like the CLS-TA as the intended depth of Suprachoroidal Injections is only 1.0mm. Clearside Biomedical device is able to achieve this because their total needle measures 900 or 1100 µm. With the Clearside device, the needle is directed perpendicular to the sclera to the full depth of the needle till the hub holding the needle touches the sclera, further pressure is exerted to create a dimple and the drug injected. The drug (Triamcinolone acetonide, Zuprata, CLS-TA) spreads instantaneously through the potential SCS.

Numerous authors (conference presentations, anecdotal reports and personal communication) have tried to circumvent the problem of long bevel length of 30 Gauge needle by creating a micro needle made by passing a 30 G Needle through a large bore needle long enough to have a short bevel exposed and joining the two needles. This methodology being non-standardized has its obvious inconsistencies and sterility issues. Different workers have injected drugs and tamponade materials in the SCS using a specially developed illuminated micro catheter that needs to be inserted through a partial thickness sclerotomy and is an invasive procedure with its learning curve.⁴ ⁵

The aim of this paper is to test a novel device of SCS injections developed by the author (AA) using the commercially available 30 G needle obviating the need of a micro needle.

**METHODS**

**CONCEPT AND PRINCIPLE**

To reach the suprachoroidal space the intended average depth to penetrate sclera in the pars plana area is 1.0 mm.

Microneedles are specially constructed needles with a short bevel and overall short length can achieve this depth by perpendicular scleral entry. However, microneedles are not commercially available.

Author (AA) proposes to achieve this goal by entering the sclera obliquely with commercially available 30 G needle, travelling intrasclerally assisted by a specially
constructed device that allows the bevel of the commercially available 30 G needle to eventually place the drug at the intended depth of 1.0 mm.

**NOVEL DEVICES USED**

*(Photographs not included as under Patent application process)*

Two devices were tested on Goats eyes in a pilot study.

**DEVICE 1:**

The concept of device 1 was to create a dimple on the sclera using a forceps and then inject with the 30 G BD needle, with the needle passing through a predetermined track whose angulation to the sclera was fixed.

**DEVICE 2:**

The concept of device 2 was to run 30 G needle through a fine track supported on an angulated base allowing defined entry of needle into the sclera.

Device 2 (SCID Suprachoroidal Injection Device) was selected for subsequent experimentation and clinical use.

**PROCEDURE FOR SUPRACHOROIDAL TRIAMCINOLONE INJECTION**

Device 2 (SCID) was chosen for suprachoroidal Injections and manual injection technique appeared safe and effective for SCS injection of Triamcinolone.

The bevel of the 30 G BD Needle was inserted through the SCID such that the needle was intrascleral just past the bevel. When the bevel is in correct plane, it was easy to inject but if the bevel was still intrascleral, there was significant resistance noted. The bevel was always kept facing downwards.

After initial experimentation with Goats eyes, and initial pilot study in five eyes of five patients this study was extended to 44 eyes of 40 patients (Table1) who had recalcitrant macular edema of diverse pathologies. Decanted triamcinolone (0.075 to 0.1ml), decanted was injected in the SCS using SCID after obtaining due consent. A 30 G BD needle, bevel down was used. The injections were done at 4mm from the
limbus. The decantation was done by loading the Triamcinolone (Aurocort) in a 1cc syringe, making it stand at 45° for 15 or more minutes, the supernatant was discarded and 0.075-0.1ml of TA used for injection. All eyes underwent Slit Lamp Exam, Indirect Ophthalmoscopy, Best Corrected Visual Acuity (BCVA) assessment, Intra Ocular Pressure (IOP) measurement with Icare tonometer, Central Subfield Thickness (CST) measurement with SD OCT. All these measurements were done on day 1, 7, 30, 60 & 90 post injection.

RESULTS

Suprachoroidal Injections using the SCID was easy and safe with some initial training. It was possible to inject TA (Aurocort) with commercially available 30G needle in the suprachoroidal space using SCID. The injection was pain free when done away from the horizontal meridian (long posterior ciliary nerves).

Mean baseline CST (475.60ì) decreased to normal range (256 m) at D7; was maintained at 229.3m/ D30 & 318.3 m/ D90. Edema resolution occurred in 62.5% at D30 & 50% eyes remained edema free at D90. BCVA improved 1 line in 50% & 3 lines in 30% at D30. No eye had increased IOP (Table1). There was no eye that developed any vitreous or Choroidal Hemorrhage. Two eyes had accidental injection in the vitreous of a small amount of TA. One occurred in the initial part of the study and one when sufficient experience had been acquired.

Fig 1 and 2 show flattening of Macular Edema after Supra Choroidal injection of Triamcinolone in a patient with persistent Diabetic Macular Edema who had received multiple intravitreal injections of antiVEGF and Ozurdex. Fig3a and 3b are of a one eyed, 45 years old vasculitis patient who had been lasered in the past and had received multiple intravitreal injections of antiVEGF. He developed Cystoid Macular Edema after Cataract Surgery done under steroid cover. He was treated with nepafenac and steroid eye drops, but did not respond and was then administered suprachoroidal
injection of TA. The macula flattened dramatically and has remained stable. His VA improved from 6/36 to 6/9.

DISCUSSION

Injections of drug formulations in the suprachoroidal space increases the bioavailability of medications to retina and choroid. Upto 1.0 ml of fluid can be accommodated in the SCS as demonstrated in animal studies. Injections of 10 to 50 mL into the SCS are well tolerated with a low risk of ocular complications.

It’s been shown that Suprachoroidal injection of Triamcinolone (CLS-TA Clearside Biomedical Triamcinolone Acetonide) using a microneedle (special single use microinjector system) is safe and effective in the treatment of Macular edema due to Diabetic retinopathy and Uveitis and when used in combination with Aflibercept reduced the number of Aflibercept injections in macular edema due to retinal vein occlusion when compared with intravitreal Aflibercept injections alone. (6)

Injection of SCS with Healon-5 has been recently shown to be effective in treating cases of retinal detachment as shown by Reyes et al 7. They however, injected Healon-5 using a special illuminated catheter, which has its own learning curve and complications.

The SCID is Autoclavable and hence can be used repeatedly. It obviates the need of a special injector or doing a Sclerotomy or using a catheter, as the routinely available 30-gauge hypodermic needle and syringe can be used. Potentially it will allow the injection of any drug in the SCS.

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</table>

Table 1: Macular thickness after Suprachoroidal Injection of Triamcinolone with SCID
In the present study no patient had an increase in IOP. BCVA improved by 1 line in 50% eyes and three lines in 30% eyes. There was a significant reduction of macular edema in the eyes studied (Table 1). This reduction was <50ìm in eyes of retinitis pigmentosa with macular edema; post PPV ERM with macular edema and Posttraumatic Macular Edema. Though the study numbers are small it can be said that in selected cases of macular edema, suprachoroidal injection of Triamcinolone is a safe option. A larger study is however required before a conclusive comment can be made.

CONCLUSION

This study shows the safety of using SCID for SCSI of triamcinolone in human eyes without the use of microneedle/Sclerotomy/catheter. However, larger human trials are needed to assess the safety and efficacy of Triamcinolone injection into the SCS using the SCID. Use of SCID may allow us to inject other drugs that are routinely injected intravitreally. Also in few selected cases of retinal detachment, Healon 5 can be injected with SCID for local tamponade.

REFERENCES

1. KENALOGt-40 Injection (triamcinolone acetonide injectable suspension), Prescribing Information 2016, Bristol Myers Squibb, Princeton, NJ, USA.
5. Samirkumar R Patel, Damian E. Berezovsky, 2 Bernard E. McCarey et al:


ME Macular edema; CRVO Central Retinal Venous Occlusion; BRVO Branch retinal venous occlusion; RP retinitis pigmentosa; PPV Pars plana vitrectomy; ERM Epiretinal Membrane; SOI Silicon Oil injection; VH Vitreous Hemorrhage; RD Retinal Detachment; IOFB Intraocular Foreign Body; MPLT Micropulse Laser therapy
Fig1 : A 58 years obese, female, T2DM 18 yrs HT 6 yrs, BE Pseudophakic, Lasered PDR with CME; C:D 0.7 on anti Glaucoma drops; Had received BE Anti VEGF (Avastin Lucentis) 8 times in each eye and intravitreal injection of Ozurdex 4 times each eye; Last Inj 2 months ago. Shows severe cystoid macular edema pre injection Fig 1b shows complete flattening of macula after suprachoroidal injection of 0.1ml of TA using a 30G BD Hypodermic needle with SCID
Outcomes of Ruthenium-106 (Ru106) Plaque Brachytherapy in OSSN With Scleral Invasion. (FP2025)

Dr. Raksha Rao, Dr. Kaustubh Mulay, Dr. Santosh G Honavar, Dr. Sumeet Lahane

Ruthenium-106 (Ru106) Plaque Brachytherapy in the Management of Ocular Surface Squamous Neoplasia with Scleral Invasion: An Analysis of 42 Cases

ABSTRACT:

OBJECTIVES:

To evaluate the safety and efficacy of Ruthenium-106 plaque brachytherapy in the management of Ocular Surface Squamous Neoplasia (OSSN) with scleral invasion.

DESIGN:

Retrospective, non-comparative, interventional case series.

PARTICIPANTS:

Forty-two eyes of 42 consecutive patients with OSSN and histopathology-proven scleral invasion were included in the study.
METHODS:
Ruthenium-106 plaque brachytherapy was provided to the ocular surface to treat the residual scleral invasion.

MAIN OUTCOME MEASURES:
Tumour regression, eye salvage, final visual acuity and treatment complications.

RESULTS:
At the time of presentation, the mean basal diameter of the tumour was 9.3 mm (median, 8.7 mm; range, 5 - 26 mm) and the mean tumour thickness 2.1 mm (median, 2 mm; range, 1.5 - 3 mm). The primary treatment in all 42 cases was wide surgical excision, alcohol kerato-epitheliectomy for the corneal epithelial component, lamellar sclerectomy and cryotherapy to the resected conjunctival edges. On histopathology, scleral invasion of OSSN was confirmed in all cases with the base displaying positivity for residual tumour cells. Ruthenium-106 surface plaque application was done for a thickness of 2 mm and a total dose of 5000cGy was provided over a mean duration of 19.7 hours (median, 18.9 hours; range, 7 - 41 hours). Over a mean follow-up of 36.9 months (median, 30.4 months; range, 22.3 - 72 months), complete tumour regression was achieved in 37 eyes (88%). Two eyes (5%) showed tumour recurrence remote from the site of radiotherapy, necessitating repeat plaque brachytherapy. Visual acuity was maintained at e”20/60 in 29 eyes (74%), with a loss of >2 Snellen lines in 5 eyes (13%). There was no evidence of systemic metastasis.

CONCLUSION:
Histopathology-guided use of Ruthenium-106 surface plaque brachytherapy is a safe and an effective adjuvant therapy in the management of scleral invasion of OSSN.
**MAIN TEXT:**

Ocular surface squamous neoplasia (OSSN) is an umbrella term for premalignant and malignant epithelial tumours of the conjunctiva including dysplasia, carcinoma-in-situ and invasive squamous cell carcinoma (SCC).\(^1\text{-}^5\) While carcinoma-in-situ extends through the entire thickness of the conjunctival epithelium and does not invade beyond the basement membrane, invasive SCC has gross or microscopic invasion into the adjacent tissue.\(^1\text{-}^2,^5\) The mucoepidermoid type, a histopathological variant of OSSN, especially tends to be more aggressive with increased propensity for local invasion.\(^6\) Patients with human immunodeficiency virus (HIV) infection and other immunodeficiency diseases also frequently have recurrent and aggressive tumors.\(^1\text{-}^3,^5\) Invasive OSSN commonly extends to involve the corneal epithelium and rarely, corneal stroma.\(^1\text{-}^5\) The tumour can also extend into the sclera, anterior segment, or the orbit in advanced cases.\(^1\text{-}^5\)

Radiotherapy for the management of ocular surface tumours is gaining popularity in the past few decades, both as an adjuvant treatment and as a part of the primary management.\(^7\text{-}^16\) Initially, X-rays were used with good tumour control, but plaque brachytherapy soon gained popularity. Plaque brachytherapy helps in providing targeted therapy to the tumour base with minimal exposure of the normal tissue to the effects of radiation. The earliest reports of the use of plaque brachytherapy in OSSN were using strontium-90, a source of beta radiation, which is known to be safe by providing precise, low-penetration radiation, thus limiting exposure to the deeper and surrounding normal tissue.\(^8\text{-}^12\) This study evaluates the efficacy of yet another source of beta radiation, ruthenium-106 (Ru-106), as an adjuvant treatment in the management of OSSN with scleral invasion.

**METHODS**

This is a retrospective, non-comparative, interventional case series of 42 eyes of 42 patients with ocular surface squamous neoplasia (OSSN) with histopathology-proven scleral invasion following excision biopsy. The primary objective was to assess tumour control with plaque brachytherapy. The study setting was an integrated
ocular oncology centre at a tertiary care eye hospital. Institutional review board approval was obtained.

The medical records of 42 patients who underwent plaque brachytherapy were retrospectively reviewed. Demographic data included age at presentation (in years), gender (male or female), race, presence of systemic immunosuppression (HIV positivity, post-organ transplantation, iatrogenic immunosuppression), and systemic diseases (diabetes, xeroderma pigmentosum and hepatitis B). Ocular features included the presenting complaint, laterality of OSSN, eye involved, best corrected visual acuity (BCVA), intraocular pressure (in mm Hg), tumour number, tumour location (limbal, bulbar), quadrantic location (nasal, temporal, superior and inferior), maximum tumour basal diameter (in mm) and thickness (in mm), corneal involvement, fixation to underlying sclera, and presence of any intraocular or orbital extension. The tumour basal diameter and thickness were measured with slit lamp biomicroscopy and, whenever possible, using anterior-segment optical coherence tomography (AS-OCT). Photographic and diagrammatic documentation of the tumour pre and post treatment was performed to monitor any local recurrence of tumour. The primary treatment protocol in all patients included excision of the clinically visible tumour with 4-mm clinically clear margins and double freeze-thaw cryotherapy to the resected conjunctival edges. The corneal epithelial component was managed by alcohol kerato-epitheliectomy, corneal stromal invasion by lamellar keratectomy and the scleral component by lamellar sclerectomy followed by ocular surface reconstruction with preserved amniotic membrane graft (AMG) and fibrin glue. The biopsy specimen was carefully placed over a sterile filter paper, oriented well in its anatomical position with margins unrolled and marked, and submitted for histopathological examination. The pathologist was requested to report on the tumour invasion of the excised scleral base, its location and extent. Patients with confirmed scleral base invasion on histopathology were treated secondarily by plaque radiotherapy after complete epithelization of the ocular surface, generally around 4 - 6 weeks after the primary surgery. The time interval between the primary surgery and plaque brachytherapy was noted.
Written informed consent was obtained from every patient. Dosimetry was performed by a radiation physicist for a depth of 2 mm after excluding intraocular extension using Anterior segment optical coherence tomography (AS-OCT) and Ultrasound biomicroscopy (UBM). A Bebig CCA or COB Ru-106 plaque (types of Ru-106 Eye applicators for ophthalmic brachytherapy) was applied over the excised scleral base ensuring complete coverage of the base with an additional 2 mm margin. After the completion of treatment, the patients were monitored 3 monthly for 1 year and 6-monthly thereafter. The clinical data were tabulated and analyzed with regard to the main outcome measures – tumour regression, eye salvage, final visual acuity and treatment complications.

RESULTS

42 eyes of 42 consecutive patients were treated with Ru-106 plaque brachytherapy over an 8-year period. The demographics of the patients are listed in Table 1. The mean patient age was 49.5 years (median, 48 years; range, 26-83 years) and the most common presenting symptom was the presence of a painless mass (n = 38, 90%) followed by redness (n = 4, 10%). Of the 42 patients, HIV and Hepatitis B infection was present in 2 (5%) and 3 (7%) patients, respectively.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>n = 42 patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Mean, years</td>
<td>49.5</td>
</tr>
<tr>
<td>Median (range), years</td>
<td>48 (26-83)</td>
</tr>
<tr>
<td>Race</td>
<td>42 (100)</td>
</tr>
<tr>
<td>Asian Indians</td>
<td>42 (100)</td>
</tr>
<tr>
<td>Sex</td>
<td>28 (74)</td>
</tr>
<tr>
<td>Male</td>
<td>14 (26)</td>
</tr>
</tbody>
</table>
Presence of systemic disease
Diabetes 4 (10)
HIV positivity 2 (5)
Hepatitis B 3 (7)
0 (0)

Xeroderma Pigmentosum

Presenting complaint
Painless mass 38 (90)
Redness 4 (10)

<table>
<thead>
<tr>
<th>Table 1. Plaque brachytherapy in scleral-invasive OSSN: Patient demographics (Total number of patients n=42).</th>
</tr>
</thead>
</table>

The clinical features of the patients at the time of presentation have been elaborated in Table 2. At the time of diagnosis, 38 eyes (90%) had visual acuity > 20/200. All patients had unilateral involvement and all eyes presented with a single tumour. Majority of the tumours were located at the limbus (n = 40, 95%) followed by nasal/temporal bulbar conjunctiva (n = 40, 95%). Papillomatous morphology was present in 3 eyes (7%), diffuse OSSN in 2 eyes (5%), while rest of them were nodular (n = 37, 88%). The mean basal diameter of the tumour was 9.3 mm (median, 8.7 mm; range, 5- 26 mm) and the mean tumour thickness was 2.1 mm (median, 2 mm; range, 1.5 - 3 mm). While 39 eyes (93%) showed corneal extension of the tumour and 39 eyes (93%) had clinically apparent scleral fixity, none of the eyes in the series had evidence of intraocular or orbital extension at the time of presentation.

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>n = 42 eyes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumour laterality</td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>42 (100)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Eye involved</td>
<td></td>
</tr>
<tr>
<td>Right Eye</td>
<td>22 (52)</td>
</tr>
<tr>
<td>Left Eye</td>
<td>20 (48)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td><strong>Visual acuity</strong></td>
<td></td>
</tr>
<tr>
<td>20/20-20/40</td>
<td>28 (67)</td>
</tr>
<tr>
<td>20/50-20/200</td>
<td>10 (24)</td>
</tr>
<tr>
<td>&lt; 20/200</td>
<td>4 (10)</td>
</tr>
<tr>
<td><strong>Intraocular pressure, mm Hg</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (median, range)</td>
<td>17 (16, 11-22)</td>
</tr>
<tr>
<td><strong>Number of tumours per eye</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (median, range)</td>
<td>1 (1,1)</td>
</tr>
<tr>
<td><strong>Tumour location</strong></td>
<td></td>
</tr>
<tr>
<td>Limbal</td>
<td>40 (95)</td>
</tr>
<tr>
<td>Bulbar</td>
<td>2 (5)</td>
</tr>
<tr>
<td><strong>Quadrantic location of tumour</strong></td>
<td></td>
</tr>
<tr>
<td>Nasal</td>
<td>19 (45)</td>
</tr>
<tr>
<td>Temporal</td>
<td>21 (50)</td>
</tr>
<tr>
<td>Inferior</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Superior</td>
<td>1 (2)</td>
</tr>
<tr>
<td><strong>Tumour morphology</strong></td>
<td></td>
</tr>
<tr>
<td>Nodular</td>
<td>37 (88)</td>
</tr>
<tr>
<td>Papillomatous</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Diffuse</td>
<td>2 (5)</td>
</tr>
<tr>
<td><strong>Tumour basal diameter, mm</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (median, range)</td>
<td>9.3 (8.7, 5-26)</td>
</tr>
<tr>
<td><strong>Tumour thickness, mm</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (median, range)</td>
<td>2.1 (2, 1.5-3)</td>
</tr>
<tr>
<td><strong>Corneal involvement</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>39 (93)</td>
</tr>
<tr>
<td>No</td>
<td>3 (7)</td>
</tr>
<tr>
<td><strong>Scleral fixity</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>39 (93)</td>
</tr>
<tr>
<td>No</td>
<td>3 (7)</td>
</tr>
</tbody>
</table>
Table 2. Plaque brachytherapy in scleral-invasive OSSN: Clinical features

Table 3 elaborates the treatment and outcomes. Every patient in the series underwent primary excision with 4 mm clinically clear margins and histopathological evaluation. Prior treatment before referral included excision biopsy in 2 patients (5%), incision biopsy in 1 (2%), and topical interferon in 1 (2%). On histopathology, 1 eye (2%) showed excision margin positivity with carcinoma-in-situ while all the 42 eyes (100%) had tumour involving the excision base. Adjuvant treatment with plaque brachytherapy was performed after a mean period of 4 weeks (median, 4 weeks; range, 4 - 15 weeks) after the primary surgery. A total dose of 5000 cGy (5000 centigrays) was provided to all tumours over a mean duration of 19.7 hours (median, 18.9 hours; range 7 - 41 hours).

<table>
<thead>
<tr>
<th>Tumour extent</th>
<th>Intraocular</th>
<th>Orbital</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 (0)</td>
<td>0 (0)</td>
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<table>
<thead>
<tr>
<th>Treatment and Outcomes</th>
<th>n = 42 eyes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous treatment*</td>
<td></td>
</tr>
<tr>
<td>Topical interferon</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Incision biopsy</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Excision biopsy</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Histopathology</td>
<td></td>
</tr>
<tr>
<td>Excision margin positivity</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Excision base positivity</td>
<td>42 (100)</td>
</tr>
<tr>
<td>Time interval between excision and plaque radiotherapy (weeks)</td>
<td></td>
</tr>
<tr>
<td>Mean (median, range)</td>
<td>4 (4, 4-15)</td>
</tr>
<tr>
<td>Total dose, cGy</td>
<td>5000 (5000, 5000)</td>
</tr>
</tbody>
</table>
### Table 3. Plaque brachytherapy in scleral-invasive OSSN: Treatment and Outcomes

<table>
<thead>
<tr>
<th>Duration of treatment, hours</th>
<th>Mean (median, range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>19.7 (18.9, 7-41)</td>
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</table>

<table>
<thead>
<tr>
<th>Duration of follow-up, months</th>
<th>Mean (median, range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>36.9 (30.4, 22.3-72)</td>
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</tbody>
</table>

<table>
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<tr>
<th>Complications from plaque radiotherapy</th>
</tr>
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<tbody>
<tr>
<td>Recurrent corneal epithelial defect</td>
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<table>
<thead>
<tr>
<th>Management of tumour recurrence, n=5</th>
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</thead>
<tbody>
<tr>
<td>Repeat plaque brachytherapy treatment</td>
</tr>
<tr>
<td>Enucleation</td>
</tr>
<tr>
<td>Exenteration</td>
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</tbody>
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<tr>
<th>Visual acuity, n=39</th>
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<tbody>
<tr>
<td>20/20-20/40</td>
</tr>
<tr>
<td>20/50-20/200</td>
</tr>
<tr>
<td>&lt;20/200</td>
</tr>
</tbody>
</table>

*1 patient underwent incision biopsy prior to referral to our institute, 1 patient received topical interferon therapy for 3 months, and 2 patients underwent excision biopsy twice.

---

**Figure 1**
Over a mean follow-up duration of 36.9 months (median, 30.4 months; range, 22.3–72 months), 37 (88%) patients did not show local tumour recurrence (figure 1a-d). Five eyes (12%) manifested a recurrent tumour at a site distant from the primary tumour at a mean follow-up of 5 months (median, 5 months; range, 4–7 months). Of these, 2 eyes (5%) with limited conjunctival and scleral recurrence were treated with plaque brachytherapy. None of the patients had regional lymph node metastasis or systemic metastasis. Two patients had post-radiotherapy recurrent epithelial defects which resolved with conservative therapy. Best corrected visual acuity at the final follow-up was >20/40 in 24 eyes (62%), 20/50 to 20/200 in 10 (26%) and <20/200 in 5 (13%) eyes. While 10 (24%) had visual improvement >2 Snellen lines and 27 (64%) were stable, 2 patients (5%) had deterioration of vision >2 Snellen lines.

**DISCUSSION**

OSSN is primarily managed by complete excision using the traditional “no-touch” technique.\(^{17}\) In the past decade, the use of topical chemotherapy (mitomycin-C and 5-fluorouracil) and immunotherapy (topical or injection interferon alpha-2b) as alternatives to surgical resection of OSSN has been widely reported.\(^{18-20}\) Topical
therapy for OSSN can achieve good tumour control, especially in eyes with small tumours and extensive corneal involvement.\textsuperscript{18-21} Topical chemotherapy and immunotherapy, however, have a longer course of treatment and is reliant on the patient’s capability to administer the drops in a timely and precise manner. In addition, a recent literature analysis by Siedlecki et al concluded that surgical excision is the best primary treatment for OSSN and the use of topical therapy is favoured only as an adjuvant treatment for cases with positive excision margins.\textsuperscript{21}

The “no touch” technique in the surgical management of OSSN involves wide excision without any direct handling of the tumour mass and only manipulating the surrounding normal tissue.\textsuperscript{17} A 4-mm wide margin is ensured around the conjunctival component, followed by excision of the tumour base.\textsuperscript{17} Double freeze-thaw cryotherapy is then applied to the resected conjunctival edges.\textsuperscript{17} Conjunctival reconstruction is done using advancement or sliding flaps, or with the use of an amniotic membrane graft.\textsuperscript{17} For tumours with scleral involvement, lamellar sclerectomy is additionally performed.\textsuperscript{17} However, for deeper scleral invasion, deeper sclerectomy is generally avoided for fear of scleral thinning, necrosis and inadvertent perforation. The use of topical therapy is also limited in these eyes as they do not penetrate the sclera.\textsuperscript{1,16}

For deeper scleral invasion in OSSN, radiotherapy has been known to achieve good success.\textsuperscript{7-16} An important prerequisite is the placement of the plaque over the sclera to cover the entire scleral base of the tumour adequately. The plaque is sutured directly onto the sclera and the duration of the treatment calculated based on the radiation dose, thickness of the scleral invasion and the type of radiation being used. In a report by Lommatzsch who treated 15 patients using strontium-90 (beta radiation) plaque brachytherapy, only 1 eye (7%) was noted to have a delayed recurrence 5 years after the radiation therapy for which enucleation was necessary.\textsuperscript{8} Of the 15 eyes, 11 eyes (73%) received radiation as a primary treatment after an incision biopsy to confirm the diagnosis.\textsuperscript{8}

Lecuona described 69 eyes with OSSN that underwent primary surgical excision without lamellar sclerectomy.\textsuperscript{11} Histopathology revealed either carcinoma-in-situ (n = 28, 41%) or invasive squamous cell carcinoma (n = 41, 59%).\textsuperscript{11} Although the
authors did not analyse the specimen for excision base positivity, margin positivity was noted in 39 eyes (57%).

Regardless of the histopathology result, all patients received plaque radiotherapy with strontium-90. Recurrence was noted in 8 eyes (11%), and the authors ascribed it to inadequate radiation coverage. Cerezo et al and Kearsley et al also used strontium-90 both as primary therapy in eyes with OSSN and obtained excellent results. In all these series, histopathology after surgical excision did not guide the use of plaque radiotherapy. Similarly, a study from Liverpool recommended the use of radiation in all cases of invasive OSSN irrespective of surgical clearance. In their series, Ru-106 brachytherapy was used as a source of radiation and whenever the tumour location was inaccessible to plaque brachytherapy, proton beam radiotherapy was used. In contrast, Arepalli et al described the use of plaque brachytherapy only in those eyes where histopathology confirmed excision base positivity. In their case series consisting of 15 eyes with OSSN, all patients primarily underwent excision. On histopathology, in addition to the presence of deep scleral involvement in all 15 eyes, 3 eyes (20%) had tumour extension into the anterior chamber and Iodine-125 plaque brachytherapy was used to manage the residual tumour and intraocular extension. Of the 15 eyes, 4 developed recurrence at a site remote from the area of irradiation, and the overall eye salvage rate was 67%. The authors speculated that immunosuppression is an important underlying factor that could have led to remote progressive recurrence in these cases.

In our series, we followed a histopathology-guided adjuvant treatment protocol. All eyes with OSSN primarily underwent excision biopsy. Adjuvant radiotherapy using Ru-106 plaque brachytherapy was used only when the excision base was positive for tumour cells on histopathology. In case of anterior chamber extension of OSSN, the authors preferred enucleation. It must be noted that in our series of 42 eyes, 39 eyes (93%) had scleral fixity noted clinically at the time of presentation. This is an important finding that can perhaps help in planning a primary plaque radiotherapy at the time of primary excision biopsy. In our series, of the 5 patients (12%) with tumour recurrence, 2 patients (40%) had hepatitis B infection. The recurrences were noted at a mean duration of 6 months post-plaque tretament and at a site
distant from the original tumour, which perhaps indicates aggressive multifocal tumour that evolved over a period of time.

Ruthenium-106 is a source of beta radiation, and like strontium-90, it provides a sharply cut-off, precise, low-penetration radiotherapy which is relatively safe to the deeper and surrounding normal tissue.\textsuperscript{8-12} This results in fewer side effects as compared to Iodine-125 which is a source of gamma radiation.\textsuperscript{14-16} Gamma radiation has a deeper penetrability and hence carries a greater chance for cataract and secondary glaucoma, especially when the radiation plaque is placed directly over the cornea, exposing the lens and angle structures to a higher dose of radiation.\textsuperscript{14-16} While the most frequently reported symptoms with strontium-90 are dry eyes and conjunctival telangiectasias, scleral thinning has also been reported.\textsuperscript{11,13} In contrast, Kenawy et al did not observe any complications after Ru-106 application in 14 eyes with OSSN.\textsuperscript{12} However, in a recent single case report of use of Ru-06 plaque for OSSN with corneal endothelial extension, the authors noted sectoral cataract formation at a 4-year follow-up.\textsuperscript{22} In our series, we noted recurrent corneal epithelial defect in 2 eyes (5%), which was managed conservatively. None of the patients developed cataract or glaucoma at the final follow-up.

**CONCLUSION**

Ruthenium-106 plaque brachytherapy achieves excellent tumour control in OSSN with scleral invasion. However, the indications for the use of plaque brachytherapy for OSSN differ widely, leading to wide variations in the tumour recurrence and eye salvage rates. Plaque brachytherapy in the management of OSSN must be guided by the histopathology and is best used as an adjuvant therapy for excision base positivity. More studies in this regard are necessary to define the absolute indications for plaque brachytherapy in OSSN.

**REFERENCES:**


Goniotomy – A Useful Procedure for Initial and Re-Do Surgery for Childhood Glaucoma in Indian Eyes. (FP482)

Dr. Sushmita Kaushik, Dr. Pandav Surinder Singh, Dr. Manpreet Kaur, Dr. Deepika

ABSTRACT

PURPOSE:
To describe the effectiveness of Goniotomy for childhood Glaucoma in Indian eyes.

METHODS:
Consecutive patients with Paediatric Glaucoma who underwent Goniotomy between July 2017 and April 2019, were prospectively analysed. Goniotomy was done as a primary procedure or a re-do surgery of the untreated angle in failed filtering surgery.

RESULTS:
151 eyes of 112 children were analyzed. Goniotomy comprised 151 of 550 (27.4%) of all Pediatric Glaucoma surgeries and 121 of 212 (57.1%) primary pediatric glaucoma surgeries in the study period. 105, 81, 64 and 33 eyes completed 6 weeks, 3 months, six months and one-year follow-up respectively. At one year, success rates in Primary Congenital Glaucoma (PCG) were 95.5%
for primary surgery and 42.9% for re-do surgery. For non-PCG eyes, the success rate was 75% at one year. Among PCG subgroups, both newborn and infantile glaucoma had similar success rates and need of additional surgery. On multivariate analysis, baseline IOP was the most important factor for success.

**CONCLUSIONS:**

Goniotomy appears to be an effective surgery for childhood glaucoma in Indian eyes. Being minimally invasive, it obviates the need for conjunctival and scleral dissection and antifibrotic agents.

**KEY WORDS:**

Goniotomy; Childhood Glaucoma; secondary goniotomy

**INTRODUCTION**

Congenital Glaucoma is caused by a developmental arrest of some of the structures within the anterior segment. The trabecular meshwork itself becomes thicker and the drainage within the meshwork is impaired. These changes lead to an increased Intraocular Pressure (IOP), and the consequent changes leading to buphthalmos.

Goniotomy is a surgical procedure, first described in 1938, primarily used to treat Congenital Glaucoma. The traditional staged approach outlined in most textbooks or review papers on primary Congenital Glaucoma involves what has been denominated as “angle surgery” (goniotomy in cases with relatively clear corneas) and trabeculotomy (for those with cloudier cornea). The main aims and steps of the procedure have remained unchanged and include entering the anterior chamber through a clear corneal incision and crossing the anterior chamber to the opposite side to incise the trabecular meshwork (while visualizing the angle with a surgical gonio lens) and covering an arc of 100–110 degrees. The Goniotomy procedure has the advantage of being less invasive, is a faster procedure, spares conjunctiva for future glaucoma surgery and being a closed technique has the potential to have lesser intraoperative and postoperative complications of hypotony, suprachoroidal haemorrhage.
A study from India in 1983 reported that 80% of congenital glaucoma cases presented with hazy cornea. Following Mandal et al’s reported success with Combined Trabeculectomy with Trabeculotomy (CTT), his procedure has largely been the most commonly done surgery across the spectrum of childhood glaucoma. There have been no reports of the outcome of goniotomy in Indian eyes.

However, a recent Cochrane review exploring the best surgical procedure for congenital glaucoma however reported that no conclusions could be drawn due to paucity of data.

However, not all patients presenting with congenital glaucoma in India have severely hazy corneas not amenable to goniotomy. We present our data of a prospective evaluation of a cohort of congenital glaucoma who underwent goniotomy. We used this procedure as both a primary and re-do surgery.

**MATERIALS AND METHODS:**

**DESIGN:**

Prospective non-randomized interventional study

**PATIENTS:**

Consecutive infants with congenital glaucoma requiring surgical lowering of IOP, presenting between 1st August 2017 and 30th April 2019, who were scheduled for goniotomy were analyzed. Both primary surgery and re-do surgery were included. The study adhered by the tenets of the Declaration of Helsinki. Informed consent was taken from parents/ legal guardians of all patients. The Institutional Review Board gave Ethics clearance for the study. Results of those completing 6 months of follow up were analysed.

**INCLUSION CRITERIA:**

Clear visibility of angle structures on gonioscopy

Congenital glaucoma

Secondary non-acquired/acquired cases of childhood glaucoma
Juvenile open angle glaucoma

Previously operated patients of congenital/Juvenile open angle glaucoma with uncontrolled IOP

The parameters recorded during the time of general anaesthesia just prior to surgery were Intraocular Pressure (IOP), Corneal diameter and clarity, Disc evaluation, Gonioscopy characteristic of angle-type 1 or type 2, Axial length and Retinoscopy.

FOLLOW-UP

Patients were followed up at 6 weeks, 3 months, 6 months, 9 months and every 3-6 monthly after surgery depending on IOP control. Presentation patterns, complications of the procedures and outcome of surgery was determined.

Main outcome measurers: Post-operative IOP, Number of medications required, additional surgery required.


Success was determined as given below:

Complete success: IOP < 16 mm Hg under anaesthesia or < 21 mm Hg on GAT without need of medications.

Qualified success: IOP < 16 mm Hg under anaesthesia or < 21 mm Hg on GAT with upto 2 topical antiglaucoma medications.

Failure: IOP not satisfying success criteria or need of additional surgery for IOP control.

STATISTICAL ANALYSIS

Descriptive data- mean, median, Frequency was computed. Success rates were calculated at 6 months, 9 months, 1 year, 1.5 years.

Outcomes in different subgroups of glaucoma and primary and secondary goniotomy were determined. Comparison between groups (PCG vs Non-PCG, primary vs secondary goniotomy, primary goniotomy newborn vs infantile) were compared. Categorical
variables by chi-square test, and quantitative variables were analyzed by Student test/Mann Whitney U test.

Univariate and multivariate analysis were done to determine if there were any baseline factors to predict success

RESULTS

151 eyes of 112 children underwent goniotomy during study period. Goniotomy comprised 151/550 (27.4%) of all pediatric glaucoma surgeries and 121/212 (57.1%) primary pediatric glaucoma surgeries. 105, 81, 64 and 33 eyes completed 6 weeks, 3 months, six months and one-year follow-up respectively.

Pre-operative data of PCG and Non-PCG babies are depicted in Table 1 and Table 2

<table>
<thead>
<tr>
<th>PCG (n=114, 75%)</th>
<th>Non-PCG (n=37, 25%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn (NB)-48</td>
<td>Sturge Weber Syndrome (SWS)-11</td>
</tr>
<tr>
<td>Infantile-66</td>
<td>Axenfeld-Rieger (AR)-8</td>
</tr>
<tr>
<td></td>
<td>JOAG-12</td>
</tr>
<tr>
<td></td>
<td>Steroid induced-1</td>
</tr>
<tr>
<td></td>
<td>Uveitic-1</td>
</tr>
<tr>
<td></td>
<td>Post-traumatic-1</td>
</tr>
<tr>
<td></td>
<td>Post-cataract surgery-3</td>
</tr>
</tbody>
</table>

Table 1: Diagnosis of the patients

<table>
<thead>
<tr>
<th></th>
<th>PCG</th>
<th>Non-PCG</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at surgery (months)</td>
<td>15.41 ± 23.97</td>
<td>130.75 ± 143.18 (0-480)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Mean corneal clarity</td>
<td>1.07 ± 0.78 (0-3)</td>
<td>0.59 ± 0.86 (0-3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Primary: secondary goniotomy*</td>
<td>87 (76.3%):27 (23.6%)</td>
<td>28 (75.6%):9 (24.3%)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Table 2: Baseline data of patients
Outcome at 3 months, 6 months and 1 year is depicted in Table 3 and Figure 1. PCG group had significant decrease in IOP whereas non-PCG group did not have significant reduction at all time periods (Figure 1). PCG group required less topical medications in postoperative period and had better success rates (76 -88%) compared to non-PCG (50 - 75%) with less requirement of additional surgery.

<table>
<thead>
<tr>
<th></th>
<th>3m</th>
<th>6m</th>
<th>1y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Total 42</td>
<td>Total 39</td>
<td>Total 22</td>
</tr>
<tr>
<td>Good</td>
<td>27 (64.28%)</td>
<td>25 (64.1%)</td>
<td>16 (72.72%)</td>
</tr>
<tr>
<td>Fair</td>
<td>9 (21.43%)</td>
<td>12 (30.7%)</td>
<td>5 (22.73%)</td>
</tr>
<tr>
<td>poor</td>
<td>6 (14.3%)</td>
<td>2 (10.5%)</td>
<td>1 (4.54%)</td>
</tr>
<tr>
<td>Secondary</td>
<td>Total 19</td>
<td>Total 13</td>
<td>Total 7</td>
</tr>
<tr>
<td>Good</td>
<td>6 (31.6%)</td>
<td>2 (15.4%)</td>
<td>1 (14.28%)</td>
</tr>
<tr>
<td>Fair</td>
<td>5 (26.32%)</td>
<td>7 (53.8%)</td>
<td>2 (28.57%)</td>
</tr>
<tr>
<td>poor</td>
<td>8 (42.1%)</td>
<td>4 (30.76%)</td>
<td>4 (57.14%)</td>
</tr>
</tbody>
</table>

P value: 0.02 0.0033 0.0029

Table 3: Outcome of patients in PCG and non-PCG groups

Figure 1: IOP in the post operative period in the PCG and non-PCG groups
Both newborn and infantile glaucoma had equal success rates and similar need of additional surgery. At one year, Primary goniotomy success rates were 80 - 90%, and secondary goniotomy successful in 40-60% (Table 4)

<table>
<thead>
<tr>
<th></th>
<th>3 months</th>
<th>6 months</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PCG</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>Total-61</td>
<td>Total- 52</td>
<td>Total-29</td>
</tr>
<tr>
<td></td>
<td>33 (54.09%)</td>
<td>27 (51.92%)</td>
<td>17 (58.62%)</td>
</tr>
<tr>
<td>Qualified</td>
<td>14 (22.95%)</td>
<td>19 (36.53%)</td>
<td>7 (24.13%)</td>
</tr>
<tr>
<td>Failure</td>
<td>14 (22.95%)</td>
<td>6 (11.53%)</td>
<td>5 (17.24%)</td>
</tr>
<tr>
<td><strong>Non-PCG</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete</td>
<td>Total-20</td>
<td>Total-12</td>
<td>Total-4</td>
</tr>
<tr>
<td></td>
<td>8 (40%)</td>
<td>6 (50%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Qualified</td>
<td>2 (10%)</td>
<td>3 (25%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Failure</td>
<td>10 (50%)</td>
<td>3 (25%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>P value</td>
<td>0.02</td>
<td>0.22</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Table 4: Outcomes in primary and secondary or re-do Goniotomy

In both univariate and multivariate analysis, baseline IOP emerged as the most significant pre-operative determinant of outcome at 6 months and one year.

Complications: Postoperative hyphaema was common (> 90%), grade 1 - 2 with spontaneous resolution. One eye developed cataract, likely iatrogenic. The infant underwent a successful phacoaspiration with IOL implantation and is on regular amblyopia treatment.

**DISCUSSION**

Goniotomy has been described to be most effective in eyes fulfilling the following features: No other ocular or systemic abnormalities, disease noted at least one month after birth but before one year of age, and with corneal clarity allowing reasonable view of the angle and corneal diameters less than 14 mm. 7 Shaffer8 analyzed 287 operated eyes and reported that one or two goniotomies cured 94% of patients
diagnosed with glaucoma between 1 month and 24 months of age. However, this success rate dropped to 30% when glaucoma was present at birth or after the age of two years. Broughton and Parks9 reported an overall 88% success rate (with a mean followup of five years) after one or more goniotomies their 20 year experience with 50 eyes of patients who underwent goniotomy.

Our study showed that Goniotomy could be successfully performed in nearly half of the cases of childhood glaucoma. The PCG group had success rates of 80 - 90% with similar results in newborn and infantile subgroups compared Shaffer’s study which reported success rate of 26% in the Newborn group.

Non-PCG group including JOAG (success rate 41.66%), Axenfeld Rieger, secondary glaucoma, Sturge weber syndrome (success rate 50%) showed relatively less then optimum outcomes. Primary goniotomy success rates in our series were higher (80- 90%) compared to secondary goniotomy which was successful in 40 - 50% of the cases. However, in infants requiring a re-do surgery, if the morbidity of conventional second surgery such as a re-do trabeculectomy or a Glaucoma Drainage implant could be avoided in half the children, it may be well worth our effort.

Goniotomy in Indian eyes appears to have favourable outcomes in both new born and infantile types of primary congenital glaucoma when performed as a primary surgery. Its advantages of no conjunctival dissection, no anti metabolite use and an excellent safety profile should prompt us to consider this in our armamentarium of surgeries for congenital glaucoma

REFERENCES


Safety an Efficacy of Incisional Goniotomy And Phacoemulsification in Angle Closure Glaucoma. (FP938)

Dr. Shikha Gupta, Dr. Viney Gupta, Dr. Ramanjit Sihota, Dr. Anin Sethi

**ABSTRACT**

**PURPOSE**

To evaluate the Intraocular Pressure (IOP) – lowering efficacy and safety of goniotomy with phacoemulsification in mild, moderate and advanced staged Primary Angle Closure Glaucoma.

**SETTING**

Tertiary care referral ophthalmic center.

**DESIGN**

Prospective interventional case series.

**METHODS**

Consecutive patients with Primary Angle Closure Glaucoma who were deemed fit for undergoing phacoemulsification plus goniotomy were enrolled in this study. These patients had either high IOP, or borderline IOP control with medications or controlled > 1 medication. Following phacoemulsification
and IOL Implantation, incisional goniotomy was performed under Viscoelastic device cover using a disposable Microvitreo-retinal blade through two side ports ranging from 90°-210° in extent. Gonio syncheyiolysis was also performed if peripheral anterior synchiae precluded angle view with a 26 G canula. Patient demographic profile, clinical data, including baseline and postoperative IOP at serial follow up, change in the number of medication use post-operatively and adverse events if any, were analyzed during at least a 6 month follow-up period. Success was defined as IOP ≤ 18 mm Hg with or without medications.

RESULTS:

Of the 36 eyes (34 patients) included in this study, 64% eyes were classified as having severe glaucoma. The mean baseline IOP decreased from 21.89 mm Hg ± 5.65 to 13.54 ± 1.82 mmHg at 6 months postoperatively (P < 0.001; paired t test); with mean percent reduction in IOP of 34.71 ± 19.16%. Hypotensive medication use decreased from 3.14 ± 1.07 to 1.25 ± 1.15, respectively (P < 0.001; Wilcoxon Signed rank test). The most common complication was hyphema (36.12%; 13 eyes) followed by IOP spike (5.56%; 2 eyes) and cyclodialysis (2.8%; 1 eye). There was a positive correlation between pre-operative IOP and percent reduction in IOP (Spearman’s correlation coefficient: 0.689). The cumulative survival probability at the end of 6 months was 94.7%.

CONCLUSIONS

Single-use blade assisted incisional goniotomy combined with phacoemulsification resulted in a significant and sustained reduction in IOP in cases with angle closure glaucoma, both mild and advanced staged along with a significant decrease in number of glaucoma medications at 6 months of follow-up.

INTRODUCTION

Current glaucoma therapy involves lowering of the intraocular pressure (IOP) by means of medical therapy, lasers, conventional filtering surgery, drainage devices
or minimally invasive glaucoma surgery. Although, the conventional filtering surgery, trabeculectomy with or without antimetabolites, has proved to be the most efficient and cost effective in control of intraocular pressure, it is associated with substantial complications; especially complications pertaining to bleb.\textsuperscript{1,2} Bleb which is an internal fistula, besides being unsightly and causing cosmetic blemish, is also an important source of infection in the post-operative period.\textsuperscript{1,2} Thus in the recent past, efforts have been made to find alternative modalities to control IOP in cases of moderate and severe glaucoma.

Thus in an attempt to move past trabeculectomy in cases of Angle Closure Glaucoma (ACG), various surgical procedures have been researched upon to look at IOP lowering efficacy in the long run. This also meant a shifting paradigm from combined lens extraction and filtering surgery performed at the same sitting.\textsuperscript{3} The newer approaches included phacoemulsification combined with goniosynechialysis\textsuperscript{4-6} and phacoemulsification with goniotomy in angle closure glaucoma eyes.\textsuperscript{7}

Phacoemulsification has been shown to deepen anterior chamber and increase the angle opening distance with a proportionate reduction in IOP. Early phacoemulsification has been shown to prevent acute angle closure attacks, more than laser iridotomy in patients with resolved acute primary angle closure attack\textsuperscript{8} besides also being more efficacious and cost effective.\textsuperscript{9} Clear lens extraction when compared with trabeculectomy in patients with ACG has been shown to have a comparable reduction in IOP with lesser post-operative complications at two years, albeit with requirement of more number of medicines.\textsuperscript{10}

Majority of resistance to aqueous outflow has been attributed to trabecular meshwork, juxtacanalicular connective tissue and Schlemm’s canal endothelium.\textsuperscript{11-13} Through goniotomy and trabeculotomy, attempt is made to bypass this resistance totally or partially; rather than creating an alternate conduit for aqueous outflow in trabeculectomy.\textsuperscript{14} Incisional Goniotomy is a relatively non-invasive procedure that incises the iridocorneal angle across the anterior chamber to treat glaucoma and can be easily combined with phacoemulsification at any stage of open angle glaucoma.\textsuperscript{15,16} Thus, in early and moderate glaucoma, goniotomy has the potential to reduce the
need for medications significantly post-operatively \textsuperscript{17,18} and in severe advanced glaucoma, it may aid to defer trabeculectomy along with reduced dependence on post-operative anti-glaucoma medications. \textsuperscript{19} A clear cornea and good visualization of angle structures are mandatory pre-requisites for performing this angle surgery. However, presence of peripheral anterior synechiae may preclude visualization of anterior chamber structures in ACG eyes, thus making goniotomy difficult. In such eyes, goniosynechiolysis may be performed first in order to approach the angle and then proceed for goniotomy unlike in open angle glaucoma.

Therefore, in a continuing effort to find adjunctive procedures that offer some IOP lowering efficacy, phacoemulsification combined with goniosynechiolysis and incisional goniotomy was envisaged in this study for angle closure glaucoma subjects.

METHODS

This interventional, prospective study was conducted at Dr. Rajendra Prasad Centre for Ophthalmic Sciences, AIIMS, New Delhi. The study was done in accordance to the tenets of the Declaration of Helsinki. Institutional ethical clearance was obtained (Ref no: IEC- 382/06.07.2018, RP-28/2018).

In consecutive established primary angle closure glaucoma (PACG) patients, who were undergoing phacoemulsification, goniotomy was performed after lens extraction and IOL implantation. PACG was defined on gonioscopy as visibility of only anterior trabecular meshwork or structures anterior to it (in at least 180 degrees of the angle) in primary gaze, with or without visualisation of posterior structures on manipulation with or without elevated intraocular pressure, with either structural and/or functional dysfunction of the optic nerve, corresponding to glaucomatous optic neuropathy. Glaucoma was classified as early, moderate or advanced based on HodappParisch Anderson Criteria. \textsuperscript{20} Severe glaucoma was defined as cup to disc ratio of e"0.9:1 or a mean deviation score on Humphrey Visual Field as d"-18.0 dB.

INCLUSION CRITERIA

- Patients with PACG undergoing phacoemulsification with a need for reduction in IOP
• Patients with PACG undergoing phacoemulsification with a need for reduction in IOP lowering medications, while avoiding the formation of a filtering bleb and its associated risks

• Those with senile cataract requiring phacoemulsification

• Those giving consent for surgery and follow-up.

EXCLUSION CRITERIA

Those patients who had secondary glaucoma, previous trabeculectomy or any other filtering surgery, established peripheral anterior synechiae precluding goniosynechiolysis, minimal cataract, hazy cornea / corneal opacity or those not giving consent for surgery were excluded from enrollment.

The patients were followed up for at least 6 months following surgery.

In history taking, information regarding history of previous ocular surgery, any medical therapy received, drug allergies and any systemic illness, was sought. Pre-operative assessment included recording Uncorrected Visual Acuity (UCVA), Best Corrected Visual Acuity (BCVA) in Snellen’s fraction which was converted to LogMAR for purpose of analysis, baseline IOP recorded using Goldmann Applanation Tonometry and following administration of medications, baseline vertical cup disc ratio of the disc, baseline Visual field analysis in terms of mean deviation score on HVF, ASOCT evaluation for Angle Opening distance and irido-trabecular contact (ITC) index on CASIA SS-OCT (Tomey Corporation, Nagoya, Japan),biometry for IOL implantation amongst others. Intra operatively, following phacoemulsification, if the nasal half of the angle could be visualized, goniotomy was proceeded with using Swan Jacob hand held lens. However, in presence of goniosynechiae, goniosynechiolysis was performed first using a Healon canula. Any intraoperative event like inability to release the dense synechiae, occurrence of hyphema, requirement to drain hyphema, inadvertent creation of cyclodialysis and iridodialysis etc and post-operative complication if any were noted.
The CASIA SS-OCT allows image acquisition circumferentially across the entire anterior chamber angle by means of an inbuilt semi-automated software. It calculates ITC index, expressed as a percentage, which is a quantitative measure of angle closure extent across the entire circumference of the angle. It uses cross-sectional meridional images of the anterior segment to determine the percentage of contact between the trabecular meshwork and the iris after the scleral spur and ITC end-point are manually marked on the image frames. For the purpose of this study, ITC index was calculated using a total of 32 frames.

**SURGICAL TECHNIQUE (FIGURE 1 A-F)**

Phacoemulsification was performed as per standard protocol through a clear corneal temporal incision (Fig 1a). Following IOL implantation in the bag, cohesive ophthalmic viscosurgical device (OVD) (Healon, AMO Inc) was left in situ (Fig 1b) and miosis achieved by instillation of intracameral 0.5% pilocarpine. This helped in bringing about partial opening of the anterior chamber angle in angle closure eyes. An additional OVD if required was injected to provide globe turgidity, for maintenance of the anterior chamber as well as tamponade of any active bleeding that ensued upon goniotomy. The patient’s head was then rotated 30 to 45 degrees away from the surgeon, and the microscope was also tilted 30 to 45 degrees downwards toward the surgeon. A direct gonioprism (Swan Jacob) held by the assistant in his dominant hand, was placed on the corneal limbus nasally and the anatomic landmarks, including the trabecular meshwork, were brought into focus under higher magnification.
If significant firm Peripheral Anterior Synechiae (PAS) precluded goniosynechiolysis or an attempt to release them resulted in excessive angle bleeding, goniotoxy was aborted. However, in presence of immature goniosynechiae which could be easily separated, synechiolysis was achieved by use of a 26 G Healon canula (Fig 1c) through superior and inferior side ports advanced along the angle to enable falling back of the iris (Fig 1d).²²

An MVR (Alcon Surgical, Fort Worth, Texas) was then introduced via the temporal side port used for phacoemulsification through the dominant hand, while the non-dominant hand of the surgeon held the globe with a Lim’s forceps. The tip of the blade then incised the trabecular meshwork, wherever possible at two different levels, that is, anterior and posterior to the pigmented trabecular meshwork band (Fig 1e). The blade was then advanced along anterior chamber angle in a counterclockwise manner. A whitish band in the incised angle confirmed goniotoxy in that area. After sufficient trabecular meshwork incision was performed in one direction, the blade
was positioned through the superior side port. The handle of the gonioprism was rotated by the assistant towards the location being treated. Following successful trabecular incision, blade was then removed from the eye and irrigation/aspiration done using coaxial hand piece for removal of viscoelastic and/or refluxed blood. In order to prevent blood from refluxing again, the anterior chamber was tamponaded with air through the side port as soon as the irrigation probe was withdrawn and corneal wounds were hydrated thereafter.

Post-operatively, evaluation was performed on day 1, week 1, 1 month, 3 months and 6 months by a single observer. Visual acuity, IOP, number of ocular Hypotensive drugs and fundus evaluation was performed at each visit, whereas AS OCT was performed for angle parameters and ITC index at 1, 3 and 6 months following surgery by a single operator.

Primary outcomes were the percentage reduction in IOP and the drop in number of ocular hypotensive drug use following goniotomy. Failure was defined as an IOP >18mm Hg with medications (2), proportion of patients requiring >1 medications postoperatively (14) was also analyzed. Absolute success was defined as IOP < 18mm Hg without medications while qualified success was defined as IOP < 18mm Hg on medications. The secondary outcomes were occurrence of any intra or post-operative complications. An IOP spike was defined as IOP > 21 mm Hg despite being on topical anti-glaucoma medications.

DATA ANALYSIS

The details of the participants and their parameters were meticulously documented under the various subsections as mentioned in the patient proforma. These were recorded in Microsoft Excel spreadsheet.

Appropriate statistical methods were applied and data was analyzed in conjunction with Biostatistics department at AIIMS, New Delhi using SSPS Software. Paired t test was used to compare preoperative and post-operative data if parametric and Wilcoxon Signed rank test was used for comparison between non-parametric data. A p value < 0.05 was considered as statistically significant.
RESULTS

The mean age of the patients was 58.06 ± 28.26 years (28 - 75 years). The mean baseline IOP was 27.68 ± 8.81 mmHg (14 - 48). Preoperatively the patients were using a median of 3 medications, (mean 3.22 ± 1.07; range 0-5); 5 of these were taking diamox tablets additionally. The mean irido-trabecular index at baseline was 83.82 ± 24.95 (11 eyes). Of the 36 eyes (34 patients) included in this study, 64% (23) eyes were classified as having severe glaucoma. Intraoperatively, following lens removal, the nasal angle could be accessed in 21 eyes whereas the remaining 15 eyes required goniosynechiolysis. The mean duration of follow up following surgery was 6.64 ± 3.87 months (range: 3 - 12 months). Baseline demographic details of the patients are listed in table 1.

<table>
<thead>
<tr>
<th>Age</th>
<th>58.06 ±28.26 years (28-75 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>19 males: 15 females</td>
</tr>
<tr>
<td>Mean baseline IOP</td>
<td>27.8±7.8 mmHg (14-48 mmHg)</td>
</tr>
<tr>
<td>Mean treated IOP pre-surgery</td>
<td>21.44 ±6.6 mmHg (10-45 mmHg)</td>
</tr>
<tr>
<td>Mean irido-trabecular index</td>
<td>79.9±26.2; median 94.5 (25-100).</td>
</tr>
<tr>
<td>Pre-operative mean number of medications</td>
<td>3.28±1.01; (range 0-5)</td>
</tr>
<tr>
<td>Mean duration of follow up</td>
<td>11.7±5.5 months (range: 6-25 months)</td>
</tr>
<tr>
<td>Goniosynechiolysis</td>
<td>19 eyes</td>
</tr>
<tr>
<td>Mean treated angle</td>
<td>141.3±42.7° (90-240°)</td>
</tr>
<tr>
<td>Severe glaucoma</td>
<td>69.6% (32) eyes</td>
</tr>
<tr>
<td>Preoperative MD on HFA</td>
<td>-15.1 (3.6 to -34.5) SD: 9.2</td>
</tr>
</tbody>
</table>

Table 1: Demographic features of the recruited study population
The mean angle that was treated was 130.83 ± 43.71° (0 - 240°). ASOCT confirmed the presence of cleft in the post-operative nasal angles of the patients along with improvement in ITC index post-operatively (Fig 2a,b). The mean post-operative ITC index was 66.45 ± 34.36; median: 83 (6 - 100) (p value: 0.02; Wilcoxon signed rank test). The mean baseline IOP decreased from 21.89 ± 5.65 mm Hg to 13.54 ± 1.82 mm Hg at 6 months postoperatively (P < 0.001; paired t test; figure 3). 10 eyes achieved absolute success at the end of last follow up (IOP < 18 mm Hg without medications) while 24 eyes achieved qualified success (IOP d” 18 mm Hg on medications). Post-operatively, the median reduction in IOP was 8 mm Hg (range, -2 to 24 mm Hg) and the median percentage reduction in IOP being 36.36% (Mean: 32.78; range: -16.67 to 63.15 mm Hg). Hypotensive medication use decreased from 3.14 ± 1.07 to 1.4 ± 1.2 at final follow up, respectively (P < 0.001; Wilcoxon Signed rank test; figure 4). 32 eyes used 1 or more than 1 fewer medications postoperatively, whereas 24 eyes used >1 fewer medications postoperatively.

The most common complication was hyphema (36.12%; 13 eyes) (Fig 5a) followed by postoperative IOP spike (8.34%; 3 eyes) and cyclodialysis (2.8%; 1 eye). An IOP spike was defined as IOP > 21 mm Hg despite being on topical anti-glaucoma medications. Three eyes required post-operative hyphema drainage while the rest settled on their own with no further intervention. In one patient, the hyphema was delayed and presented at his fourth day post-operative visit. In another patient, hyphema recurred after drainage but it was managed conservatively at recurrence. The IOP spike that was observed had to be controlled with anti-glaucoma medications. Two eyes developed normalization of IOP within a week whereas one eye was operated upon for trabeculectomy a month after initial surgery after it failed to achieve IOP control. At 1 month following surgery, 3 eyes had persistent intraocular inflammation for which continued steroidal cover in tapering doses was administered for another month while one eye had developed PCO (Fig 5b,c). At 6 months, the only adverse effect noted was persistent PCO in 1 eye which had to be Yag lasered.

There was a positive correlation between pre-operative IOP and percent reduction in IOP at final follow up (p: 0.02; rho: 0.40) and absolute decrease in IOP (p: 0.006; Spearman’s correlation coefficient: 0.45). The cumulative survival probability for
absolute success when IOP <18 mmHg was considered as the end point was 5.4% (SE: 0.05; 95%CI: 0.004-0.21) at the end of 12 months (figure 6a); indicating the need for medications in most. The cumulative survival probability for qualified success at the end of 12 months was 94.4% (SE: 0.04; 95% CI: 0.80-0.98) when IOPd”18 mmHg was considered the end point while it was 49% (SE: 0.14; 95% CI: 0.20-0.72) when IOPd”14 mmHg was considered the end point. (Figure 6 b,c). There was failure in 2 eyes to achieve success criterion despite use of medications. There was no difference in the success rate in eyes with severe glaucoma or those with mild-moderate glaucoma (p: 0.59; Fischer Exact Test)

**DISCUSSION**

Goniotomy is a minimally invasive surgical option, which provides the aqueous with direct access to the collector channels and the distal outflow system by incising trabecular tissue which is the site offering maximum impedance to aqueous outflow.\textsuperscript{14-16} The literature on goniotomy in angle closure glaucoma is scarce due to the limited visibility of angle structures from presence of peripheral anterior synechiae/pigmentation, iris concavity and high lens vault precluding angle surgery in these eyes. However, lens extraction followed by goniosynechiolysis allowed us easy angle view in this study. Ours was the first study which evaluated the feasibility, efficacy and safety of incisional goniotomy using disposable MVR with or without goniosynechiolysis in combination with phacoemulsification in lowering IOP in eyes in different stages of primary angle closure glaucoma. We observed that the procedure was effective in lowering IOP significantly in these eyes including eyes with advanced stages of glaucoma and in reducing the dependence on anti-glaucoma medications.

Being ab-interno in nature, the advantages over a filtering surgery include non-violation of the scleral wall and also in being a bleb less surgery.\textsuperscript{23} The risk of hypotony related issues and need for future cataract surgery is circumvented.\textsuperscript{24} Since the subjects with PACG with cataract are generally elderly, the need for secondary interventions should be minimal to cause little discomfort. However, a trabeculectomy calls for frequent secondary interventions like anterior chamber reformation, needling, releasable suture removal etc.\textsuperscript{25} Hence a single procedure of phacoemulsification with
simultaneous glaucoma surgery is desirable. The advantages of incisional goniotomy over minimally invasive glaucoma surgeries (MIGS) include absence of need for any costly external implantable device and thus avoiding any associated adverse effects like implant migration, extrusion, dislocation, issues related to MRI compatibility, endothelial cell loss, conjunctival erosion and tube blockade.\textsuperscript{24,26}

Dorairaj and Tam performed a series on use of Kahook dual blade (KDB) goniotomy along with goniosynechiolysis in angle closure glaucoma eyes.\textsuperscript{7} They observed that KDB can be used to perform goniosynechiolysis as well along with excisional goniotomy. They found favorable results in their short term follow up of 6 months in 42 eyes. However, theirs was a retrospective study and they used KDB instead of MVR goniotomy performed in this series. Furthermore, their series does not mention the proportion of eyes needing GSL. In our series we noted that not all ACG eyes required goniotomy, especially more so in younger population which had primarily plateau iris or in those with angle closure secondary to a high lens vault. Priced at an approximate 350\$, this disposable device marketed for one-time use, excises a part of TM, thus achieving lowering of IOP by decreasing resistance through TM.\textsuperscript{27} However, the availability of KDB worldwide is limited and is yet to be introduced in our part of the world. Contrarily, incisional goniotomy performed by a 23 G Microvitreo-retinal blade theoretically may offer higher chances of failure postoperatively due to adhesion of the incised TM leaflets over time. However, in the absence of any long term studies on evaluation of the feasibility and efficacy of incisional goniotomy in conjunction with phacoemulsification in eyes with ACG, the question has remained unanswered so far. Unlike other procedures marketed for angle surgery which directly excise (KDB) or ablate the TM Trabectome (Neo Medix),\textsuperscript{28} incisional goniotomy by MVR does not require a capital outlay; the cost is limited to that of the blade which is usually priced at 5\$. This results in a per-case cost that is several times lower than other devices.

Previously, goniotomy using disposable KDB combined with phacoemulsification has been shown to be efficacious in achieving IOP lowering in eyes suffering from OAG primarily with different severities of involvement.\textsuperscript{17,19,29,30}KDB assisted excisional
goniotomy was shown to lower IOP by 24-36% and reduce the need for Hypotensive medications by 37-63% at 6-12 months following intervention combined with cataract surgery or as a standalone procedure.\textsuperscript{6,17,31,32} Other open angle glaucomas including JOAG\textsuperscript{33} and pseudoexfoliation glaucoma when combined with small cyclodialysis\textsuperscript{34} have also shown favorable outcomes with KDB goniotomy.

Looking at the outcomes of phacoemulsification alone in cases with ACG, it may reduce IOP by up to 50%, the proposed mechanisms being increased anterior chamber depth and opening up of irido-corneal angle leading to a decrease in IOP.\textsuperscript{35} In a comparative study by Tham et al to study the outcomes of clear lens extraction versus trabeculectomy in medically uncontrolled angle closure glaucoma patients over 2 years, they found that both reduced IOP by approximately 35%.\textsuperscript{36} However, patients who underwent lens extraction had to be dependent on post-operative anti-glaucoma medications more often, suggesting the need for addition of some adjunctive procedure to help lower IOP further following phacoemulsification alone. In a comparative analysis of randomized controlled trails each on phacoemulsification and phacotrabeculectomy, it was observed that in those PACG eyes which had higher preoperative IOP, cataract or were on an increased number of glaucoma drugs, the probability for failure was high with either phacoemulsification or phacotrabeculectomy alone, however cases which underwent phacotrabeculectomy had a higher likelihood of success.\textsuperscript{37} This study showed that advanced PACG eyes or those PACG with cataract have a higher likelihood of failure if phacoemulsification alone is done and an adjunctive procedure if performed would be valuable to control IOP in such cases. Hence the need for goniotomy.

In a meta-analysis on studies performed to look at the benefit of phaco-goniosynechiolysis over phacoemulsification alone, it was concluded that phaco-goniosynechiolysis surgery does not reduce the dependence of patients on anti-glaucoma eye drops post-operatively. It thus suggested that goniosynechiolysis does not provide extra benefit over phacoemulsification in subjects with PACG.\textsuperscript{38} The reasons suggested for failure of goniosynechiolysis are diverse and include increased inflammation following synechial release leading to re-formation of PAS, direct surgical trauma
during the procedure, dysfunctional trabecular meshwork due to chronic synechiae, proliferation of iris or fibrous tissue into TM, and atresia of distal outflow channels due to chronic deprivation from aqueous flow.\textsuperscript{38} Hence the efficacy of goniosynechiolysis as a standalone procedure in ACG is questionable.\textsuperscript{39,40} On the contrary, looking at the efficacy of KDB goniotomy alone without phacoemulsification, Erin G et al found it to be safe and effective in reducing IOP as a standalone procedure in striking contrast to goniosynechiolysis alone.\textsuperscript{18} Thus, the benefit of goniosynechiolysis in our cases may be short term, acting more as an aid to help expose the trabecular meshwork for goniotomy incision. An incised angle may further help to prevent synechiae formation in future at the same site.\textsuperscript{16} The air tamponade provided at the end helps in preventing the undesirable re-adhesions at the goniotomy site as well as acting as a haemostatic agent. It thus derives that in the procedure goniotomy plus goniosynechiolysis following phacoemulsification, goniotomy works to lower the IOP in the long term by removing the resistance to aqueous outflow at the level of TM while the main role of goniosynechiolysis is to facilitate goniotomy in angle closure eyes.

Incisional goniotomy in our study achieved significant reduction in the median number of medication requirement post-operatively. Greenwood et al had found a mean reduction of 0.7 medications at 6 months postoperatively.\textsuperscript{17} Use of fewer medications correlate positively to quality of life as well as medication adherence.\textsuperscript{41} The need for fewer medications improve compliance and is helpful in better preservation of ocular surface from chronic inflammation. Patient convenience improves with the use of fewer bottles and lesser frequency of medication use leading to better adherence.\textsuperscript{41} Cost effectiveness studies have linked fewer medications with more patient satisfaction as well as lower costs.\textsuperscript{42} Higher levels of satisfaction and convenience was reported with lower frequency of drops, in a survey amongst 2500 patients in New Zealand.\textsuperscript{43} In an analysis on trabeculectomy outcome, Broadway et al found a higher failure rate to be associated with long-term usage of multiple medications with corresponding subclinical inflammation in conjunctiva.\textsuperscript{44} Notably, preservatives, excipients and buffers used in topical medications can adversely affect the ocular surface.\textsuperscript{45}
Hyphema is one of the commonest complications following incisional goniotomy followed by increased intraocular inflammation. Greenwood et al found the incidence of hyphema after goniotomy to be 39.4% after surgery in their series, 36.5% in severe glaucomas by Salinas et al and 19% in a series on angle closure glaucoma by Dorairaj et al. The causes for hyphema include exposure of the anterior chamber to blood filled Schlemm’s canal, the presence of granulation tissue at the wound edges or due to injury to uveal vessels following trauma with MVR. However certain precautions taken during the surgery such as performing goniotomy with Healon in the anterior chamber, using air tamponade towards the end, doing good hyphema aspiration intraoperatively and leaving the IOP little towards the higher side with the anti-glaucoma cover takes care of recurrence of hyphema postoperatively.

We found no difference in the success outcomes between patients with mild – moderate or severe glaucoma. Two-third of our participating patients had severe glaucoma, indicating that goniotomy as an adjunct to phacoemulsification can work well in advanced angle closure glaucomas as well. Conventionally the treatment options for more advanced glaucomas remain trabeculectomy, deep sclerectomy, glaucoma drainage devices (all of which produce a dysthetic bleb) and cyclodestruction in poor visual prognosis cases. However, bleb calls for its own set of complications related to bleb fibrosis with eventual surgical failure or leakage leading to hypotony or infection. In another study on the effect of excisional goniotomy in severe glaucoma, favorable outcomes were reported. However, theirs was a multi centric study which demonstrated the efficacy of KDB goniotomy, the surgery was performed by different surgeons across different centers and included only 11 cases of angle closure glaucoma.

The merits of our study include the inclusion of a homogenous set of population consisting of North Indians with angle closure glaucoma, surgery performed by a single surgeon and the prospective design of the study. However, the limitations include a small sample size and a short follow up. In the absence of a control arm, this observational study lacked randomization leading to biases and a non-inferiority hypothesis-testing trial could not be performed. Nevertheless, it could be derived from this study that goniotomy if performed simultaneously as an adjunct with
phacoemulsification is helpful in achieving significant reduction in IOP and lowering the need for medications in eyes with any severity of angle closure glaucoma. Possibly by stabilization of IOP, it can help defer the need for filter by few years in advanced glaucoma. Thus even in the absence of availability of KDB, incisional goniotomy has an important role to play in the management of angle closure glaucomas as an adjunct to phacoemulsification.

**BIBLIOGRAPHY**


FIGURE LEGENDS

FIGURE 1 SURGICAL STEPS

a. Standard Phacoemulsification is performed using usual technique.
b. A posterior chamber intra-ocular lens is placed in the capsular bag.
c. Miosis is achieved with intracameral pilocarpine, this is followed by goniosynechialysis if goniosynechiae are present.
d. A fallen back iris can be visualised in areas with goniosynechialysis.
e. Using a 23G MVR blade and under visualisation with a Swan-Jacobs lens, a nasal goniotomy is performed.
f. Arrow indicates angle with incised area which can be visualised as a white band.
Figure 2

ASOCT of one representative patient (a) Preoperative picture showing occludable angles and shallow anterior chamber before phacoemulsification. ITC showing contact percentage to be 95% (b): Postoperative ASOCT image showing a cleft in the trabecular meshwork in the nasal angle following phacoemulsification with goniotomy, with ITC contact percentage falling to 32% after goniotomy.

Figure 3

Line graph showing IOP preoperatively and at subsequent follow ups. It shows statistically significant decline in IOP at all time points when compared with preoperative levels. (p value: Multiple comparison test with Bonferroni adjustment)
FIGURE 4

a. An eye with hyphema showing layering of red blood and hazily appearing inferior iris on first post-operative day. Superiorly placed air bubble can be seen.

b. Intraoperative appearance of layered blood in a case of hyphema.

c. Post operative appearance showing increased inflammatory reaction in the eye appearing as early post-operative posterior capsular opacity.

d. An inflammatory membrane visible on the anterior surface of IOL.

FIGURE 5

Kaplan Meir Cumulative survival curve showing a) Absolute success probability (5.4%) at the end of 12 months when IOP < 18 mm Hg was considered as the end point (SE: 0.05; 95%CI: 0.004-0.21) b) Qualified success probability (94.4%) at the end of 12 months (SE: 0.04; 95% CI: 0.80-0.98) when IOP < 18 mmHg was considered the end point. c) Qualified success probability (49%) at the end of 12 months (SE: 0.14; 95% CI: 0.20-0.72) when IOP < 14 mm Hg was considered the end point.
A Comparative Study on The Effects of Dorzolamide Versus Timolol On Ocular Blood Flow in Normal Tension Glaucoma Patients (FP88)

**Dr. Pratheeba Devi Nivean, Dr. Murali Ariga, Dr. Nivean M**

**INTRODUCTION**

Total human ocular blood flow is estimated to be approximately 1 ml/min, most of which supplies the vasculature of the uvea (primarily the choroid); only 2-5% supplying the retina\(^1\). The vascular supply to the eye is primarily from the ophthalmic artery (branch of internal carotid artery). The retinal and the choroidal circulation have important clinical implications. The posterior ciliary arteries make provision for much of the optic nerve head and choroidal blood supply while the central retinal vessels supply the retina. Autoregulation of blood flow occurs with changes in blood pressure, ocular perfusion pressure and intraocular pressure\(^2\). Ocular hemodynamics though complex, can be assessed to an extent. The quantification of blood flow in these vessels can give great lengths of information with regards to the pathological processes behind retinal and optic nerve head diseases such as glaucoma.

**MATERIALS AND METHODS**

This investigation will be conducted at MN Eye Hospital. All experimental procedures conform to the tenets of the Declaration of Helsinki and will be approved by the...
institutional review board at MV Diabetic Hospital Royapuram. Subjects will sign informed consent prior to entry into the study.

All participants will be confirmed OAG patients referred by Glaucoma consultants at M N Eye Hospital and RIO GH. Treatment naïve patients with mild to moderate glaucoma would be included in the study.

30 glaucoma patients will participate in a prospective, parallel comparative trial, over a period of 12 weeks. Baseline measurements would be done followed by treatment with either dorzolamide (n = 15 patients) or timolol (n = 15 patients) 2 or 3 times a day for 12 weeks. Final measurements would be done at the end of 12 weeks of the study (final visit).

All study visits (2) (excluding the recruitment visit) will be conducted at approximately the same time of day by the same research team to eliminate user-initiated variations in the evaluations of ocular blood flow.

At each study visit, measurements will include: medical questionnaire, brachial artery pressure (systolic and diastolic), radial pulse, slit lamp examination, IOP, Color Doppler Imaging (CDI) of the retrobulbar blood vessels, and calculated ocular perfusion pressures including systolic, diastolic and mean ocular perfusion pressures.

All examinations will be performed on one qualified eye, which will be randomly chosen (if only one eye qualifies for inclusion the study that eye will be examined). All measurements will be in the same order at the same time of day for each patient.

**MEASUREMENT SPECIFICS**

Brachial artery blood pressure and pulse will be assessed after a five-minute rest period using a calibrated automated sphygmomanometer at the beginning and end of each study visit.

IOP will be assessed using Goldmann Applanation Tonometry. Ocular Perfusion Pressures (OPP) will be calculated using the following equation:

(Systolic Perfusion Pressure (SOPP), Diastolic Perfusion Pressure (DOPP) and the mean Perfusion Pressure (MOPP) will also be calculated as systolic BP-IOP, diastolic
BP-IOP and mean arterial pressure-IOP respectively.) This will allow for a comprehensive assessment of IOP and various measures of ocular perfusion pressure during treatment with both therapies.

COLOR DOPPLER IMAGING

CDI imaging of the blood vessels supplying the retina and optic nerve will be conducted using Philips HDI 5000 SonoCT Ultrasound System with the microvascular small parts clinical option (Philips Medical Systems, Bothell, WA) with a 7.5 MHz linear probe as described in detail previously.\textsuperscript{21-24} In brief, samples of pulsed-Doppler signal from within a 0.2 x 0.2mm sample area will be analyzed to calculate blood velocities in the retrobulbar vasculature. Ultrasound power settings will comply with local and national guidelines as required, if no guidelines are set by locality a mechanical index equal to or less than 0.22 will be set. This technique has been shown to yield reproducible measurements of retrobulbar blood flow velocities.\textsuperscript{21} CDI measurements will be taken in the Ophthalmic (OA), Central Retinal (CRA), and Nasal (NPCA) and Temporal (TPCA) short posterior ciliary arteries. In each vessel, peak systolic velocity (PSV) and End Diastolic Velocity (EDV) will be determined, and Pourcelot’s resistive index will be calculated (RI = (PSV-EDV)/PSV). This will allow for a comprehensive assessment of all of the blood vessels supplying the retinal ganglion cells and optic nerve during treatment with both therapies.

PATIENT DEMOGRAPHICS, INCLUSIONS AND EXCLUSIONS

INCLUSION CRITERIA

Patients will meet all of the following inclusion criteria to enter the study:

- Age: 40 years or older.
- Diagnosis: Treatment naïve patients with mild to moderate normal tension glaucoma in at least one eye
- Best corrected visual acuity at least 20/40 in at least one eye.
- Study would also include normal healthy subjects with no ocular abnormality, normal optic discs, and IOP below 20 mm Hg in both eyes
- Patients willing to follow up of 12 weeks
EXCLUSION CRITERIA

- Exfoliation glaucoma, pigmentary glaucoma, history of acute angle closure or a narrow, occludable anterior chamber angle by gonioscopy, mean deviation (MD) of visual field testing (Humphrey 30-2 program) >12
-Patients with cardiovascular disorders on hypotensives, bradycardia (heart rate < 50 beats/min), second and third degree Heart Block, Asthma Bronchiale, Chronic Obstructive Pulmonary Disease, Congestive Heart Failure
- Intraocular surgery or argon laser trabeculoplasty within the last 6 months
- History of Chronic or Recurrent Inflammatory Eye Diseases (e.g., Scleritis, Uveitis) or Infection
- History of Intraocular Trauma.
- Any Abnormality Preventing reliable Applanation Tonometry.
- Current use of any Ophthalmic or Systemic Steroid, which may interfere with this investigation.
- Severe, unstable or Uncontrolled Cardiovascular, renal, or Pulmonary Disease (creatinine clearance < 1.8 l/h)
- Any opacity or patient uncooperativeness that restrict adequate examination of the ocular fundus or anterior chamber in the study eye or poor follow-up
- History of hypersensitivity to one of the study drugs or drugs with similar chemical structure
- Pregnancy

RESULTS

We had 11 patients in each group. The average ocular perfusion pressure was 42.61. The mean resistive index in ophthalmic artery was 0.83 pre treatment which reduced to 0.79 post treatment in Timolol group and in Dorzox group it was 0.79 (pre treatment) and 0.75 (post treatment). The average RI in the central retinal artery was 0.72 and
0.70 pre and post treatment in timolol group and 0.73 pre treatment and 0.71 post treatment in Dorzox group. The mean RI in the short posterior ciliary artery was 0.70 and 0.70.5 pre and post treatment in timolol group and 0.70 and 0.69 in Dorzox group. There was reduction in resistive index with both the groups. However the reduction was significant only in short posterior ciliary artery.

CONCLUSION

Technology through decades has brought us to this golden era of imaging where we can visualize and understand the subtle physiological and pathological processes that lead to the diseases we treat. Although there is an association between measurements of ocular blood flow and glaucoma progression, a causal relationship has not yet been established. There is insufficient data to support the measurement of blood flow in the treatment of retinal diseases and glaucoma. Further studies with better study designs are required to validate its use with respect to treatment and prognosis. In the future, through evolving methods of estimation of ocular blood flow, we can evaluate and characterize ocular circulation and this may become an integral element in our clinical practice.
Epiphora is a very common complaint. It has a broad differential diagnosis. One of the least discussed among the etiologies of epiphora is stenosis of the lacrimal punctum. The most common presenting symptom is tearing, but patients may also give vague complaints of ocular discomfort. Stenosis must be distinguished from complete occlusion of the puncti, which differs in its treatment and prognosis. This review article has given emphasis only on punctal stenosis.

The Lacrimal Puncti are positioned at the medial part of the eyelid margins. They open into the tear lake near the plica semilunaris and the bulbar conjunctiva. The upper punctum is generally located 0.5 – 1 mm medial to the lower punctum according to the laterally sloped caruncle shape. When the eyelids are closed, these two puncti are usually adjacent to one another.

The puncti are located within an elevated structure referred to as the lacrimal papilla. They are considered to be 0.2 – 0.3 mm in diameter and are surrounded by a fibrous ring. The papillae are surrounded by the muscle of Riolan, and are pulled medially and posteriorly by the muscle fibers. Lower puncti is larger than the upper. Upper punctal stenosis is more common than lower punctal stenosis. The punctual diameter is inversely proportional to age.
There are no studies which addresses the issue of the predictive value of epiphora in diagnosing acquired punctal stenosis. Therefore, the incidence and prevalence of punctal stenosis have yet to be determined, and it is also unclear whether a complaint of tearing warrants a meticulous search for this condition.

**TREATMENT**

Apart from stent and plugs, there are many surgeries that have been advocated. It includes Vertical slit, horizontal slit, one/two/three snip surgeries. Punctal plugs are also advocated as an adjunct to these surgeries.

Surgeries have been probably advocated because of easy, quick and cheap option but there is a high incidence of recurrence mainly due to fibrosis on account of wound healing or chronic blepharitis. On the other hand the stent and plugs are costly.

**AIM**

The purpose of this study was to find out a cheaper version of such plugs which can be commonly made and which can prevent the recurrence of punctual stenosis resulting in epiphora.

Period of study - 3rd March 2016 to 5th April 2019

**MATERIALS AND METHOD**

- We examined the cases complaining of watering with punctal block/occlusion or stenosis seen under slit lamp.
- Other causes of epiphora were excluded.
- All these patients underwent punctal dilatation.

**GROUP A**

Syringing without any obstruction at canaliculi or the naso lacrimal duct

**GROUP B**

If there were any obstructions while syringing- fluid regurgitation from same punctum.
GROUP C
If there were obstruction to the flow while syringing and the regurgitation was from the other punctum.

GROUP D
If there were mucoid fluid or pus regurgitation.

We included patients of group A only.

GROUP A1
There was a follow up on 1st day and 7 days. No return of the patients by one month.

GROUP A2
If the patients remained asymptomatic for 7 days but come back later on with the same complaints. The term “later on” means any day from first syringing to 30 days.

In Group A we had excluded patients of group A1 because of non availability of cases.

In Group A2, we examined the patients and again excluded all the causes of epiphora.

In these cases we have inserted “Bicautpron plug”. The cost calculated is less than one US Dollar.

DETAILS OF THE “BICAUTPRON PLUG”

This plug is made by the proline rod of 0/0.

Flat knob, 1st arm - 2 mm and 2nd arm – 10 mm.

Video detail of the plug, it’s insertion and removal is available.
METHOD OF INSERTING “BICAUTPRON PLUG”

• Puncti were dilated using punctual dialator.
• Syringing done.
• Plug inserted as one does it in Mini Monoca plug/stent.
• The proximal end of the plug which is like a flat knob is inserted in the punctum.

INSTRUCTIONS TO THE PATIENTS

• Patients may feel foreign body sensation, but should not rub the eyes.
• While touching the eye, the patient may feel the elevation of the flat knob end, but are advised not to remove it.
• Moxifloxacin eye drops were put 4 times a day x 40 days.
• Lid hygiene to be maintained.
• In case if they feel something protruding and coming out by itself, then they must report immediately.
• Should ignore little watering initially for 7 days.
• Should follow up after every 10 days.
• Should report after 40 days for removal of the “Bicautpron plug”

After removal of the “Bicautpron plug” all patients were followed up monthly for six months.

RESULTS

Group A - 253 patients

Subgroup - Group A1 - 97 patients. Since they did not return back with any complaints, we take it that punctal dilatation and syringing solved their problem.

Subgroup - Group A2 - 156 patients.

39/253 patients had “Bicautpron plug” in both the puncti.

All other had in one eye.
There were self extrusion also as shown in table 1.

TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>Within 10 days</th>
<th>Within 20 days</th>
<th>Within 30 days</th>
<th>Before 40 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self Extrusion</td>
<td>3</td>
<td>10 (3+7)</td>
<td>70 (10+60)</td>
<td>109 (70+39)</td>
</tr>
<tr>
<td></td>
<td>None from both lids plugs</td>
<td>Includes 10 days patients also None from both lids plugs</td>
<td>Includes 10 and 20 days patients None from both lids plugs</td>
<td>Included 10, 20 and 30 days patients None from both lids plugs</td>
</tr>
</tbody>
</table>

After the self extrusion, patients were asked to continue with Moxifloxacin eye drop with lid hygiene.

After 40 days all “Bicaupron plugs” were removed and patients were followed up monthly till six months for recurrence of watering as shown in table 2

TABLE 2

Watering

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>10 Days ( After plug insertion )</td>
<td>2</td>
</tr>
<tr>
<td>20 Days ( After plug insertion )</td>
<td>4 (2+2) Including previous complaint</td>
</tr>
<tr>
<td>30 Days ( After plug insertion )</td>
<td>4 (4+0) Including previous complaint</td>
</tr>
<tr>
<td>40 Days ( After plug insertion the date of removal)</td>
<td>5 (4+1) Including previous complaint</td>
</tr>
<tr>
<td>Time Period</td>
<td>Description</td>
</tr>
<tr>
<td>---------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>2 months</td>
<td>After plug insertion (20 days after plug removal)</td>
</tr>
<tr>
<td>3 months</td>
<td>After plug insertion (50 days after plug removal)</td>
</tr>
<tr>
<td>4 months</td>
<td>After plug insertion (80 days after plug removal)</td>
</tr>
<tr>
<td>5 months</td>
<td>After plug insertion (110 days after plug removal)</td>
</tr>
<tr>
<td>6 months</td>
<td>After plug insertion (140 days after plug removal)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

- By 40 days there was extrusion of 109 plugs.
- None of the plugs extruded where it was inserted in both eye lids.
- Early extrusion happened in early post plug insertion.
- On retrospective investigation, it was found that those cases were very apprehensive and did not follow the instruction properly. They also came from poor background and were less educated.
- But if we see the recurrence of watering, it happened in only 2 cases.
- By the end of 40 days the extrusion was in 109 cases but the watering remained controlled in (148/156) cases.
CONCLUSION

Bicautpron Plugs are a very cheap and an alternative measure in cases of punctal stenosis / occlusion treatment to control epiphora.

REFERENCES


Status of AQP4-Ab Antibody in Optic Neuritis in A Tertiary Eye Center And Its Implications. (FP1294)

Dr. Anita Ambastha, Dr. Srishtee Shree, Dr. Gyan Bhaskar, Dr. Rakhi Kusumesh

ABSTRACT

AIM

Long-term visual and neurological outcome of optic neuritis according to status of AQP4-Ab antibody in them.

METHODS

96 patients with Optic Neuritis (mean age 34.2 ± 20) underwent serological test for AQP4-Ab. MRI, VEP, fields and haemogram for autoimmune status was done in all cases. Kaplan-Meier survival analysis was used to investigate the visual outcomes and prognostic characteristics of aquaporin-4 antibody seropositive patients.

RESULTS

AQP4-Ab was positive in thirteen female patients with Atypical Optic Neuritis. Among the seropositive patients, 7 developed neuromyelitis optica (NMO). 3 patients with seronegative Atypical optic neuritis also developed NMO. Difference
in presenting BCVA in both seropositive and seronegative was not significant. However difference in final BCVA at the end of 6 weeks in both groups was significant (p = .03)

CONCLUSION

Examination for AQP4-Ab positivity in ON is important in predicting the prognosis, possibility of developing NMO and starting timely intervention.

INTRODUCTION

Optic neuritis is an inflammatory disorder of the optic nerve often resulting in a demyelination process. In the west and in Caucasian populations, the optic neuritis treatment trial demonstrated good recovery and visual outcomes with a significant risk of conversion into multiple sclerosis. However recent reports from the Asia and Africa have noted a significantly different clinical profile and outcomes are reported to be worse than the West while the risk of conversion to multiple sclerosis is low and between 0-5% 1. The difference in outcome of optic neuritis between the west and the east has been attributed to the higher incidence of atypical optic neuritis and possibly a racial difference in the course of the disease 2. The discovery of a specific serum marker for NMO-IgG antibody [aquaporin 4 antibody/ AQP4 Ab] has revolutionised the treatment of demyelinating diseases. Severe vision loss can be seen in optic neuritis (ON) associated with both multiple sclerosis (MS) and NMO. Identifying this antibody in optic neuritis patients can help us to establish the likelihood of these patients developing NMO. It is important to differentiate these two entities as the treatment strategies of MS and NMO are different. In our study, we decided to screen all patients of Isolated optic neuritis coming to our Neuro ophthalmology clinic, for AQP4 Ab (ELISA technique) and to know the clinical course and long term visual outcome over a three year old study in both positive and negative cases. It has been reported that about one-half of NMO patients present with isolated ON 3 and the ON in NMO is characterized by profound and persistent visual function damage.
AIM

Short term outcome of patients with Isolated Optic Neuritis and visual and neurological outcome of optic neuritis according to status of AQP4-Ab antibody and their comparative analysis.

MATERIAL AND METHOD

This was a prospective analysis of patients diagnosed with optic neuritis in our Neuro-ophthalmology clinic over a period of three years from 2016-2019. Evaluation was done by anterior segment examination, dilated fundus examination, Humphreys visual field analysis (HFA) and Visual Evoked potential (VEP). All patients have undergone detailed neurological evaluation by a referral neurologist. MRI Brain was done in all patients. MRI orbit and Spine was done in suspected Opticospinal MS and NMOSD. Apart from laboratory testing for serum AQP4Ab, complete hemogram, blood sugar, ESR, rheumatoid arthritis factor[RA], antinuclear antibody[ANA], ACE, serum creatinine, P-ANCA, C-ANCA, Mantoux, chest x-ray was done. CSF analysis was done in severe optic neuritis. AQP4 Ab was detected using the ELISA technique. Best Corrected Visual Acuity (BCVA) was examined by Snellen chart and converted into a Logarithm of the Minimal Angle of Resolution (LogMAR) units for statistical analysis. The number of recurrent attacks in the affected and fellow eye were recorded. Clinical data at final visit were collected and analysed. A good visual outcome was determined as final BCVA equal to or better than 20/60, and a poor visual outcome was determined as final BCVA of less than 20/200. For patients with simultaneous bilateral involvement, clinical data of the worse eye would be selected for statistical analysis. Based on their seropositive status, patients’ management was revised. Patients were started on acute phase treatment of intravenous methylprednisolone therapy 1 g/day 3 – 5 days with a short oral steroids taper for 11 days for all patients. Patients diagnosed with NMOSD and MS received further long-term immunosuppressants or immunomodulator at neurology clinic. Follow up was done over a three year period for visual, neurological outcome and recurrence. Clinical features were compared between the seropositive and the seronegative groups, on presentation and at the
final follow-up. Statistical analysis was performed with Epi info version 7. Institutional ethical committee clearance was taken. Tenets of Helsinki adhered to.

**CASE DEFINITION**

Optic neuritis was defined by history of unilateral or bilateral visual loss of acute onset associated with at least 2 of the following criteria: color vision abnormality, pain on eye movement, afferent papillary defect, centrocecal scotoma, and abnormal visual-evoked response. [5]. A diagnosis of OPN was confirmed by an ophthalmologist or neurologist at onset. Multiple sclerosis was diagnosed using the McDonald criteria [6] and NMO by the criteria proposed by Wingerchuck. [7] Neuromyelitis optica (NMO) was considered to be a monophasic disorder causing bilateral Optic neuritis and severe transverse myelitis simultaneously or in rapid succession within few weeks. ON was classified as bilateral if both eyes were involved simultaneously or sequentially within 3 weeks. Recurrent ON (RON) was defined as a new unilateral attack occurring after an interval $\geq 4$ weeks. Chronic recurrent idiopathic OPN (CRION) was diagnosed in patients with recurrent OPN, steroid responsive/dependent and normal MRI brain and no evidence of systemic illness on long-term follow-up. [8] Severe visual loss was defined as visual loss of 20/200 or more in worst affected eye. A good response to steroid therapy was defined as the recovery of VA to more than 20/40, within 1 – 2 months, after steroid pulse therapy. Steroid dependency, based on previously reported characteristics of CRION [8], was defined as a relapse or exacerbation of ON, occurring within 2 months from the time of cessation or dose reduction of steroid treatment.

**INCLUSION CRITERIA**

- Clinically isolated Optic neuritis.
- Bilateral optic neuritis
- Recurrent optic neuritis
- CRION
EXCLUSION CRITERIA

• Cases with neurological abnormality at presentation
• Other optic neuropathies [ischemic, compressive, hereditary, toxic, metabolic, vascular, and infective].

RESULTS

A total of 96 patients were evaluated and followed up for a period of three years. (Jan 2015-Jan 2018). Of the 96 patients followed, 84 patients were followed-up from the day of onset of ON and in 12 patients history revealed ON as the initial presenting feature. Mean follow-up period was 26.8 ± 8.2 months. Mean Age at onset was 34.2 ± 20 years. There were 75 female patients and 21 male patients. M:F ratio was 1:3.6. Serum AQP4 Ab was positive in 13 of the 96 (13.5%) patients with greater frequency in the female, bilateral, and recurrent ON groups. Transverse myelitis developed in two patients in following two months. Among the seropositive patients, 7 developed neuromyelitis optica (NMO). Only 2 of the seronegative patients developed NMO. Among the seronegative patients, 10/83 (10.4%) developed to MS, 21 had recurrent isolated optic neuritis (RION) out of which 10 were chronic recurrent isolated optic neuritis (CRION). Rest of the seronegative cases did not progress further and remained as monophasic. Overall, 10 patients developed MS, 7 NMO, 21 had RION out of which 10 were CRION. No CRION patients were aquaporin positive. MS was diagnosed in 6 patients at MRI done at presentation. Follow up over three years showed 4 patients developing MS. On comparing the seropositive with seronegative groups, visual acuity on presentation between the two groups, was almost comparable [i.e. profound visual impairment on presentation was seen in both the groups] but on final follow up, the seropositive group had a poorer visual recovery as compared to the seronegative group which had a better visual recovery and the value was statistically significant (p =< .05). Complete visual recovery occurred in none of the 13 seropositive patients. Baseline evaluation including the age and the clinical presentation between the two groups were not statistically significant. At 3-year follow-up, the ON recurrence rate was higher in the seropositive AQP4-
Ab patients (13/1, 100%) than in the seronegative patients (32/91, 35%). ANA was more positive in seropositive group.

Lumbar puncture was not performed routinely in patients with MS or NMO.

Comparison of the V/A at presentation and the final visual outcome between the seropositive and the seronegative group

<table>
<thead>
<tr>
<th></th>
<th>Seropositive</th>
<th>Seronegative</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial mean BCVA (log MAR)</td>
<td>1.88</td>
<td>1.301</td>
<td>0.21</td>
</tr>
<tr>
<td>Final mean BCVA (log MAR)</td>
<td>1.78</td>
<td>0.58</td>
<td>0.03</td>
</tr>
<tr>
<td>p Value</td>
<td>0.94</td>
<td>0.03</td>
<td></td>
</tr>
</tbody>
</table>

Visual outcome in both groups of optic neuritis patients

<table>
<thead>
<tr>
<th>Visual acuity</th>
<th>Seropositive (%)</th>
<th>Seronegative (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete recovery 6/6</td>
<td>NIL</td>
<td>49 (56.32%)</td>
</tr>
<tr>
<td>Partial/incomplete recovery (Snellens 1–2 line improvement)</td>
<td>11 (84.6%)</td>
<td>11 (12.64%)</td>
</tr>
<tr>
<td>Deterioration (dropped from presenting visual acuity by 1–2 lines)</td>
<td>2 (15.3)</td>
<td>27 (31%)</td>
</tr>
</tbody>
</table>

DISCUSSION

AQP4-Ab is considered to be a pathogenetic and prognostic factor of NMO-related ON. The distinctive nature of the optic nerve lesion between AQP4-Ab seropositive and seronegative patients with ON has been reported. However, the prevalence of AQP4-Ab in acute ON is not clear in the Indian population, and its relationship with
the severity of visual function of ON patients at onset has not been fully studied yet. In a study by Ambika et al\textsuperscript{9}, they noted that Indian population with severe optic neuritis have 20% seropositivity for AQP4 Ab and all seropositive patients were females and had a relatively poorer visual outcome as compared to the seronegative patients. However this study has limited itself to severe optic neuritis. In our study we attempted to find out seroprevalence and course of disease in all patients with isolated optic neuritis. Our study showed an incidence of 13 percent with more bilateral, recurrent and those with severe visual impairment being seropositive. Pandit et al\textsuperscript{[10]} analysed the NMO-IgG status in 78 cases with 81% belonging to the NMO spectrum and found only 3.8% seropositivity in the study group. In another study by Pandit et al\textsuperscript{(11)} 59 patients were identified with optic neuritis as the initial presentation of neurologic disease. During the follow-up: 29 patients developed MS, 3 NMO, 13 CRION, and 14 did not progress further and remained as monophasic OPN. In our study, 10 patients developed MS, 7 NMO, 21 had RION out of which 10 were CRION. In our study all CRION patients were seronegative with one becoming seropositive at the end of three years. They showed lesser improvement in median logMAR visual acuity. Recent literature has shown that race and ethnicity has a bearing on the demography, clinical profile and outcomes of optic neuritis. The outcome of optic neuritis in the Asian countries has been shown to be poorer than the west \textsuperscript{(12,13,14)} Saxena et al\textsuperscript{15} examined the clinical profile and short-term visual outcome of all forms of optic neuritis in 99 eyes of 83 Indian patients.\textsuperscript{19} The patients were examined and followed up for a mean period of 10 months. The median logMAR visual acuity improved significantly from 1.6 \pm 0.8 to 0.2 \pm 0.6, though only 64% of eyes achieved a final visual acuity of 20/40 or more as against 94\% in the Optic Neuritis Treatment Trial.\textsuperscript{16,17} These results are similar to ours as we too found a poorer visual outcome in patients presenting with severe visual impairment and though median logMAR visual acuity improved significantly, it was less than in the ONTT trial. Lesser number of patients converted to MS but this could be due to shorter followup.
A multicentric study was conducted by Wakakura et al.\textsuperscript{12} to establish the baseline characteristics of optic neuritis in Japanese patients. In the study, it was observed that the clinical profile of optic neuritis was significantly different from the western population (compared to a US study) with a lower risk of multiple sclerosis. However, the study demonstrated similar visual function changes and outcomes as the western population. Neurologists should work in close partnership with ophthalmologists in their practice so that this vital link between the benign disease of isolated OPN and chronic inflammatory CNS disorders, such as MS, NMO and CRION is not missed. Valuable time is lost and often irreversible neurologic dysfunction will set in before diagnosis is made. AQP4-Ab seropositive ON patients tend to be predominantly female and younger, with worse visual acuity. AQP4-Ab seropositivity indicates patients with ON might have worse visual function and prognoses.

**CONCLUSION**

Serum AQP4-Ab should be tested in all bilateral, recurrent and severe cases of Optic Neuritis so that timely and appropriate treatment can be started.

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17. Beck RW, Trobe JD, Optic Neuritis Study Group. What we learned from the Optic
Assessment Of Retinal Manifestations Of Parkinson’s Disease Using OCT: A Study In Indian Eyes. (FP805)

Dr. Shishir Verghese, Dr. Parag K Shah, Dr. Virna Shah

Key Words: Parkinson’s disease, OCT

ABSTRACT

BACKGROUND

Despite the abundance of OCT studies in PD in various populations, study of OCT changes in the Indian population are lacking. Here, we explored OCT changes in patients with Parkinson’s disease compared to healthy controls.

METHODS

A prospective cohort of eleven patients with Parkinson’s disease and eleven age-matched controls (total forty-four eyes) were recruited at Aravind Eye Hospital. Central fields for superior, inferior, nasal, and temporal macular subfield, GCC, NFL, ORL, RNFL, in addition to PMB and choroidal thickness were measured with SD-OCT. Cumulative measures for temporal, nasal, and global thickness were compared. Inter-eye asymmetry was assessed by comparing average OCT parameter asymmetries in patient groups.
RESULTS
Statistically significant differences were found for the average values of NFL S2, 33.11 vs. 37.65 (p = .045), ORL Central 90.86 vs. 85.68 (p=.008), ORL T1 81.59 vs. 79.09 (p = .020), ORL T2 78.18 vs. 76.23 (p = .007), ORL S1 81.50 vs. 79.23 (p = .028), for healthy control and Parkinson’s patients, respectively. Inter-eye asymmetry was significantly different for NFL N2 1.73 vs. 9.64 (p = 0.0296), RNFL Center 2.64 vs.6.27 (p = 0.0292), RNFL ST 9.91 vs. 21.64 (p = 0.0251) between healthy control and Parkinson’s patients, respectively. No statically significant differences were found between global, gross temporal, or gross nasal RNFL parameters.

CONCLUSIONS
Significant OCT differences shown here support the investigation of OCT biomarkers for parkinsonism in the Indian population. Larger studies focused on the effects of medication, other types of dementia, and combination imaging are warranted.

INTRODUCTION
The gold standard for Parkinson’s disease (PD) diagnosis is expert clinical evaluation, with special attention to cardinal features of bradykinesia, tremor, rigidity and postural instability, as well as clinical response to dopaminergic therapy. Global estimates of the prevalence of PD are variable, though estimates suggests roughly six thousand cases per hundred thousand, with a burden of roughly three thousand daily-adjusted life years (DALYs) per hundred thousand.\(^1\)

Attempts to quantify disease burden, such as the clinimetric assessment, the Movement Disorder Society-Sponsored Revision of the Unified Parkinson’s Disease Rating Scale (MDS-UPDRS), are often used in clinical research.\(^2\) However, early, reliable, objective biomarkers for Parkinson’s disease presence and severity remain to be elucidated.
Parkinson’s has a complex etiopathology influenced to varying degrees by genetics, exposures, and lifestyle factors which complicate diagnostic clarity and epidemiologic studies. In the past twenty years, alpha-synuclein, a filamentous protein, was found to be the predominate component of Lewy Bodies and Lewy Neurites, the pathologic hallmarks of the disease.

Misfolded and abnormal alpha-synuclein is believed to underly neurotoxic sequelae in dopaminergic neurons, contributing to cell loss in PD. The progression of neuronal lesions in PD follows a well-studied progression beginning in the medulla oblongata and pontine tegmentum, and progressing to the midbrain and higher cortical areas, which serves as the basis for post-mortem staging.

Interestingly, the retina utilizes dopaminergic signaling via D1 and D2 receptors which helps explain visual phenomena in Parkinson’s disease. While retinal neuroarchitecture dysfunction related to changes in dopaminergic neuroarchitecture has historically been explored via histologic analysis; studies of living patients have not been possible until more recent, non-invasive OCT technology. OCT studies have become very prevalent in the literature, with varying degrees of evidence for changes in RNFL thickness and macular thickness. Despite the abundance of OCT studies in PD in various populations, study of OCT changes in the Indian population are lacking. Consequently, the investigation here sought to determine whether prior findings are replicable in the Indian population.

METHODS

Approval from the Institutional Review Board was received for the single-site study at the Neuro-ophthalmology and Retina outpatient departments at Aravind Eye Hospital, Coimbatore, Tamil Nadu. Patients with Parkinsonism diagnosed at the Neurology department of Kovai Medical Centre and Hospital, Coimbatore, Tamil Nadu, India, were recruited. Age-matched controls without Parkinsonism as determined clinically were recruited for controls. Exclusion criteria included any pre-existing ocular disorder, retinal pathology, or advanced motor dysfunction prohibiting OCT acquisition. Patients received a comprehensive eye exam including visual acuity and refraction (Snellen
chart), intraocular pressure with applanation tonometer, color vision (Ischiara/Ishiha)
and contrast sensitivity (Mars contrast sensitivity test), central fields (Bjerrum screen),
anterior and posterior segment evaluation by slit lamp biomicroscopy, dilated fundus
evaluation with indirect ophthalmoscopy, and optical coherence tomography after dilation
(Heidelberg/Heidelberg Retinal Angiogram). Eleven healthy control (7 female, 4 male) and
eleven parkinsonism patients (7 male, 4 female) were enrolled. Patients carried a diagnosis
of parkinsonism on average for 5.2 years, with most patients taking syndopa (8 patients),
or other regimens of pramipex, ropark, syncapone, amantrel pacitane or syndopa (3 patients).
All patients remained medicated during the study. Baseline patient characteristics are in Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Healthy Control</th>
<th>Parkinsonism</th>
<th>p-value</th>
</tr>
</thead>
</table>
| **Average Age**           | 59.7 years (+/-
5.33 years) | 68 years (+/-6.19 years)            | .073    |
| **Average Contrast**      | 1.44            | 1.39                                | .329    |
| **Visual Acuity**         | 20/20 (11 patients) | 20/20 OU (6 patients), 20/20-20/30 (1 patient), 20/40-20/200 (1 patient), 20/30 OU (2 patients), 20/40 OU (1 patient) |         |
| **IOP**                   | 15.5            | 14.7                                | .437    |
| **Systemic Conditions**   | DM (4), HTN (4) | DM (6), HTN (10), CAD (3), CKD (1), CVA (1) |         |
| **Anterior Segment**      | WNL             | PCIOL OU (4) WNL OU (2) NS1 OU (2), NS2 PSC OU (2) NS 1-PCIOL (1), Mild lens changes (1) |         |
| **Posterior segment**     |                 | Lamellar hole OD (1) Photocoagulation scars OU (1) Drusen OS (1) ERM OS (1) Drusen OU (2) moderate NPDR OU (1) |         |
Statistical analysis was performed using R studio and Microsoft Excel. Average values for each parameter were compared using student’s t-test with 2 tails (alpha = .05). Inter-eye asymmetry was compared by taking the absolute value of the difference between each eye per patient, followed by T-tests with 1 tail (based on the null hypothesis of increased asymmetry in Parkinson’s disease) comparing disease and healthy groups. Regional values not captured on OCT were excluded from analysis, and any patient missing values from either eye were removed from inter-eye analysis.

RESULTS

Central fields for superior, inferior, nasal, and temporal macular subfield, GCC, NFL, ORL, RNFL, in addition to PMB and choroidal thickness were measured with OCT. There were statistically significant differences found for several parameters on average between disease groups (Table 2) and on average for inter-eye asymmetry (Table 3).

<table>
<thead>
<tr>
<th>NFL S2</th>
<th>Average Healthy Control</th>
<th>Average Parkinsonism</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>33.11</td>
<td>37.65</td>
<td>.045</td>
</tr>
<tr>
<td>ORL Central</td>
<td>90.86</td>
<td>85.68</td>
<td>.008</td>
</tr>
<tr>
<td>ORL T1</td>
<td>81.59</td>
<td>79.09</td>
<td>.020</td>
</tr>
<tr>
<td>ORL T2</td>
<td>78.18</td>
<td>76.23</td>
<td>.007</td>
</tr>
<tr>
<td>ORL S1</td>
<td>81.50</td>
<td>79.23</td>
<td>.028</td>
</tr>
</tbody>
</table>

Table 2: Statistically significant average differences observed on OCT

<table>
<thead>
<tr>
<th>NFL N2</th>
<th>Healthy Control</th>
<th>Parkinsonism</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.73</td>
<td>9.64</td>
<td>0.0296</td>
</tr>
<tr>
<td>RNFL Center</td>
<td>2.64</td>
<td>6.27</td>
<td>0.0292</td>
</tr>
<tr>
<td>RNFL ST</td>
<td>9.91</td>
<td>21.64</td>
<td>0.0251</td>
</tr>
</tbody>
</table>

Table 3: Statistically significant average inter-eye differences observed on OCT
Of note, RNFL Temporal and ORL S1 inter-eye differences were actually significantly greater in healthy controls compared to Parkinsonism. Sengupta et al\textsuperscript{17} explored gross temporal and nasal RNFL thickness on OCT. Supplemental Table 1 shows the results of assessments using their formulas. No statistically significant differences were found between PD and healthy controls for average temporal, nasal, or global RNFL thickness. There were no statically significant differences for temporal-nasal difference (TND) or temporal-nasal ratio (TNR).

<table>
<thead>
<tr>
<th></th>
<th>Healthy Control</th>
<th>Parkinsonism</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporal side average RNFL thickness</td>
<td>209.318</td>
<td>204.955</td>
<td>0.683</td>
</tr>
<tr>
<td>( T_{\text{avg}} = (TS + [2 \times T] + TI) \text{ divided by} 4 )\textsuperscript{17}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal side average RNFL thickness</td>
<td>205.068</td>
<td>206.568</td>
<td>0.846</td>
</tr>
<tr>
<td>( N_{\text{avg}} = (NS + [2 \times N] + NI) \text{ divided by} 4 )\textsuperscript{17}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average global thickness ( G_{\text{avg}} ) was extrapolated from the formula ( G = (TS + NS + 2T + 2N + TI + NI)/8 )\textsuperscript{17}</td>
<td>207.193</td>
<td>205.761</td>
<td>0.840</td>
</tr>
<tr>
<td>Temporal-nasal difference (TND) = ( T_{\text{avg}} - N_{\text{avg}} )\textsuperscript{17}</td>
<td>4.250</td>
<td>-1.614</td>
<td>0.626</td>
</tr>
<tr>
<td>Temporal-nasal ratio (TNR) = ( T_{\text{avg}}/N_{\text{avg}} )\textsuperscript{17}</td>
<td>1.025</td>
<td>0.998</td>
<td>0.640</td>
</tr>
</tbody>
</table>

Supplemental Table 1
CONCLUSION

The present study was minimally powered to identify strong differences between Parkinsonism and healthy controls on OCT; however, there were statistically significant differences in nerve fiber layer and the outer retinal layer in the central, temporal, and superior quadrants.

Although myriad studies have been performed globally, very few have focused on the Indian population. Sengupta et al\textsuperscript{17} studied thirty-four Parkinson patients and fifty healthy age-match controls with OCT, finding significantly thinner RNFL thickness in PD patients, and diminished macular volumes correlating with disease severity. Despite similar RNFL regional findings in the literature\textsuperscript{13,18-20}, these findings were not explicitly corroborated here perhaps due to medication effects\textsuperscript{21} and the small patient cohort here with heterogenous disease severity.

Nevertheless, the significantly different inter-eye nerve fiber layer volumes here, especially in the RNFL, may be connected to the laterality of symptoms in this disease. Parkinson’s disease displays laterality with regard to motor symptoms\textsuperscript{22,23} perhaps related to asymmetric central neuronal loss\textsuperscript{24}. In fact, interocular asymmetry on OCT has been reported in Parkinson disease for foveal thickness\textsuperscript{24-26} and suggested in the RNFL\textsuperscript{27}. Therefore, these trends should be explored further in higher-powered cohorts.

Ultimately, this pilot study allows for interesting hypothesis generation regarding OCT findings in Parkinsonism in the Indian population. Larger studies exploring the effects of medication, Parkinson-like syndromes, and the addition of other types of retinal imaging such as visual evoked potentials or electroretinography\textsuperscript{28} may augment the predictive power of OCT biomarkers for neurodegeneration.

REFERENCES


Sleep Deprivation and Its Impact on The Quality of Vision—A Clinical and Molecular Analysis (FP2141)

Dr. Nikhil Balakrishnan, Dr. Rohit Shetty, Dr. Tejal S.J.

ABSTRACT

AIM
To understand the effect of lack of sleep on clinical metrics and molecular profile on the ocular surface.

MATERIALS & METHODS
30 healthy volunteers (60 Eyes) underwent routine dry eye evaluation (Schirmer’s & Tear Break Up Time (TBUT) along with OSDI questionnaire, Lipid Layer assessment using LipiView Interferometer, Objective Scatter Index (OSI) using the OQAS (HD Analyzer) at Baseline, following Sleep Deprivation (for 24 hours) & after 3 nights of sufficient sleep (>8 hours). Eye wash & Tears (Schirmer’s strip) were collected & different cytokine levels were measured by multiplex ELISA using a flow cytometer.

STATISTICAL ANALYSIS USED
Wilcoxon matched-pairs signed rank test
RESULTS

Sleep Deprivation resulted in significant decrease in Schirmer’s test value 1, TBUT & LipiView metrics and an increase in Scatter (OSI and Mean OSI) and OSDI. Tear cytokines and chemokines including IL-1a, IL-1b, IL-6, IL-12, IL-17F, MCP1, ICAM1 etc., showed similar increase. The magnitude of tear cytokine changes was proportional to the severity of TBUT, Schirmer’s test 1, Lipid Layer Thickness and Optical Scatter changes. A significant (p<0.05) reversal of these changes was observed following a period of adequate sleep.

CONCLUSION

Sleep deprivation causes significant detrimental alteration in tear fluid dynamics, along with an increase in inflammatory cytokines on the ocular surface. It leads to increase in ocular scatter and decrease in lipid layer thickness, inducing dry eye & in turn leads to poor quality of vision. These improve, but do not return to normal levels even after 3 days of adequate sleep.

KEY-WORDS

Sleep Deprivation
Ocular Scatter
Visual Quality
Lipid Layer Thickness
Tear Cytokines

INTRODUCTION

Sleep Deprivation has numerous detrimental effects on the body, hindering daily functioning and adversely affecting health and longevity. Loss of sleep is known to cause fatigue, mood swings, difficulty in concentration, memory loss, paranoia, fatigue and hallucinations.
The cumulative long term effects of sleep loss include an increased risk of hypertension, diabetes, obesity, heart attacks and depression. But the effect of sleep deprivation on the ocular surface is insufficiently studied. Through our study we wish to highlight the effect of Sleep Deprivation on the Ocular Surface and in turn on Visual Outcomes and to identify Tear Biomarkers correlating with the same.

SUBJECTS AND METHODS

The study was a Prospective Interventional Study conducted over a six month period at a Tertiary Care Eye Hospital after prior ethics committee approval.

A total of 30 healthy volunteers (60 eyes) were recruited for the study. All volunteers were between 20 to 40 years old, had no previous history of Dry eye or any systemic conditions associated with the same, had regular sleep routines and were not on any kind of medications or eye drops. Contact Lens Users, patients with ocular disease/disorders of the lid margin/nasolacrimal duct, and post refractive surgery patients were excluded from the study.

Each volunteer was tested at 3 time intervals namely: Baseline, Sleep Deprivation (24 hours) and after 3 days of Good Sleep (8 hours of sleep).

At each interval volunteers were made to undergo a Dry Eye Evaluation i.e.- Schirmer’s 1, Tear film breakup time (TBUT) and fill up an Ocular Surface Disease Index (OSDI) Questionnaire. OQAS HD Analyser (Optical Quality Analysis System High Definition Analyser) was used to gauge the optical quality using the Objective Scatter Index (OSI), and the Tear Film Analysis using the Mean OSI. Lipid layer assessment was performed using the LipiView Ocular Surface Interferometer. Tears were collected using sterile Schirmer’s strips (5*35mm² Tear Strips, CC ContacareOphthalmics and Diagnostics, India) and put in Microcentrifuge Eppendorf tubes and stored at -80 C. The tears were extracted from the stored Schirmer’s strips in 300uL phosphate-buffered saline (PBS) solution & were used to measure associated inflammatory associated molecules such by Multiplex ELISA using flow cytometry based cytometric bead array. An eye wash was given with a 5 cc syringe on the ocular surface of each eye covering both the bulbar and palpebral conjunctiva using normal saline stored.
at room temperature and collected by placing wash tubes (15 ml polypropylene tubes) at the angle of the eye. The eye wash sample was fixed using equal amounts of (minimum 2 ml) 0.1% paraformaldehyde to preserve cell markers and morphology. These were then transported at 4 degree C in an ice box. They underwent centrifugation at 200 RCF (relative centrifugal force) for 5 minutes at 4 degrees. This was followed by tagging of the different cell markers and quantification of cells using flow cytometry. All data was collected using Microsoft Office Excel. Statistical Analysis of the data was conducted using Wilcoxon matched-pairs signed rank test.

RESULTS

Following Sleep Deprivation, the Schirmer’s 1 test values reduced to 13mm/5 minutes from the baseline value of 28mm/5min. This value rose up to 22mm/5min after 3 nights of adequate sleep. Similarly Tear Break UpTime values dropped to 4.3 seconds from 7.8 seconds following Sleep Deprivation and increased to 6.9 seconds following Good Sleep. OSDI questionnaire scores increased to an average of 28.7 following Sleep Deprivation from the baseline of 10.2 and fell back to 14.6 after adequate sleep. The Objective Scatter Index (OSI) showed similar trends increasing from 0.4 to 1.8 following sleep deprivation and dropping back to 0.8 following Good sleep. Similar patterns were observed in Mean OSI scores that increased to 2.64 from a baseline score of 0.74 following loss of sleep and returned to 1.23 following 3 nights of adequate sleep. Lipid layer thickness values fell from an average of 92 to 64 following Sleep Deprivation and increased to 83 following Good Sleep.

Tear cytokines IL1a, IL2, IL4, IL6, MPO, EPO, TNF, MMP 9, ICAM 1 were observed to increase almost two fold following sleep deprivation as compared to baseline which returned to near normal following Good Sleep.

DISCUSSION

Statistical Analysis of the data revealed Schirmer’s 1, TBUT and LipiView values decreased significantly after Sleep Deprivation and returned to near normal but not to the baseline levels following 3 nights of Good Sleep. Similarly OSI, Mean OSI and OSDI values increased following loss of sleep and the values reversed but did
not reach the baseline values after adequate sleep. A twofold increase in cytokines were noted which correlated strongly to the severity of the above tests. These cytokine levels too returned to near normal levels following good sleep.

This study highlights that Sleep Deprivation leads to alteration in the ocular surface. Inflammatory pathways play a pivotal role in the disruption of the ocular integrity. Disintegration of the ocular surface leads to decrease in the lipid layer thickness, increase in optical scatter and symptoms of dry eye.

This in turn leads to worsening of the Optical Quality.

Another noteworthy finding is the improvement of these values following adequate sleep. But even 3 days of Good Sleep doesn’t totally return the Ocular Surface to its normal state.

This study is a first of its kind. Never has the effect of Sleep Deprivation on the Ocular surface and its molecular correlation been documented. We further wish to broaden our horizons and find out if any drop could act to prevent the degradation of the Ocular Surface despite Sleep Deprivation. Another arm of our study would involve the effect of Sleep Deprivation on Ophthalmologists and how it would affect their practice.

This seemingly simple to sound study, is actually novel and noteworthy in many aspects and is a paradigm for future work.
Comparative Study Of Recovery Of Ocular Motor Nerve Palsies – YES Or NO To Treatment With Steroids?

Dr. Sumitha Muthu, Dr. Rohit Shetty, Dr. Abdul Rawoof, Dr. Jyoti Matalia

We conducted a prospective study to determine etiologies of 4th and 6th nerve palsy in a tertiary eye care center and to compare the recovery of these nerve palsies with intervention (treatment with oral steroids & antiplatelet agents) versus non-intervention. Both arms received treatment for any systemic condition if present.

The inclusion and exclusion criteria were as below:

The patients were divided into arms – an intervention arm and a non-intervention arm. The intervention received steroids and antiplatelet agents in addition to systemic treatment whereas the non-intervention arm received treatment for any systemic condition if present only.

In the intervention arm we had a total of 90 patients with a mean age of 58 years and the non-intervention arm included 85 patients with a mean age of 53 years. The mean follow up in the intervention arm was 92 days and mean follow up in the non-intervention arm was 115 days.
The most common etiologies for the nerve palsies in both arms were diabetes mellitus, hypertension, dyslipidemia and hyperhomocystinemia. Other less common etiologies included trauma and idiopathic etiology.

There was no statistically significant difference in the final outcome that is the between the 2 arms. However, time to recovery was faster in intervention arm and ranged between 3 - 6 weeks with a mean of 25 days as compared to non-intervention arm which ranged between 6 - 12 weeks with a mean of 57 days which was statistically significant.
CONCLUSION

There is no difference in the final outcome when steroids are used in nerve palsies but they do speeden up the recovery. Hence steroids may be considered for speedy recovery of nerve palsies and in the absence of systemic comorbidities like poorly controlled DM which contraindicate its use.
Targeted Retinoblastoma Therapy: Specific Tumor Killing by Cationic Peptides (Caps). (FP2164)

Dr. Gagan Dudeja,

**TITLE**

Novel cationic anti-microbial peptides (CAPs) for targeted therapy for retinoblastoma

**PURPOSE**

Current multimodal treatment of Intra-ocular retinoblastoma (RB) includes focal treatment (LASER, Cryotherapy, Thermotherapy or Brachytherapy) Chemotherapy (systemic, periocular, intra vitreal, intra arterial) or enucleation of affected eyes. The existing chemotherapy drugs not only attack tumour cells, but also affect other dividing cells in body like bone marrow or normal retinal cells. Any drug which selectively targets RB tumour cells sparing other normal cells in body is the need of the hour for in ocular oncology.

The outer membranes of RB tumour cells have been reported to have more negatively charged molecules compared to normal cells. Tumor cell membranes contain charged moieties such as phosphatidylserines, acidic glycoproteins,
and glycosaminoglicans. Therefore we hypothesized using charged cationic peptides carrying unnatural amino acid sequence for selective targeted activity against RB tumour cells sparing the normal cells.

Thus we tested anti-cancer activities of a series of cationic anti-microbial peptides (CAP) in vitro against RB cell line and 3-D RB tumour model.

METHODS

Cytotoxic effects of CAPs were tested on retinoblastoma cell line WERI-RB1 and Human Retinal Pigment Epithelial cells (ARPE-19). Cells were treated with a dose escalation regime and cell viability was assayed using Trypan Blue assay and Propidium Iodide based flow cytometry. Checkerboard assay was performed in WERI-RB1 to determine the effect of CAPs and chemodrug topotecan, individually or in combination on cell viability over time. Effects of CAP’s in regulating DNA damage and repair, mitochondrial membrane disruption, apoptosis were analyzed at the protein level by immunoblotting and immunostaining the cells or cellular extracts post treatment. We developed 3D tumour spheroids using WERI-RB1 cells and evaluated the treatment response of CAP’s and topotecan monotherapy. The tumor spheroids were also analyzed for DNA damage by gamma-H2ax staining.

RESULTS

Cell viability assay demonstrated cytotoxic and cytostatic effect of two CAPs HC3 & HC5 (out of 5 initial designs) in WERI-RB1 cells, while no cell toxicity was observed in ARPE-19 cells. HC3 and HC5 showed synergistic effects with Topotecan in the combination therapy evaluated by checkerboard assay. Monotherapy of CAPs on 3D tumor spheroids (n=12) resulted in size reduction and shrinkage of spheroids, which were measured using automated microscopy based high content screening. CAPs at IC50 dosage shows activation of Caspase-3, Caspase-9, the key mediators of apoptosis. Besides, CAPs showed PARP cleavage and activation of p53 and αH2A.X at the protein level which were evaluated by western blot and immunofluorescence.
CONCLUSIONS

CAPs (HC3 and HC5) are a novel molecules which can be used for targeted therapy as they demonstrate selective cytotoxicity against tumour cells and spare retinal epithelial cells. CAPs can synergistically enhance the effect of Topotecan. In particular, the data demonstrate selective induction of cell death in Rb null tumor cells, but to in retinal epithelial cells. The in vitro spheroid model demonstrates significant shrinkage of tumour by CAP treatment. Additional animal xenograft studies need to be performed to validate these data in the future. Together, the results provide new insights into CAP function regarding how selective targeting of cancerous cells while sparing the healthy surrounding tissue is achieved.

ACKNOWLEDGEMENTS

Vishnu Suresh Babu, AmuthaBarathiVeluchamy, Laxminarayan Rajamani, Navin Kumar Verma, Arkasubhra Ghosh
Dynamic Ophthalmoscopy (DO): A Novel Objective Technique for Estimation of Accommodation in Children. (FP2337)

Dr. Mihir Trilok Kothari, Dr. Rishika Jain, Dr. Daneshwar Verma

INTRODUCTION

Several accommodative abnormalities exist in young children (Table 1). Majority go unrecognised due to lack of evaluation by the ophthalmologists. Of all the available methods for evaluation of accommodation (Table 2), dynamic retinoscopy (DR) is considered the gold standard. However, due to its learning curve, time taken for evaluation, problems with off axis aberrations under mydriatic conditions and inability to be performed on both eyes simultaneously, DR is not used routinely. In this manuscript, we have described a novel objective technique, dynamic ophthalmoscopy (DO), for the evaluation of accommodation in children and compared it with the current gold standard. We describe its usefulness that has allowed us to recognise hitherto unrecognised accommodative abnormalities in children.
<table>
<thead>
<tr>
<th>Type of accommodative abnormalities</th>
<th>Description / definition</th>
<th>Associated clinical conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoaccommodation or accommodative insufficiency[1]</td>
<td>Reduced accommodative amplitude for the age</td>
<td>Down Syndrome,[2] Cerebral Vision impairment,[3] Accommodation insufficiency with asthenopia,[4] Convergence excess esotropia,[5] Association with convergence insufficiency,[6] Foveal hypoplasia, Aniridia, Albinism and Ectopia lentis</td>
</tr>
<tr>
<td>Accommodative inertia</td>
<td>Time between the application of an accommodativestimulus and the response of the eye is delayed.</td>
<td>Asthenopia[7]</td>
</tr>
<tr>
<td>Accommodative in facility</td>
<td>The inability to focus back and forth quickly</td>
<td>Asthenopia[8]</td>
</tr>
<tr>
<td>Ill sustained accommodation</td>
<td>Accommodation is normal in amount, but is sustained only with effort and soon gives out</td>
<td>Children with brain damage</td>
</tr>
<tr>
<td>Paralysis of accommodation</td>
<td>Inability to accommodate</td>
<td>Trauma, Syphilis (Tabes dorsalis), Diphtheria</td>
</tr>
<tr>
<td>Lag accommodation</td>
<td>Reduced accommodation for a particular amount of stimulus</td>
<td>Juvenile onset myopia (Association)</td>
</tr>
</tbody>
</table>
Aniso-accommodation

Accommodation in the two eyes is not the same

Syphilis, diphtheria

Anti -accommodation

More accommodation for distance than for the near target

Amblyopia and Pre presbyopia

Spasm of accommodation

Persistently fixed and high accommodation

Pseudomyopia, Acquired esotropia with spasm of near reflex

Lead of accommodation

Accommodation lies persistently above the usual normal limit

Pseudomyopia

<table>
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<th>SUBJECTIVE METHODS</th>
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<tr>
<td><strong>Name</strong></td>
</tr>
<tr>
<td>1.Near vision assessment</td>
</tr>
<tr>
<td>2.Near point of accommodation</td>
</tr>
<tr>
<td>3.Accommodative amplitude (positive relative accommodation and negative relative accommodation)</td>
</tr>
<tr>
<td>Test Method</td>
</tr>
<tr>
<td>-------------------------------------</td>
</tr>
<tr>
<td>4. Accommodative flipper test</td>
</tr>
<tr>
<td>5. Near duo-chrome test</td>
</tr>
<tr>
<td><strong>OBJECTIVE METHODS</strong></td>
</tr>
<tr>
<td>1. Dynamic ophthalmoscopy</td>
</tr>
<tr>
<td>2. Dynamic retinoscopy</td>
</tr>
<tr>
<td>3. Open field autorefractometry</td>
</tr>
<tr>
<td>4. Dynamic Aberrometry</td>
</tr>
</tbody>
</table>

Table 2: Common methods of assessment of accommodation and their limitations.
DESCRIPTION OF THE ‘NEW’ TECHNIQUE

Dynamic ophthalmoscopy (DO):

- Full correction of refractive error,
- Child reads letters from 6 meter chart.
- Examiner looks at pupil from one meter
- The child reads at 40 cm and target moved closer in small steps from 40 cm to 30 cm and then to 20 cm, 10 cm and 8 cm.

Estimation Dynamic Ophthalmoscopy (eDO):

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- Full correction of refractive error,
- Child reads letters from 6-meter chart
- Examiner looks at pupil from one meter
- The child reads at 40 cm and target moved closer in small steps from 40 cm to 30 cm and then to 20 cm, 10 cm and 8 cm.

Lens interjected to neutralise the crescent

**SUBJECTS AND METHODS**

This prospective study was performed from 1\textsuperscript{st} March, 2010 till 22.9.2019 in three parts

<table>
<thead>
<tr>
<th>Aims</th>
<th>Objectives</th>
<th>Inclusion criteria</th>
<th>Design</th>
<th>Sample Size</th>
</tr>
</thead>
</table>
| Comparison of DO with DR | Comparison in a routine pediatric ophthalmology clinic | ØChildren 1-16 years age  
ØVisiting pediatric eye clinic for various eye disorders  
ØCooperative for DO and DR | Observational, comparative, unmasked | 1000 patients |
| Comparison for assessment of drug induced cycloplegia | \( \text{Children 5-16 years age} \)
| | \( \text{Visiting pediatric eye clinic} \)
| | \( \text{Underwent cycloplegic refraction} \)
| | \( \text{Cooperative for DO and DR} \)
| Observationa, comparative, masked | 32 \( \pm \) 5 (patients)

| Comparison of eDO with eDR | Collection of normative data | \( \text{Children 6-16 years age} \)
| | \( \text{Normal eyes} \)
| | \( \text{Visiting pediatric eye clinic} \)
| | \( \text{Cooperative for eDO and eDR} \)
| Observationa, comparative, unmasked | 60 eyes of 60 children

| Evaluation of interobserver variation | \( \text{Children 5-16 years age} \)
| | \( \text{Visiting pediatric eye clinic} \)
| | \( \text{Cooperative for eDO and eDR} \)
| Observationa, comparative, masked | 10 eyes of 5 patients

| Comparison for assessment of drug induced cycloplegia | \( \text{Children 1-16 years age} \)
| | \( \text{Visiting pediatric eye clinic for any problem} \)
| | \( \text{Cooperative for DO} \)
| Observationa, non comparative | Not defined

Use DO for routine examination in the clinic

Detection of frequently unrecognized or unreported accommodative abnormalities in children

\( \text{Children 1-16 years age} \)

\( \text{Visiting pediatric eye clinic for any problem} \)

\( \text{Cooperative for DO} \)

Observational, non comparative

Not defined

- Sample size calculations:
FOR PART 1 STUDY:

We calculated sample size to detect a difference of 1.0 D (effect size) in accommodation (continuous variable) between two techniques (paired variable) namely, DR and DDDO, with 5% significance level ($z_{1-a/2}$) and 80% power of the study ($z_{1-b/2}$) and for 2.0 D standard deviation in accommodation using the formula, $n = (Z_{1-a/2}^2 + Z_{1-b/2}^2)S^2/d^2$ we needed 32 eyes/patients in our study.

For Part 2 study:

We used the formula $n = (Z_{1-a/2} - Z_{1-b/2})^2 Sc^2/d^2$, $Z_{1-a/2} = level\ of\ significance = 1\% = 2.58$

$Z_{1-b/2} = power\ of\ the\ study = 90\% = 1.28$, $Sc = standard\ deviation = 0.5D$, $d = effect\ size = 0.25D$

Putting this value in above formula, $n = (2.58 - 1.28)^2 (0.5)^2 / (0.25)^2 = (3.96)^2 \times 0.25 / 0.625, = 14.8996 \times 4$

$= 59.596, = 60$

STATISTICAL METHODS

FOR PART 1 STUDY

$2 \times 2$ Bayesian tables were made to calculate the sensitivity, specificity and predictive values of DDDO in comparison to DR. Ninety five percent confidence interval and clinical agreement (Cohen’s kappa coefficient) between the two techniques were calculated.

FOR PART 2 STUDY

Two tailed, paired t test for samples with equal variance was used as a test of significance. Correlation coefficient (Pearson r) and 95% confidence intervals were calculated.
for the statistical analysis. T value (statistical significance of Pearson correlation coefficient) was calculated for the given sample size.

RESULTS

1. Dynamic ophthalmoscopy (DO/DDDO) had excellent (>90%) sensitivity, specificity

2. Estimation dynamic ophthalmoscopy (eDO or eDDDO) had excellent correlation with eDR (Tables 1 and 2 below) and the inter observer variation (Table 3 below).
3. Part 3 of the study

‘New’ abnormalities of accommodation recognised by the authors using DO in their pediatric eye clinic

Left pupil more dilated than right in all lighting conditions. Accommodation equal in both eyes in a child using 0.01% atropine drops


Left eye accommodating less than the right eye in a child using 0.01% atropine drops
3. Anti accommodation (Accommodation relaxes for near and induced for far objects)
Patient accommodating more for 33cm than at 10cm and 20cm
4. Convergence insufficiency with accommodation failure in a child with oculocutaneous albinism
5. Convergence insufficiency without accommodation failure

6. Hypoaccommodative esotropia

7. Intermittent exotropia controlled with accommodation
6. Intermittent exotropia controlled with fusional control (without excess accommodation)

**DISCUSSION**

In this study we have described novel techniques of DO and eDO and compared it with DR and eDR for the clinical assessment of accommodation in young children. eDO and eDR utilized the same ‘lens insertion’ technique. Response accommodation measured by eDO was comparable to that measured on eDR and the correlation between the two techniques was excellent.

DO and eDO were observed to be easier to perform at close fixation distances (i.e. 10 and 8 cm) compared to DR and eDR. Using an openfield autorefractor or photoscreener is warranted for future studies where these observer dependent techniques would be compared with a more objective technique.

We realize that DO has a higher chance of going wrong in presence of an uncorrected refractive error, specifically a hyperopia or hyperopic astigmatism. This is simply because, a clinician relying excessively on disappearance of bright crescent from the top of the pupillary area may be foxxed by a larger than normal superior crescent to begin with, in patients with hyperopia. However, with experience, false positive test results are likely to decrease provided the examiner learns to take into account the thickness of the superior crescent in hypermetropes before they commence accommodation.

An important and common utility of DR or DDDO would be to assess the completeness of cycloplegia after pharmacological dilatation of pupil in children with ametropia. Under the condition of mydriasis, retinoscopy is known to become less reliable.\textsuperscript{[10]} This can happen due to either interference from peripheral aberrations, especially
spherical aberrations, from the crystalline lens that produce two conflicting reflexes, exactly in the opposite direction, one from the center of the lens and another one from the periphery or the examiner is simply refracting ‘off’ the visual axis due to mydriasis. Although, both these phenomena can influence the results and interpretation of DO, we found DO to be more reliable than DR (two false negatives on DR) under the condition of mydriasis.

We believe DDDO is more objective test than DR. Location of bright crescent moving from top to the bottom of the pupil is probably easier to recognize than change in the movement of the retinoscopy reflex from with to against, more so when the pupils are dilated. This may also be the reason that DDDO could detect the onset of accommodation failure after instillation of cycloplegic eye bit earlier than DR in all the five patients that we examined in the later part of the study.

The eDO over estimated the accommodation by a mean of 0.17D. The probable reason for these differences lie in the fact that eDO follows the principles of photorefraction. Photorefraction involves the use of a still image, addition of the lens, and observation of the pupil, while retinoscopy requires movement (to produce the moving shadow), on top of addition of the lens and observation of the pupil. Thus, photorefraction is a simpler process. When the light rays from a direct opthalmoscope are reflected back from an emmetropic eye, they form a superior crescent due to divergence of the reflected light rays in front of the opthalmoscope. As subject accommodates, the refractive status of the eye changes from emmetropic (diverging rays) to pseudomyopic (converging rays), making the reflected light rays emerge in more convergence causing the disappearance of superior crescent and appearance of an inferior bright transpupillary crescent.

We found that the neutralization of the crescents on eDO was easier than neutralization of the light reflex on eDR, especially for closer fixation distance. It is important to note, however, spherical aberration, astigmatism, and irregular astigmatism can make it difficult to perceive the crescents when the pupils are dilated using DO. In addition, there is an increase in the dead zone when the size of the pupil is constricted. eDR may be more accurate in patients with media opacity, irregular cornea and
high astigmatism than eDO. Future studies are needed before eDO is used in such situations.

The correlation between DO and DR is high, and both the techniques were equally effective under cycloplegia and mydriasis. Overall reproducibility of DO and eDO (interobserver difference) was similar to eDR (0.9 D with eDO in this study versus 0.8 D with eDR by León et al.\cite{11}). However, it needs to be reassessed in future studies with masked observer, larger sample and in younger children with various ocular comorbidities.

A possible limitation of eDO and eDR is that children are often anxious of objects near their faces, and hence this technique may be limited in applicability to older children, though the use of free lenses could help to employ this technique on younger children. Further studies with larger sample are required to better assess the interobserver agreement and the performance of eDO in various disorders of accommodation affecting young children. The greatest limitation of this technique, like eDR, is that this method relies on the brief introduction of minus trial lenses for neutralizing the respective type of reflex while the patient is continuing to focus on a near target. It is possible that accommodation is significantly stimulated even with such brief introductions. While the latency in human accommodation, in response to adding minus powered lenses, is about 400ms, it is possible that the accommodation reflex happens even faster due to an automatic reflex when an object suddenly comes that close to the patient’s face. In this way, it is not necessarily to the lens that the patient is accommodating, but to the the near distance of an object. In order to avoid this issue, eDDDO can easily be adapted to the Nott technique and further investigated. Although it might provide more accurate results, it may be challenging to measure distances when working with children.

In summary, DO is a simple, quantitative, reliable and objective technique of assessing accommodation in children. The DO was found to be a faster technique, but the greatest advantage that DO distinctly presents, is that, it allows for the simultaneous assessment of both eyes. While technically it is also possible to perform DR binocularly by holding the streak in a horizontal position and moving away far enough to illuminate
both eyes simultaneously, eDR is difficult to perform, especially for those with shorter arms, as the distance can be too much for placing lenses in front of the patient’s eye for measuring accommodation. Further studies are required to rigorously and quantitatively compare both the techniques in these regards.

REFERENCES


A Case Series of Immunoglobulin G4-Related Ophthalmic Inflammation: An Emerging Disease. (FP455)

Dr. Amrita Sawhney, Dr. Shaloo Bageja, Dr. Anurag Mittal, Dr. Ashok Kumar Grover

PURPOSE

To present the spectrum of clinic-radiological manifestations in thirty cases of IgG4-related Ophthalmic disease (IgG4-ROD), along with their epidemiological and histopathological data. Also, to evaluate the clinical outcomes of the disease with targeted therapies like Rituximab and to monitor the response of glucocorticoid therapy in relation to serum IgG4 levels.

Immunoglobulin G4-related disease, an immune-mediated condition, is characterized by mass forming lesion, lymphoplasmacytic infiltration rich in IgG4 positive plasma cells and raised IgG4 levels in 60 - 70 % cases.\textsuperscript{1} It was first identified in a group of patients with autoimmune pancreatitis with raised serum IgG4 levels\textsuperscript{2} and was recognized as a systemic condition in 2003.\textsuperscript{3}

IgG4–RD can involve several organs of the body including orbit, lymph node, skin, lungs, salivary glands, thyroid, aorta, biliary tract, breast, kidney, retroperitoneum and CNS. Orbit is the most common extra-pancreatic site to be involved by this disease entity.\textsuperscript{4} The most frequently involved site in IgG4–related orbital disease is the lacrimal gland (IgG4–related dacryoadenitis). Other sites in the orbit that can be involved
are – extraocular muscles (IgG4–related orbital myositis), orbital soft tissues (IgG4-related orbital inflammation), eyelids and orbital nerves. Orbital IgG4–related disease is predominantly seen in adults with no gender predilection. Albeit, few Paediatric cases have been described with similar distribution of disease localizations as adults.

Microscopic features which are characteristic of IgG4–RD are -Lymphoplasmacytic infiltrate (predominantly T-lymphocytes), storiform/cartwheel pattern of fibrosis and obliteratorive phlebitis. However, in lacrimal gland involvement both storiform fibrosis and obliteratorive phlebitis may not be present.

The new diagnostic criteria for IgG4-ROD has been given by Goto et al in 2015:

**Imaging studies** showing Enlargement of the Lacrimal Gland, Trigeminal Nerve, or Extraocular Muscle.

Serum IgG4: $\geq 135$ mg/dl

Histopathologic examination showing:

a) Marked Lymphocyte and Plasmacyte Infiltration and Fibrosis

b) A Germinal Center

c) Infiltration of IgG4+ Plasma Cells:

  \[
  \text{Ratio of IgG4+/ IgG + cells } \geq 40 \% \quad \text{or} \quad \geq 50 \text{ IgG4 + Plasma Cells / HPF}
  \]

Definite IgG4-ROD: (1) + (2) + (3), Probable: (1) + (3), Possible: (1) + (2).

Long term follow-up is required as there is a risk of recurrence and chances of development of Lymphoma.

**MATERIALS AND METHOD**

We conducted a prospective interventional case series of Thirty patients between 2014-2019. All the cases were diagnosed on the basis of published diagnostic criteria for IgG4-related Ophthalmic disease given by Goto et al in 2015. Their epidemiological profile (including age and sex), presenting complaints, laboratory results (CRP, ESR and serum IgG4), orbital imaging and histological findings were recorded (Figure 1).
All the patients were started on oral steroids (0.6mg/kg/day) with tapering of 5mg 2 weekly and Azathioprine (50mg OD or 100 mg OD), which was used as a steroid sparing agent. One of the patients, who presented with proptosis and signs of compressive optic neuropathy, was given Intravenous Methylprednisolone (1gm OD for 3 days). Eight patients with steroid resistance were given one cycle of Rituximab (1gm IV infusion, repeated after 15 days, a total of two doses given).

RESULTS

We diagnosed thirty cases of IgG4 related orbital disease from 2014-2019.

The average age at presentation in our study was 40 years (12-68 years) with Male: Female ratio of 1:1.1 (14 males and 16 females).

CLINICAL PRESENTATIONS

(Figures 2, Figure 3 a-d) included swelling of upper lid due to dacryoadenitis in 16/30 cases (53.3%) with unilateral involvement in 6/16 (37.5%) and bilateral involvement in
10/16 (62.5%); proptosis with extraocular muscles (EOM), intraconal fat or infraorbital nerve (IONE) involvement in 10/30 cases (33.33%) with bilateral involvement in 4/10 cases (40%); proptosis with lid swelling due to both lacrimal gland and extraocular muscle involvement in 4/30 cases (13.33%). Overall, bilateral lesions were seen in 14/30 cases (46.6%).

Figure 2 – Pie chart showing distribution of Clinical presentation

Figure 3a – Clinical presentation in IgG4-ROD
Figure 3 b- NCCT Orbits

Figure 3 c- LE medial rectus muscle Incision biopsy done
Figure 3(a-d)- A Clinical case presentation of IgG4 -ROD

The histopathological diagnosis was based on IgG4 positive plasma cells with fibrosis. Isolated Ophthalmic disease was seen in 25/30 cases (83.3%) and Systemic involvement was noted in 5/30 cases (16.66%). Salivary glands enlargement was present in 3/30 cases (10%), lymphadenopathy (cervical or mediastinal) in 2/30 cases (6.66%) and pancreatitis was seen 1/30 case (3.33%).

The number of cases diagnosed as definite, probable and possible IgG4 related orbital disease were 16, 6 and 8 respectively.

In our study, 22/30 patients had good and stable clinical outcomes with steroids and azathioprine. However, 8/30 patients were given Rituximab (1gm intravenous infusion to be repeated after 15 days, total two doses) as there was resistance to steroids.

**CONCLUSIONS**

- The diagnosis of IgG4-ROD is critical, as it responds well to targeted therapies like Rituximab.
• Significant reduction was seen in Serum IgG4 levels along with clinical improvement in response to glucocorticoid therapy.
• Serum IgG4, when elevated, can be used in disease activity monitoring after initiating treatment.

DISCUSSION

This study depicts the spectrum of manifestations in orbital IgG4 related disease along with their epidemiological, radiological, laboratory and histological data. Standard treatment for this disease remains oral steroids with immunosuppressants as maintenance therapy. However, in our study 8/30 patients had to be given Rituximab due to resistance to steroid therapy and it proved to be beneficial as patients had better clinical outcome.

Rituximab is a monoclonal antibody which acts against CD-20 positive B lymphocytes. These B lymphocytes differentiate into short acting plasma cells that produce IgG4 antibodies. This therapy has shown promising results in inducing clinical remission and is also associated with fall in serum IgG4 levels, especially in resistant and recurrent cases\(^8\).

The average age at presentation in our study was lower (40 years) as compared to other studies (Plaza et al – 59 years, Ebbo et al – 55.1 years).\(^9,10\) The M: F ratio in our study was 1:1.1, depicting no gender predilection. This is similar to study conducted by Plaza et al (M:F 1:1).\(^9\)

In our study, isolated Ophthalmic disease was seen in 25/30 cases (83.3%) and systemic involvement was noted in 5/30 cases (16.66%). However, in study conducted by Ebbo et al, extraophthalmic manifestations reported in 78.9 % cases.\(^10\)

Earlier, diagnostic criteria given by Umehara et al was followed \(^11\), however, now we make the diagnosis according to the specific criteria given by Goto et al\(^7\) for IgG4-related ophthalmic disease.
We would conduct more studies in future with larger sample size to look into the role of Rituximab in management of IgG4 related disease and correlate Serum IgG4 levels with Rituximab therapy.

REFERENCES

Rhino-Orbital Mucormycosis: A Clinical Spectrum and Decision Making for Orbital Exenteration. (FP456)

Dr. Anurag Mittal, Dr. Shaloo Bageja, Dr. Amrita Sawhney, Dr. Ashok Kumar Grover

**PURPOSE**

To present the spectrum of clinical manifestations in forty cases of proven rhino-orbital mucormycosis with radiological, microbiological data and to highlight the factors in decision making for orbital exenteration (a retrospective analysis between 2009 to 2019).

**METHOD:**

Liposomal amphotericin B (L AmB) mono-therapy was given in 7/40 cases while 33/40 received both L AmB and Posaconazole. All patients underwent Functional Endoscopic Sinus Surgery (FESS). Orbital exenteration (OE) was done in patients with no perception of light and Central Retinal Arterial Occlusion, complete ophthalmoplegia along with radiological features suggesting either risk of or presence of intracranial extension.

**RESULTS:**

Cerebral involvement was seen in 18/40 cases. FESS with OE was done in 25/40 cases while 15/40 underwent FESS alone. Overall death rate was 30% with 12% mortality in OE with FESS and 60% in FESS alone.
CONCLUSION
Early diagnosis and timely exenteration in the appropriate cases may help improve survival rates.

INTRODUCTION
Mucormycosis is well known as an opportunistic fungal infection that rarely arises in healthy individuals. Fungi undergo spore formation, and inhalation of the airborne spores provides them access to the human oral and nasal mucosa. In healthy individuals, these spores are easily cleared by phagocytosis, but in the immunocompromised host, germination and hyphae formation can occur. Hyphae formation allows the organism to invade blood vessels. The most critical decision in the management of orbital mucormycosis is whether and when to exenterate. The literature fails to provide information on the indications and factors for considering exenteration in mucormycosis. Exenteration can be life saving at the price of a mutilating procedure. The decision for exenteration often depends on the judgement of the treating otolaryngologist and the ophthalmologist.

MATERIAL AND METHODS
A 10 year retrospective analysis of forty patients was carried out from January 2009 to January 2019 at a tertiary care hospital in New Delhi, India. All the patients who had been histopathological and microbiologically proven rhino-orbital mucormycosis were included in the study. The parameters analysed included the epidemiological profile, laboratory and radiological data along with the management outcomes. Seven out of forty patients were started on Liposomal amphotericin B (L AmB) (AmBisone 5mg /kg / day, I.V. infusion over 30-60min) whereas 33/40 received a combination of L AmB with Posaconazole. Posaconazole was given either 200mg four times a day or 400mg twice daily. All the patients underwent Functional endoscopic sinus surgery (FESS).
The decision making for orbital exenteration was based on three factors, namely aggressiveness of the disease at the time of presentation, the underlying predisposing disease process and the response to the initial medical therapy.

The aggressiveness of the disease was further defined by disease’s initial presentation. Most of the patients presented initially with foul smelling nasal mucosal crusts along with proptosis, chemosis, orbital congestion and complete ophthalmoplegia (CN III, IV, VI involvement) which signified superior orbital fissure involvement. In the patients who presented with or progressed to no perception of light, central retinal artery occlusion and corneal anaesthesia along with all the aforementioned signs, indicated orbital apex syndrome. Signs of cranial nerve V₂ involvement that includes facial numbness and facial anhidrosis have a linear correlation with further increase in severity and progression of disease suggesting the intracranial spread (cavernous sinus spread).

According to the European Society for Clinical Microbiology and Infectious Diseases and European Confederation of Medical Mycology Joint Clinical Guidelines, a diagnostic nasal endoscopy was done in all the patients presenting with necrotic ulcers of nasal mucosa and a wedge biopsy specimen was sent immediately for microbiological and histopathological evaluation.

On Direct microscopy of the biopsy specimen using optical brighteners, non-septate, ribbon like, 90degree or wide angle branching hyphae of Mucoales were identified and a rapid presumptive diagnosis of mucormycosis was made and initial medical therapy was started immediately. Recovery of the species of mucorales was done on culture. Characteristic hyphae along with angioinvasion, prominent infarcts and perineural invasion on histopathology, allowed the differentiation between hyphae of aspergillus or morphologically related fungi from the hyphae of Mucoales and finally confirmed the diagnosis of mucormycosis.

The clinical presentation was confirmed on radiological evaluation. MRI Head, bilateral orbits and Paranasal Sinuses confirmed the extent of spread of disease and ruled out any extensive intracranial spread.
Fig 1: Direct Microscopy
KOH Wet Mount

Fig 2. Rhizopus Species on Culture Petri Dish

Fig 3. Angioinvasion & Characteristic Hyphae on Histopathology
The irreversibility or rapidly deteriorating underlying disease process or the predisposing factor along with no or minimal response the initial medical therapy with intravenous L AmB and Posaconazole within first forty eight hours, paved the way for decision making for orbital exenteration.

The relative contraindications for orbital exenteration were bilateral disease, extensive intracranial spread and the little chance of survival.

RESULTS

The average age of presentation noted was 51 years (18-80 years) with male female ratio of 2.8:1. Diabetes mellitus was the most common predisposing factor seen in 36/40 patients followed by chronic steroid use in 2/40, solid organ transplant in 1/40 and chronic myeloid leukaemia in 1/40. Twenty two out of forty had rhino-orbital disease only whereas 18/40 had cerebral involvement. Twenty five out of forty underwent FESS with Orbital exenteration and 15/40 underwent fess alone. Highest mortality rate of 60% was seen in patients who underwent FESS alone compared to 12% mortality in FESS with orbital exenteration. Overall death rate was 30%.

CONCLUSIONS

Based on our study, it can be concluded that uncontrolled diabetes mellitus with or without diabetes ketoacidosis was the most common predisposing factor. Early diagnosis of mucormycosis and reversibility of underlying disease was associated with lower mortality. Survival outcome was significantly better in patients managed with FESS with orbital exenteration compared to who underwent FESS alone.
Early exenteration in the patients, after 48 hours of no response to the intensive initial medical therapy to reverse the underlying disease process and targeted antifungal regimen of a combination of L AmB with Posaconazole, along with signs of further progression of the disease, can possibly be lifesaving and can significantly decrease the mortality rate in cases of Rhino-orbital mucormycosis, as can be seen in our study.

**DISCUSSION**

Mucormycosis is well known as an opportunistic fungal infection that rarely arises in healthy individuals. Fungi undergo spore formation, and inhalation of the airborne spores provides them access to the human oral and nasal mucosa. In healthy individuals, these spores are easily cleared by phagocytosis, but in the immunocompromised host, germination and hyphae formation can occur. Hyphae formation leads to angioinvasion resulting in thrombus formation and ischaemia of surrounding tissue.

Therefore functional endoscopic sinus surgery in every patient of mucormycosis was done to debride the infarcted and necrosed tissue that does not respond to systemic medical therapy as a result of poor vascular supply and instead acts as an environment that promotes the fungal proliferation.

Based on data from global fungal registry, malignancy is the predominant underlying condition for mucormycosis. In contrast, our study reported uncontrolled diabetes mellitus with or without diabetic ketoacidosis to be the predominant risk factor. This is similar to the results of other studies done in India where diabetes mellitus continues to be the major underlying cause of ROCM.

Serum of normal humans has inhibitory activity against Rhizopus. But in diabetics along with diabetic ketoacidosis, acidosis and hyperglycaemia are ideal environments for the fungal growth. Several layers of innate host defences are simultaneously impaired due to intrinsic and iatrogenic abnormalities in macrophages, neutrophils, decreased phagocytic activity, abnormal polymorphonuclear chemotaxis and reduced myeloperoxidase activity.
Macrophages provide the first line of defence by preventing the germination of hyphae from spores and neutrophils form the second line of defence that damage the hyphae and prevent the invasion of the surrounding tissue. Rhizopus thrives on high glucose content and reaches the peak metabolic activity at acidic pH. In acidotic conditions, the iron binding protein Transferrin dissociates and unbound iron is released further leading to high iron content in the blood which is taken by Rhizopus for hyphal growth.

The unusually high incidence of rhino-orbito-cerebral mucormycosis in diabetics is a reflection of poor diabetic control and also at times poor socioeconomic factors along with the low levels of patient education and awareness. Diabetes is an underlying metabolic derangement which is most amiable to treatment and so the patients with diabetes as predisposing factor for rhino-orbital mucormycosis have the best chance of survival. An underlying condition, metabolic or immunological that can be rapidly corrected is one of the criterion for conserving orbits.

In the Retrozydo study, lower mortality rate has been reported in patients with diabetes mellitus and diabetic ketoacidosis, where controlling blood glucose is possible, as compared to other risk factors like malignancy or solid organ transplant, where reversal of immunosuppression and metabolic derangement is difficult. Diabetes was found to have a positive predictive value for survival as compared with Mucor with other underlying diagnoses such as palate necrosis, frontal sinus involvement and steroid use.

In our retrospective analysis, the mortality rate at 3 months follow-up was 12% in OE+ FESS group as compared to 60% in cases who underwent FESS alone. Our study emphasizes the significance of orbital exenteration in reducing fungal load and achieving local control of the disease in cases with presence or threatened intracranial spread. This is similar to the study done by Blitzer et al.

Our study is a retrospective study and no emphasis has been given on debridement of pterygopalatine fossa, it being a reservoir of infection. There is no definite protocol for management of different stages of Orbital involvement in a case of mucormycosis.
It is ethically & morally not possible to carry out a controlled study with such a disease and so we are planning a Prospective Study pertaining to the variables mentioned in the lacunae with a larger sample size.

REFERENCES


Outcomes Of ‘All-Nasal’ Approach For 25-Gauge Lens Sparing Vitrectomy in Stage 4B Retinopathy of Prematurity (FP1613)

Dr. Simar Rajan Singh, Dr. Mohit Dogra; Dr. Mangat Ram Dogra, Dr. Deeksha Katoch

ABSTRACT

PURPOSE

To describe a novel ‘all-nasal’ approach for lens sparing vitrectomy (LSV) in stage 4B retinopathy of prematurity (ROP).

METHODS

This is a pilot study in infants with stage 4B ROP. Eyes included had tractional retinal detachment approaching the retrolental space temporally. The surgeon sat nasal to the eye being operated. Infusion was placed in the centre between the supero-nasal and infero-nasal ports. We described the surgical technique and anatomical outcomes in the eyes undergoing ‘all-nasal’ LSV.

RESULTS

Eight eyes with stage 4B ROP were operated using this approach. All surgical objectives were achieved using this technique. Lensectomy could be avoided in 7 of the 8 eyes (87.5%). At 6 months of follow up, retina was attached in 6 eyes (75%).
CONCLUSION

All-nasal approach for LSV appears safe and effective in stage 4B ROP.

KEY WORDS

Lens sparing vitrectomy, Retinopathy of Prematurity, ROP, All-nasal Vitrectomy, Stage 4B ROP

BACKGROUND

Lens Sparing Vitrectomy (LSV) has been established as the standard of care for management of retinal detachment associated with advanced retinopathy of prematurity (ROP).\textsuperscript{1,2} With the advent of small gauge vitrectomy systems, LSV has gained wide acceptance with success rates varying between 80-90% in stage 4 ROP.\textsuperscript{1-3} The standard technique involves 3 ports in the infero-temporal, supero-temporal and supero-nasal quadrant, with the infero-temporal port being reserved for the infusion canula. But in some cases of stage 4 ROP, especially stage 4B, the temporal retina maybe pulled up so far behind the lens that placement of sclerotomies in the temporal half runs the risk of inadvertent retina injury. Such cases require either a limbal approach or a more horizontal entry which may involve sacrificing the crystalline lens, thereby taking away the advantages of LSV. We describe a novel ‘all-nasal’ approach for LSV in such cases of stage 4B ROP.

SURGICAL TECHNIQUE

This pilot study was approved by the institute ethics committee and adhered to the tenets of the declaration of Helsinki. Eight eyes of 8 infants presenting with stage 4B ROP and tractional retinal detachment of the temporal retina, approaching up to the retrolental space were selected for this approach. Six eyes had received prior laser treatment.

Examination under anaesthesia was done before starting the procedure to document the extent of retinal detachment behind the crystalline lens. Routinedraping and painting was done to ensure asepsis. The surgeon sat on the nasal side of the eye to be operated
with the operating microscope oriented accordingly (Figure 1A). The first sclerotomy for the infusion canula was placed nasally along the horizontal meridian, at 3 or 9’o clock position for the right and left eye respectively. The infusion was turned on after checking the position of the canula in the vitreous cavity. Two more sclerotomies were placed in the supero-nasal and infero-nasal quadrant for the vitreous cutter and endoilluminator, 1 millimetre from the limbus (Figure 1B). The central placement of the infusion canula facilitated better rotation of the globe during surgery, as a superior / inferior placed infusion canula would impinge on the lids in the small palpebral aperture of an infant. The nasal bridge also helped in keeping the canula stable and away from the crystalline lens. The supero-nasal and infero-nasal ports could be used effectively to achieve the surgical objectives. The vitreous planes were dissected from ridge to lens, ridge to periphery, ridge to ridge, ridge to disc and circumferentially along the ridge. The case was closed after a partial fluid-air exchange and the sclerostomies were sutured with 7-0 vicryl sutures.

**DISCUSSION**

Lens Sparing Vitrectomy has been established as the standard of care for stage 4 ROP. Sparing the lens provides for faster post-operative visual rehabilitation and has been shown to have better outcomes than scleral buckling / lensectomy with vitrectomy. However, in cases with stage 4B ROP with peripheral traction, the standard approach for surgery necessitates lensectomy in a large number of cases. In the series by Gadkari et al, lensectomy was required in 11 of the 32 eyes (34.4%) of stage 4 ROP with peripheral traction. Similarly in the series by El Rayes et al, 57.1% of the eyes with stage 4B ROP required lensectomy with vitrectomy. We describe a novel ‘all-nasal’ approach of 25-gauge LSV for the management of stage 4B ROP. This approach appears safe for tractional retinal detachments with the temporal retina approaching the retro-lental space. Using this approach, lensectomy could be avoided in 87.5% of the eyes with stage 4B ROP.

Placement of nasal sclerotomies for LSV has been suggested earlier by Bhende et al, but details of the technique were not described. The placement of the infusion canula in the centre is an important part of this approach. The shallow nasal bridge of an
infant not only provides support to the infusion canula, but also helps in keeping the tip of the canula away from the crystalline lens. The placement of the infusion canula between the endoilluminator and vitreous cutter minimises the chances of displacement as the surgeons hands rarely cross during surgery. The central canula remained stable even during globe manipulation. The superior and inferior ports allowed for all intraoperative manoeuvres to be performed with ease. Entering from the nasal side in such eyes not only facilitates dissection at the posterior pole, but also provides easy access to the opposite temporal retina where the bulk of the fibro-vascular tissue lies. This approach may also be suitable for tractional retinal detachments associated with familial exudative vitreoretinopathy which predominantly involves the temporal retina. To date, we have operated eight eyes using this approach. Clinical characteristics and outcomes of these eyes with a minimum follow up of 6 months are listed in table 1. Overall we were able to achieve retinal reattachment in six eyes (75%) of the 8 eyes.

This approach is not without its drawbacks. Temporal traction anterior to the equator may not be fully addressed by this technique, as reaching up till that area would require sacrificing the lens and hence, take away the entire advantage of the technique. Extensive dissection of this anterior fibrous tissue may not significantly alter the outcome of surgery and any retinal break created in the process would be detrimental. Using a scleral buckle as an adjunct to support this anterior proliferation has been reported to not alter the outcome significantly.9 Lensectomy was required in one case (case 6 – table 1) in our series. This case had an extensive stage 4B ROP with the fovea pulled up behind the crystalline lens close to the equator. Attempt to release the fovea with the vitreous cutter resulted in accidental lens touch.

In conclusion, we describe a novel surgical approach for LSV in premature infants with stage 4B ROP. To the best of our knowledge, this is the first report of an ‘all-nasal’ approach with central placement of canula for LSV in an infant. Though more experience is required to validate the wider applicability of this approach, our initial experience demonstrates the safety and efficacy of this approach in stage 4B ROP.
REFERENCES


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<tr>
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M, Male; F, Female; GA, Gestational Age
FIGURE 1.

Surgeon positioning and trocar placement for all-nasal lens sparing vitrectomy. (A) Surgeon is seated on the right side of the patient to operate on the left eye from the nasal side. (B) Surgeon’s view with the surgeon seated nasally, showing the placement of the infusion cannula in the centre and the other two ports on the sides along with orientation of the eye. (I – Inferior, N – Nasal, S – Superior, T – Temporal)
Optic Disc and Retinal Vessel Changes In Children With Surgically Treated Hydrocephalus. (FP655)

Dr. Tanmay Gupta, Dr. Smitha K.S., Dr. Arvind Tenagi, Dr. Bhagyajyothi B.K.

ABSTRACT

AIM

To study the optic disc and retinal vessel morphology, using both indirect ophthalmoscopy and Optical coherence tomography in children with surgically treated hydrocephalus.

METHODS

A prospective, cross-sectional study was performed in 50 children (median age 4 years) with early surgically treated hydrocephalus. All children were examined by indirect ophthalmoscopy and optical coherence tomography was done for evaluation of optic disc and retinal vessel changes.

RESULTS

Optic atrophy was found in six out of fifty children (12%). In comparison with reference group, median optic disc area were significantly smaller (p<0.0001) in children with hydrocephalus. There was not much difference in cup area but the rim area was smaller (<0.0001). On Indirect Ophthalmoscopy, children with hydrocephalus had abnormal retinal vascular pattern.
CONCLUSION

Children with surgically treated hydrocephalus are found to have subnormal optic disc and neuroretinal rim areas with abnormal vascular pattern. Our study reflects a lower frequency of optic atrophy than previously reported indicating improvement in perinatal care and timely management of raised intracranial pressure.

KEYWORDS

Hydrocephalus, disc area, cup area, Optical Coherence Tomography

INTRODUCTION

Hydrocephalus is a condition that reduces the absorption or outflow of cerebrospinal fluid in the cerebral ventricles and increases the intracranial pressure.[1] Systemic symptoms such as nausea, vomiting, headache, fatigue, irritability, and increased head circumference are helpful to diagnose hydrocephalus.[2] Medical and surgical management are the two treatment options available to restore the pressure to optimum levels.[3] Both anterior and posterior visual pathways may be affected in children with hydrocephalus resulting in mild deterioration to marked loss in visual acuity.[1] The incidence of hydrocephalus during the first year of life is around 1 in 1000.[4]

Visual signs of hydrocephalus in children include double vision, gray outs, misaligned eyes, reduced vision, and visual field defects.[4, 5] Papilledema is one of the most important signs of hydrocephalus; if undetected, it can lead to irreversible damage such as optic atrophy.[2] However, in infants and young children papilledema is rare or absent probably due to open suture permitting the head to enlarge in response to increased intracranial pressure. It was reported that hydrocephalus might also cause cognitive visual problems such as decreased depth perception, impaired recognition, impaired motion perception, and simultaneous perception.[4] Hence, every individual either children or adult diagnosed with hydrocephalus must undergo baseline ophthalmic evaluation.
Recent research has reported that hydrocephalus affects the neural tissue and resulted in the less than normal optic disc and rim areas and also an abnormal vascular pattern, indicating a pre/perinatal influence on the development of neural and vascular tissues in children.[1] Moreover, to the best of our knowledge, in India, no population-based morphometric study has been performed on the ocular fundus of children with surgically treated hydrocephalus. The present study was therefore intended to detect and quantify visual dysfunction in children who have received surgical treatment for hydrocephalus.

MATERIALS AND METHODS

STUDY DESIGN AND SETTING

The present prospective cross-sectional study was conducted from September 2018 to September 2019 at the Department of Ophthalmology, Dr. Prabhakar Kore Hospital and Medical Research Center (MRC), Belagavi, after obtaining the ethical approval from the Institutional Review Board and the protocol adhered to the tenets of the Declaration of Helsinki. The procedure of the study was briefed to the parents and guardians and written consent was obtained. The study consists of a total of 50 children.

STUDY POPULATION

Children presenting to ophthalmology OPD in the age group 1 to 14 years with head circumference > 2 standard deviation score (SDS), enlarged ventricles present at birth or developing during first year of life who underwent surgical intervention were included in the study. Children who did not fit the criteria mentioned, did not survive during or post-surgery or whose parents/guardian opted out of the study were excluded.

SAMPLE SIZE

Sample size calculation is done using Cochran's formula. According to the publication by S. Andersson et al[1], 14% of surgically treated patients with hydrocephalus had
optic atrophy. Using the above-mentioned formula for calculation, the minimum sample size was calculated as 50. More the sample size, greater is the precision.

REFERENCE GROUP

50 healthy Indian children between the age group 1 to 14 years presenting to ophthalmology OPD for routine evaluation were constituted as a reference group for evaluation of ocular fundus morphology by optical coherence tomography.

STUDY PROCEDURE

Demographic data including clinical and family history of the patients were recorded. A thorough history of the child and mother was noted and duly filled in the proforma. Maternal history including data of last menstrual cycle, number of antenatal visits, gestational age, type of delivery, iron and folic acid supplementation was also recorded. Neonatal characteristics such as birth weight, head circumference, history of NICU admission, and duration of hospital stay were taken. With informed consent, all the patients underwent an eye examination, including disc evaluation with the Optical Coherence Tomography (TOPCON) using the 3D disc mode in glaucoma protocol. “This protocol acquires six 4.0 mm radial scans. These line scans are arranged like the spokes of a wheel centered in the middle of the disc. For all scans, internal fixation was used as it provides a higher degree of reproducibility”. Images were automatically analyzed by the software. The OCT imaging and quality assessment of the scans were done by the examiner. Focused ocular fundus video image, an adequate signal strength (>7) and the presence of linear scans centered on the disc were requirements for acceptable quality. For optic disc topography, the automated determination of the disc margin as the end of the retinal pigment epithelium (RPE) was used for this analysis. The straight blue line which connects the edges of the RPE represents the disc diameter. The cup diameter is denoted by a parallel red line constructed 150 µm anterior to the disc diameter. Structures below the red line are defined as the cup and structures above the red line, the neuroretinal rim. Previous reports estimate the mean morphometric optic disc size of $2.58 \pm 0.65 \text{ mm}^2$ in less than 20-year-olds in the Indian population.\textsuperscript{[6]}

[6]
RETROSPECTIVE REVIEW OF MEDICAL FILES

Hydrocephalus has multiple aetiology. Twenty children out of fifty were born preterm. The last menstrual period of the mother was recorded and foetal sonography performed at 12 weeks of gestational age for any prenatal insult. Also, sonography was used to determine GA at birth.

We observe that, mean gestational age at birth in the sample was 36.04 weeks with range 30 to 39 weeks and the mean birth weight in the sample was 2.19 kg with range 1 to 3 kg (Table 1).

<table>
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<th>Mean ± SD</th>
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<tr>
<td>Age (in years)</td>
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<td>Birth weight (in kg)</td>
<td>2.19 ± 0.66</td>
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<td>Gestational Age (in weeks)</td>
<td>36.04 ± 3.17</td>
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DEMOGRAPHIC DATA

Here, 50 children 16 boys and 34 girls of median age 4 [1.5,14] (in years) were studied. Strabismus was noted in eight out of fifty children (16%). We also note that, 20 (40%) of subjects in the sample had history of NICU admission whereas 30 (60%) subjects mothers reported taking iron and folic acid supplementation during the pregnancy.

STATISTICAL ANALYSIS

R i386 3.5.1 was used to analyse the data. Continuous data was represented in the form of mean ± SD and the categorical variables were represented using the frequency table. P < 0.05 was considered statistically significant.
RESULTS

OPTIC-NERVE MORPHOLOGY AND CLINICAL FINDINGS

Optic disc variables for children with hydrocephalus and reference group as shown in Table 2. Using sign test, we conclude that the children with hydrocephalus had a smaller median optic disc area of 2.39 mm$^2$ than reference group of healthy children 2.42 mm$^2$ (p<0.0001). Neuroretinal rim area was 2.01 mm$^2$ which was smaller from 2.07 mm$^2$ of reference group. Median of Horizontal D.D. and vertical D.D. was 1.42 mm and 2.10 mm which was significantly different from 1.66 mm and 2.04 mm in reference group respectively. On indirect ophthalmoscopy, six out of fifty children (12%) showed optic atrophy. Children born preterm were found to have a smaller neuroretinal rim area as reported on OCT in comparison to children born at term.

RETINAL VESSEL MORPHOLOGY

Examination by indirect ophthalmoscopy showed increased tortuosity of central retinal vessels.

DISCUSSION

Children with hydrocephalus were found to have abnormal optic disc area in comparison with reference group, illustrated by smaller optic disc and rim areas along with abnormal retinal vascular pattern. Neuroretinal rim area had significant difference between hydrocephalus children and reference group. These findings were consistent with a study by Anderson et al.[1] The horizontal and vertical cup/disc diameter ratios show marked inter-individual variability, so it has relatively low diagnostic power to differentiate between normal eyes and eyes with early glaucoma. Their diagnostic power increases significantly if their dependency on the optic disc size is taken into account.[8] Our study did not show significant difference in vertical and horizontal disc diameter when compared to reference group. Raised intracranial pressure causes compressive optic neuropathy at junction of lamina cribrosa and optic nerve sheath leading to blockage of axoplasmic flow in retinal ganglion cell axons causing their loss resulting in pale optic disc and optic atrophy. In our study, six out of fifty children (12%) had optic atrophy. Histologically optic nerve head is characterised by a reduction
in both number of axons and optic nerve diameter. Variation in optic disc morphology has been suggested to be caused by lot of other factors such as secondary degeneration of ganglion cells and their fibres (retrograde, transsynaptic, or non-trans-synaptic), defective trophic mechanisms or deficient myelinisation. A study by McLoone et al showed no significant association was found between disc morphology and timing of cerebral insult. Also in a similar study in the past no correlation had been found between etiology of hydrocephalus and ocular fundus variables. Our study results correlated with the results of the study mentioned above. A non-specific response to neurological insult was found in the form of strabismus, eight out of fifty children (16%) had strabismus. Six had exotropia and two had esotropia. None of the children with hydrocephalus who presented to our OPD had nystagmus or epilepsy.

CONCLUSION

Hydrocephalus has been associated with a high frequency of optic atrophy, but our results show a relatively low frequency. Hydrocephalus is known to affect neural tissues resulting in abnormal disc morphology, smaller disc area and cup area and abnormal vascular pattern as observed by us in our study. These abnormal findings indicate pre-/perinatal influence on neural and vascular tissue development in children with hydrocephalus. Complete antenatal visits coupled with iron and folic acid supplementation, avoiding consanguineous marriages, timely ultrasound scans are some of the factors that can help us in preventing or early diagnosis and treatment. In a developing country like ours, it is imperative for the healthcare infrastructure to keep up with the demands of the growing population. Low frequency of optic atrophy imply improvement in medical care being given to children with hydrocephalus.

REFERENCES


7. Hoyt CS et al. Do we really understand the difference between optic nerve hypoplasia and atrophy?


Table 2

<table>
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<tr>
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<td>Cup Area (mm²)</td>
<td>0.38 ± 0.19</td>
<td>0.33 [0.25,0.95]</td>
<td>0.34</td>
<td>0.0002</td>
</tr>
<tr>
<td>Rim Area (mm²)</td>
<td>1.99 ± 0.23</td>
<td>2.01 [1.32,2.25]</td>
<td>2.07</td>
<td>0.0002</td>
</tr>
<tr>
<td>Horizontal Disc Diameter (mm)</td>
<td>1.42 ± 0.35</td>
<td>1.42 [0.74,2.11]</td>
<td>1.66</td>
<td>0.0002</td>
</tr>
<tr>
<td>Vertical Disc Diameter (mm)</td>
<td>2.10 ± 0.29</td>
<td>2.01 [1.80,2.98]</td>
<td>2.04</td>
<td>0.0114</td>
</tr>
</tbody>
</table>
Scattered plot of optic disc area, cup area and rim area, the dotted lines represent the median values
Analysis of Visual Outcomes Following Cyclotorsion Compensation Versus None in SMILE for Astigmatism. (FP1189)

Dr. Shreyas Ramamurthy, Dr. Gitansha Sachdev

Analysis of visual outcomes following cyclotorsion compensation versus none in SMILE for astigmatism

STUDY TITLE

Comparative analysis of manual cyclotorsion compensation with triple centration versus no cyclotorsion compensation in eyes undergoing Small Incision Lenticule Extraction for correction of myopic astigmatism: contralateral eye study

STUDY OBJECTIVE:

To assess the visual outcomes in patients undergoing SMILE for correction of myopic astigmatism (greater than or equal to -1.50D cylinder) and compare the outcomes following manual cyclotorsion compensation and no compensation in a contralateral eye study

INTRODUCTION:

SMILE does not provide an active cyclotorsion compensation for astigmatism correction at present. Under correction of higher cylinders by 13-17% has been reported in
published literature. Various methods using preoperative manual marking have been described to compensate for intraoperative cyclotorsion and have demonstrated superior results in comparison to earlier studies.\(^{1-2}\) However, none of the studies have compared the outcomes between intraoperative cyclotorsion compensation and no cyclotorsion in a contralateral cohort.

**MATERIALS AND METHODS:**

The study adhered to the tenets of declaration of Helsinki, ethics committee approval was obtained and an informed consent was taken from all patients.

Inclusion criteria were as follows: Age greater than 18 years, stable refractive error [change in Manifest Refractive Spherical Equivalent (MRSE) of not more than 0.25D] over one year, patients undergoing Small Incision Lenticule Extraction (SMILE) for astigmatism of 1.50 D or greater in both eyes, intraoperative cyclotorsion of 5 degrees or greater in both eyes and contact lens discontinuation for 2 weeks prior to corneal tomography.

Following eyes were excluded from the study: Simple myopic astigmatism with no spherical power in one or both eyes, inadequate pachymetry (less than 500 microns) or residual stromal bed post SMILE of lower than 280 microns, corneal tomographic abnormalities including Keratoconus or Pellucid marginal degeneration, Corneal scars, Pregnancy or lactation and ocular comorbidities including cataract, glaucoma or inflammation.

SMILE procedure was performed under topical anesthesia using the Visumax femtosecond system. In this contralateral eye study, one eye received treatment with manual cyclotorsion compensation using triple centration method. Contralateral eye received no cyclotorsion compensation. Table of random numbers was used to allow randomization.

Following investigations were performed at preoperative, one-month and three-months postoperative visit: Visual acuity and refraction, IOP measurement (Goldmann applanation tonometry), Slit lamp bio microscopy and dilated fundus evaluation, Corneal tomography
(Pentacam, Oculus, Optikgerate, Gmbh), Corneal biomechanics measurement (Corvis ST, oculus Optikgerate GmbH) and contrast sensitivity measurement.

A single trained optometrist of greater than 15 years’ clinical experience carried out the refraction at all visits. The procedure performed (cyclotorsion compensation versus no compensation) was masked to the patient and optometrist.

Postoperative medication regimen included e/d L-Pred four times a day for 2 weeks, e/d Vigamox four times a day for one week and e/d Systane Ultra four times a day for 3 months.

**STATISTICAL ANALYSIS:**

The sample size calculation to prove the “non superiority” of manual cyclotorsion over cyclotorsion compensation in eyes with cyclotorsion of 5 degrees or greater is 56 eyes. A sample size of 60 eyes (30 patients) has been calculated to account for data attrition secondary to loss of follow up

CDVA, sphere, cylinder, axis, keratometry and pachymetry values were considered as outcome variables. Study group (cyclotorsion compensation versus no cyclotorsion compensation) were considered as primary explanatory variables.

All quantitative variables were checked for normal distribution within each category of explanatory variables by using visual inspection of histograms and normality Q-Q plots. Shapiro Wilk test was conducted to assess normal distribution, wherein a p value of > 0.05 was considered as normal distribution.

For normally distributed Quantitative parameters the mean values were compared between study groups using Independent sample t-test (2 groups). For non-normally distributed Quantitative parameters, Medians and Interquartile range (IQR) were compared between study groups using Mann Whitney u test (2 groups). Categorical outcomes were compared between study groups using Chi square test/Fisher’s exact test. P value d” 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis. (3) Astigmatic outcomes were analyzed using Alpins criteria. (4)
RESULTS:

A total of 30 subjects were included in the final analysis. The patients underwent bilateral SMILE surgery, with cyclotorsion compensation in one eye (n = 30 eyes) and no cyclotorsion in the other eye (n = 30 eyes).

PATIENT DEMOGRAPHICS:

Groups were matched in terms of sphere, cylindrical error treated and preoperative corneal tomographical parameters. (Table 1)

<table>
<thead>
<tr>
<th>Pre-Operative parameters</th>
<th>Study group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cyclotorsion</td>
<td>No Cyclotorsion</td>
</tr>
<tr>
<td>Age Median (IQR)</td>
<td>22.5 (20, 29)</td>
<td>22.5 (20, 29)</td>
</tr>
<tr>
<td>Gender N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>15 (50%)</td>
<td>15 (50%)</td>
</tr>
<tr>
<td>Female</td>
<td>15 (50%)</td>
<td>15 (50%)</td>
</tr>
<tr>
<td>Sphere (Mean ±SD)</td>
<td>-2.97 ± 1.34</td>
<td>-2.93 ± 1.77</td>
</tr>
<tr>
<td>MRSE (Mean ±SD)</td>
<td>-4.07 ± 1.49</td>
<td>-3.98 ± 1.74</td>
</tr>
<tr>
<td>Mean Keratometry (Mean ±SD)</td>
<td>43.96 ± 1.7</td>
<td>44.31 ± 1.28</td>
</tr>
<tr>
<td>Flat Keratometry (Mean ±SD)</td>
<td>42.92 ± 1.69</td>
<td>43.41 ± 1.11</td>
</tr>
<tr>
<td>Steep Keratometry (Mean ±SD)</td>
<td>45.06 ± 1.77</td>
<td>45.32 ± 1.62</td>
</tr>
<tr>
<td>Thinnest Pachymetry (Mean ±SD)</td>
<td>536.33 ± 26.59</td>
<td>538.63 ± 29.65</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>Cylinder Median (IQR)</td>
<td>-2 (-2.75, -1.5)</td>
<td>-1.75 (-2.5, -1.5)</td>
</tr>
<tr>
<td>Cylindrical axis Median (IQR)</td>
<td>165 (35, 175)</td>
<td>77.5 (10, 160)</td>
</tr>
<tr>
<td>CDVA Median (IQR)</td>
<td>0 (0, 0)</td>
<td>0 (-0.025, 0)</td>
</tr>
</tbody>
</table>

Table 1: Comparison of pre-operative demographic parameters between the study groups (N=60)

**VISUAL OUTCOMES:**

No significant differences were noted in MRSE, CDVA and refractive error between the two groups at three-months postoperative visit (Table 2)

<table>
<thead>
<tr>
<th>Post-Operative</th>
<th>Study group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cyclotorsion</td>
<td>No Cyclotorsion</td>
</tr>
<tr>
<td>1st month period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sphere Median (IQR)</td>
<td>0 (0, 0)</td>
<td>0 (0, 0)</td>
</tr>
<tr>
<td>Cylinder Median (IQR)</td>
<td>-0.5 (-0.75, 0)</td>
<td>0 (-0.125, 0)</td>
</tr>
<tr>
<td>MRSE Median (IQR)</td>
<td>-0.25 (-0.375, 0)</td>
<td>0 (-0.25, 0)</td>
</tr>
<tr>
<td>BDVA Log Mar Median (IQR)</td>
<td>0 (0, 0)</td>
<td>0 (0, 0.1)</td>
</tr>
<tr>
<td>Thinnest Pachymetry Median (IQR)</td>
<td>446 (431, 465.25)</td>
<td>451 (431.5, 484)</td>
</tr>
</tbody>
</table>
### Table 2: Comparison of Post-Operative 1st month and 3rd month various parameters between the study groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1st month (Mean ±SD)</th>
<th>3rd month (Mean ±SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Keratometry (Mean ±SD)</td>
<td>40.26 ± 2.03</td>
<td>41.52 ± 1.82</td>
<td>0.014</td>
</tr>
<tr>
<td>Flat Keratometry (Mean ±SD)</td>
<td>39.75 ± 1.91</td>
<td>41.06 ± 1.72</td>
<td>0.007</td>
</tr>
<tr>
<td>Steep Keratometry (Mean ±SD)</td>
<td>40.89 ± 2.19</td>
<td>42.01 ± 1.97</td>
<td>0.041</td>
</tr>
<tr>
<td>3rd month period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sphere Median (IQR)</td>
<td>0 (0, 0)</td>
<td>0 (0, 0)</td>
<td>0.766</td>
</tr>
<tr>
<td>Cylinder Median (IQR)</td>
<td>-0.375 (-0.75, 0)</td>
<td>0 (-0.5, 0)</td>
<td>0.097</td>
</tr>
<tr>
<td>MRSE Median (IQR)</td>
<td>-0.25 (-0.40625, 0)</td>
<td>0 (-0.375, 0)</td>
<td>0.096</td>
</tr>
<tr>
<td>UDVA Logmar Median (IQR)</td>
<td>0.1 (0, 0.2)</td>
<td>0 (0, 0.2)</td>
<td>0.719</td>
</tr>
<tr>
<td>Mean Keratometry (Mean ±SD)</td>
<td>40.2 ± 2.03</td>
<td>41.51 ± 1.81</td>
<td>0.011</td>
</tr>
<tr>
<td>Flat Keratometry (Mean ±SD)</td>
<td>39.71 ± 1.94</td>
<td>41.05 ± 1.78</td>
<td>0.007</td>
</tr>
<tr>
<td>Steep Keratometry (Mean ±SD)</td>
<td>40.81 ± 2.17</td>
<td>41.97 ± 1.95</td>
<td>0.033</td>
</tr>
<tr>
<td>Thinnest Pachymetry (Mean ±SD)</td>
<td>447.43 ± 20.16</td>
<td>459.93 ± 34.09</td>
<td>0.089</td>
</tr>
</tbody>
</table>
ASTIGMATIC OUTCOMES:

Astigmatic outcomes were measured using Alpins criteria with no statistically significant differences between the two cohorts (Table 3).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study Group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cyclotorsion (Mean ±SD)</td>
<td>No Cyclotorsion (Mean ±SD)</td>
</tr>
<tr>
<td>Target Induced Astigmatism</td>
<td>2.2 ± 0.71</td>
<td>2.1 ± 0.76</td>
</tr>
<tr>
<td>Surgically Induced Astigmatism</td>
<td>2.23 ± 0.83</td>
<td>2.13 ± 0.9</td>
</tr>
<tr>
<td>Difference Vector</td>
<td>3.6 ± 1.88</td>
<td>3.72 ± 1.98</td>
</tr>
<tr>
<td>Angle of Error</td>
<td>15.53 ± 79.62</td>
<td>50.97 ± 66.87</td>
</tr>
<tr>
<td>Magnitude of Error</td>
<td>0.03 ± 0.44</td>
<td>0.03 ± 0.35</td>
</tr>
<tr>
<td>Correction Index</td>
<td>1.02 ± 0.19</td>
<td>1.01 ± 0.18</td>
</tr>
<tr>
<td>Index of Success</td>
<td>1.69 ± 0.72</td>
<td>1.8 ± 0.64</td>
</tr>
</tbody>
</table>

Table 3: Astigmatic outcomes using Alpins criteria

DISCUSSION:

SMILE does not provide an active cyclotorsion compensation for astigmatism correction. Under correction of higher cylinders by 13-17% has been reported in published literature. Sriganesh and coworkers have demonstrated an under correction of 3% and 7% in low (less than 1.5D) and high (1.5D or more) astigmatism respectively, following manual cyclotorsion compensation in SMILE. However, a limitation of this study is the lack of a control group. The data is compared with earlier studies of astigmatic correction in SMILE, and the results demonstrated are superior to earlier cohorts. However, Sriganesh and coworkers have applied an additional nomogram correction.
of 10% for the astigmatic refraction, which may attribute to the superior outcomes. They recommend cyclotorsion compensation in eyes with preoperative high cylinder (>1.5D) or an intraoperative cyclotorsion greater than 5 degrees.

Jun et al demonstrated a 4% under correction in SMILE for high astigmatism (>2.5D) following triple centration technique, and superior outcomes in comparison to wavefront guided transepithelial PRK. However, they do not compare their outcomes with a control group (SMILE with no cyclotorsion compensation).

Our study compares the visual outcomes with and without cyclotorsion compensation in a contralateral study, in eyes with high astigmatism (>1.5D) with intraoperative cyclotorsion of 5 degrees or greater.

We demonstrated no significant differences between the two groups in terms of refractive and astigmatic outcomes at three months' postoperative visit. Moreover, no additional nomogram correction was applied in our cohort. The non superiority of cyclotorsion compensation using triple centration, may be secondary to errors associated with manual marking techniques. An average variation of 3 to 5 degrees has been demonstrated with manual marking techniques in toric IOLs. Additionally, spreading or smudging of the ink marks can result in a further loss of precision and accuracy.

CONCLUSION:

Our study demonstrates non superiority of cyclotorsion compensation with triple centration vis-à-vis no cyclotorsion compensation in eyes undergoing SMILE for high myopic astigmatism. Refinement in current marking techniques may be the next step forward to further enhance visual outcomes.

NO FINANCIAL DISCLOSURE

NO CONFLICT OF INTEREST
REFERENCES:


Surgical Outcomes of Plication Versus Resection in Intermittent Exotropia: A Comparative Study (FP161)

Dr. Siddharth Baindur, Dr. Shweta, Dr. Anju Rastogi, Dr. Kamlesh

INTRODUCTION

Intermittent exotropia [X(T)] comprises about 50-90% of cases of all exotropias.\textsuperscript{1} Small exophorias are frequently discovered in adult population and 60 - 70% of newborns present a transitory deviation which can resolve by 4 - 6 months after birth.\textsuperscript{2} The patient should be followed over time to determine whether their exotropia is stable or deteriorating as in some cases it may be intermittent to begin with and later on becomes constant. Correction of ocular alignment is vital for achieving and maintaining binocular single vision as stereopsis is acquired during growth from 0 - 2 years until approximately 8 years of age after which children tend to maintain it. If binocularity fails to mature, it may become difficult to restore it.\textsuperscript{3}

The treatment in X(T) is essentially surgical although non-surgical modalities can be considered in some cases.\textsuperscript{4} The primary goal of surgery is to improve the alignment of the visual axis which helps to re-establish binocularity, increase stereoacuity and restore peripheral visual field. The most preferred surgery in basic type of X(T) is unilateral resection and recession.\textsuperscript{5} Resection is the time tested muscle strengthening procedure, however it has the disadvantage of irreversible removal of muscle tendon, chances of slipped or lost muscle and typically involves severing of ciliary vessels.
which increases the risk of anterior segment ischemia. Plication is considered as an alternative by some strabismologists for strengthening of the horizontal rectus muscles. It offers several advantages over resection including a less likelihood of muscle loss, decreased risk of anterior segment ischemia, permitting more than two recti muscles to be operated simultaneously in a single eye. There is a paucity of comparative data for relative surgical & cosmetic advantages and dose effects. We designed this study to compare the functional and cosmetic outcomes of plication and resection in basic type of intermittent exotropia.

**MATERIAL AND METHODS**

We conducted a prospective interventional study in a tertiary eye care centre. Approval was taken from the Institutional Ethics Committee (F.No./11/IEC/MAMC/2017/08) and research adhered to the tenets of the Declaration of Helsinki.

60 patients of basic type of intermittent exotropia, above 6 years of age with deviation of 35 PD to 55 PD were enrolled in the study after taking informed consent and divided in two groups of 30 patients each. Group A underwent lateral rectus (LR) recession and medial rectus (MR) plication (RP group) and Group B underwent LR recession and MR resection (RR group). For allocation of the participants, a computer-generated list of random numbers was used. Odd digits were assigned to group A and even digits to group B. The allocation sequence was concealed in sequentially numbered, opaque, sealed and stapled envelopes. Randomization was done before the start of procedure and a member of the surgical team besides the operating surgeon and the investigator knew the group to which the patient belongs. The patient, operating surgeon and the investigator were all blinded towards the group of the patient.

A constant amount of lateral rectus (LR) recession of 8 mm was done in all cases whereas the amount of resection/plication of medial rectus (MR) was calculated on the basis of pre-existing horizontal deviation. Patients with incommittant strabismus, history of previous squint surgery, unilateral or bilateral amblyopia, pattern strabismus (A, V, X, ë), systemic neurologic disorders were excluded from the study. A detailed history was taken with em-
phasis on the age of onset of strabismus, progression, duration of tropic phase, asthenopic symptoms, diplopia, previous treatment and family history of squint.

A thorough preoperative examination was done including unaided and best corrected visual acuity (BCVA) obtained after cycloplegic refraction as per age, accommodative convergence/accommodation (AC/A) ratio by lens gradient method. Deviation was measured by Prism bar cover test (PBCT) for near (at 33 cm) and distance (with patient fixing on 6/12 symbol on Snellen's chart at 6m distance), in all 9 gaze after occlusion for 24 hours. Office control method was used to assess the control of deviation. Assessment of binocularity was done by Worth 4 dot test, synaptophore and Titmus fly test.

Postoperative analysis was done on day 1, and at end of 1, 3, 6, and 12 weeks in terms of postoperative alignment. A surgical outcome was considered to be successful if the distance post patch deviation was between 10 PD of exophoria or exotropia to 10 PD of esophoria or esotropia at all examinations.

The postoperative followup included assessment of horizontal alignment for distance (measured by post patch PBCT), binocularity, near stereoacuity and exodrift (at last follow-up). Cosmetic outcomes were assessed in terms of visible hump/scar, foreign body sensation and persistence of congestion.

SURGICAL TECHNIQUE

All surgeries were performed by same surgeon under anaesthesia appropriate to age. Time taken for each procedure was noted. A constant amount of LR recession of 8 mm was done in every case. A temporal para limbal conjunctiva incision was given, lateral rectus muscle was identified and hook was passed, and all the attachments to the muscle were dissected, followed by passage of interlocking loops of double armed polyglactin 910 suture (Vicryl 6-0; Ethicon) at insertion. Muscle was cut and 8 mm recession was done after marking on the sclera by conventional technique. The conjunctiva was then closed with a second polyglactin suture (Vicryl 9-0; Ethicon).

FURTHER IN GROUP A (PLICATION TECHNIQUE)
A nasal para – limbal conjunctival incision was made. The medial rectus muscle was hooked and connective tissues were gently retroplaced. A double armed polyglactin 910 suture (Vicryl 6-0;Ethicon) was passed through the muscle at the distance from the insertion corresponding to the plication amount in an interlocking manner. The two ends were then each passed through the partial thickness of the sclera adjacent to the corresponding pole of the insertion. A pincer forceps was applied to the muscle beyond the sutures placed and an iris sweep was placed temporarily between the tendon and the sutures forming a fulcrum over which the anterior tendon was folded flat between the muscle and globe. The conjunctiva was then closed with a second polyglactin suture (Vicryl 9-0;Ethicon).

As shown in figure 1
A: Amount of plication to be done marked from insertion after separating muscle
B: Polyglactin 910 suture passed posterior to mark with locking sutures at each end
C: The sutures are passed again through the respective edges of the insertion to form two loops on either side of the muscle
D: Pincer forceps used to hold muscle posterior to sutures and iris repositor placed between muscle and suture loops
E: Pincer forceps brought forward folding muscle upon itself
F: Sutures tied and instruments removed

FURTHER IN GROUP B (RESECTION TECHNIQUE)

A nasal para limbal conjunctival incision was given, a hook was passed after identifying borders of medial rectus, marking was made by caliper corresponding to the amount of resection. A double armed polyglactin 910 suture (Vicryl 6-0; Ethicon) was passed in an interlocking manner at the mark. The part of the muscle between the insertion and mark was excised and rest of the muscle was sutured with the stump at insertion. The conjunctiva was then closed with a second polyglactin suture (Vicryl 9-0; Ethicon).

As shown in figure 2
A: Amount of resection to be done marked from insertion after separating muscle
B: Polyglactin 910 passed posterior to mark with locking sutures at each end
C: Muscle crushed with artery forceps and cut just ahead of the marking
D: Sutures passed through sclera at respective ends of insertion of muscle
E: Muscle is pulled towards the insertion and held in place with a forceps
F: Suture is tied and forceps removed

Patients were prescribed steroid and antibiotic eye drops along with a lubricant post operatively for 6 weeks.
STATISTICAL METHOD

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± standard deviation (SD). Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non parametric test was used. Statistical tests were applied as follows-

1. Quantitative variables were compared using Independent t test/Mann-Whitney Test (when the data sets were not normally distributed) between the two groups.

2. Qualitative variables were correlated using Chi-Square test/Fisher’s exact test.

A p value of <0.05 was considered statistically significant.

The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 17.0.

RESULTS

60 patients aged > 6 years with basic type of intermittent exotropia with deviation between 35 PD and 55 PD were divided equally into two groups. Group A underwent recession and plication and Group B underwent recession and resection. The mean age was 20.67 ± 9.22 years in group A while the mean age in group B was 19.13 ± 8.3 years.

The mean preoperative deviation for distance was 44.67 ± 4.54 PD in group A and 43.17 ± 4.82 PD in group B. The mean postoperative deviation for distance at the end of 12 weeks was 10.13 ± 3.56 PD in group A and 9.47 ± 3.23 PD in group B. The difference was not statistically significant between the groups (p = 0.423). Successful outcome was seen in 20 out of 30 patients (66.67%) in Group A and 23 out of 30 patients (76.67%) in group B. The difference was statistically not significant (p = 0.390) as shown in table 1.

In our study, the postoperative exodrift for distance at 12 weeks followup was 4.4 ± 2.8 PD in group A and 4.67 ± 3.29 PD in group B. This difference was not statistically significant (p = 0.856) as shown in table 2.
<table>
<thead>
<tr>
<th></th>
<th>Post patch PBCT Distance (Primary gaze) in Prism Diopters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre op</td>
</tr>
<tr>
<td>Group A</td>
<td>Mean</td>
</tr>
<tr>
<td></td>
<td>Std. Dev</td>
</tr>
<tr>
<td>Group B</td>
<td>Mean</td>
</tr>
<tr>
<td></td>
<td>Std. Dev</td>
</tr>
<tr>
<td>P-value</td>
<td>0.280</td>
</tr>
</tbody>
</table>

Table 1: showing post patch PBCT for distance in primary gaze for group A and group B

<table>
<thead>
<tr>
<th></th>
<th>EXODRFIT FOR DISTANCE (Mean ± Std Dev)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A (PD)</td>
<td>Group B (PD)</td>
</tr>
<tr>
<td>1 week to 12 weeks</td>
<td>4.4 ± 2.8</td>
<td>4.67 ± 3.29</td>
</tr>
</tbody>
</table>

Table 2: showing the postoperative exodrift for distance in group A and group B

No patient in either group had consecutive esotropia or complaints of postoperative diplopia. The maximum postoperative under correction noted was 16 PD seen in 1 case in the RP group and 2 patients in the RR group. All the patients in the study were satisfied with the postoperative cosmetic outcome and hence no prism therapy or reoperation was done in any case.

Preoperatively, grade 1 binocularity was seen in 8 (26.67%) patients in group A and 6 (20.0%) patients in group B, grade 2 binocularity in 9 (30.0%) patients in both groups and grade 3 binocularity in 13 (43.33%) patients of group A and 15 (50.0%) patients of group B. Postoperatively at 12 weeks, none of the patients with grade 1 binocularity improved, while in group A, 4 patients with grade 2 binocularity improved to grade 3 and in group B, 5 patients with grade 2 binocularity improved to grade 3. Preoperatively, all the cases had near stereoacuity between 3000-100 sec of arc. Postoperatively at 12 weeks, improvement was seen in 11 patients in Group A and 12 patients in group B as shown in table 3 and table 4.
### BINOCULARITY

<table>
<thead>
<tr>
<th>Grade</th>
<th>GROUP A</th>
<th></th>
<th>GROUP B</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre op</td>
<td>Post op</td>
<td>Pre op</td>
<td>Post op</td>
</tr>
<tr>
<td>GRADE 1</td>
<td>8 (26.67%)</td>
<td>8 (26.67%)</td>
<td>6 (20.0%)</td>
<td>6 (20.0%)</td>
</tr>
<tr>
<td>GRADE 2</td>
<td>9 (30.0%)</td>
<td>5 (16.66%)</td>
<td>9 (30.0%)</td>
<td>4 (13.33%)</td>
</tr>
<tr>
<td>GRADE 3</td>
<td>13 (43.33%)</td>
<td>17 (56.67%)</td>
<td>15 (50.0%)</td>
<td>20 (66.67%)</td>
</tr>
</tbody>
</table>

Table 3: showing improvement in binocularity in group A and Group B

<table>
<thead>
<tr>
<th>Grade of stereoacuity (sec of arc)</th>
<th>GROUP A</th>
<th></th>
<th>GROUP B</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PREOP</td>
<td>POSTOP</td>
<td>PREOP</td>
<td>POSTOP</td>
</tr>
<tr>
<td>20 - 50</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>100</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>160</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>200</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>400</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>3000</td>
<td>5</td>
<td>6</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>No stereoacuity</td>
<td>17</td>
<td>13</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>TOTAL N(%)</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

Table 4: showing improvement in near stereoacuity in group A and group B

The bump/scar was assessed on the slit lamp. A visible scar/bump was noticed in all patients in both groups on day 1 post op and at 1 week postop. Visible scar/bump disappeared in 12 (40.00%) patients in group A and in 16 (53.33%) patients in group B at end of 3 weeks. At the end of 6 weeks, Visible scar/bump disappeared in 14 (46.67%) more patients in group A and 12 (40.0%) more patients in group B. At the end of 12 weeks none of the patients in either groups had a visible scar/bump. The time taken for disappearance of the visible scar/bump was comparable between the two groups and was statistically not significant (p = 0.499)
DISCUSSION

Various muscle strengthening procedures have been described in literature such as resection, plication, advancement and transposition.\textsuperscript{5} Though resection is historically accepted procedure, the exact reason for its preference over plication is not clear. Literature has generally favored tendon-to-tendon plication for the superior oblique and resection procedure for the rectus muscles as standard approaches to strengthening.\textsuperscript{8} Since there is paucity of studies comparing plication and resection in terms of ocular alignment and surgical dose, we compared the two in patients with intermittent exotropia.

A study by Kimura et al which included all types of X(T) achieved successful outcome in 55\% cases in RP group and 50\% cases in RR group (p = 0.66) at final follow up of 21 ± 7.6 months in RP group and 24 ± 8.6 months for RR group. Our study also showed similar results, though our success rates were slightly higher in both groups. This may be attributed to the shorter follow up in our study. However in this study, the surgical dose was aimed on lesser side than usual which resulted undercorrection in significant cases at last followup. Besides that, the amount of LR recessed was variable in both groups which could have confounded the amount of ocular alignment achieved.\textsuperscript{9}

Huston et al found similar results in both procedures. Successful outcome was seen in 77.4\% patients in the RP group and 96.6\% in the RR group at 4 to 16 weeks after surgery. However, this study has not commented whether the difference in success rates between RP and RR is significant or not. Also, the range of follow up period is large, though overall follow up is short.\textsuperscript{10}

Alkharashi et al included both esotropes and exotropes in their study and showed a significantly higher success rate and lesser reoperation in resection over plication. However, success rate for LR and MR was not defined individually and sample size in resection group outnumbered the plication group. This may have confounded their results.\textsuperscript{11}
In our study, a constant amount of LR recession was performed to nullify the aforementioned confounding factor. Successful outcome was seen in 66.67% in Group A (RP) and 76.67% in group B (RR). The difference was statistically not significant (p = 0.390). Our study also showed similar results, though success rates were slightly higher in our groups. 10 patients in RP group and 7 in RR group who did not meet the success criteria had mean preoperative deviation of 48.5 ± 3.37 PD and 46.43 ± 3.78 PD respectively which was near the higher range of our inclusion criteria. Of 10 unsuccessful cases in RP group, 3 cases had poor control, 6 had fair and 1 (undercorrected by 2PD) had good control whereas in RR group, of 7 unsuccessful cases, 3 had poor, 3 had fair and 1 case (preop deviation-50PD, undercorrected by 4 PD) had good control. The amount of MR operated was kept similar for both groups (min -4mm and max-5.5mm). Univariate logistic regression was performed to check for association of independent variables like age, pre op post patch PBCT, pre op binocular status, control of deviation, type of surgery (group A and B) and type of refractive error with successful outcome of surgeries.

Significant association was found with pre op post patch PBCT. Every unit increase in pre op post patch PBCT decreased the chances of success by 27.9% (OR= 0.721, 95% CI= 0.597-0.871, p=0.001). All other factors including type of surgery (OR= 1.643, 95% CI= 0.527-5.120, p=0.390) were found to have no significant association with successful surgical outcome. A multiple regression model was performed to determine the effect of each variable adjusted for all other variables in the model. Pre op post patch PBCT (OR= 0.592, 95% CI= 0.432-0.811, p=0.001) was found to be the only significant factors.

Studies comparing postoperative drift after plication or resection have reported variable results. Kimura et al found an exodrift of 5.5 ± 6.7 PD in plication group and 8.3 ± 8.2 PD in resection group (p = 0.09) at 12 months whereas it was 6.8 ± 7.0 PD and 10.7 ± 9.8 PD respectively at last followup with p=0.04. Alkharashi et al found an exodrift of 15PD in plication group and 11 PD in resection group. In our study, the exodrift for distance at 12 months followup was 4.4 ± 2.8 PD in RP group and 4.67 ± 3.29 PD in RR group which was statistically not significant. (p = 0.856).
Chaudari et al compared the surgical dose effect of plication and resection. The mean effect of MR plication was 7.10 (1.65) PD/mm initially which increased to 8.08 (1.63) PD/mm at last follow-up (p > .05) and that of MR resection was 7.26 (1.23) PD/mm initially which decreased to 6.81 (1.58) PD/mm at last follow-up (p > .05). They found that plication showed equivalent surgical effect to that of rectus muscle resection. However, they included previously operated cases also in their study. The sample size of exotropes was small (9 cases-plication and 19 cases-resection) and non-comparable in both the groups. Besides this, the nature of exotropia was not defined and success rate of the two procedures was not commented. In our study, the mean effect of MR plication initially and at last followup was 4.42 ± 0.57 PD/mm and 3.56 ± 0.54 PD/mm respectively whereas that of MR resection was 4.41 ± 0.87 PD/mm and 3.47 ± 0.62 PD/mm respectively (p = 0.938) considering a constant amount of LR effect according to Stallard et al.

In our study, overall improvement in binocular status was seen in 9 cases whereas 23 cases had improvement in near stereoacuity, stressing the importance of timely correction in ocular alignment in intermittent exotropia. The cosmetic outcome i.e. persistence of congestion, foreign body sensation and visible hump was comparable between the groups showing no relative superiority. Similar cosmetic results are seen in other studies also. The time taken to perform each procedure was comparable. No complications were encountered in any case.

We conclude that both procedures are equally effective in achieving acceptable ocular alignment with no cosmetic superiority. Resection involves severing of ciliary arteries, interrupting this source of circulation to the anterior segment of eye. Plication preserves the ciliary blood flow hence decreasing the risk of anterior segment ischemia allowing surgery of more than two muscles in same eye. Plication can be performed readily under topical anesthesia as it does not involve relatively painful muscle crushing. Also, there are less chances of slipped or lost muscle with an early postoperative surgical reversibility. Given such added advantages, plication is a good alternative for resection as a muscle strengthening procedure.
REFERENCES


Clinical Profile and Visual Outcome of Pellet Gun Related Ocular Trauma. (FP901)

Dr. Tariq Syed Qureshi

INTRODUCTION

The American Medical Association’s ‘Guides to the Evaluation of Permanent Impairment,’ rates permanent impairment to the visual system on an almost equal rate of impairment as to the “whole man’.

Ocular trauma -> major and preventable cause of ocular morbidity -> leading cause of monocular blindness.

WHO has reported some 55 million eye injuries restricting activities more than one day to occur each year; 750,000 cases will require hospitalization each year, including some 200,000 open-globe injuries; there are approximately 1.6 million blind from injuries.

Pellet guns are used worldwide for hunting, pest control, recreational shooting and competitive sports and are an important cause of ocular injuries worldwide.

Used for crowd control in India, Canada, Egypt, South Africa, Israel, Argentina etc. Used in Kashmir to control protesting mobs has emerged as a significant cause of ocular morbidity over the last few years.
The guns used in Kashmir to curb agitated mob, is 12 Bore Pump-Action Shotgun, pellet type 8/9 (commonly known as riot gun) manufactured at the Ordinance Factory, Ishapor.

Cartridge disperses few hundred pellets over few hundred metres: 8 number shot contains approximately 410 pellets of 2.26mm diameter while number 9 contains 585 pellets of 2.01mm diameter.

Modern air gun pellets exceed the critical velocity for penetration of human skin by a pellet (38 and 70 m/sec).

Eyes are particularly vulnerable to injury from pellet guns and direct hits invariably result in severe damage and significant loss of vision.

The 2016 unrest in Kashmir, resulted in a series of violent protests in Kashmir Valley where pellet gun was used as a crowd control measure.

The protests started on 9 July 2016 and are continuing till date.

AIMS

The goal of our study is to characterize clinical profile of such injuries, determine visual outcome and elucidate factors affecting visual outcome.

MATERIAL AND METHODS

SMHS Hospital Tertiary Care Center of 1066 patients who reported with ocular trauma during this period, 664 eyes of 643 patients were included in the study and were treated in Department of Ophthalmology of SMHS Hospital. Hospital-based, prospective, observational study. Duration of the study was one and a half years. Primary variables studied were visual acuity, pupillary reaction, zone of injury, grade of injury and anatomical status of eye in accordance with BETTS and OTCS. Ocular Trauma Score was calculated was calculated for each eye.

INCLUSION AND EXCLUSION CRITERIA

All patients with pellet gun related eye injuries were included. Those who gave informed consent were included.
Patients with previous trauma, previous vitrectomy, retinal diseases, glaucoma were excluded.

**RESULTS**

Age

- 2 - 59 years
- Mean age 23.5 \( \pm 7.73 \) years

Gender

- 98.6% males
- 1.4% females

**VA**

<table>
<thead>
<tr>
<th>Presenting Visual Acuity</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VISUAL ACUITY</strong></td>
<td><strong>PERCENTAGE</strong></td>
</tr>
<tr>
<td>( \geq 20/40 )</td>
<td>14.9</td>
</tr>
<tr>
<td>20/50 to 20/100</td>
<td>10.8</td>
</tr>
<tr>
<td>19/100 to 5/200</td>
<td>11.7</td>
</tr>
<tr>
<td>4/200 to Light Perception</td>
<td>60.6</td>
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<tr>
<td>No Perception of Light</td>
<td>6.6</td>
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## Type of injury

<table>
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<tr>
<th>Type of injury</th>
<th>Frequency</th>
<th>Percentage</th>
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</thead>
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<tr>
<td>Open Globe Injury</td>
<td>975</td>
<td>67.9</td>
</tr>
<tr>
<td>Closed Globe Injury</td>
<td>461</td>
<td>32.1</td>
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## Anterior segment findings

<table>
<thead>
<tr>
<th>Findings</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>SCH</td>
<td>66.7</td>
</tr>
<tr>
<td>Hyphema</td>
<td>54.7</td>
</tr>
<tr>
<td>Traumatic cataract</td>
<td>41.2</td>
</tr>
<tr>
<td>Exudates in AC</td>
<td>3.1</td>
</tr>
<tr>
<td>AC Foreign body</td>
<td>3.3</td>
</tr>
<tr>
<td>Lens matter in AC</td>
<td>5.9</td>
</tr>
<tr>
<td>Iridodialysis/iris lacerations</td>
<td>18.2</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>3.3</td>
</tr>
</tbody>
</table>

## Tissue in wound

<table>
<thead>
<tr>
<th>Tissue in wound</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uvea prolapse</td>
<td>41.2</td>
</tr>
<tr>
<td>Vitreous prolapse</td>
<td>62.1</td>
</tr>
<tr>
<td>Retinal tissue prolapses</td>
<td>3.3</td>
</tr>
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</table>
### Posterior segment findings

<table>
<thead>
<tr>
<th>Condition</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Vitreous Hemorrhage</td>
<td>83.4</td>
</tr>
<tr>
<td>Vitreous incarceration</td>
<td>23.1</td>
</tr>
<tr>
<td>Necrotic retina</td>
<td>4.7</td>
</tr>
<tr>
<td>ERM</td>
<td>1.8</td>
</tr>
<tr>
<td>Subretinal hemorrhage</td>
<td>44.6</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>18.2</td>
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<tr>
<td>Retinal break</td>
<td>13.5</td>
</tr>
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</table>

### Foreign body location

<table>
<thead>
<tr>
<th>Location</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subretinal FB</td>
<td>7.3</td>
</tr>
<tr>
<td>Intravitreal FB</td>
<td>16.6</td>
</tr>
<tr>
<td>Anterior Chamber FB</td>
<td>3.3</td>
</tr>
<tr>
<td>Perforation (orbital)</td>
<td>57.9</td>
</tr>
</tbody>
</table>

**CONCLUSION**

Pellet gun injuries mostly cause open globe and perforating type injuries. Our study suggest we can offer good visual rehabilitation with properly timed intervention in the form of primary and secondary repairs.
Clinical Audit of Ocular Trauma Across Six Tertiary Centers Over 10 Years. (FP2218)

Dr. Moreker Sunil Ratilal, Dr. Harshavardhan Ghorpade

INTRODUCTION

Ocular trauma is an important, preventable, worldwide public health problem. Worldwide, there are approximately 1.6 million people are blind due to ocular injuries, an additional 2.3 million have bilateral visual impairment, and 19 million have unilateral visual loss.(1) However preventive measures are by and large lacking in most of the places probably due to lack of awareness (2). While considering eye injuries which needed hospital admission, rates have ranged from 8 to 57 per 100,000 (3)(4). In India there are only four population-based studies of eye injuries that have been published in the recent past. There is no major epidemiologic survey done in western India and to fill this gap in knowledge we undertook the study

AIM:

To study the epidemiology of eye injuries in patients with major trauma in two cities, in India, determining the incidence, etiology, outcomes of ocular injuries, and their association with fractures.
METHODS:

An analysis of the Trauma Audit database, data from 43,982 general trauma patients from six centers across Mumbai and Navi Mumbai over ten years was done. Patients with ocular trauma were separately analysed. The research adhered to the tenets of the Declaration of Helsinki. Patients’ data was protected.

Ocular Trauma was defined as any injury affecting the eye or adnexa that required emergency care in the outpatient or needed hospital admission and described as a principal or secondary discharge diagnosis as per the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM). Patients were traced as per their address in the hospital to look for present status if possible.

The data was analyzed on basis of age, sex, etiology and classification of trauma. Visual acuity (VA) at presentation and discharge was recorded. Details of slit lamp examination and indirect ophthalmoscopy examination were noted. The injuries were classified according to the Ocular Trauma Classification System (OTCS) and Birmingham Eye Trauma Terminology (BETT). We used the Ocular Trauma Score (OTS) in evaluating the final visual outcome.

A Medline search done using PubMed and Medline plus for a combination of cluster of keywords – prevalence, incidence, epidemiology, eye, ocular, trauma, injury, Birmingham Eye Trauma Terminology system, OTS open globe, close globe, rupture, laceration, penetrating, perforating, incidence, and outcome. All papers were compared with our data.

RESULTS:

After correction for the effects arising out of demographic distribution, we found that the risk for open globe injury was the highest in young adults and lowest in seniors.

79% were men, median age was 37 years. 65.8% of ocular injuries were due to road traffic accidents. 82% had good outcomes.
The most common eye injuries in men were associated with outdoor activities (29.5%) and work (26.6%). In women too, outdoor activity was associated with trauma most of the times (20%).

Closed globe injuries (CGI) were less severe with better final visual outcome than open globe injuries (OGI). The incidence of OGI and CGI differed in work-related injuries ($p < 0.0001$), sport-related injuries ($p < 0.0002$), and assaults ($p = 0.023$).

Of the 43,982 patients with major trauma, 8% patients had associated ocular injuries and 8699 had a facial fracture (zygoma, orbit or maxilla).

The risk of an eye injury with a facial fracture is 8.2 times Vs no facial fracture (95% confidence interval 6.7 to 9.6).

Odds of poor prognosis were high with complex fractures, multiple fractures, poor GCS at presentation.

Initial visual acuity was found to be strongly correlated with final visual acuity (Spearman’s correlation coefficient = 0.648; $p < 0.001$).

Mean follow up of 7.3 years +/- 1.8 years

**DISCUSSION**

To the best of our knowledge, this study is the first of its kind to measure accurately the magnitude of ocular trauma in a large sample of western Indian population across two cities and twelve draining areas and adequately puts down the incidence; sociodemographic pattern and visual outcome of ocular trauma in western India which has hitherto not been reported. We had a higher percentage of men compared to some other studies (7) and that could be due to an increased uptake of healthcare by the male population. We had better outcomes in few cases and that was attributed to availability of multiple specialists and more so when the care was given immediately. Across various hospitals the results were better due to more advanced care and hence the results are probably skewed towards positive outcome as compared to other studies (8)(9). Our results in Navi Mumbai rural population were comparable to results from other studies (10). The epidemiology in terms of incidence and prevalence
compared with other studies (11) (12) (13) (14). Our study shows that, the epidemiology in urban areas, compares well with other studies in urban areas (15) Our study may have potentially excluded patients who might have suffered minor ocular trauma which may have resolved on its own and those individuals with ocular trauma who may have not sought any medical treatment for unknown reasons.

CONCLUSIONS:

This largest multicentric clinical audit across two cities and with longest follow up gives important insights for planning management strategies not only in local area but a large geographical expanse and can aid in health policy formulation as well as formulation of educational material directed towards preventive aspects

REFERENCES:


Utility of Anterior Segment Optical Coherence Tomography (AS-OCT) In Diagnosis Of Anterior Scleritis. (FP49)

Dr. Murthy Somasheila I, Dr. Rashmi Ranjan, Dr. Abhinav Loomba

INTRODUCTION

Scleritis is the inflammation in the scleral tissues with injection in both superficial and deep episcleral vessels. It is a chronic inflammatory process involving sclera and adjacent structures which can result in potentially blinding complications. It is characterized by edema and cellular infiltration of sclera which may also involve adjacent cornea, uvea and even retina which may threaten vision. A majority of about 32 – 57% of patients with scleritis have evidence of an underlying systemic disease.¹

Most acceptable and widely used classification for scleritis was given by Watson and Hayreh which groups scleritis anatomically and on clinical features.² Various other clinocopathologic and severity scoring system has been advised but are rarely used.²³ Diagnosis is mainly clinical with other investigations aids to rule out any systemic involvement or infectious causes. Among all anterior scleritis being the commonest accounts for 40% cases

Clinically, anterior scleritis may have several distinct patterns including diffuse scleritis, nodular scleritis, and necrotizing scleritis. The treatment of scleritis involves the
use of topical and oral steroids and long term immunosuppression. At present, the only way to prognosticate the improvement in the treatment of scleritis is by clinical examination and signs and symptoms of the patient. It is difficult to quantify the severity and the response to therapy based on clinical signs alone.

Shoughy SS et al described the optical coherence tomography (OCT) findings in eyes with active anterior scleritis and compare the findings to those with episcleritis and normal controls and showed that patients with active anterior scleritis showed increased thickness of the sclera and presence of intra-scleral hypo-reflective areas of edema by OCT compared to patients with episcleritis and normal eyes and concluded OCT adds both qualitative and quantitative information to diagnosis and monitoring of patients with scleritis. Christakopoulos C and Amar Agarwal have published case reports on Anterior segment OCT to evaluate cases of nodular scleritis. However, none of them talked about using this tool in a large cohort of patients with anterior scleritis. At present, no diagnostic modality is used to objectively quantify scleritis and evaluate the morphological features with this non-contact based procedure.

The aim of this study is to characterize the optical coherence tomography (OCT) findings in eyes with scleral inflammation.

**MATERIALS AND METHODS:**

This was a prospective study and the protocol was approved by the institutional review board of LVPEI. Patients gave written informed consent to participate in the research study.

A total of 40 eyes of 40 patients were included. All patients had the clinical diagnosis of unilateral scleral inflammation in the period from May-Oct 2018. The clinical diagnosis of scleritis was made based on symptoms of gradual onset of moderate to severe ocular pain that radiates to the surrounding tissues, moderate to severe tenderness, photophobia, and blurring of vision and signs of congestion.

All patients presenting with anterior scleritis were included in the study. The exclusion criteria consisted patients with episcleritis, uncooperative patients and patients...
suffering from other causes of ocular surface inflammation such as infectious keratitis or conjunctivitis, pterygia and pingueculae.

A complete ocular and systemic examination was done in collaboration with physician and rheumatologists. After complete slit lamp examination, slit lamp photographs were taken in all gazes and Anterior segment OCT was done of the areas which had maximum bogginess or congestion clinically. Patient were asked to keep their gaze accordingly and probe was focused to the area of maximum congestion and measurement were taken in both horizontal and vertical lines either of which did include a part of cornea also. The measurements were done using the digital calipers provided in the tools and the area with the maximum thickness was manually measured from posterior to anterior border. In cases where posterior border was not very well defined Descemet’s membrane was considered as the baseline. The presence of vessels was identified with areas of localized hypo-reflective areas with underlying shadow. This shadowing was not appreciated in areas of intra-scleral edematous pockets caused due to fluid collection.

RESULTS

Out of the 40 patients majority 80% presented with nodular scleritis and 20% diffuse scleritis with age ranging between 10-74 years with the mean age being 45 years. The majority being females (67.5%) presented in active disease stage with a mean scleral thickness of 1276 +/- SD: 374.9 microns on AS-OCT scanning with a range of 670-2000microns.

There were 11(27.5%) patients with scleral thickness between 500-1000 microns, 18(45%) patients in between 1000-1500 microns and 11(27.5%) patients with thickness >1500 microns.

The active area of inflammation showed presence of conjunctival inflammation 16/40(40%) patients with 14/40(35%) patients showing presence of large caliber vessels in form of large irregular hypo-reflective areas with underneath shadowing and medium sized vessels in 19/40(47.5%) patients. 25/40(62.5%) patients showed significant intra-scleral edema with shadowing of posterior scleral margin in which sclera thickness
measurement is approximated with corneal Descemet’s membrane which included majority with large calibervessels. 100% patient showed a linear fluid demarcation line in between deep episcleral plexus and scleral tissues suggestive of areas of fluid pockets

**DISCUSSION**

Scleral inflammation in scleritis is most of the times associated with both episcleral and conjunctival congestion. Slit-lamp examination with the narrow slit beam is used to detect the depth of inflammation, indicating which network of vessels is predominantly affected. In episcleritis, anterior edge of the narrow slit beam is displaced forward while the posterior edge remains flat against the sclera, however, in scleritis both anterior and the posterior edges of the narrow slit beam are displaced forward due to involvement of deep episcleral plexus. As topical application of 10% phenylephrine only blanches the superficial episcleral plexus and not the deep episcleral plexus. The eye remains congested in scleritis. Red-free light is helpful in revealing areas of maximal vascular congestion and new vascular channels. However, many times it is still very difficult to differentiate both clinically.

Anterior segment OCT has been extensively used to study pathologies in cornea and serves as a non contact tool to study about various layers anomalies. Same can be utilized in sclera and episclera and AS-OCT can be used as a tool for radiological histology of the sclera and episcleral tissue.

Out of the 40 patients studied, majority 80% presented with nodular scleritis. The majority of population was middle aged with average age of 45 years with a female preponderance.

In this study we have analyzed the ability of AS-OCT to characterize the morphological changes in the scleral thickness and architecture in cases of anterior scleritis. We also correlated the changes with the clinical presentation. In our study, we categorized patients in three categories, first category with scleral thickness between 650-950microns, second one 1000-1500 microns and third category with thickness > 1500microns. The morphological features were measured in terms of involvement
of conjunctiva, intra-scleral edema, caliber of vessels (clinical interpretation) and presence of demarcation fluid line in between sclera and episclera.

27.5% (11/40) of patients were in first and third category with sclera thickness < 1000 microns and > 1500 microns respectively. Majority 45% (18/40) presented with sclera thickness in between range of 1000-1500 microns.

The active area of inflammation showed presence of conjunctival inflammation 16/40 (40%) patients which was irrespective of the amount of sclera thickness. 14/40 (35%) patients showing presence of large caliber vessels in form of large irregular hypo-reflective areas with underneath shadowing and medium sized vessels in 19/40 (47.5%) patients but this also didn’t correlate with the amount of sclera thickness. One explanation for this could be the way scanning is being done at that cross-section which might show have arrangement of vessels differently. This could be explained by the fact that findings in a histopathology slide depends on the area of cut section.

This demarcation lines denotes the fluid collection in areas of deep episcleral vascular plexus. This demarcation line can help us identifying involvement of episclera and sclera as well as episcleral tissue alone and can serve as a tool in differentiating scleritis with episcleritis. Furthermore, AS-OCT of sclera tissue also showed hypo-reflective areas of fluid collection within the sclera which confirmed the diagnosis of scleritis. Shoughy SS et al\(^1\) described the OCT findings in eyes with active anterior scleritis and compare the findings to those with episcleritis and also explained to differentiate on basis of OCT findings. The amount of fluid collection also corroborated with the sclera thickness, however, with increasing sclera thickness the ability of AS-OCT in defining the posterior margins also decreased. In such cases posterior margins of sclera was presumed along the Descemet’s membrane of the cornea.

Anterior segment OCT appears to be a promising tool in identifying cases of scleritis and episcleritis and also in objectively quantifying the severity of the disease based on scleral thickness and morphological characteristics of involved sclera. This can further help in assessing prognosis of the disease.
The strength of this study is good number of data with reproducible imaging property with AS-OCT, with the paper uniquely describing the various morphological changes seen in cases of scleritis. The limitations is AS-OCT being an expensive tool and requires proper training for handling and measurement purpose. The other limitation of the study being difficulty in identifying posterior border of sclera in cases of significant edema as in such cases the fluid filled spaces create a shadowing effect and limit the imaging of posterior border. There is no gold standard test for measuring the sclera thickness so the OCT findings also cannot be compared with any reference level.

CONCLUSION:

Patients with active scleritis presented with areas of increased sclera thickness with intra-scleral edema which may or may not be associated with conjunctival edema. Presence of localized hypo-reflective areas in OCT imaging showed amount of dilatation of blood vessels with presence of fluid pockets in deep episcleral plexus. Anterior segment OCT imaging could also do a quantitative analysis of the disease by correlating the severity of disease with amount of thickness and inflammation in affected area and can be a promising tool in grading the severity of disease.

REFERENCES:


ABSTRACT

PURPOSE:

Age-related macular degeneration (AMD) is one of the leading causes of irreversible central vision loss in the elderly population. The current study aims to find non-invasive prognostic biomarkers in the urine specimens of the AMD patients.

DESIGN:

Peripheral blood and urine samples were collected from 23 controls and 61 AMD patients. Genomic DNA was extracted from the buffy coat of peripheral blood. Allele specific PCR was used to assay SNPs in complement factor H (CFH), complement component 3 (C3). Protein was concentrated using 3Kda cut off ultra-centrifugal filters from urine. Comparative proteomic analysis of urine from AMD versus control patients was also performed using isobaric labelling followed by mass spectrometry. Validation was performed using enzyme-linked immunosorbent assay (ELISA).
RESULTS:

Comparative proteomic analysis of urine samples from early AMD, Choroidal Neovascular Membrane (CNVM), Geographic Atrophy (GA), and healthy controls was performed using Tandem Mass Tags (TMT) followed by mass spectrometry. Of 751 proteins identified, 383 proteins were found to be differentially expressed in various groups of AMD patients. Gene ontology classification of differentially expressed proteins revealed the majority of them were involved in catalytic functions and binding activities. Pathway analysis showed cell adhesion molecule pathways (CAMs), Complement and coagulation cascades, to be significantly deregulated in AMD. Upon validation by ELISA, SERPINA-1, TIMP-1, APOA-1 were significantly over-expressed in AMD (n=61) patients compared to controls (n=23). A logistic model of APOA-1 in combination with CFH and C3 polymorphisms predicted the risk of developing AMD with 82% accuracy.

CONCLUSION:

This study gives us a preliminary data on non-invasive predictive biomarkers for AMD, which can be further validated in a large cohort and translated for diagnostic use.

INTRODUCTION

Age-Related Macular Degeneration (AMD) adversely affects the lifestyle of the elderly population by causing central vision loss.1 The global prevalence of early and late AMD is 8.01% and 0.37%, respectively.2 In India, the prevalence of early AMD is about 46.2% and of late AMD at 1.2%.2 Diagnosis of AMD is most commonly established by clinical examination of the retina. Based on the clinical features, late AMD is further classified into neovascular AMD with features of choroidal neovascularisation (CNV) and non-neovascular AMD with geographic atrophy (GA) and extensive retinal pigment epithelium (RPE) degeneration. Although anti-vascular endothelial growth factor (VEGF) therapy is helpful in controlling the severity of neovascular AMD, a complete cure for non-neovascular AMD is still elusive. Maintaining a healthy life
style along with antioxidant supplementation are recommended for controlling the progression of the disease\textsuperscript{3}. It is suggested that the early detection of the disease plays a pivotal role in the better management of the disease and allows patients to incorporate lifestyle changes. So, the need of the hour is to identify early-stage biomarkers for AMD that will enable optimal screening of population at high risk of developing AMD.

AMD being a chronic low-grade systemic inflammatory disease, biomarkers from body fluids may reflect the status of AMD. Over the past decade, identification of biomarkers for AMD has been widely explored through proteomic approaches on various body fluids such as plasma\textsuperscript{4 –6}, vitreous and aqueous humor\textsuperscript{7} which shows an association of several serum cytokines and plasma proteins to the development of AMD. These markers have included C-reactive protein (CRP), CC chemokine ligand-2 (CCL2), Eotaxin (CCL24), Interferon α-Inducible factor 10 (IP-10), interleukin (IL)-2, interleukin (IL)-6, soluble intercellular adhesion molecule (sICAM)-1, tumor necrosis factor (TNF-α), and C3a-desArg, where higher levels were found by researchers to be associated with AMD in comparison to controls\textsuperscript{8 –14}.

The use of serum, vitreous and aqueous humor for diagnostics is disadvantageous because it requires an invasive mode of collection and presence of albumin in the serum and vitreous would be a major hindrance to proteomics studies. In contrast, urine is a rich source of the biomarker, which is widely explored in the field of clinical proteomics even in non-renal disorders because of its non-invasiveness, less complexity and relative stability of the proteome\textsuperscript{1 5}.

In addition, urine is specifically useful as a clinical specimen in AMD because of certain similarities between the eye and kidney. Earlier studies showed that the kidney and eye share striking structural, developmental, physiological, and pathogenic pathways. (i) The vascular networks of the glomerulus of kidney and choroid of the eye are structurally similar; (ii) The developmental pathways of the inner retina and glomerular filtration barrier are similar; (iii) renin–angiotensin–aldosterone hormonal cascade is found in both the eye and kidney\textsuperscript{1 6}; (iv) CFH gene variants
implicated in AMD, is also found to be also associated with membranoproliferative glomerulonephritis type II (MPGN Type II), a rare kidney disease. (v) In MPGN type II, there are also drusenoid deposits in the macula along with dense deposition of substance within the glomerular capillary walls \(^{17-19}\). There are evidence for associations of chronic kidney disease (CKD) and AMD in many studies. The Blue Mountains Eye Study (BMES) reported that there is a reduced renal function in AMD cases, with a decreased estimated glomerular filtration rate (eGFR) and creatinine clearance when compared with age-matched controls \(^2\). The above-mentioned reports suggest the possibility that AMD indeed is a manifestation of a systemic disease that includes mild abnormalities in renal function.

Studies have identified urinary pro-inflammatory cytokines TGF-â-1, MCP-1 and C3a desArg as potential non-invasive biomarkers for monitoring AMD in the Australian population\(^2\). However, a pilot study from our lab suggested that these markers were not significant to predict AMD in an Indian cohort (Supplementary figure S2-4). So, we chose a global proteomics approach to find out urinary biomarkers for AMD amongst Indian subjects. We carried out the study to identify early-stage urinary biomarkers for AMD. In this study, we performed a comparative urine proteome profiling between AMD and controls to analyse the differential proteomic signature. Besides, we also studied the polymorphism in CFH and C3 genes that are associated with high risk of AMD to discriminate AMD patients from controls. In addition, we analysed the diagnostic utility of the urinary proteomic markers along with the gene polymorphism for identifying as well as stratifying AMD patients. Our results suggested that a logistic model of APOA-1 in combination with CFH and C3 polymorphisms predicted the risk of developing AMD with 82% accuracy. The approach of combining proteomic marker along with the genetic polymorphism is suggested for potentially identifying patients at high risk of developing AMD and its complications.

**MATERIALS AND METHODS STUDY POPULATION:**

Participants were recruited from the vitreo-retinal outpatient clinic (Medical Research Foundation, Sankara Nethralaya, Chennai, India) from April 2013 to August 2015
for this cross-sectional study. The study was approved by institute’s ethics committee (ethical clearance number-270-2011-p dated 02-09-2011). The study adhered to the tenets of the Declaration of Helsinki. A standard health interview was undertaken by the patient giving particular attention on the history of smoking, any known renal disease, systemic inflammatory disease(s), hypertension, diabetes mellitus, use of drugs, etc. apart from basic demographic data. Patients with uncontrolled hypertension, or any other systemic inflammatory disease such as arthritis were excluded from the study.

Patient’s dilated fundus examination was done using a slit lamp and indirect ophthalmoscopy and the disease severity was graded. Optical Coherence Tomography (OCT) and fluorescein fundus angiography (FFA) were used to confirm cases of CNVM. AMD stages were classified according to the international system of classification.¹ Patients were classified into three groups as: (i) early AMD who had drusen > 63 μm in diameter; (ii) late AMD with geographic atrophy (GA) involving the centre of the fovea; and (iii) CNV (choroidal neovascularization). The control group had no or few small drusen (<63 microns in diameter).

**CLINICAL SPECIMEN COLLECTION AND PROCESSING:**

A written informed consent was obtained from all patients before collecting samples.

**A) PERIPHERAL BLOOD**

Approximately 4 ml of venous blood samples were drawn from the patients. After aliquoting 1 ml for biochemical tests such as estimation of plasma creatinine and subsequent estimation of eGFR, the remainder is centrifuged on a Histopaque density gradient to isolate PBMCs. Genomic DNA was extracted from isolated PBMC using QIAamp DNA isolation kit and stored at -80°C until further use. Allele-specific PCR was performed on AMD samples and control samples for rs1061170 (Tyr-402-His) (T/C) polymorphism on the Complement Factor H (CFH) gene and rs2230199 (Arg-102-Gly) (G/C) polymorphism on the Complement component 3(C3) gene. Three primers were used for each set of SNPs, with a common forward primer (F) and wildtype (W) and mutant reverse primer (M).
(CFH (rs106170) F – 5’TTGTGCAAACCTTTGTTAGT 3’, R-M-5’CTGTACAAACTTCTTCCAGA3’; W - 5’CTGTACAAACTTCTTCCAG3’; C3 (rs2230199) – F- 5’ACTGGGGAGAGACAAAGAGG3’ R- M- 5’GGAGTTCAGCAAAAGGGAG3’, R-M- 5’GGAGTTCAGCAAAGGGGAC3’.

B) URINE:

Midstream urine sample was collected from patients and stored at ice immediately upon collection. Urine sample was centrifuged at 1200 rpm for 10 mins at 4°C and the supernatant was again centrifuged at 4000 rpm for 15 mins at 4°C to remove cell debris and precipitates. It was then passed on 0.22μm filters to remove bacterial contamination and are concentrated using 3kDa cut off filters and aliquoted and stored in -80°C until further use.

TMT labeling and fractionation and Mass Spectrometry analysis:

A detailed workflow of the experiment is depicted in Figure I. Protein estimation was carried out using BCA assay (Pierce). Ten patient samples were taken in every group. SDS PAGE was performed to see the intactness of the protein. (Supplementary Information-1) Approximately 50μg of protein was added from each sample and pooled. Briefly, 200μg of the pooled samples were reduced and alkylated by using Dithiothreitol and Iodoacetamide, respectively. The samples were digested overnight with trypsin (Promega) (1:20) at 37°C. Pre and post digests were loaded on SDS-PAGE for checking digestion efficiency. Peptides from each group were labelled using 8plex tandem mass tags with technical replicates as per manufacturer’s protocol (Catalogue # 90110 Thermo Fischer Scientific). Peptides derived from control were labelled by 126 and 127N, Early AMD was labelled by 127C and 128N, CNVM were labelled by 128C and 129N, GA was labelled by 129C and 130N and are pooled.

The labelled peptides were subjected to basic reversed-phase liquid chromatography (bRPLC) fractionation as described previously2 2. A total of 96 fractions were initially collected in 96- well plates with 0.1% formic acid added to each well. The
fractions were then concatenated into 12 fractions and dried using speedvac. The fractions were analyzed using Orbitrap Fusion mass spectrometer (Thermo Scientific, Bremen, Germany) interfaced with Proxeon Easy NanoLC system as described previously\(^2\). The raw data was processed using Proteome Discoverer software (Thermo Fisher Scientific, Bremen, Germany) and database searches were carried out using Mascot and Sequest human protein database NCBI Ref Seq (Version 65, containing 36211 protein entries along with common contaminants).

VALIDATION OF CANDIDATE MARKERS:

Validation was performed for three differentially expressed proteins SERPINA-1 (Human SERPINA-1 ELISA kits, Abcam), TIMP-1 (Human TIMP-1 ELISA kits Enzo Life Sciences, Inc.) APOA-1, ( Human APOA-1ELISA kit, R&D Systems, Inc. Minneapolis, MN ) which were selected based on criteria explained in Figure IIIa using ELISA. The urinary levels of each protein were normalized to the total protein measured by BCA assay.

STATISTICAL ANALYSIS:

Student’s t-test and Mann-Whitney U test were employed to find the significance of ELISA results. In order to evaluate the diagnosing ability of the markers, ROC curves were plotted using the sensitivity and specificity. Graph pad prism (Version-6) software was used performing these tests. Statistical analysis for mass spectrometry proteomics data was done using Perseus and R.

RESULTS:

COMPARATIVE URINE PROTEOMIC ANALYSIS OF VARIOUS GROUPS OF AMD PATIENTS WITH REFERENCE TO CONTROL

The study included 61 AMD patients and 23 controls. The demographic characteristics of the patients are detailed in Table 1. Differential proteomics analysis of urine from AMD patients and controls identified about 750 proteins. These proteins were represented by 24,140 peptide spectral matches which corresponded to 2,122 unique peptides. A fold change cut-off of e\(^{-} \pm 1.5\) fold between AMD and controls revealed
about 383 proteins to be differentially expressed. Among the differentially expressed, 224 proteins were found to be upregulated and 107 proteins were downregulated in early AMD, 98 and 44 proteins were up and downregulated respectively in CNVM, and 64 and 22 proteins were up and downregulated respectively in GA. Figure IIa and IIb show Venn diagram representing proteins that are differentially regulated in AMD (>1.5 and <0.6 fold cut-off was considered as differentially expressed). List of pr

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**GENE ONTOLOGY AND PATHWAY ANALYSIS**

The differentially expressed proteins were analysed based on the information available on human protein reference database (HPRD) to determine their cellular localization, molecular function, and participation in biological processes. The gene ontology analysis pertaining to cellular localization revealed that majority of proteins identified were extracellular. This result validates our proteomics data since urine is a secretome and expected to contain extracellular proteins (Figure IIc). Majority of the deregulated proteins were involved in catalytic and binding activities. Functional annotation of the deregulated proteins revealed 11 signalling pathways to be significantly associated with AMD. Table 2 lists the top 5 signalling pathways.

**VALIDATION OF THE PROTEOMIC RESULTS**

We proposed a schema for choosing the candidate proteins for validation (Figure IIIa). Briefly, the schema involved the following criteria: 1. Differentially expressed in all the three groups; 2. Concordance with previous proteomic studies on AMD; 3. Proteins that have shown gradual increase in fold change from early AMD to advanced stages of AMD and 4. Commercial availability of ELISA kits. Novel proteins identified in the proteomic analysis were not considered for validation studies, since their non-correlation with the disease and would be difficult correlate in the absence
of information on their role in the disease or their expression in the local environment (retina or ocular tissues). Their presence in a systemic sample such as urine might be due to other systemic unknown factors. Based on the above-mentioned criteria, 3 differentially expressed proteins SERPIN A-1, TIMP-1, and APOA-1 were chosen for validation on a larger cohort of patient samples. The proteomic fold changes of the proteins are listed in Table 3. Fold changes of 0.6 and 1.5 were used as cut-off for down and upregulated proteins, respectively. Spectral images of peptides of the respective proteins that were chosen for validation are shown in Figure IV. ELISA Assay of all the three proteins revealed significant up-regulation in the urine of AMD patients compared to controls (p< 0.05; Mann-Whitney U test) (Table 4, Figure IV).

DIAGNOSTIC UTILITY OF THE VALIDATED PROTEINS AS CANDIDATE BIOMARKERS

We performed the receiver operating characteristic curve for the validated proteins, since the diagnostic utility of the biomarker depends on their power to discriminate the diseased individuals from the normal individuals. The result of the ROC revealed that the area under the curve AUC was around 0.65 for all the three proteins which is considered to be low number for discriminating the groups. In order to increase the discriminatory power of the diagnosis, we incorporated SNP genotypes of the patients along with the protein levels in a logistic regression model and fitted with ROC curve (Figure V). SNPs on CFH and C3 gene, which are previously known to be associated with AMD were chosen.

We analysed the diagnostic utility of biomarkers along with the SNP status using ROC curves. A logistic combinatorial model of the proteins and genotype data gave a better performance of these biomarkers in diagnosing AMD patients of Indian cohort. TIMP-1 alone could discriminate AMD and controls with 65% (Sensitivity - 88%, Specificity - 50%) accuracy. In combination with CFH and C3 polymorphism in a logistic regression model, the discrimination accuracy of TIMP-1 increased to 80% (Sensitivity - 88%, Specificity - 60%) with a P value <0.0001. Similarly, APOA-1 alone could discriminate AMD and controls with 66% (Sensitivity - 80%, Specificity - 50%) accuracy. In
In combination with CFH and C3 polymorphism in a logistic regression model, the discrimination accuracy of APOA-1 increased to 82% (Sensitivity - 58.5%, Specificity - 90%) with a P value <0.0001. SERPINA-1 alone could discriminate AMD and controls with 65% (Sensitivity - 74%, Specificity - 62%) accuracy. In combination with CFH and C3 polymorphism in a logistic regression model, the discrimination accuracy of SERPINA-1 increased to 72% (Sensitivity - 88%, Specificity - 60%) with a P value <0.002 (Supplementary information Table 2).

**DISCUSSION**

Proteomics-based approaches have developed a new platform for discovery of biomarkers and therapeutic targets in diseased conditions. Previous studies exploring the proteome in various clinical samples of AMD had concentrated on identifying differentially expressed proteins between controls and AMD patient. However, in the current study, we tried to stratify the AMD patients into early AMD, CNVM, and GA. Additionally, we utilized comparative proteomics methods to identify the proteins that gradually increased during the progression of the disease. This method will let us know how proteins are deregulated between various stages of AMD. This approach might be more advantageous since AMD is a slowly progressing disease.

We found proteins involved in complement pathway to be deregulated in AMD. In our dataset, the complement inhibitor proteins such as SERPINF2, SERPIND1 (supplementary table 1) were downregulated in early AMD which indicated the increased complement and coagulation pathway activation in early stages of AMD. Our study identified extracellular matrix-receptor interaction to be dysregulated in AMD. Previous studies have shown that ECM plays an important role in the pathogenesis of AMD 2-9. Extracellular matrix (ECM) metabolism is highly regulated by MMPs and TIMPs which were also altered in our dataset (Supplementary information 2). It has been known that the increased conversion of pyruvate to lactate in AMD 3-0. Lactate dehydrogenase A/B, the enzymes involved in the conversion of pyruvate to lactate under anaerobic conditions, was found to be upregulated in all stages of AMD. Loss of retinal phagocytosis have been observed in age-related
blindness and impaired phagolysosomal processing of photoreceptor outer segments were also observed in AMD. In our proteomic data set FC à receptor-mediated phagocytic pathway was down regulated especially in early AMD and impaired lysosomal pathway was observed in all stages of AMD.

Our results suggested that SERPINA1 may be more useful than APOA1 and TIMP1 in discriminating the controls from early AMD (p<0.044), hence had an edge over the other two markers for initial screening purpose. SERPINA-1 (Alpha 1 anti-trypsin) is an acute phase protein of the Serpin family. It is a serine protease inhibitor and thereby protects tissues from serine protease enzymes generally secreted by inflammatory cells. SERPINA-1 levels were found to be higher in all stages of AMD particularly in early AMD, suggesting that inflammatory responses and injury could play important roles in the development of AMD. With respect to CNVM, all the three markers were significantly up-regulated over the control; however, APOA1 levels clearly distinguished the CNVM (15-fold increase) from early AMD (4-fold increase). Apolipoprotein (APOA-1), a major component of high-density lipoprotein, is a key factor regulating reverse cholesterol transport and has antioxidant, anti-inflammatory, and anti-endotoxin effects.

GA was best distinguished from both early AMD and CNVM groups by TIMP1 with greater than 2-fold difference with respect to other two groups (Table 4). TIMP-1 is (Tissue inhibitor of matrix metalloproteinase-1), an inhibitor of matrix metalloproteinases which regulate ECM metabolism was found to be altered in AMD. TIMP-1 levels are progressively increasing from early to late stage of AMD in our study, thereby correlating with the pathogenesis of AMD.

The limitation of our study was the sample size of the GA cohort and the significant difference in the age of the controls compared to the AMD groups. In addition, the lack of history of smoking and alcohol was more pronounced in the control group which can influence the urinary proteome. In order to avoid the discrepancies of our analysis, we incorporated allele
status of risk-conferring SNPs in AMD in our study which is not affected by person’s behaviour or any other co-morbidity.

**CONCLUSIONS:**

This study identified candidate predictive biomarkers SERPINA-1, TIMP-1, and APOA-1 proteins for AMD using the in-depth analysis of the urine proteomes of AMD patients and controls. Our data also demonstrated the significant association of the Y402H polymorphism on the CFH gene and R102G polymorphism on C3 gene and AMD in Indian subjects. Moreover, our data identified that TIMP-1 in combination with CFH and C3 polymorphism serves to be a better predictive diagnostic tool in predicting the risk of developing AMD in patients. Our results may enable the diagnosis of AMD using urine samples, thereby permitting early detection, introduction of lifestyle changes and possibly leading to the prevention of macular degeneration mediated complications in the elderly population.

**FIGURE LEGENDS**

Figure I : Study design for comparative proteomics based mass spectrometry for identifying candidate biomarkers in AMD.
200 mg pooled samples were reduced and alkylated by using Dithiothreitol and Iodoacetamide, respectively. The samples were digested overnight with trypsin (Promega) (1:20) at 37°C. Peptides from each group were labelled using 8plex tandem mass tags with technical replicates as per manufacturer’s protocol (Catalogue # 90110 Thermo Fischer Scientific). Peptides derived from control were labelled by 126 and 127N, Early AMD was labelled by 127C and 128N, CNVM were labelled by 128C and 129N, GA was labelled by 129C and 130N and are pooled. The fractions were analyzed using Orbitrap Fusion mass spectrometer and the Raw data was analysed using Proteome discoverer software. The data was further validated using ELISA.

Figure II

![Venn diagram](image)

Figure II: Representation of proteins that are up and down regulated using Venn diagram. A) Number of urine proteins that are upregulated in each condition B) Number of urine proteins that are downregulated in each condition. A total of 24 proteins were commonly upregulated and 12 were commonly downregulated irrespective of stages of AMD. C) Gene ontology classification of deregulated proteins in urine of AMD patients based on their localization
Figure III: A) Selection criteria used for filtering out molecules for validation. B&C) Venn diagram matching proteins published in previous Proteomic datasets for AMD. B) Represents matched proteins with fluid proteomes while C) Represents matched proteins with Tissue proteome. Proteins were shortlisted for validation based on the criteria shown in the figure. Out 751 proteins totally identified, 383 were differentially expressed between AMD patients and healthy control, of which 48 proteins matched with previous proteomic datasets in AMD. Out of the 48, 16 proteins were upregulated in both early and late stages and 3 were finally selected for validation based on the availability of ELISA kits.
Figure IV

Representative spectral Images of MS/MS spectra after HCD for peptide SEEFLIAGK TIMP-1 (a), peptide AVLTIDEK of SERPINA-1 (b) and peptide ATEHLSTLSEK OF APOA-1 (c). m/z 126.1 represents mass tag intensities from control samples and 127.1, 128.1 and 129.1 represents intensities from Early AMD, CNVM and GA respectively.
Figure V: ROC curve of TIMP-1(a), APOA-1(b) and SERPINA-1(c) in differentiating AMD patients and controls based on various combinations with the genotypic data.

TABLE LEGENDS

Table 1: Demographics of the cohort (p-values are calculated based on logistic regression analysis and chi-square analysis)

Table 2: Pathways De-regulated in AMD. The table lists the signalling pathways that got maximum hit obtained using annotation tools.

Table 3: Mass spectrometric fold change of proteins selected for validation with reference to control. All the three proteins chosen were showing upregulation trend in proteomics data.

Table 4: Validation of differentially expressed proteins in AMD patients using ELISA.
### Table 1

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### Table 2

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### Table 3

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**Table 4**

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**Table 4**

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<td>(n=22)</td>
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Hyperreflective Dots in Optical Coherence Tomography May Prompt A Change in Treatment. (Best paper of Telangana Ophthalmological Society)

**Dr. Simakurthy Sriram**, Dr. Mahesh P Shanmugam, Dr. Rajesh Ramanjulu, Dr. Divyansh Mishra

**ABSTRACT**

**TITLE:**

Hyperreflective dots in optical coherence tomography may prompt a change in treatment

**PURPOSE:**

To characterize optical coherence tomography (OCT) biomarker - Hyperreflective dots (HRDs) and its influence on disease management.

**MATERIALS AND METHODOLOGY:**

Retrospective analysis of all cases with fluid at macula due to various chorioretinal vascular diseases with anti VEGF resistance, who received intravitreal dexamethasone implant ± anti VEGF in the last one year duration. The patients were evaluated on swept source OCT (SS-OCT) to look for hyperreflective
dots and followed up serially post intravitreal injection to look for a response in terms of decrease in macular fluid and need for further interventions.

RESULTS:

A total of 23 eyes were diagnosed with anti VEGF resistance requiring addition of steroid implant. Hyperreflective dots were noted in 43% of cases with anti VEGF resistance. The decrease in hyperreflective dots precedes decrease in the fluid at the macula. Mean central macular thickness decreased from 397µ to 262.5µ in group with HRDs, while it decrease from 416µ to 289.3µ in group without HRDs. Though there was no statistically significant difference between the two groups, the response was sustained in the group with HRDs. The group with hyperreflective dots showed 4 fold decrease in the frequency of add on intravitreal anti VEGF at 6 months post dexamethasone implant injection.

CONCLUSION:

Hyperreflective dots sized <30µ with an absence of back shadowing and reflectivity similar to nerve fibre layer act as surrogate markers of inflammation and predict a better response to dexamethasone implant. Addition of steroids to the treatment regimen reduces the burden of anti VEGF injections.

KEYWORDS:

hyperreflective dots, dexamethasone implant, retinal imaging

FINANCIAL DISCLOSURES:

No financial disclosures.

INTRODUCTION

Hyperreflective dots (HRDs) are small, punctiform, reflective lesions seen on Optical Coherence Tomography (OCT) B scans in various chorioretinal vascular disorders such as Age related macular degeneration (AMD)	extsuperscript{1}, diabetic macular edema (DME)	extsuperscript{2}, retinal vein occlusion (RVO)	extsuperscript{3} etc. and degenerative disorders such as Best disease,
vitelliform dystrophy. These HRDs are not demonstrable on any monochromatic or angiographic photos. They can be demonstrated in any layer of the retina, though they are more commonly located near intraretinal fluid collection, or within the cysts or in the cyst wall. HRDs are thought to be a novel OCT biomarker, which represent the clinical activity of inflammation. They are known to be helpful to predict the photoreceptor status and also to determine the final visual acuity. The main purpose of this study was to identify and characterize HRDs in cases with fluid at macula due to various chorioretinal vascular diseases with anti VEGF resistance.

MATERIALS AND METHODOLOGY

Non-randomized, hospital-based, retrospective study. Retrospective analysis of all cases with fluid at macula due to various chorioretinal vascular diseases with anti VEGF resistance (mean of 3 anti VEGF injections), who received intravitreal dexamethasone implant ± anti VEGF in the last one year duration was done. The patients were evaluated on SS-OCT (DRI Triton, Topcon Inc., Japan) to look for HRDs and followed up serially post intravitreal injection for a period of 6 months to look for a response in terms of decrease in macular fluid and need for further interventions.

HRDs were defined as scattered, punctiform dot reflective lesions seen on OCT (B scan image- raster or radial scan) either in isolation or in clumps, the size of the dot being <30 microns with reflectivity that of nerve fibre layer without any back shadowing. Care was taken to differentiate these dots from hard exudates and microaneurysms (higher reflectivity with back shadowing). The aid of special software – enhanced vitreous visualization (EVV) inbuilt within the DRI Triton OCT platform was taken, wherein EVV set at -4 helped in identification of hyperreflective dots, while hard exudates persist till EVV -5. (Figure 1)

RESULTS

23 eyes were diagnosed with anti VEGF resistance (mean of 3 anti VEGF injections) over last one year period at our Centre, who required further management with dexamethasone implant ± anti VEGF. These 23 eyes include 13 eyes with diabetic macular edema (DME), 4 eyes with retinal vein occlusion (RVO), 6 eyes with wet
Age related macular degeneration (AMD). Out of these 23 eyes, 10 eyes had HRDs (43%).

On further analysis of two subgroups (with HRDs, without HRDs), the mean age of patients in both the groups was comparable (66 vs 61 years, \( p > 0.05 \)), both groups had received a mean of 3 intravitreal anti VEGF injections before addition of dexamethasone implant. The central macular thickness (CMT) in the group with HRDs decreased from a mean of 397 \( \mu \) at baseline to 253.3 \( \mu \) at 1 month post addition of dexamethasone implant and 6 months was 262.5 \( \mu \), while in the group without HRDs, CMT decreased from a mean of 416 \( \mu \) at baseline to 341.6 \( \mu \) at 1 month post addition of dexamethasone implant and 6 months was 289.3\( \mu \). There was a reduction in central macular thickness in both groups, however the difference between the two groups was not statistically significant. The mean period before relapse of fluid was 2.38 months in the group with HRDs while it was 2.36 6 months in the group without HRDs (\( P > 0.05 \)). However, the group with HRDs required four times less frequent add on anti VEGF injections over the next 6 months compared to the group without HRDs (mean of 0.3 vs 1.3 add on anti VEGF injections respectively). On further analysis, it was noted that group with RVO required early re-intervention (mean of 0.75 months duration), while the group with DME was most responsive and required delayed re-intervention (mean of 2.3 months duration).

**DISCUSSION**

This study was performed to analyze hyperreflective dots characteristically detected only by OCT imaging. Unrelated to specific changes in either fundus photography, autofluorescence imaging or infrared imaging such as haemorrhage, lipofuscin deposits or hard exudates, these HRDs can be seen in any layer of the retina. These HRDs have reflectivity similar to nerve fibre layer while hard exudates have higher reflectivity similar to that of RPE – Bruch’s membrane complex\(^7\). Enhanced vitreous visualization (EVV\(^\text{TM}\)) software in DRI TRITON SS- OCT helps in altering the contrast of the scan similar to the gain function of ultrasound B scan, thus areas of interest can be highlighted selectively. For example, with EVV set at higher levels (+1 to +5) weaker signals like vitreous becomes better appreciated and with EVV set at lower levels (-1 to -5)
only hyperreflective layers of the retina are visible. We noted that hard exudates having reflectivity similar to RPE – Bruch’s membrane persists till EVV -5, while HRDs having reflectivity similar to nerve fibre layer persist till EVV -4. This function avoids the need for elaborate tools in photographic software.

There are several hypotheses on the origin of the biomarkers – biomarkers of inflammation\(^1\), precursors of hard exudates\(^2\), degenerated photoreceptor cells\(^8\), anteriorly migrated RPE cells\(^9\), and retinal vessels. Using SS OCT, we investigated the presence of HRDs and followed up post treatment. We noted that up to 43% of the eyes contained HRDs which responded on the addition of the steroid implant strengthening the role of inflammation in the disease causation. Coscas et al\(^1\), Vujosevic et al\(^10\), Hwang et al\(^11\) have shown similar response to the addition of steroid implant in a study done in AMD, DME and RVO respectively. The group without HRDs also responded to the addition of steroid implant indicating the inflammatory pathogenesis of the disease per se, but the response in the group without HRDs was not sustained and they required frequent add on anti VEGF injections in the next 6 months period. In our study HRDs were noted to disappear before the reduction in edema and reappear before clinically significant edema, thus representing early changes of inflammatory reaction (Figure 2) similar to previous studies\(^{1,12}\). In our study, we noted that the response was sustained for a longer period in the group with DME, while the effect was short-lasting in RVO requiring further anti VEGF injections on follow up. However the current study is retrospective in nature with limited sample size, the significance is limited. In our study, we did not quantify the number of HRDs and grade the response. A prospective study with a larger sample size and longer follow up is planned to better study the role of HRDs.

To conclude, HRDs act as a surrogate marker of inflammation and show a better response to the addition of steroid implant. Addition of steroid implant in HRDs reduces the burden of add on anti VEGF injections.
REFERENCES


**FIGURE LEGENDS**

**Figure 1**: a) Hyperreflective dots at EVV -4 highlighted within red circle, appearing as hyperreflective as nerve fibre layer b) disappearance of hyperreflective dots at EVV -5 c) Hard exudate clump at EVV -4 d) persistence of hard exudate clump at EVV -5, appearing as hyperreflective as RPE – Bruch’s membrane

**Figure 2**: serial follow up of a case of DME post dexamethasone implant + antiVEGF injection showing disappearance of hyperreflective dots prior to disappearance of cystic edema
Change in Vessel and Perfusion Densities with Varying Signal Strength on OCTA (FP160)

Dr. Saurabh Verma, Dr. Atul Kumar, Dr. Rohan Chawla, Dr. Amar Pujari

**ABSTRACT**

**PURPOSE**

To evaluate change in vessel and perfusion densities with varying signal strengths on optical coherence tomography angiography (OCTA).

**METHOD**

Quadrant wise vessel densities and perfusion densities in superficial capillary plexus were measured using 3*3 mm OCTA scans. Images were obtained in 26 normal eyes, out of which 10 were finally evaluated to study the variations in the aforementioned parameters with signal strengths (SS) 8, 9 and 10.

**RESULT**

The total vessel and perfusion densities increased significantly from SS 8 to 10 and 9 to 10. The mean vessel densities along the superior, inferior, temporal and nasal quadrants showed a consistent increase in values with a progressive increase in the scan strengths. (Figure 1, Table 1, graph 2) Similarly, the perfusion...
densities along all four quadrants also showed a progressive increase in the percentage values with increasing signal strengths. (Figure 1, Table 1, graph 3)

CONCLUSION

Even minor variation in signal strength of OCTA, even within the generally accepted scan strengths, affects the quantitative analysis. Therefore, future studies using OCTA must specify the signal strength of the scans for a head to head comparison or interval analysis.

INTRODUCTION

Following the introduction of optical coherence tomography angiography (OCTA), a significant number of studies have been performed to understand the anatomical changes along the retinal and choroidal microvascular networks.\textsuperscript{[1]} It provides insights into capillary densities and the perfusion densities by analysing the white and dark pixels in a given area. The white pixels are assumed as areas with perfusion and the dark areas as non-perfused regions or areas lacking any form of vasculature. However, the brightness or the quality of the scan improves as the acquisition signal strength increases. In routine clinical practice on a scale of 10, scans with more than 7 signal strength are considered as adequate for assessment.\textsuperscript{[2-4]}

MATERIALS AND METHODS

Here in this observation, we assessed the effect of variation of signal strength from 8 to 10 on OCTA automated vessel density and perfusion density values. A total of 26 eyes of 15 healthy ophthalmic residents were evaluated. However, only 10 eyes were considered for final assessment after excluding those with artefacts. Under dim room light conditions and without use of any mydriatics, all subjects underwent 3*3 mm OCTA (Ziessangioplex OCT, Carl Zeiss AG, Jena) scan of the macula. At least three scans were obtained for each eye with signal strengths of at least 8/10, 9/10, or 10/10. All the scans were obtained by a single observer and the best scan in
each category of individual signal strength was included for the final analysis. The acquired scans were assessed for the automated vessel densities and perfusion densities along the superficial retinal plexus. Values were documented along each quadrant with increasing signal strengths (SS) for each individual. The data were entered in an excel sheet, statistical analysis was performed using strata software 12.2, and p values less than 0.05 were considered as statistically significant.

RESULTS

The average age was 26 years and six subjects were females (M: F= 2:3). The total vessel and perfusion densities increased significantly from SS 8 to 10 and 9 to 10. (Table 1,2 and Graph 1) The mean vessel densities along the superior, inferior, temporal and nasal quadrants showed consistent increase in values with progressive increase in the scan strengths. (Figure 1, Table 1, graph 2) Similarly, the perfusion densities along all four quadrants also showed progressive increase in the percentage values with increasing signal strengths. (Figure 1, Table 1, graph 3) On inter strength density comparison, between 8 and 9 SS, the change in the values obtained were not statistically significant along any of the quadrants; (Table 2) whereas the values between SS 9 and 10, and 8 and 10 showed a statistically significant increase in the superior, nasal and inferior quadrants (p<0.05). Likewise, changes in the perfusion density values were also statistically significant between SS 8 and 10, and between 9 and 10 along all four quadrants; and only along the inferior quadrant between the SS 8 and 9. Rest of the values, however, did not show any significant statistical difference. (Table 2)

DISCUSSION

OCTA with its three-dimensional imaging capability maps the vessels by observing the movement of the blood cells against the static retinal tissue background. Therefore, based on the perceived movements detected by analysing the decorrelation of the optical coherence tomography signals, a vascular map is constructed. The vessel areas are depicted with white pixels and the non-vessel or non perfused areas as dark pixels. Therefore, the quantification of vascular parameters such as vessel density,
perfusion density, non-perfusion areas and the longest vessel length are mere expressions of the perceived pixels within the captured image.[1]

There are a different set of algorithms devised by the researchers for the quantification of pixels within a given image. But till now, there are no universally defined algorithms for these examinations. In routine studies, signal strength of 7/10 or more is considered as satisfactory for the assessment of vascular changes. (1-4) But our study shows that even change in the signal strength by 1 point beyond 8/10 alters the vessel density by 3.5 % (min) to 9.9% (max), and perfusion density by 6.69% (min) to 14.21% (max) amongst the total values.

In certain pathological conditions of the eye with low vision, the scan qualities are often poor and this can alter the pixel densities significantly. Thus, results of the studies comparing the quantitative data of such poor scans with the data of scans in normal eyes may not be correct as they would have overlooked the bias/error which can occur by a mere variation of signal strength by 1 point. In a study by Lim et al, they noted significant changes in vessel and perfusion densities from signal strengths 7 to 9 but not between 9 and 10., However, in our observation, we noted statistical significant changes in the values between the signal strengths of 9 and 10, and between 8 and 10.[3]

In our observation, even though we performed scans on twenty-five eyes, acquisition of scans without artefacts and with consistently high signal strengths (8, 9, and 10) was challenging. We could acquire 9/10 and 10/10 signal strengths in our subjects as they were very co-operative and young with 20/20 visual acuity and very clear media. Though our sample size is small, it definitely highlights the variations in the automated vessel and perfusion density values obtained with change in signal strengths. Other limitation of this study is that we did not assess the deeper retinal and choroidal plexuses.

To conclude, from our observations, it is evident that a minor variation in signal strength, even within the generally accepted scan strengths of OCTA, can affect the
quantitative analysis. Therefore, future studies using OCTA must specify the signal strength of the scans for a head to head comparison or interval analysis.

Keywords: OCTA; Signal strength; Vessel and perfusion densities.

REFERENCE:


FIGURE CAPTIONS

Figure 1A, B, C: Automated vessel density values along four quadrants with increasing signal strength. (A=8 SS, B=9 SS, C=10 SS) (Three images on the left side of panel)

Figure 1D, E, F: Automated perfusion density values along four quadrants with increasing signal strength. (D= 8 SS, E=9 SS, F=10 SS) (Three images on the right side of panel)
Graph 1: Vessel density changes along the four quadrants with increasing signal strength.
Graph 2: Perfusion density changes along the four quadrants with increasing signal strength.
Legend/caption of graph 3 has to be added.

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<th>SS 8</th>
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Table 1: Vessel and perfusion density changes (Total and quadrantic) with increasing signal strengths (8, 9, 10). (SS= Signal Strength)

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Table 2: P value after comparing the signal strengths of 8 (S1, I1, T1, N1), 9 (S2, I2, T2, N2) and 10 (S3, I3, T3, N3). VD= Vessel density, PD= Perfusion density, S=Superior, I=Inferior, T=Temporal, N=Nasal. VDT= Vessel density total, PDT= Perfusion density total.
Human Induced Pluripotent Stem Cell Derived Enriched Rpe Cultures: An Ex-Vivo Animal Safety Study. (FP1449)

Dr. Vivek Dave, Dr. Indumathi Mariappan, Ms. Savitri Maddileti, Mr. Vinay Kumar Pulimamidi

AIM

To evaluate the safety of human induced pluripotent stem cell (iPSC) derived retinal pigmented epithelial cells (RPE) in immune compromised nude mice model.

SETTING

A prospective ex-vivo animal study.

METHODS

A healthy control iPSC line generated in-house was differentiated into retinal cell types, and pure cultures of RPE cells were established at our cGMP cell culture facility. Two million cells (roughly 10 times the sub-retinal dose), were suspended in 20% Matrigel solution and injected subcutaneously in nude mice (N = 8), with strict adherence to animal handling protocols and ethics as per ARVO guidelines. At 8 weeks post-transplantation, the animals were euthanized and the pigmented cell mass at the site of injection was excised for further
evaluations by immunohistochemistry using human antigen and RPE-specific markers.

RESULTS

The transplanted human iPSC-derived RPE cells survived for up to 8 weeks in the sub-cutaneous space of nude mice and remained confined to the transplant site. No abnormal growth and migration of pigmented cells to ectopic sites were noted. The injected cells formed a compact pigmented mass of about 3 - 5 mm size. Histopathological examination showed monolayered pigmented epithelial cells, organized into circular clusters, with clear basal and apical polarity. Immunohistochemistry confirmed that the pigmented cells were of human origin and expressed the human mitochondrial antigen. The pigmented cell clusters were also positive for RPE-specific markers such as PAX6 and RPE65. No abnormal cell proliferation or differentiation was noted and the RPE clusters were negative for the cell proliferation marker, Ki67; thus confirming the human RPE identity and their non-proliferative status in vivo.

CONCLUSION

Pure cultures of iPSC derived human RPE cells neither proliferated abnormally nor induced any teratomas in nude mice. This demonstrated the efficiency of our cell preparation protocols and the safety of RPE cells for future in vivo applications in cell therapy for retinal regeneration.

INTRODUCTION

Currently diseases like age related macular degeneration and retinitis pigmentosa do not have any definitive curative therapy. But several studies have shown that there is promise in sub-retinal cell replacement therapy using pluripotent stem cell derived retinal cells. [1-5] Pluripotent stem cells such as embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) have the capacity to differentiate into cell types of all three germ layers. [6,7] Newly derived iPSCs have to be extensively characterized to demonstrate their stemness, pluripotency and genomic integrity
before considering their use in downstream experiments. The common methods used to characterize these iPSCs include quantitative polymerase chain reaction (PCR), immunocytochemistry (ICC) and Fluorescence Activated Cell Sorting (FACS) analysis for various stem cell markers. These techniques check for the stable expression of pluripotency genes such as Oct4, Sox2, c-Myc, KLF4 and Nanog.\[8-12\] However, a teratoma assay is considered the gold standard to confirm the pluripotency of any iPSC lines. This assay is carried out in immune compromised animal model such as the nude mice or the NOD/SCID mice to prevent immune rejection of the transplanted human cells. It checks for the ability of iPSCs to proliferate \textit{in vivo} and differentiate into cell types belonging to all three germ layers and form a complex, well differentiated and encapsulated tumor called a teratoma.\[13,14\]

We have generated a healthy control iPSC line (hiPSC-F2-3F) in-house and reported its molecular characterization earlier.\[15\] iPSC derived enriched RPE cells in culture may contain a small population of undifferentiated stem cells/early neuro-retinal progenitors that may proliferate and form tumors post transplantation. Hence it is important to check if the fully differentiated RPE cells are devoid of any contaminating undifferentiated cells and are safe for transplantation purposes. Here, we report the safety and purity of iPSC derived enriched RPE cells in athymic nude mice for regenerative applications.

METHODS

This was an ex-vivo pre-clinical animal study performed at LVPEI and at NCLAS, NIN, Hyderabad. This study was approved by the LVPEI institutional review board (IRB), Institutional Committee for Stem Cell Research (IC-SCR) and the NIN Animal Ethics Committee (AEC). All animal handling were done in adherence to the ARVO statement. A normal iPSC line (hiPSC-F2-3F) was derived by reprogramming human dermal fibroblasts established from skin biopsy cultures of a healthy control. Extensive characterization of this line for stemness, pluripotency and genomic integrity was reported earlier.\[15\] Similarly, in-house developed and optimized protocol to obtain enriched neuro-retinal cells and RPE cells from hESCs was reported earlier.\[16\]
In this technique, hiPSC-F2-3F was cultured on Matrigel™-inmTeSR-1™. Embryoid body (EB) formation in suspension on non adherent plates containing differentiation medium, for 3 days. EBs were transferred onto Matrigel™ coated dishes containing neural induction medium for 1 week to obtain neural rosettes. Neural rosettes were shifted to retinal differentiation medium for 4 weeks to obtain pigmented patches of retinal progenitors. Pigmented RPE patches were manually picked using a flame-pulled glass Pasteur pipette and sub-cultured on Matrigel™ coated dishes containing RPEM for 2 to 3 months to get enriched cultures of RPE.

In order to check for the safety and purity of hiPSC-derived RPE cells, 2 months old enriched and mature RPE cells were suspended in 20% Matrigel solution. 50 µL of the above suspension containing 2 million cells were injected subcutaneously into 7 to 8 week old nude mice (Foxn1<sup>nu</sup>/Foxn1<sup>nu</sup>), using an insulin syringe with a 26 G needle and the animals were monitored for up to 8 weeks. The study animals were then sacrificed and the pigmented tissue that developed subcutaneously at the site of injection was excised, fixed in 10% formalin for 24 hours and paraffin embedded. Tissue sections of 4 micron thickness were analyzed by haemotoxylin and eosin (H&E) staining and by immunohistochemistry.

RESULTS

No abnormal growth or migration of pigmented cells to ectopic sites were noted. Histological examination showed monolayered pigmented epithelial cells, organized into circular clusters within the pigmented cell patch. The pigmented cell clusters at the transplant site expressed the human mitochondrial antigen and we could not detect any human cells beyond the pigmented patch. This confirmed that the human iPSC-derived RPE cells survived and remained confined to the injection site. The cells within the pigmented patch were positive for RPE-specific markers such as, PAX6 and RPE65, thus confirming that the human RPE cells maintained their cellular identity in nude mice. The RPE cells within the pigmented clusters did not express the cell proliferation marker, Ki67; thus confirming their non-proliferative status in vivo.
DISCUSSION

In the current paper, we report the safety and purity of iPSC derived enriched RPE cells in athymic nude mice for regenerative applications. The current study shows that pure cultures of iPSC derived human RPE cells neither proliferated abnormally nor induced any teratomas in nude mice. This demonstrated the efficiency of our cell preparation protocols and the safety of RPE cells for future in vivo applications in cell therapy for retinal regeneration. A large body of literature evidence has confirmed that adult mammalian and primate retina are amenable for cell replacement therapy. Transplantations of human fetal retinal progenitors or photoreceptor precursors are shown to preserve or improve visual functions in animal models of retinal dystrophy. However, a reliable and renewable source of donor cells such as the hESCs and iPSCs are being intensely explored for adopting them in cell replacement therapies. As mentioned earlier, many reports have shown that retinal cells derived from hESCs are amenable for scaling up and are effective in delaying disease progression and in improving visual functions in preclinical animal studies. Recent reports on the clinical outcomes of FDA-approved, phase I/II trials have established the safety and tolerability of subretinal transplantations of iPSC-derived RPE cells in the treatment of patients with Stargardt’s macular dystrophy and dry AMD. It is well known that the eye is an immuneprivileged site, being established by the barrier functions of RPE cells and the endothelial cells of retinal vasculatures. The early observations and outcomes of this trial confirm that in spite of being an allogeneic cell source, the iPSC-derived RPE cells transplanted in the subretinal space of the patient’s eye did not elicit any significant immunologic response. The reports also revealed that there were no signs of hyperproliferation, tumorigenicity, or ectopic tissue formation. Fundus photographs and optical coherence tomography images of transplantation sites of the retina in treated eyes have confirmed that the RPE grafts survived, proliferated/expanded in vivo for up to 37 months post transplantation, and contributed to marginal improvements in visual parameters. These developments were encouraging to consider BJNhem20- derived retinal cells for possible preclinical and clinical applications.
iPSC derived enriched RPE cells in culture may contain a small population of undifferentiated stem cells/early neuro-retinal progenitors that may proliferate and form tumors post transplantation. Hence it is important to check if the fully differentiated RPE cells are devoid of any contaminating undifferentiated cells and are safe for transplantation purposes. Our study is an ex-vivo study. The safety of the injected RPE cells was tested in the subcutaneous space of the animal. This was done as the subcutaneous space is amenable to easy examination and one is capable of picking up subtle side effects if any easily. In an obvious next step, we intent to repeat our experiments in rats by injecting these cells in the subretinal space and then looking for the response. Those results would give an exact idea of the reaction of the host eye to the cells in the subretinal space and would augur well for further cell procedures to achieve favorable transplant based therapy outcomes.

REFERENCES


FIGURE LEGENDS

1. Hematoxilin and eosin stained sections of human iPSC-derived RPE patch

2. The transplanted pigmented RPE cell clusters showing the cytoplasmic expression of human mitochondrial antigen
3. Pigmented RPE clusters showing nuclear expression of PAX6 and cytosolic expression of mature RPE specific marker RPE65

4. No abnormal cell proliferation or differentiation was noted and the RPE clusters were negative for the cell proliferation marker, Ki67; thus confirming the human RPE identity.

Hematoxilin and eosin stained sections of human iPSC-derived RPE patch

The transplanted pigmented RPE cell clusters showing the cytoplasmic expression of Human Mitochondrial Antigen
No abnormal cell proliferation or differentiation was noted and the RPE clusters were negative for the cell proliferation marker, Ki67; thus confirming the human RPE identity.

Pigmented RPE clusters showing nuclear expression of PAX6 and cytosolic expression of mature RPE specific marker RPE65.