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Cover Photo

Nocardia Endophthalmitis

Courtesy : Rajesh Sahay, Lucknow, India

"WHEN GOING GETS TOUGH, THE TOUGH GETS GOING"

The above words of wisdom and encouragement are befitting the situation caused by Corona pandemic.

I am happy to note that inspite of all miseries and difficulties the new issue of U.P. state Ophthalmological society is in your hands.

"THE PESSIMIST SEES DIFFICULTY IN EVERY OPPORTUNITY,

THE OPTIMIST SEES OPPORTUNITY IN EVERY DIFFICULTY"

All the credit goes to Dr. Shalini Mohan the dynamic editor of U.P. State Ophthalmological society and I am sure that U.P. State Ophthalmological society will maintain highest level of integrity ensuing consistency and scientific flavor in each research articles My utmost desire that U.P. State Ophthalmological society should be indexed journal with high impact factor.

Wishing you this great scientific treatise.

Dr. Shrikant, MS
President, UPSOS
Former Professor & Head, Regional Institute of Ophthalmology
Institute of Medical Science BHU, Varanasi
Presently Prof. & Head Department of Ophthalmology
Heritage Institute of Medical Sciences, Varanasi

The Power of Reading

Dear Friends,

Reading as a hobby, culture and necessity in academics evolved over the times we know of human existence and is the commonest way of communication even today.

As technology evolved and social paradigms changed, text reading started; getting modified into e-reading and printed text started losing its monopoly.

As an Ophthalmologist, I myself noticed the declining trend of reading printed journals and increasing ease and access to the online study material which often gives biased and incomplete information too.

So why this printed Journal? Is this the time to change? Or we need to revisit our thoughts?

I accept, online access is easy, available on phone, and easy to read but let's trace back our steps...

We studied throughout via book reading, we see our kids reading books. We never had computer vision syndrome? We had prolonged sittings with books without instilling eyedrops.

There is some beauty in book reading and books have been our best friends. Actually we read in between the lines with less ocular fatigue, improve our vocabulary and that also inculcates habit of writing, improving creativity and generates further reading ability.

I would like to have feedbacks on this issue from everyone but I personally feel that one must sit with printed text, read and write more.

I am thankful to President Dr. Shrikant, Secretary Dr. Mohita Sharma, CSC Dr. Deepak Mishra, Joint Editor/Associate Editors and whole editorial board along with executive body for their whole hearted support and cooperation.

I hope everyone will enjoy this edition of journal.

All the best

Warm regards

Dr Shalini Mohan
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"COVID ERA"

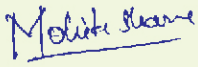
Dear Members,

Welcome to COVID times !! In an era where almost everything seems to have come to a standstill the UP Journal of Ophthalmology continues to come out and impart scientific knowledge to all its members. This journal signifies that life can never stop and scientific upgradation is a continuous process.

As a State society UPSOS is committed to imparting scientific knowledge. On behalf of the whole executive committee my Congratulations to the editor and the editorial team.

As doctors we took the hippocratic oath and promised to serve humanity. My appeal to all our dedicated members is to continue to work whole heartedly and simultaneously be updated about all precautions which can keep you safe. Take special care of yourself especially from the ophthalmology point of you. And since workload is less ours being mostly an elective branch, spend more timing reading good journals like this one. You also have the opportunity to do what you never got the time to do. In this one important thing is studies and publishing. So let's get started on this academic front too. And hope to see more contributions of structured study results from our own state of Uttar Pradesh.

Stay safe, stay healthy and stay working



Dr Mohita Sharma,

General Secretary, UPSOS

Panel Discussion on Glaucoma Practice Patterns

UPSOS Correspondent : **Mohit Khattri**
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Expert Panel

Dr Vineet Ratra (VR)
Senior Consultant,
Sankara Nethralaya, Chennai

Prof. Rajiv Nath (RN)
Ex Professor, KGMU, Lucknow

Dr Sagarika Patyal (SP)
Senior Glaucoma Consultant
Centre for Sight, New Delhi

Dr Manish Pandey (MP)
Glaucoma Consultant
Ratan Jyoti Netralaya, Gwalior

Glaucoma is a disease which has involved maximum interest in terms of pharmacological developments and technical advancements. Due to the multifactorial nature and ambiguity, it still remains a Pandora box to be explored further. Hence is the need to be guided with the practice patterns of experts and make our own algorithms to have safe and confident glaucoma practice. In this issue, we bring forward a panel discussion on practice patterns in glaucoma involving four eminent glaucoma experts across the country. Hope you all shall gain and incorporate the conclusions in your practice.....

Q.1 What minimum investigations you would like to be done in all your glaucoma patients?

VR: All my glaucoma patients undergo intra ocular pressure checked by an application tonometry. They undergo Indentation gonioscopy, 90 D Slit lamp bio microscopic examination, pachymetry and an automated visual field with Humphrey. In glaucoma suspects or in early glaucoma patients I do optic disc photography and optical coherence tomography of retinal nerve fiber, the GCC and the macula.

MP: For any patient with suspected or confirmed glaucoma, a comprehensive eye examination including applanation tonometry, four mirror indentation gonioscopy and stereoscopic optic disc examination, I would ask for ultrasound pachymetry and visual field testing (24-2, SITA-Standard and/or 10-2 in central involvement). In addition to these, if necessary I may need further imaging modalities like OCT, HRT or GDx. For OCT (which I have access to) I use nerve fibre analysis (RNFL) and ganglion cell complex (GCC) in glaucoma suspects, ocular hypertensives or early glaucoma. I am also vary of the limitations of these imaging modalities especially false positive (red disease) or false negative (green disease). I also document optic disc photographs in both colour and red free for suspect cases.

SP: Tonometry on multiple occasions and at different times of the day with applanation tonometer, CCT, optic nerve and nerve fibre layer (red free) assessment by 90 D, Perimetry:24-2 Sita std.

RN: Careful ocular examination includes SLE, Optic disc and RNFL evaluation with 90D, GAT, CCT, and Gonioscopy (in that order), followed by other detailed evaluation after mydriasis (unless contraindicated) as a routine in all cases when suspected. Minimum Ophthalmological Investigations should include Automated perimetry, Optic disc photographs. However several other investigations are to be advised on suspicion of NTG, or secondary glaucomas.

Q.2 Where do you feel is the need of GDx in current glaucoma practice?

VR: My go-to machine for the retinal nerve fibre layer analysis is the OCT. This is because I would like to do the macula and the Glaucoma evaluation RNFL and the GCC all in one go.

MP: I did use the GDx till around 3 years back but stopped now due to technical issues. All imaging techniques give supplemental information which may vary to some extent. But none of them gives diagnostic accuracy needed in all glaucomas. The current OCT technology has evolved to a point where most information is both comprehensively and rapidly acquired in a reliable manner.

SP: Only if the patient is unable to do perimetry /OCT is unavailable or in glaucoma suspects.

RN: GDx or other imaging techniques should be taken as additives after a careful clinical evaluation. Their role starts in diagnosis if their findings go with clinical Diagnosis. These investigations support the clinical diagnosis and correct it if clinical diagnosis is wrong. Treatment should not be started on basis of these investigations alone. They help in explaining the patients better about their ocular illness. Their important role is in picking up or ruling out subtle progressions during follow up. However, these are expensive, and economic burden on patient must be considered when advising them repeatedly.

Q.3 Where do you feel is the need for SLT in today's glaucoma practice?

VR: Selective Laser Trabeculoplasty (SLT) is a good armamentarium to have in our practice and I do use it now as mainly a third or last line in patients who are at high risk for surgery. There have been studies to show that when used as the first line management and in virgin eyes the outcome is better .. and it reduces intraocular pressure by 20% i.e. approximately 3 -5 mms of Hg and the effect lasts for a duration of 3 to 5 years when the treatment can again be repeated.

MP: I usually start with medications and SLT is an add on if IOP is not under good control. Some advocate SLT as a primary therapy due to compliance with drops and issue of reduced efficacy of medication if given after SLT. SLT has a role to play especially if my aim is to reduce or delay anticipated progression despite antiglaucoma therapy. The efficacy is higher with a greater baseline IOP. I know it may fail with time necessitating further applications. I also understand it is not a modality for all glaucoma subtypes especially pigmentary glaucoma and eyes with inflammation. The IOP reduction would be less for normal tension glaucoma. There are reports of using SLT in angle closure after YAG iridotomy if sufficient angle opens up. The typical situation would be the point where open angle glaucoma patient is on maximum tolerated medicines with inadequate control of IOP or surgery for glaucoma could be deferred/not feasible. A short term IOP control in pregnancy with glaucoma could be achieved where I would like the medications to be reduced or stopped. However the cost and availability of laser are constraints.

SP: For POAG esp in pregnant/lactating female patients; patients who cannot instil meds especially with neurological diseases, dementia patients.

RN: Selective Laser Trabeculoplasty in POAG is helpful in postponing surgery for cases where surgery cannot be taken up for any reason. These are not very promising nor very safe procedures.

Q.4 Do you use neuroprotective drugs in glaucoma? If Yes, then which one?

VR: I only use gingko biloba in very advanced glaucoma patients, only in patients who do not have a gastric ulcer, bleeding diathesis and those who are not on any anticoagulants.

MP: I do not advocate the use of drugs per se for 'neuroprotection' alone. Neither I am against the concept if pushed to the wall in certain patients. In these, a combination therapy with IOP lowering may be needed. Neuroprotection would mean protection of retinal ganglion cells independent of IOP control. For me, the best 'protection' to the patient with glaucoma is rational and regular use of antiglaucoma medications, close monitoring and surgery for the progressing patient despite therapy. However in certain situations, where I believe mere IOP control is not helping, I may choose to use these agents (most commonly, brimonidine) despite their inconclusive evidence.

SP: Brimonidine, if that can be considered one. I also advise antioxidants containing Resveratrol or Citicoline to patients with advanced glaucoma. Since Tumeric (containing curcumin) is easily available and is cheap, I also advise patients to take it.

RN: Neuroprotective having an established role in glaucoma is not available as yet.

Q.5 Which drug do you use as first line therapy in open angle glaucoma?

VR: My first choice of drug in open angle glaucoma is a

prostaglandin analogue. However in fair skinned individuals and unilateral Glaucomas especially where cosmesis is an issue (due to the skin pigmentation, enophthalmos, the eyelash growth and the mild congestion) I would use a Beta blocker as my first line, if there is no systemic contraindications. If systemic contraindications are present I prefer to use a Topical CAI which has a safer systemic profile.

MP: The first line could be a prostaglandin analogue. Concerns about their cost is partly taken care by generic variants. The advantage being a once daily dosage, greater efficacy and greater effect on nocturnal curve. However, if the situation warrants or there is a contraindication to PG analogues, I freely use any of the available drugs including beta blockers, alpha agonists or CA inhibitors. This is true because not all patients require a maximal reduction of IOP.

SP: Depends on how advanced the glaucoma is/patient' ability to purchase medicines. PGA is my first choice.

RN: The first drug of choice for POAG is prostaglandin analogues unless contraindicated or unaffordable for long term use. Now these topical preparations are widely available in our country also, but cost of treatment may still limit the patient's compliance. Several pharmaceutical companies have cheaper and effective preparations. They also have support programmes to help patients. Poor patients should be advised early Trabeculectomy, because they are more non- compliant with medical treatment.

Q.6 With PI available, where do you find the use of Pilocarpine in Narrow angle Glaucoma?

VR: Yag PI is the mainstay in Angle closure Glaucoma. The use of pilocarpine is mainly in patients with Plateau Iris which is confirmed by a UBM.

MP: Though, being the oldest and still widely available drug, personally, my use is now limited. Pilocarpine eyedrops have been used both in open and angle closure glaucoma. Most common use in angle closure disease would be in plateau iris (post iridotomy) and prior to YAG iridotomy. But I do not use it as a 'substitute' for YAG iridotomy at all in angle closure disease. I am careful and explain side effects to patients who may find it uncomfortable due to induced miosis and/or headaches in patients with anticipated prolonged use.

SP: Before doing the PI; when all other meds are unable to get to target IOP, I add Pilocarpine.

RN: Pilocarpine is to be used for PNAG till a PI has been done. Some cases show a persistent high IOP even after PI. If gonioscopy reveals occludable angles even after PI, pilocarpine shall work best in such eyes, otherwise other drugs can be used.

Q.7 Do you practice measurement of ocular blood flow in glaucoma patients? If yes, then how?

VR: No I do not measure ocular blood flow routinely.

MP: My practical use of measuring routine OBF clinically is very limited due to procedural constraints. Epidemiological studies have linked the role of low ocular perfusion pressure (OPP) to development and progression of glaucoma. Ocular hemodynamic studies as a diagnostic modality have evolved in recent times especially with use of Doppler and OCT among others. With time, we should be doing more testing of OBF in susceptible individuals (having IOP independent component) to establish association of improved ocular hemodynamic parameters to improved patient outcomes.

SP: Blood flow with ambulatory BP is helpful so that BP control can be attempted and measuring blood flow blood flow corroborates findings. OCTA is helpful for aiding diagnosis

RN: Ocular blood flow measurement is done by Doppler ultrasound and is difficult to master clinically. I have no experience clinically.

Q.8 Would you like to treat on OCT findings in pre perimetric glaucoma?

VR: It's important to understand that management of glaucoma is not treating an IOP, an OCT or a field. No my treatment of pre-perimetric glaucoma is not based just on OCT... it is based on all the above and the risk factors. Glaucoma is a disease of change so it's only if I see a progression in an OCT or visual field would I want to treat... if there is no change I would still prefer to watch.

MP: I never treat on a positive finding on OCT parameters. I am wary and aware of the pitfalls of imaging. The machine may give false flagging of disease if none exist such as in lack of acquired data in normative database of imaging ex high myopics (red disease), or give normal outputs in glaucoma patients (green disease). Single measurements on these devices should not be considered as diagnostic. A more pragmatic approach is to look for changes over time from baseline which may be suggestive of glaucoma and to correlate it to other clinical and investigational parameters (optic disc evaluation, Visual fields etc) to reach a final conclusion on treating.

SP: No, not as of now.

RN: OCT findings alone should not be used to start treatment.

Clinical or investigational documented progression in glaucomatous damage can be a flag to start treatment in absence of other signs.

Q.9 What has been your experience with micropulse laser?

VR: I have not personally used the micro pulse laser.

MP: The micropulse laser could be used either for micropulse laser trabeculoplasty (MDLT) or micropulse trans-scleral cyclophotocoagulation (MP-TSCPC). Micropulse has been reported a fairly comparable efficacy and better intraoperative and postoperative safety profile as compared to conventional treatment options. Again the cost and availability are major issues.

SP: I have still to use it.

RN: I have no experience with micro-pulse laser though many Ophthalmologists have found it to be very promising.

Q.10 Trabeculectomy with Phacoemulsification. Do you like to combine the two procedures or do them separately?

VR: In a patient with advanced open angle Glaucoma who also has a cataract, I would prefer to combine both Phacoemulsification with a trabeculectomy. In a patient with Angle closure I would discuss with the patient and prefer to do a cataract surgery alone with a sequential trabeculectomy if the IOP is not within the target even with maximum medical therapy.

MP: If there is "visually significant" cataract and I decide for a possible need for glaucoma surgery (high IOP, inadequate control, advanced glaucoma, compliance issues, progression), I combine the two procedures in most of my patients. This may be a single site or twin site surgery. I do staged surgery only if patient does not immediately or in near future require the other. In early cataract, with inadequate control of IOP, I may choose to do glaucoma surgery alone first and explain patient that cataract may progress faster and require surgery later. Similarly in patients with good control of IOP, on one or two antiglaucoma medications and early field defects with no progression, I may choose to do a clear corneal cataract surgery alone and follow up. This is underlined by the fact that I understand there may be some reduction of IOP by cataract surgery alone, especially in angle closure disease.

SP: I do the combination when indicated as it becomes a single surgery and the results are good otherwise doing a single procedure of Trabeculectomy gives better results and inflammation is lesser.

RN: Trabeculectomy and Phaco emulsification surgery should be combined if glaucoma is not controlled by MMT, and cataract is visually disabling. Otherwise it is generally more suitable to do them one after another. Combined surgery has its merits, but possibility of complications must be kept in mind.

Journal Update

Diagnostics (Basel). 2020 Jun; 10(6): 409.

COVID-19 Diagnostics, Tools, and Prevention

Mayar Allam, Shuangyi Cai, Shambavi Ganesh, Mythreye Venkatesan, Saurabh Doodhwala, Zexing Song, Thomas Hu, Aditi Kumar, Jeremy Heit, COVID-19 Study Group and Ahmet F. Coskun

The Coronavirus Disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), outbreak from Wuhan City, Hubei province, China in 2019 has become an ongoing global health emergency. The emerging virus, SARS-CoV-2, causes coughing, fever, muscle ache, and shortness of breath or dyspnea in symptomatic patients. The pathogenic particles that are generated by coughing and sneezing remain suspended in the air or attach to a surface to facilitate transmission in an aerosol form. This review focuses on the recent trends in pandemic biology, diagnostics methods, prevention tools, and policies for COVID-19 management. To meet the growing demand for medical supplies during the COVID-19 era, a variety of personal protective equipment (PPE) and ventilators have been developed using do-it-yourself (DIY) manufacturing. COVID-19 diagnosis and the prediction of virus transmission are analyzed by machine learning algorithms, simulations, and digital monitoring. Until the discovery of a clinically approved vaccine for COVID-19, pandemics remain a public concern. Therefore, technological developments, biomedical research, and policy development are needed to decipher the coronavirus mechanism and epidemiological characteristics, prevent transmission, and develop therapeutic drugs.

Practice Recommendations for Ophthalmic Outpatient Care in the COVID-19 Era

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Abstract: SARS-CoV2 (COVID-19) pandemic has caused unprecedented number of infections and deaths across the world.[1] This pandemic has forced entire nations into self-imposed quarantine to contain the transmission of this virus. For the same reason, the Government of India (GoI) too has mandated a nationwide lockdown, which is now being lifted in a phased manner. In the wake of this pandemic and various government-imposed restrictions, the practice of ophthalmology has been affected drastically. Thus, there is a need for a set of evidence-based guidelines for ophthalmic outpatient care in this COVID-19 era. In this paper, we attempt to summarize a preferred practice pattern (PPP) in these times, especially for Indian ophthalmologists, based on guidelines from various government authorities, healthcare institutions, and various international and regional ophthalmic associations. These guidelines will be required to be updated from time to time as per government protocols & recommendations as well.

PRACTICE GUIDELINES FOR OPHTHALMOLOGISTS DURING THE LOCKDOWN

Scheduled appointments

a. Postponement/Schedule of all the routine outpatient consultations as per the Government of India recommendations zone wise[2]

b. Postponement/Schedule of all elective surgeries and procedures as per the Government of India recommendations zone wise

c. Creating alternate channels for interaction with patients including phone calls, emails, and social media interaction

Ophthalmic Emergencies

The ophthalmologists should triage the patients[3,4] (Figure 1) and decide which patient requires emergent care. This has to be

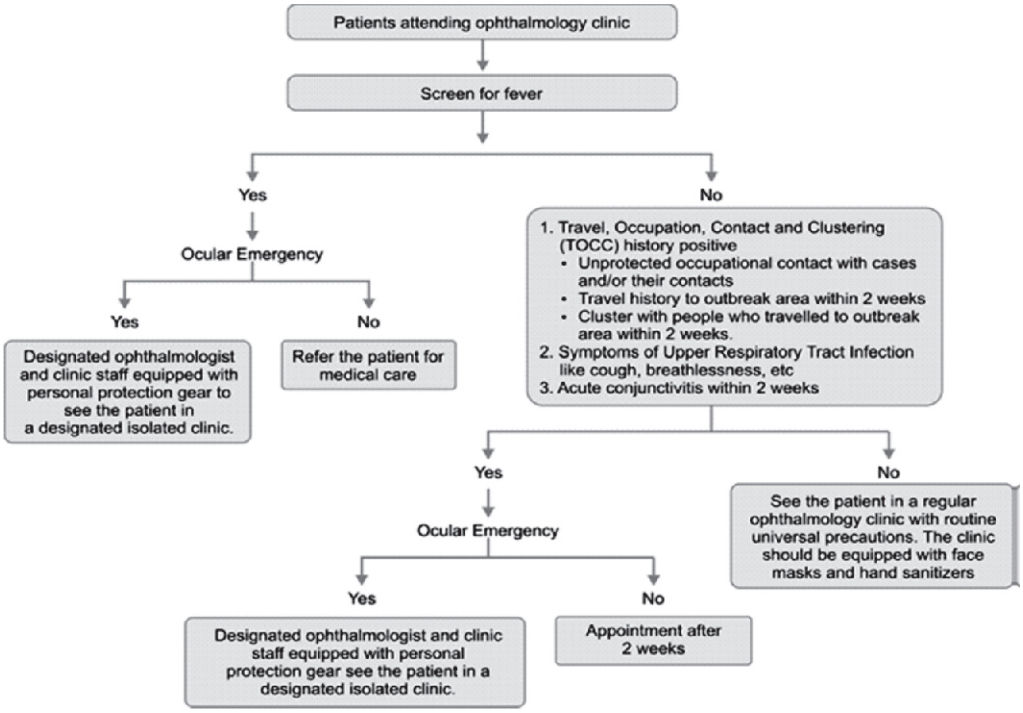

Figure 1: Flowchart showing the triage system to be used in ophthalmology[3,4]

done on case to case basis. This diagnosis-based triage can only be done after the patient has been seen by a medical practitioner. However, if the patient has contacted the call centre of the hospital for an appointment or is met with by the non-medical staff of the hospital, then they may be given a checklist of presenting complaints that may indicate true emergencies.

These include the following:

a. Injury to the eye (chemical, thermal, mechanical)
b. Sudden loss of vision
c. Acute pain
d. Acute red eye
e. Acute onset of eyelid lesions
f. Acute onset of double vision or sudden onset of droopingof the eyelid
g. Acute onset of colored halos, photo phobia, floaters orflashes of light
h. Acute onset of discharge from the eye
i. Acute or subacute (days to weeks) onset bulging of the eye.

Point of entry screening and check in

Triage should be done by an ophthalmologist or a trained ophthalmic technician or an optometrist. Telephonic tri aging to be done as far as possible. The flowchart shown in Figure 1 can be utilized to screen the patients at entry point and for further segregation of the patients.[3,4]

Waiting hall guidelines

a. Maintain a one-meter distance at every point
b. Keep the waiting time minimum in the hospital premises
c. Only one attendant per patient
d. Numbered stickers to be given to every patient
e. Provision of hand sanitizer in the waiting hall
f. Three-ply masks for all the patients and their attendants
g. Keep as many doors open as possible
h. Sanitize the waiting hall frequently

Cleaning of the emergency room and waiting halls

a. After every 2 hours or 3 patients, the emergency room areas, which come in contact such as doorknobs, handles, slit lamps (head and chin rest), tables, benches must be cleaned with freshly prepared 1% Sodium Hypochlorite or 1% Bacillocid Extra solution
b. Every day, the floor and common contact surfaces must be cleaned with 1% Bacillocid Extra solution before work begins and every 2 hours with Lizol
c. The slit-lamp apparatus, especially the joystick, switches and other parts must be thoroughly cleaned with alcohol wipes
d. The rooms should be well-ventilated and well lit
e. All HCWs must be instructed to clean and disinfect (using the standard procedure as recommended by the manufacturer) their equipment such as lenses, indirect and direct ophthalmoscopes, torches, and other such items.

Precautions at ophthalmic evaluation and OPD procedures[5]

a. Protections for head, mouth, nose, and eye (with a surgical cap, three-ply surgical mask, goggles/faceshield) for the examiner and a three-ply surgical mask for the patient. Masks should be changed every 6 hours.
b. Slit-lamp barriers or breath shields. These can be designed indigenously by cutting out a transparent plastic sheet of an appropriate thickness (Figure 2). The slit lamp touch-contact parts should be cleaned by alcohol wipes after examining every patient. Barriers can be washed with soap water, dried and reused

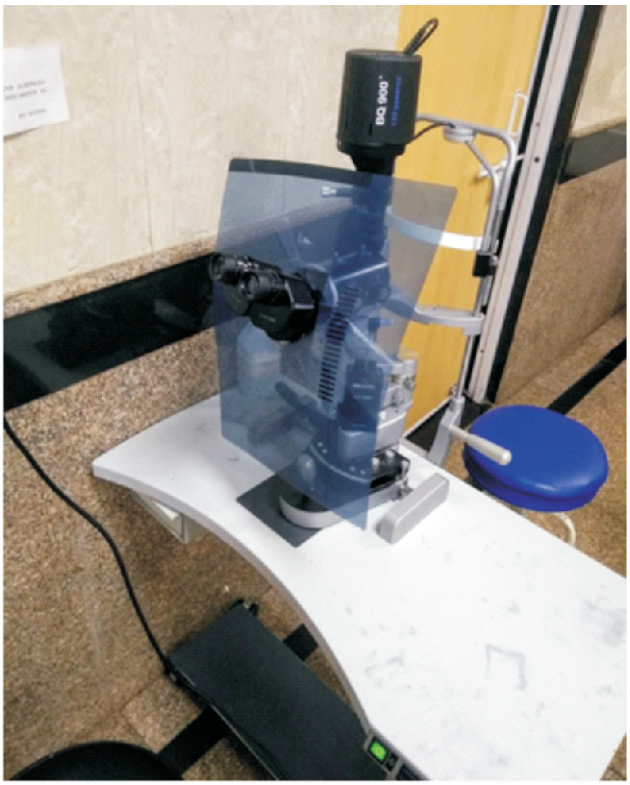

Figure 2: Breath-shield for the slit lamp made using X-ray sheet

c. Alcohol-based hand sanitizer before and after examining each patient
d. Speak as little as possible. The patient should also be informed not to speak during the examination
e. Disposable gowns, gloves and eye protection, cap and N95

mask are recommended if a procedure is planned that will result in aerosols. Details are provided in Table 1[6]

f. Avoid dilatation and nasola crimal syringing if possible. If dilatation is mandatory for a follow-up patient, home dilatation is ideal if there is no known contraindication.

g. Avoid all aerosol-based procedures including non contact Tonometer (NCT). Use of Tonopen with adisposable tip or Goldmannapplanationtonometry (with the cleaning of the applanation cone after every patient) is recommended if IOP measurement is necessary

h. Refraction can be performed using autorefractor or a streak retinoscope where mandated. Trial frame and the metal rim of the lenses used should be cleaned with alcohol-based sanitizer after use.

i. Avoid contact lens trial unless therapeutic

j. Optical dispensing and Pharmacy services should be available, but with 1-meter distancing protocolk. Retinal examination should be done in patients who need it, strictly with an indirect ophthalmoscope. Avoid direct ophthalmo scopy and contact lens-based fundus examination

l. Infants undergoing ROP screening must be placed on a designated crib with a plastic or polythene sheet, by the mother who uncovers the face of the infant and steps away more than 2 meters. The barrier sheet is replaced or sanitized between successive infants

m. In case of urgent ophthalmic problems in a patient who is at high risk for COVID-19, transmission precautions for treating ophthalmologists include full body protection (full PPE or an HIV kit)

n. Since conjunctivitis is a part of the spectrum of COVID-19,[7-10] all patients with conjunctivitis should be COVID-19 suspects and should be examined in isolation, with slit lampbreath shields, using N95 mask and disposable gloves [Table 1]

o. Prophylaxis: ICMR has advised oral Hydroxychloroquine (HCQ) 400 mg BD on day 1, followed by 400 mgOD weekly for 7 weeks.[11] This must be taken only after direct consultation with an internal medicine expert

Table 1: Recommendations on use of PPE by ophthalmologists[6]

COVID-19 status	Risk of life- or sight-threatening harm if not seen urgently (based on triage	Brief close contact (e.g., slit-lamp examination)	Prolonged close contact (e.g., laser, intravitreal procedures)	Aerosol-generating procedures (e.g., general anesthetic, ophthalmic surgery involving high-speed devices)
Asymptomatic	Low	Discharge or postpone until after pandemic or offer remote consultation.		
Asymptomatic	High	Slit-lamp breath shield, Three-ply surgical face mask, Protective goggles, Surgical cap, Surgical scrub suit	Slit-lamp breath shield, Three-ply surgical face mask, Protective goggles, Surgical cap, Surgical scrub suit	Slit-lamp breath shield, N95 face mask, Protective goggles, Surgical cap, Disposable sterile gloves, Disposable surgical gown wom over surgical scrub suit
Suspected or confirmed COVID-19	Low	Discharge or postpone until after pandemic or offer remote consultation.		
Suspected or confirmed COVID-19	High	Isolate the patient Slit-lamp breath shield, N95 face mask, Protective goggles, Surgical cap, Surgical scrub suit, Disposable plastic apron, Disposable gloves	Isolate the patient Slit-lamp breath shield, N95 face mask, Protective goggles, Surgical cap, Surgical scrub suit, Disposable plastic apron, Disposable gloves	Isolate the patient Slit-lamp breath shield, FF3 respirator, Protective goggles, Face shield, Surgical cap, Surgical scrub suit, Disposable scrub suit, Disposable plastic apron, Disposable gloves, Disposable shoe cover

Precautions at diagnostic procedures

a. Non-essential testing and imaging should be deferred

b. Gonioscopy and visual field examination should be avoided unless mandatory

c. Optical coherence tomography (OCT) and retinal imaging procedures to be done based on ophthalmologist's discretion

d. All imaging equipment should be cleaned before and after each patient, using the technique recommended by each manufacturer

Personal Protective Equipment (PPE)

PPEs are protective gear designed to safeguard the health of workers by minimizing the exposure to a biological agent.[12] Components of PPE are goggles, face-shield, mask, gloves,

coverall/gowns (with or without aprons), head cover and shoe cover. Table 1 shows recommendations for use of PPE by ophthalmologists based on the COVID status, risk of vision loss, duration of expected contact with the patient and need for aerosol-generating procedures

Infection control and prevention measures[13]

a. Hand hygiene: HCWs should perform hand hygiene using alcohol-based hand rub (minimum 20 seconds) or by washing with soap and water (minimum 20 seconds).If hands are visibly soiled, use soap and water for hand wash. Hand hygiene should be performed frequently, before and after examination of a patient

b. Mask and PPE etiquette

   i. Place the mask carefully to cover mouth and nose and tie securely to minimize any gaps between theface and the mask. Wear the PPE as instructed by experts.

   ii. While in use, avoid touching the mask

   iii. Remove the mask by using the appropriate technique (i.e., do not touch the front but remove the lace from behind)

   iv. Remove PPE in the reverse order that it was worn and discard the material in appropriately colored disposal bags for infective plastic items (red)

   v. Do not reuse or use three-ply surgical mask/N 95 masks for more than 8 hours.

   vi. Mask and PPE etiquettes should be followed by hospital staff as well.

c. Environmental hygiene: Freshly prepared 1% Sodium Hypochlorite or 1% Bacillocid Extra solution can be used as a disinfectant for cleaning and disinfection for ophthalmicinstruments between patients. Leaving thesolution for a contact time of at least 10 minutes is recommended. Alcohol (e.g., isopropyl 70% or ethyl alcohol 70%) can be used to wipe down surfaces where the use of bleachis not suitable, e.g., metals. The slit lamp contact surfaces

d. OPD areas and the OT are fumigated with 2% Bacillocid Special at the end of every day

e. Follow an open door, non-AC environment if feasible.

Guidelines for maintenance of equipment

a. Equipment maintenance to be done once a week by trained OT Technicians

b. All ACs, AHU, dehumidifiers to be switched on at least twice a week

c. All OPD and OT machines, other than Excimer and Femtosecond laser machines, to be switched on fora minimum of 15 minutes twice a week.

d. Excimer and Femtosecond laser machines need to be calibrated and tested at the end of the lockdown period and before any patient is posted for these procedures. It will be prudent to discuss maintenance guidelines with the specific manufacturer

e. For OCT, topographers, etc. all printers need to be given one print command as test print at least once a week

f. All lasers, including Nd:YAG and retina lasers, will need to fire for 50 blank spots at least once a week

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Resumption of Work after the Lockdown is Lifted

It is certain that, after the lockdown is lifted, the viral infection will still be prevalent in the population andhealth care workers, especially ophthalmologists and others who come in close contact with patients will continue to be at increased risk of contracting the infection unless some precautions are continued to be taken. A lot of the OPD and OR procedures can be adapted for routine use irrespective of a pandemic. Most of the measures mentioned above to be adopted during the lockdown should be continued even after the lockdown is gradually lifted atleast till such time whenthe virus spread is relatively high.

Discussion

The COVID-19 infectionis posing an unprecedented challenge to the health care system.[1] Ophthalmologists are at a slightly higher risk of transmissiondue to their close contact with patients,[16,17] tears[9] as well as procedures that generate aerosols. It is important tomanage patients effectively, using preferred practices and recommendations as mentioned above. Precautions to be taken during OPD and surgical services,both during and after the lockdown have been lifted.

Conclusion

SARS-CoV-2 has created a healthcare emergency all over the world and the development of vaccine against it is still in the initial stages. Thus, the fight against the SARS-CoV-2 virus appears to be a long one. Using preferred practices as far as possible will protect us in these difficult times. Various measures mentioned in this paper such as triage, PPE, sterilization techniques, tele consultation and social distancing are crucial in blunting the effect of this pandemic.

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Interesting Facts

Bats actually have good eyesight -- they just don't need it much.

Bats aren't blind. They're not even a little nearsighted. What they do have is exceptionally acute hearing. They also possess sonar so sophisticated, it tops that used by the U.S. military [source:Science Daily]. This sonar, or echolocation ability, involves the bats producing ultrasonic pulses, or sounds, which then reflect off objects. The bats process the reflected sound to avoid obstacles, to effectively hunt and to properly orient themselves.

Since bats are nocturnal animals, and have such amazing echolocation skills, their sense of sight isn't that important. Perhaps this is why the myth about their blindness arose. It also may have something to do with the fact that bats, the world's only flying mammals, have long been viewed by humans as both fascinating and repulsive -- qualities that have led to many myths about the creatures.

Newer Modifications in IOL Technology

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Abstract:

IOL technology is one of the fastest developing technologies in recent years in ophthalmology. Monofocal in the bag IOL is the most commonly used IOL all around the world. In developing countries, use of this IOL is almost standard. There are many different IOL options in the market and appropriate IOL must be individualized for each patient to reach perfect postoperative outcomes. Presbyopia correcting intra ocular lenses (IOLs) have revolutionized refractive cataract surgery, as there is continuous evolution in materials and optical designs going on which allowed ophthalmologist for a better balance of functionality of IOL while reducing unwanted symptoms. Presbyopia correcting IOLs have become a focus of attention in IOL selection discussions with patients due to the increasing number of activities that require near and intermediate vision in our modern world, such as smart phones, and computers. Numerous IOL platforms have been designed to extend the range of focus as "presbyopia correcting IOL" options, and three main categories can be identified: those including multifocality (functional bifocal and trifocal IOLs), accommodative or pseudo accommodative IOLs, and extended depth of focus (EDOF) IOLs. Regardless of the optical design or strategy chosen to achieve relative spectacle independence, a certain degree of visual compromise can still be anticipated. In this article, we have tried to enumerate all the recent developments in IOL technology, their specific mechanisms, characteristics and performances to help ophthalmologists to decide the best possible Intra ocular lens for his/her patient, to achieve the best possible visual outcome and to his patient's satisfaction.

Introduction:

IOL technology is one of the fastest developing technologies in recent years in ophthalmology. Monofocal in the bag IOL is the most commonly used IOL all around the world. In developing countries, use of this IOL is almost standard. There are many different IOL options inthe market and appropriate IOL must be individualized for each patient to reach perfect postoperative outcomes.

History:

In 1949, English ophthalmologist Dr. Harold Ridley performed first successful intraocular lens (IOL) implantation. He presented this new surgical method in 1951 Meeting of American Academy of Ophthalmology (AAO) and reported results of first 8 operations in 1952.[1] In those days, many of ophthalmologists opposed to this method because many complications were seen such as unpredictable high postoperative refractive error, uveitis, glaucoma, corneal decompensation and permanent visual loss. Nevertheless Dr Ridley continued and kept on developing newer methods for cataract extraction and IOL implantation.

Original Ridley lens was designed for use in posterior chamber. Subsequent designed IOLs were implanted in anterior chamber because there were no modern operation microscopes in those days. So along with operating instrument modification and development for microsurgery there was constant development in IOL shape, design, material etc. Finally, modern IOLs were designed for use in anatomical localization of human crystalline lens.

Changes in IOL modification is based on

- Advances in IOL materials
- Advances in IOL shapes and designs.

Material:

If we talk about materials, PMMA (polymethyl methacrylate) have ruled as best material for IOL since original Ridley lens was used. As time passes IOLs have divided in two main category's non foldable and foldable IOLs. Non foldable IOLs are made of PMMA and foldable IOLs are made of silicon and acrylic.

Acrylic IOLs

Acrylic bio material is the most commonly used optic material. Now these acrylic lenses were further divide on their bases of their behaviour inside ocular environment in two types

1. Hydrophilic acrylic lenses and

2. Hydrophobic acrylic lenses.

Hydrophilic, as the name suggests, absorbs and retains water. It is the consistency in the ability of the material to take up and retain the water, which make refractive power and elasticity deviations in intra ocular lens. While in hydrophobic lens, the material tends to absorbs minimal amount of water. The Refractive power of Hydrophobic lens is depends on the

molecular orientation and not on molecules itself. It is for this reason, the reproducibility, accuracy, and sensitivity of the refractive outcome will be high in case of hydrophobic IOLs.

Selection between hydrophilic and hydrophobic IOL depend upon capsular bio compatibility. Capsular bio compatibility of hydrophilic acrylic IOL is low. Capsular bio compatibility is very important because it affects long term visual outcomes negatively through posterior capsular opacification (PCO) and deformation of IOL surface.[2] For this reason, most of the cataract surgeons use more common hydrophobic acrylic IOL than hydrophilic acrylic IOL if possible. Uveal bio compatibility and some optical properties of hydrophilic acrylic IOL are high.[3,4] Additionally, one study reported bacterial adhesion to surface of IOL is fewer in hydrophilic acrylic IOL than other IOLs.[5] New designed hybrid acrylic IOL combine advantages of two acrylic IOLs and provides higher uveal and capsular bio compatibility. Thus, this material yields better surgical outcomes via reducing postoperative anterior chamber cells and PCO rate.[6]

Heparin coating is a surface modification that enhances the uveal bio compatibility of IOL. Fewer aqueous flare are seen after implantation of heparin coated IOL.[7] Although heparin coated IOL increases the risk of PCO, but this increase in PCO is not found statistically significant.[8] And this IOL can be used in patients with high-risk for postoperative intraocular inflammations.

Silicon IOL

Polymers of silicone and oxygen have been employed as IOL material since 1984, with the purpose of implanting the IOL through an incision narrower than IOL diameter. The refractive index is usually between 1.41 and 1.46, the optic diameter is 5.5–6.5 mm. Current models are 3 piece, with PMMA, polyvinyl difluoride (PVDF) or polyamide haptic. Because of the low refractive index, the optics is rather thick, requiring incisions larger than 3.2 mm to implant higher power lenses. However, the abrupt opening of silicone IOLs inside the anterior chamber remains a problem for surgeons.

Designs and Shapes:

The variation in optic and total diameter of IOL is limited. Larger optical size is advantageous in visualisation of peripheral retina, it is disadvantageous in terms of folding and implantation through small incision. Optic diameter of IOLs is almost standard due to this limitation. When total diameters are compared, average rotation and stabilization are similar in IOLs with 12 mm and 13 mm total diameters.[9]

There are various haptic designs on the market such as plate haptic, C haptic, modified C haptic, J haptic, quad ripod haptic and more. A study comparing various haptic types reported that double C haptic contacts the lens capsule at 4 points. Double C haptic design maintains anteroposterior and rotational stability of IOL. [10] In postoperative 3rd month, the average rotation of IOL was found as 1.85 degrees in this haptic design .[11]

Planar and angular haptics are another differentiation in haptic design. There can be 5, 10 or more degrees in optic haptic junction of IOL with angular haptic. IOL deformation is less in planar haptics while anterior capsule opacification is less in angular haptics.[12] PCO and IOL decentralization occur equally in both of planar and angular haptics.[13]

With advancement in optic design, toric IOL are in high demand for correction of astigmatism, toric IOL can correct very high degree astigmatism such as 30 dioptres but cylindrical power of toric IOL on the market are limited. High degree cylindrical power causes rotational instability and increased postoperative refractive error after cataract surgery because cylindrical power help in rotational stability of an intraocular lens. This reason, postoperative refractive predictability of surgery reduces after implantation of high degree toric IOL.[14,15]

All IOLs in the market block UV electromagnetic radiations. Additionally, some IOLs contain blue and yellow filters to protect retina from photo toxicity. Thus, the light permeability of IOL is approximated to the young human natural lens. But one study shows that blue light is necessary for scotopic vision in night and melatonin suppression in day.[16] So, benefits of these filters are controversial and further research is needed. At least, we know that colour filter coated lenses do not negatively effects postoperative visual acuity and contrast sensitivity.[17]

Refractive power of IOL is same in all over the surface of IOL in spherical optical design while, in aspheric, optic makes overrefraction in periphery of IOL and causes decreases spherical and chromatic aberrations, which is not in case of Spherical optical design, where there is an increase in spherical and chromatic aberration which reduce visual acuity and contrast sensitivity.[18] Additionally, photic phenomena such as glare and halo occur more commonly in spherical optic than aspheric optic.[19] For these reasons, IOL with aspherical optical design is used more frequently than IOL with spherical optical design.

Recent modification in Intraocular lenses

There is constant evolve in technology behind intra ocular lenses in recent years

- Aspheric IOLs, monofocal IOLs that compensate for spherical aberration;
- Toric IOLs, designed for eyes with astigmatism; and
- Presbyopia-correcting IOLs, including accommodating and multifocal lenses.

Aspheric IOLs

An aspheric IOL aligns the light rays to compensate for the positive corneal aberration, resulting in enhanced clarity and image quality. In addition, the use of thinner IOLs permits surgeons to create smaller incisions, which are more likely to be self-sealing.

Currently available aspheric IOLs manufactured by Alcon, Abbott Medical Optics (AMO), Bausch & Lomb, Hoya, Lenstec, and STAAR. Studies comparing the use of an aspheric lens with a traditional lens found that although visual outcomes were the same, eyes receiving the aspheric lens demonstrated superior functional performance in contrast sensitivity with a night-driving simulator and improvement in contrast sensitivity.[20,21]

Multifocal IOLs

These Intraocular lens are design to give us near, intermediate and far vision with single IOL, Multifocal IOLs have two distinct foci with blurry vision in between. Focusing on one, may cause glare and haloes from the other. These are the main drawbacks cause's disturbances which are especially noticeable under dim lighting conditions. However, 2 studies demonstrated good patient satisfaction and visual outcomes with the multifocal lenses .[22,23]

Bifocal IOLs

Mplus, Mplus X (Oculentis) and SBL-3 (Lenstec) aresingle-piece refractive multifocal IOL of hydrophilic acrylic with a hydrophobic surface. It has an inferior surface–embedded segment with a near addition (add) of+3.00 D. It is based on rotationally asymmetric segmented bifocal IOLs with sector-shaped near vision segment giving two focus zones for better depth of focus (Figure: 1 & Figure: 2).

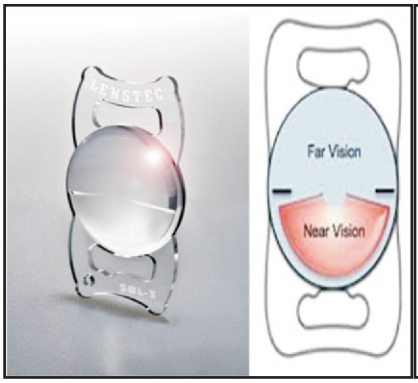

Figure 1: SBL-3: Segmented Bifocal Lens Source: https://www.lenstec.com/

Figure 2: Distance and near sectors of the aspheric nonrotational symmetric multifocal IOL. A: Plate-haptic model. B: Model with Cloop haptic.

Source: Jan A. Venter, MD, J Cataract Refract Surg 2013.

Trifocal IOLs

FineVision (PhysIOL), PanOptix (Alcon)(Figure: 3), AT Lisa (Zeiss)(Figure: 4) and AcrivaReviol (VSY Biotech) are trifocals (3 points of focus, near, intermediate and far). These trifocal lenses are also available on toric platform which help in managing astigmatism. Trifocal lens help in providing clear and better intermediate vision compared to bifocal intraocular lens by using second-order light diffraction and asymmetric light distribution.

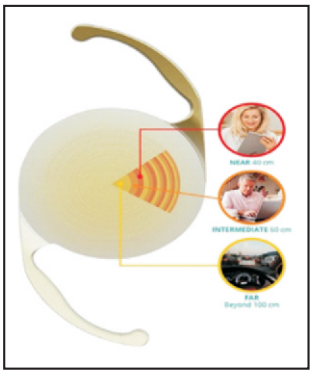

Figure 3: Acry Sof Pan Optix IOL

Figure 4 : AT LISA tri 839 MP.

Source: Wolfgang Riha, MD

Source: https://www.eyeassociatesoftallahassee.com

EDOF IOLs (Extended depth of focus)

The basic principle behind EDOF IOLs is to create a single elongated focal point to enhance the depth of focus or range of vision.[24] EDOF IOLs is based on diffractive echelette designand forms a step structure. The height, spacing, and profile of the echelettes are optimized to achieve constructive interference of light from different lens zones, thus producing a novel light diffraction pattern. In addition, proprietary achromatic technology and negative spherical aberration correction improve the image quality.[25]

EDOF IOLs have generally given good uncorrected distance and intermediate vision: however, near vision from standard multifocal may be better. Therefore, it may be implanted in the dominant eye first followed by a micromonovision strategy with EDOF IOL or a multifocal in the non-dominant eye is recommend by many leading ophthalmologist.

EDOFs like the Tecnis Symfony IOL (AMO) (Figure: 5)use a biconvex design, anterior aspheric surface, posterior achromatic diffractive surface with an echelette design to give better intermediate vision with less haloes and light scatter.We have a latest IOL from Tecnis family called Tecnis synergy IOL. The Tecnis Synergy IOL provides a broad range of continuous vision covering from distance to 33 cm; eliminates the visual gaps present in trifocal and other multifocal technology,

offering patients the freedom to focus within the range; continues to deliver superior performance in low-light conditions; and demonstrates reduction in halo intensity for tasks like night driving, as demonstrated in clinical simulations.

Tecnis Eyhance IOL is designed to extend depth of focus from distance to intermediate vision. In this, there is a continuous change in power from the periphery to the center of the lens, creating a unique anterior surface that improves intermediate vision, maintains distance image quality comparable to aspheric monofocal IOLs, delivers a profile of photic phenomena similar to monofocal and keeps on reducing spherical aberration to near zero. Tecnis Eyhance IOL, unlike other monofocal lenses, is not based on a spherical-aberration (SA) based or zonal design, but the continuous power profile is created with a higher order asphere.

AT LARA 829MP (Zeiss) (Figure: 6) is the latest EDOF lens to appear. It has a diffractive aspheric design, chromatic correction and smoother phase zones that optimise contrast sensitivity and minimise light scattering and visual side-effects.

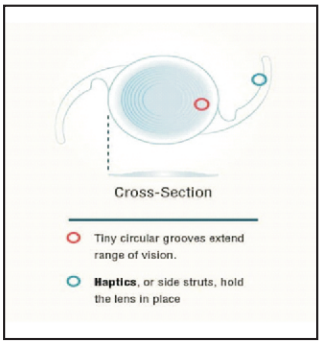

Figure 5 :
Tecnis Symfony IOL
Zeiss AT LARA toric
Source:
https://www.zeiss.com/

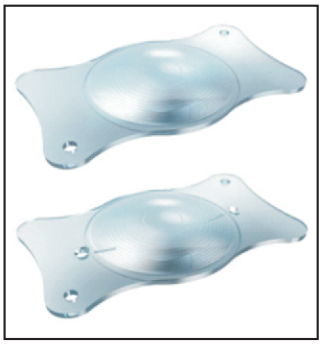

Figure 6 :
Zeiss AT LARA 829MP &
929M/MP

Source:
https://alexandria.vancethompsonvision.com

Small-aperture IOLs also extend depth of focus. These are especially effective in post LASIK, post RK eyes and in irregular corneal astigmatism. In the presbyopia eye, the natural lens cannot compensate for defocused peripheral light that degrades image quality and range of vision while The IC-8 IOL uses small aperture technology disrupting peripheral light rays and allowing central focused light to reach the retina resulting in clear vision across a broad range of distances.

IC-8 IOL combines the principle of small Aperture optics with a high quality aspheric mono focal. IC-8 is one-piece hydrophobic acrylic IOL. IC-8 IOL can compensate for up to 1.50 D of astigmatism without needing to be placed on a particular axis, just like pin hole principle. The small (1.36 mm) non-diffractive aperture of the IC-8 lens, together with the absence of diffractive surface structures in the IOL, allows it to act as a 'universal' corrective lens (Figure: 7).

XtraFocus Pinhole implant (Morcher) designed by Trinidade et al. is another small-aperture sulcus IOL made of black acrylic with a central pinhole(Figure: 8). Fundus imaging is possible and vitreo-retinal surgery can be performed when required through both these IOLs, IC-8 and XtraFocus Pinhole implant.

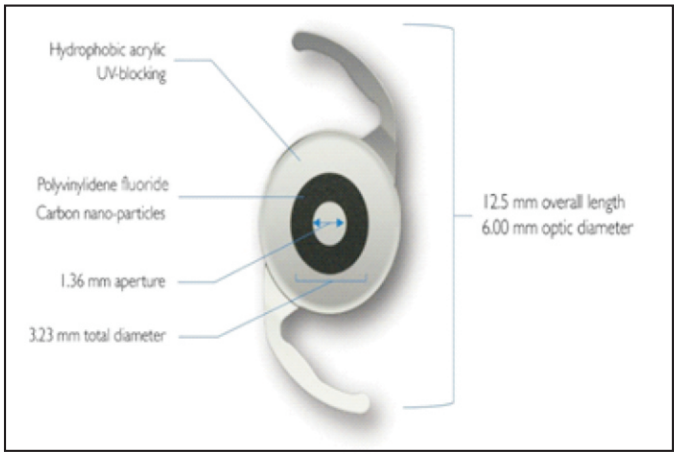

Figure 7 : IC-8 Small aperture IOL
(Lens platform to deliver the first implantable small aperture intraocular lens.)
Source: https://theophthalmologist.com/

Figure 8 :
Xtra Focus Pinhole implant
Source: https://eyetube.net/

ACCOMMODATIVE IOLs

Accommodating IOLs are designed to mimic the changes in the natural lens by inducing a transient and rapidly reversible change in the optical power of the eye

These changes can be done by two ways

1. Change in shape of IOL
2. Change in Position of IOL within bag.

Accommodative IOL help to provide good vision for near, intermediate and far. Accommodating IOLs generally are not associated with loss of contrast sensitivity, but accurate placement is essential for optimal results. There are some partial accommodating IOLs which rely on changes in axial position of the IOL like Single-optic IOLs such as Crystalens

(B&L), 1CU IOL (HumanOptics), Tetraflex (Lenstec) (Figure:10) as well as dual-optic IOLs such as Synchrony (AMO) give antero-posterior movement said to give some degree of both near and distant vision

Synchrony IOL (Visiogen, Abbott Medical Optics, AMO, and Santa Ana, Calif.) is a single-piece dual-optic, silicone lens designed to mimic the natural lens (Figure: 9). It has a 5.5 mm high plus anterior optic of +32 D, coupled to a 6.0 mm negatively powered posterior optic. The concept is that these two lenses are separated by a spring-activated mechanism. The haptic separate the lenses at a given distance under constriction of the capsule, and during relaxation of the capsule following accommodative effort, anterior movement of the positive anterior optic produces increased power for near tasks.[26]

Several options now available are getting closer to the goal of restoring accommodative vision. Some of these act by various mechanisms, including changing optic shape, curvature or thickness to change focus, In-the-bag accommodative IOLs are an interesting innovation.

Figure 9 :
Synchrony dual-optic lens
Source: Abbott Medical Optics

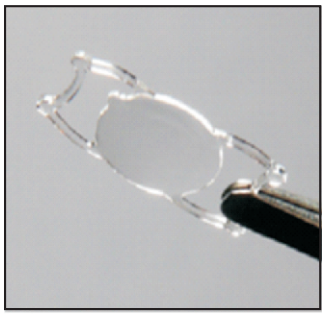

Figure 10:
Tetraflexlens
Source:
Paul. J. Dougherty. M.D

FluidVision (PowerVision) IOL

FluidVision IOL is a hydrophobic acrylic lens with a hollow optic and two hollow haptic that are filled with a refractive index-matched silicone fluid and are connected by fluid-filled channels (Figure: 11).

When the ciliary muscle contracts in response to a near stimulus, the resulting relaxation of zonular fibres causes the capsular bag to contract, forcing fluid from the haptic into the optic, making it more convex and thereby increasing its dioptric power.

"FluidVision movement translates into a true shape change for seamless vision from near to distance," said Dr Nichamin, Vail, Colorado, USA. The FluidVision 20/20 (PowerVision) can provide a broader range of focus than earlier models, according to the results of a study presented by Louis D. "Skip" Nichamin, MD at the 36th Congress of the ESCRS in Vienna, Austria. And in this study Dr Nichamin predict the ability to meet design objectives and deliver 20/20 vision at all distances .[27]

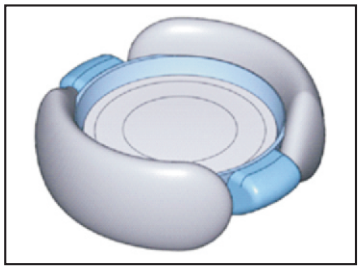

Figure 11 :
Fluid Vision IOL
Source: Power Vision

Sapphire IOL (Elenza)

ELENZA combineselectronically controlled, remotely programmable, customisable nanotechnology, artificial intelligence (neural networks-based memory), and advanced electronics to seamlessly autofocus an optic from far to near without movement focus in response to pupillary changes. Therefore, the lens doesn't have to rely on precise contact with ciliary muscles to move and accommodate properly.

Juvene (LensGen) is a two-lens modular IOL made of a monofocal base lens into which a fluid-optic accommodating component that changes curvature is placed.

WIOL-CF IOL

WIOL-CF accommodative IOL (Figure: 13) was invented by Professor Otto Wichterle and his collaborators at the Institute of Macromolecular Chemistry in Prague. Its design is based on the biomimetic principle: the hydro gel material used and the lens geometry simulate some of the key properties of the crystalline lens itself.The shape of the lens may be biconvex, planoconvex or convex–concave, according to the dioptric power. The suggested A-constant for implantation is 120 and the recommended formula for the calculation of the dioptric power of the WIOL-CF is SRK II or SRK–T. Pseudo accommodation up to 2.5 dioptres can be achieved with the WIOL-CF. Its soft material and continuous contact with the posterior capsule allows some axial movement and deformation of the lens following ciliary muscle contraction.[28]

Possible Mechanisms of pseudo accommodation is the anterior–posterior movement of the implant due to tightening and relaxation of the ciliary muscle. This type of accommodation is similar to natural accommodation, but rather than occurring due to a change in lens curvature and refractive power, the movement of the lens causes an increase or decrease in the distance between the lens plane and the retina.

Dyna curve IOL (NuLens)

NuLensDynacurve IOL (Figure: 12) uses the capsular bag as a component of a moving diaphragm, consisting of the collapsed capsular bag, zonules, and the ciliary processes. The dynamic diaphragm transfers force from the contracting and relaxing of the ciliary muscles to the device attached to it. A piston, activated by the capsular diaphragm, pressurizes a small, rigid

chamber containing a silicone gel. The chamber is fixated to the eye wall at the ciliary sulcus so that movements along the optical axis are avoided. The silicone gel is pressurized by forward movements of the capsular diaphragm and depressurized by backward movements of the diaphragm. The pressurized gel was displaced through a round hole in the anterior (or posterior) chamber wall to form a lens-shaped bulge that continuously changed its curvature in correlation with the ciliary muscle's movements. In the more current design, the "hole" has been replaced by a flexible membrane that can be modified to provide a spherical or aspherical dynamic surface. The prototype of the Dynacurve used in the pilot study required a 10- to 11-mm incision for implantation. To decrease the incision size and improve the surgical procedure, NuLens redesigned the Dynacurve IOL to what it looks like today—a base plate and a haptic unit that requires a 5-mm incision. With recent modifications to the rigid components of the lens, it is reasonable to expect a sub–3.5-mm incision version of the device .[29]

Figure 12 :
NuLensaccommodating IOL
Source: I. Howard Fine, M.D.

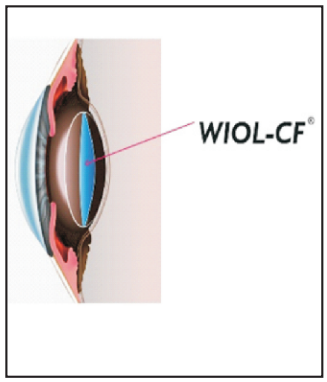

Figure 13 :
WIOL-CF
Source: behance.net

Special IOLs

Adjustable IOL

RxSight (formerly Calhoun Vision) developed the first light adjustable lens (RxLAL). The 3-piece RxLAL includes diffusible, photosensitive silicone macromers that are dispersed in the overall silicone matrix. Cataract surgery with RxLAL implantation is performed using standard techniques. Approximately 3 weeks later, the patient is refracted and a slit lamp based digital light delivery device (LDD) system is used to deliver the ultraviolet(UV) light in a precisely programmed pattern to induce a predictable change in the shape and refractive power of the optic. Treatment times rangebetween 60-120 seconds. After the newly adjusted refraction is confirmedseveral days later, a "lock-in" dose is given with the LDD to polymerizeall remaining macromer, at which point no further refractive change willoccur. Patients wear special UV blocking spectacles until the lock-in step iscompleted, after which they are no longer required. It is still under development.[30]

Perfect Lens LLC is developing a novel technology called refractive index shaping (RIS) that can modify the refractive properties of an implantedIOL in situ with a femtosecond laser.

Piggyback IOL

Piggyback lenses are best used when there is a refractive error which is large enough to correct with excimer laser treatment or IOL removal surgery.Piggyback IOL, which works best in patients with a hyperopic postoperative refractive error.[31]

For placement of piggyback lens in the capsular bag, an IOL with a negative shape factor such as the three-piece hydrophobic acrylic IOL is an excellent choice because at +30.00 D, all but 1/5th of the lens power is located on the posterior surface. For the ciliary sulcus lens, a large diameter, low profile, round edge, biconvex newer generation silicone IOL, such as the Staar AQ-2010V (+5.00 D to +30.0 D) or the extended power range Staar AQ-5010V (-4.00 D to +4.00 D) is recommended.

The Sulcoflex (Figure: 15) is a one-piece hydrophilic acrylic IOL with a 6.5-mm optic and 13.5-mm overall length. The optic has a round edge with a concave posterior surface and convex anterior surface. The haptic have 10° posterior angulation. These characteristics ensure separation of the IOL from the iris anteriorly, and the primary IOL posteriorly, resulting in significant reduction in the risks of ILO and iris chafing.

Anti Dysphotopic IOL

Dysphotopsia may be one of the most under recognized complications following otherwise unremarkable cataract surgery. Based on subjective symptoms, up to 20% of patents have negative dysphotopsia (ND), a temporal dark shadow after intraocular lens implantation. Other patients have positive dysphotopsia (PD), characterized by light streaks, arcs, central light flashing or star bursts. Some patients may have both ND and PD.[32]

Dr. Masket published reverse optic capture (ROC), either as a therapeutic or prophylactic measure for ND, in 2011. But primary ROC is not without concern. All of the eyes that underwent primary ROC placement had fibrotic PCO that required laser posterior capsulotomy within three months of the initial surgery. And long-term piggyback or sulcus placement have the potential for iris chaffing and decentration.

Dr. Masket has developed Anti Dysphotopsia IOL(Figure: 14) to avoid ND and PD, they are currently marketed in name of the Tassignon "BIL" (Morcher) and the Femtis (Occulentis).

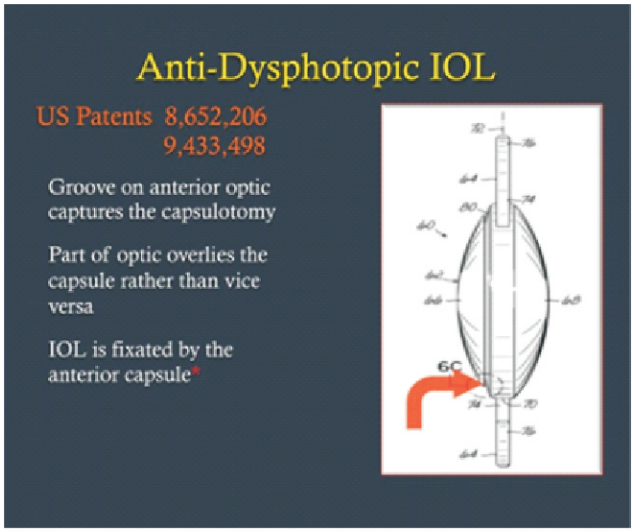

Figure 14: Anti-Dysphotopic IOLSulcoflex IOL
Source: Howard Larkin

Figure 15:
Source:
Richard S. Hoffman M.D

Age related Macular Degeneration (AMD) IOL

In 2015, a novel approach designed by Scharioth was introduced to the market: an intraocular lens (IOL), which can be placed into the ciliary sulcus as a secondary or add-on lens. Therefore, it offers a solution for pseudophakic AMD patients, as it is possible to be implanted any time after the cataract surgery. Moreover, only a small, corneal incision (approximately 2.4 mm in diameter) is required. The Scharioth macula lens for AMD has central 1.5mm diameter with +10D add giving magnification of about 2X.[33]

- The SML (Figure: 16) is made of a copolymer of Hydrophilic and Hydrophobic Acrylic with 25% water content.
- It comes with a UV absorber and is available with an additional blue light filter.
- The special convex-concave optic maintains distance between the implants, preventing IOLs from touching each other.
- Due to its round polished edges the IOL has no chafing effect.

Mode of action is using the near triad reflex of miosis accommodation and convergence.

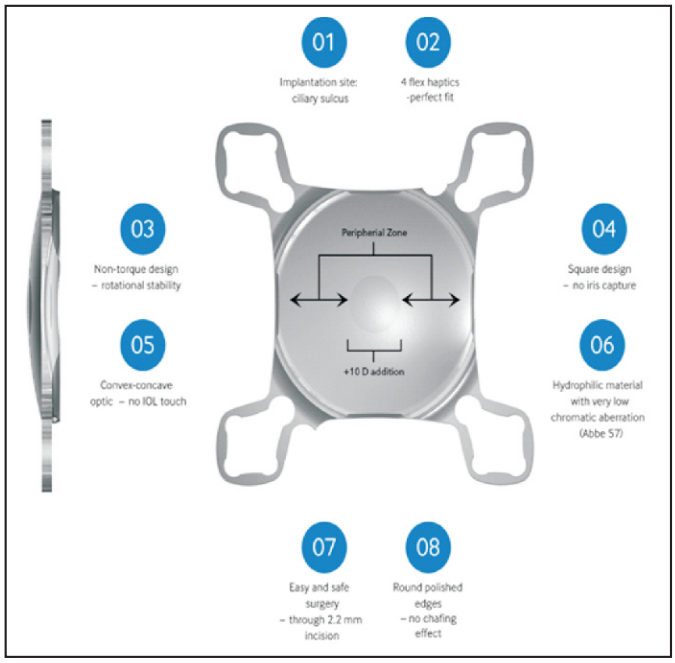

Figure 16: SML (Scharioth Macula Lens)
Source: Medicontur

Mini Well IOL

The Mini Well Ready IOL uses wavefront technology to enhance range of vision and compensate for presbyopia in cataract surgery and refractive lens exchange.The SIFI Mini WELL Ready (Figure: 17) is a preloaded, single-piece hydrophilic acrylic IOL with a hydrophobic surface. The overall diameter is 10.75mm with four closed-loop haptics with 5-degree angulation. The biconvex optic of 6mm diameter has three annuli, an outer monofocal zone and two inner zones with spherical aberrations of opposite signs. The innermost zone, or D1, is 1.8mm wide and has a positive spherical aberration, creating the intermediate focus. The middle zone, or D2, is 3.0mm wide and has a negative spherical aberration, contributing to near focus. The outermost zone, or D3, is a monofocal optic with a diameter of 6.0mm that is responsible for creating the far focus. The lens features an equivalent addition of +3.0D corresponding to a spectacle plane addition of +2.4D. Power ranges from 0 to +30D (0.5D increments from +10.5 to 30.0D). The company's estimated A-constant is 118.6.[34]

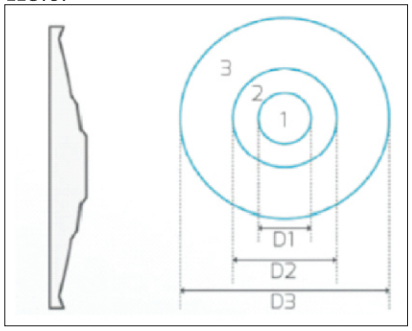

Figure 17:
MINI WELL Ready IOL
(The progressive optic has a central distance zone (1), a surrounding distance zone (2) with spherical aberration of the opposite sign, and a peripheral distance zone (3) with monofocal characteristics)
Courtesy of Sifi Medtech

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Recent Advances in Pharmacotherapy for Glaucoma Management

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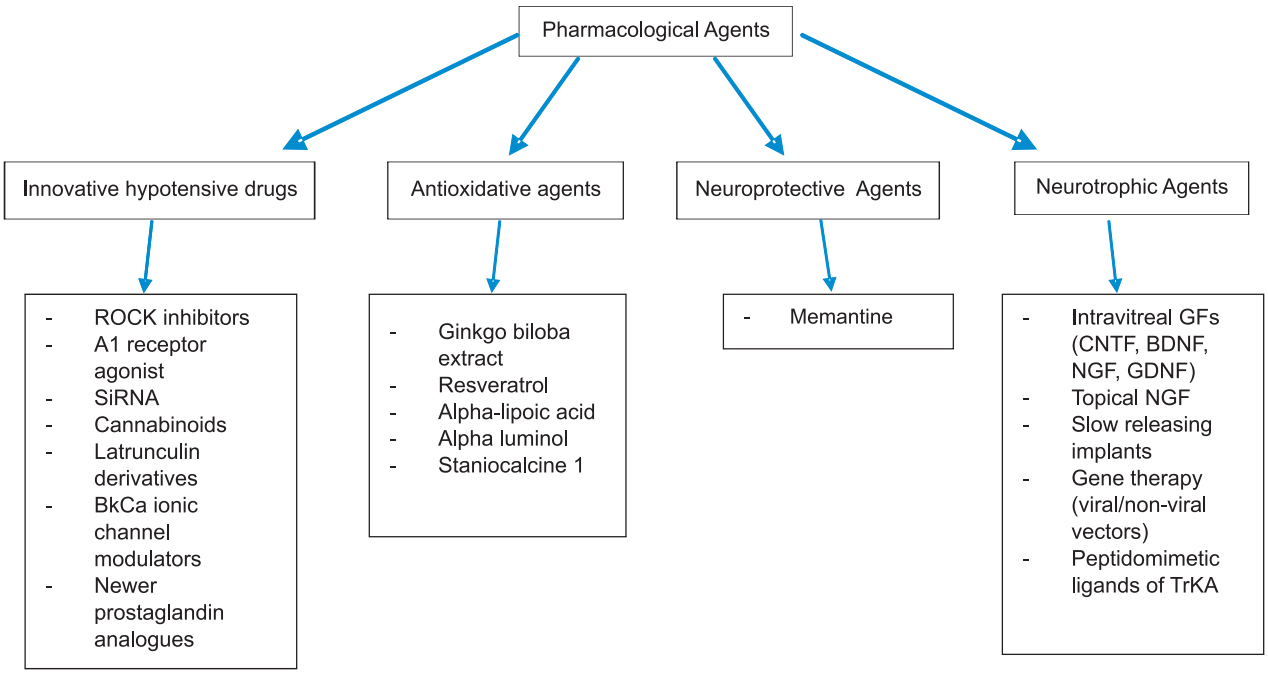
Introduction:

Glaucoma is a chronic progressive optic neuropathy caused by a group of ocular conditions, leading to damage of optic nerve with loss of vision, the most common risk factor being raised intra-ocular pressure.[1] It is a leading cause of irreversible blindness and the second leading cause of blindness worldwide.[2,3] Estimated global burden induced by glaucoma is 76 million in 2020 and expected to increase upto 111.8 million by 2040 majorly affecting the Asian and Africans .[2,4] Out of which open angle glaucoma (OAG) accounts for 70 percent of all the glaucoma.[2,5]

Axons of retinal ganglion cells are damaged leading to an earlyapoptosis and hence irreversible vision loss.[6] As the disease is mostly asymptomatic its often very late by when the diagnosis is made butpermanent visual disabilitycan be prevented by early diagnosis, appropriate management. The mainstay of treatment lies in strict intra-ocular pressure control primarily by medical management .[2,7] Multiple factors aid poor adherence and failure in management of glaucoma i.e. lack education about the disease, poor communication between patient and doctor, lifelong follow-up, timely and repetitive evaluation, complex and multi-drug therapy and financial constraints. [2,8,9]

It is necessary to understand and assess the benefit- risk ratio of medical management to achieve the target pressure without hampering the health-related quality of life (HRQL) and improve patient adherence. Hence the need for more research and introduction of newer drugs with mild or no side effects, better IOP lowering and neuroprotection.



NEWER PHARMACOLOGICAL AGENTS

A. INNOVATIVE HYPOTENSIVE DRUGS:

- **ROCK inhibitors (RHO kinase inhibitors):** The Rho family consists of guanosine triphosphate-binding protein which plays a vital role in regulating cell shape, motility, contractility, proliferation, and apoptosis.[2] Rho-associated coiled-coil-forming protein kinase (ROCK) regulates the actin-myosin proteins that promote cellular contraction in smooth muscle and also promotes the production of extracellular matrix proteins which are responsible for anchoring of cells to their substrate. The cells oftrabecular meshwork (TM) contains smooth muscle like properties and

the resistance to aqueous drainage is controlled by the contraction of cells of TM and production of extracellular matrix components. ROCK inhibitors block the TM cell contraction and decrease the production of the extracellular matrix substance hence increasing the aqueous outflow thus reduces the IOP [10]

1. **Ripasudil-**was approved in Japan for the treatment of glaucoma and OHT in September 2014. Phase 1 and phase 2clinical trials(Mono drug), demonstrated ripasudil (0.4%) twice daily provided reduction of 2 to 4.4 mmHg of IOP from the baseline.[11-13] Phase 3 trial demonstrated ripasudil (0.4%) when used along with timolol maleate (0.5%)twice daily gave an additional lowering in IOP of 0.9 to 1.6 mmHg.The most common side effect was conjunctival hyperemia which was observed in all the phases of clinical trial.[14]
2. **Netarsudil-** It is a Rho kinase inhibitor and norepinephrine transporter inhibitor whichwas approved in 2017 for use in United States of America for management of glaucoma and OHT. It had a longer duration of action than few drugs in this category.[15] Animal trials demonstrated additional action of decreased aqueous production and additional action of decrease in episcleral venous pressure was noted in humans and rabbits too and differentiating this drug from the other drugs in this class .[16,17] In a clinical trial of single daily dose Netarsudil (0.01% and 0.02%) an average of 5.5 and 5.7 mmHg IOP lowering from the baseline was noted. Conjunctival hyperemia, increased lacrimation were few side effects of the drug. The study concluded that if used with latanoprost 0.005% provided good results. Also, the drug showed better results in patients with lower mean IOP from the baseline .[18]

- **Adenosine receptor agonist:** Various physiological and biochemical pathways in the body are facilitated through G protein-coupled adenosine receptors. Secretion of matrix metalloproteins (MMP) in the endothelial cells of TM is stimulated by these receptors leading to shrinkage of cell volume and extracellular matrix remodeling, ultimately facilitating the conventional aqueous outflow.[2] Trabodenoson is a highly selective adenosine A1 receptor agonist that causes an upregulation of protease A and matrix metalloproteinase-2 (MMP-2) in target cells. A phase 2 study on patients with POAG and OHT of Trabodenoson reported that it was well tolerated by the study group at a dose of 500 micrograms twice daily with no systemic side effects. The average IOP lowering was 4.1 mmHg .[19]

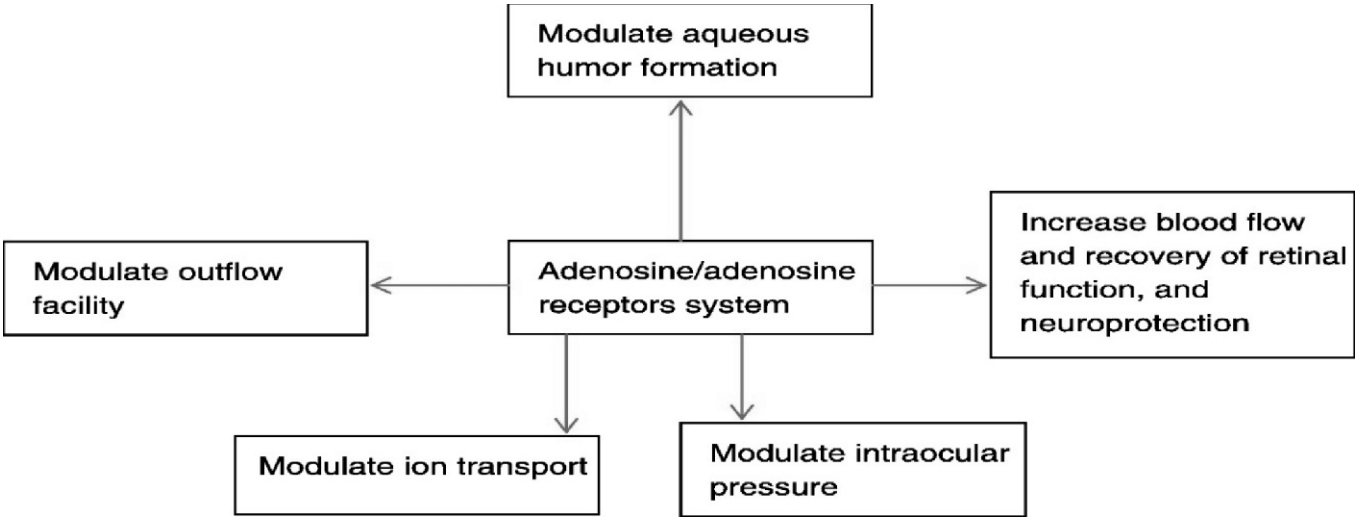


Figure 1 : Mechanism of action of Adenosine receptor agonist [20]

- **Small interference RNA (siRNA):** siRNA are small nucleotides able to interfere with mRNA translation protein. Bamosiran is a naked double stranded siRNA, it acts as agene silencer and blocks the beta-2 adrenergic receptor thus decreases the aqueous production by the ciliary body. As the drug gets absorbed very quickly in the anterior chamber, no systemic absorption of the topical drug has not been reported yet .[21] Phase 1 clinical trial have shown that 600 µg/eye/day of the Bamosiran was well tolerated with 20% IOP reduction from base line. Few animal studies have also reported neuro protective properties as well .[10] A multicenter randomized placebo controlled parallel design phase 2 trial of 89 patients revealed that 300 µg/eye/day caused statistically significant IOP reduction and was well tolerated by 80% of the patients and only one serious complication of hyponatremia was noted .[22]
- **Cannabinoids:** They not only reduce IOP but also possess neuro protective properties as well agents .[10] The presence of cannabinoid receptor 1 was seen in the TM and ciliary epithelium. They have a direct effect on the ciliary process and dilating blood vessels contributing to its property of altering aqueous humor dynamics. They also induce COX-2, PG E2 and MMP 1,3 and 9 expression adding to IOP

reduction property.[23]

- **Nitrogen Mono-oxide (NO) donors :** Nitric oxide using cGMP initiates a series of events causing structural and functional changes leading to overall relaxation of TM an inner wall of Schlemm's canal.[24] Latanoprostene bunod (0.0024%) aka LBN is a nitrous oxide donating compound which is metabolized in situ and converted to latanoprost acid and butanediol mono nitrate a NO donating species. LBN causes lowering of IOP by dual action primarily it increases the uveoscleral outflow and secondly it causes the relaxation of TM and SC leading to increased drainage of aqueous humor. Various studies comparing the efficacy of LBN (0.024%) with timolol maleate (0.5%) have been done. Studies like LUNAR and APOLLO demonstrated that LBN once daily dose of LBN (0.024%) was not inferior to timolol maleate 0.5% and was well tolerate in study group. Another study VOYEGAR concluded that the LBN 0.024% had better IOP reduction than latanoprost (i.e. 1mmHg more than Latanoprost).Some newer drugs NCX 667 (Nicox) and NCX 470 are also in the pipeline and under going animal trial .[25-29]
- **Newer Prostaglandin Analogues:**

1. **Tafluprost :** it is a newer prostaglandin analogue available in 0.0015% conc. for the management of glaucoma. The mechanism of action is same as that of latanoprost and other drugs in this class, but it has pro stanoid FP- receptor affinity 12 times greater than latanoprost .[30] Preservative free tafluprost has been developed for patient with sensitivity against the BAC and other preservatives. A study by Hommer et al. done in 544 patients to evaluate the efficacy and tolerability of preservative tafluprost 0.0015%. The subjects for the study were on antiglaucoma drugs and tafluprost was used as an adjunct therapy or in combination with pre-existing treatment. The study found that preservative free tafluprost 0.0015% caused significant reduction in IOP from baseline. In 79.5% eyes IOP <= 18 mmHg was achieved. An overall reduction of IOP in all patients (N = 544) from 19.4 +/- 5.0 mmHg at baseline to 15.7 +/- 4.1 mmHg after 4 to 6 weeks and to 15.3 +/- 3.5 mmHg after 12 weeks. Both values were significantly lower than treated baseline IOP ($p < 0.001$) was noted.[31] Another study Tumbocon JA et al. reported preservative free tafluprost (0.0015%) to be safe and effective IOP lowering agent in routine clinical setup. The study was conducted in 329 eyes of 177 patients. Most common diagnosis was primary open-angle glaucoma (POAG) (34.9%), followed by primary angle-closure (PAC) glaucoma post-laser iridotomy (24.0%), PAC post-laser iridotomy (15.5%), ocular hypertension (OHT) (14.6%), secondary glaucoma (6.7%), and normal-tension glaucoma (4.3%). Mean IOP change at month 3 was 6.18 mmHg (SD 4.06), a 26.37% reduction ($p<0.001$) and IOP reduction was sustained throughout the study period. Conjunctival hyperemia was noted in 15% patients in the study.[30]
2. **Unoprostone:** IOP-lowering docosanoid and belongs to the of a family of lipid IOP-lowering agents. It is commercially available as Unoprostone Isopropyl (0.012%) ophthalmic solution. Although the mechanism of action of unoprostone may be controversial as earlier the mechanism of IOP lowering was thought to be same as latanoprost i.e. IOP lowering by increasing the uveo-scleral outflow. But according to new research it acts on BK channels which, upon activation cause cell hyperpolarization. Endothelin-1 (ET-1) in the TM induce contractility of cells which is mediated via glutamate-associated increase in intracellular Ca2+. Through BK channel activation, unoprostone is believed to block this increase in intracellular Ca2+ in TM cells leading to increased trabecular meshwork outflow and IOP reduction .[32] Unoprostone typically lowers IOP by 10%–25% from baseline, with a duration of effect of 2–5 hours .[33] Sponsel et al [34] compared the IOP-lowering and hydrodynamic effects of unoprostone and latanoprost in 25 patients with open-angle glaucoma or ocular hypertension. After one month of therapy, both agents produced significant reductions in IOP and increases in pulsatile ocular blood flow, although the changes seen with latanoprost were nearly two-fold greater than those seen with unoprostone, which was statistically significant. Another study by Nordmann et al [35] in, double-masked, randomized trial of 556 patients with glaucoma orocular hypertension receiving either unoprostone, betaxolol, or timolol twice daily for 6 months, found similar mean diurnal IOP-lowering efficacy between betaxolol and unoprostone monotherapy. When used as adjunct therapy with timolol it has shown to provide an additional 2-3 mmHg fall in IOP

B. ANTIOXIDANTS:

Under stressful conditions like OHT/ glaucoma there are micro-alterations in the blood ocular barrier as well as there is transient and prolonged ischemia this results in release of inflammatory factors and free radicals which further leads to glaucomatous neurode generation. The free radicals generated may directly or indirectly damage the astrocytes and muller cells of the retina further causing NMDA receptor hyperactivity seconded by retinal ganglion cell cytotoxicity. Mitochondrial dysfunction induced due to ischemia may also lead to RGC viability.Reducing the oxidative stress could be helpful in achieving neuro protection. Antioxidants like alpha-luminol, Ginkgo biloba extracts, resveratrol, stanniocalcine-1 and alpha-lipoic acid have been evaluated in mouse models, proving to be effective in RGC protection. [23]

C. NEUROPROTECTIVE AGENT (MEMANTINE):

Another molecule that has been evaluated for neuro protection. It is a receptor antagonist for NMDA glutamatergic and acts by blocking the exocytotoxic process mediated by glutamate .[36] It prevented retinal ganglion cell loss in animal trials but in human trials the results were not very satisfying when compared to the placebo group. [23]

D. NEUROTROPHIC AGENTS:

Ciliary neurotrophic factor (CNTF), Brain derived neurotrophic factor (BDNF) Neurotrophic factors, neuronal growth factor (NGF) and the glial cell line-derived

neurotrophic factor (GDNF) are produced by cells within the retina. In chronic conditions the intrinsic growth factors are not enough and can be administered via exogenous route.[23] intravitreal injections of 5 micrograms of BDNF and 2 µg of CNTF have reduced the death of RGC in animal models by 8 and 22% respectively after 1 month, but the effect was not sustained and the need of repetitive inject was required. Another study reported that topical administration of NGF qid for 7 weeks increases the density of ganglion cells by 37%. Functional improvements detected with electro retinography, visual evoked potentials and computerized visual field, as it was carried out in small number of patients it was still carried and in the absence of a control group the efficacy is doubtful .[37-39] The gene therapy approach to elevate endogenous retinal production of neurotrophic factors prevents the undesirable complications and problems associated with the in vivo delivery, showing good efficacy in pre-clinical trials. Furthermore, research is required for development of this approach to get desirable results with minimal side-effects.[40]

Conclusion:

As it is proven fact that glaucoma is the leading cause of irreversible blindness severely affecting the health quality of life. Its timely diagnosis and management is even more difficult due to lifelong treatment and poor patient adherence. Various drugs for glaucoma management in the pipeline are undergoing trials. Few of which like siRNA (Bamosiran), RHO Kinase Inhibitors (Ripasudil, Netarsudil), Nitrogen Mono oxide donor (LBN) and Tafluprost have shown promising results either as mono therapy, adjunct therapy or in combination with older drugs. These results have provided a ray of hope that glaucoma management wouldn't be atedious process for the patient and improvement in compliance to treatment can be seen. Although a more extensive and aggressive approach may be required for the future.

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Pirfenidone Inhibits Post-Traumatic Proliferative Vitreoretinopathy

B N M K Khanum, R Guha, V P Sur, S Nandi, S K Basak, A Konar and S Hazra Eye (Lond). 2017 Sep; 31(9): 1317–1328.

Purpose: The purpose of the study was to evaluate the efficacy and safety of intravitreal pirfenidone for inhibition of proliferative vitreoretinopathy (PVR) in a model of penetrating ocular injury.

Patients and methods: Penetrating trauma was induced on the retina of rabbit and treated either with 0.1ml of phosphate-buffered saline (PBS) or 0.1ml of 0.5% pirfenidone, and development of PVR was evaluated clinically and graded after 1 month. Histopathology and immunohistochemistry with transforming growth factor beta (TGFβ), alpha smooth muscle actin (αSMA), and collagen-1 were performed to assess the fibrotic changes. Expression of cytokines in the vitro-retinal tissues at different time points following pirfenidone and PBS injection was examined by RT-PCR. Availability of pirfenidone in the vitreous of rabbit at various time points was determined by high-performance liquid chromatography following injection of 0.1ml of 0.5% pirfenidone. In normal rabbit eye, 0.1ml of 0.5% pirfenidone was injected to evaluate any toxic effect.

Results: Clinical assessment and grading revealed prevention of PVR formation in pirfenidone-treated animals, gross histology, and histopathology confirmed the observation. Immunohistochemistry showed prevention in the expression of collagen-I, αSMA, and TGFβ in the pirfenidone-treated eyes compared to the PBS-treated eyes. Pirfenidone inhibited increased gene expression of cytokines observed in control eyes. Pirfenidone could be detected up to 48h in the vitreous of rabbit eye following single intravitreal injection. Pirfenidone did not show any adverse effect following intravitreal injection; eyes were devoid of any abnormal clinical sign, intraocular pressure, and electroretinography did not show any significant change and histology of retina remained unchanged.

Conclusion: This animal study shows that pirfenidone might be a potential therapy for PVR. Further clinical study will be useful to evaluate the clinical application of pirfenidone.

Retinopathy of Prematurity

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Abstract:

The incidence of premature births and their improved survival rates have led to an increasing number of cases diagnosed with Retinopathy of Prematurity. There is an ever-increasing need of awareness amongst Ophthalmologists and Pediatricians, to diagnose and treat these babies timely, in order to prevent advanced visual loss. This article highlights the extent of the disease and the importance of prompt diagnosis and intervention. Diagnosis is done by Retcam or indirect ophthalmoscopy and laser photocoagulation and anti-VEGF therapy have been the mainstay of treatment in these cases. Meticulous follow-ups are of paramount importance, as there is a very small window between when to treat and when to defer. Even after a successful treatment these babies have to be closely followed up till the retinal vascularization is complete. The comorbidities have to be taken into account while treating. Tele medicine plays an important role in reaching out to the periphery, and hence the need to introduce it far and wide.

Keywords- Retinopathy of prematurity,Retcam, Laser photocoagulation for ROP, Anti -VEGFs in ROP

Introduction :

Retinopathy of prematurity (ROP) is a fibrovascular proliferative disorder which affects the developing peripheral retinal vasculature of premature infants. Improved neonatal care and better neonatal survival rate has led to the diagnosis of increasing number of cases of ROP.[1] Identifying and screening of at-risk premature infants by an experienced ophthalmologist is the most important strategy in the management of ROP. ROP is a preventable cause of blindness and remains one of the leading causes of visual loss in children. STOP-ROP trial has shown that supplemental oxygen is not the sole cause of the disease;[5]studies support that both hyperoxia and hypoxia seem to be important factors in the pathogenesis of ROP, their effects being mediated by vascular endothelial growth factor, which is produced by muller cells and astrocytes. In the rural population an experienced ophthalmologist may not be available, and availability of Retcam can prove beneficial in such areas. Screening pictures of retina taken by Retcam can be sent via telemedicine to higher centers and a diagnosis made. If treatment is warranted ,the patient can be advised to come to higher centers. The mainstay of treatment has been laser photo coagulation to the avascular retina, although anti vascular endothelial growth factor injections have shown promising results in posterior disease.[6]

With the rising rate of prematurity and improving survival ,the need for ongoing ROP screening ,treatment options and long term follow up is greater than ever.

Incidence : In India, incidence of ROP varies from 38-51.9 % among low birth weight babies.[1] Approximately 2 million babies out of 26 million live births annually are born with birthweight <2000 gms and are at risk of developing ROP. According to WHO,India has the highest number of preterm births in the world.[7]

Risk Factors

- Low Gestational age
- Low Birth weight
- Number of days oxygen administered

Less common risk factors include -

- Multiple births
- Blood transfusions
- Respiratory distress syndrome
- Sepsis
- Intra uterine growth retardation(IUGR)
- Anemia
- Seizures

Whom To Screen (Recommended by American academy of ophthalmology and pediatrics)

Fundus examination of all infants with birth weight< or equal to 1500 gms or Gestational age < or equal to 30 weeks should be done. Babies between 1500-2000 gms or >30 weeks with an unstable clinical course should also undergo screening fundus examination.

Screening Criteria According To Indian Scenario

All infants with birth weight< or equal to 1700 gms or Gestational age<34 weeks should be screened for ROP. All infants requiring supplemental oxygen or with unstable neonatal course, irrespective of GA or BW should also have a screening fundus examination. This is called **SICKNESS**

CRITERIA.[9]

When to Screen

Initial eye examination should be done at 31 weeks post menstrual age or 4 weeks of chronological age whichever is earlier. The first retinal examination should be done in the first month of life.

How to Screen

Screening is done in a temperature controlled room or a nursery in the presence of a neonatologist. Such babies are susceptible to hypothermia, bradycardia, apnoiec episodes and fall in oxygen saturation. A monitor should be there to monitor the heart rate and oxygen saturation throughout the course of examination.

Instrumentation

1. Retcam-It is a digital camera for screening, provides instant and accurate documentation and provides state of the art wide field pediatric retinal imaging(130 degrees).It is a useful tool which can be used in peripheral areas, where a trained ophthalmologist is not available. A nurse or a technician can also do screening with a retcam, capture photographs and send over to an ophthalmologist. This tele screening program has been successfully implemented in Karnataka internet assisted diagnosis of retinopathy of prematurity (KIDROP) by Vinekar et.al.[4]

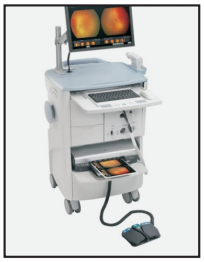

Figure 1: Retcam

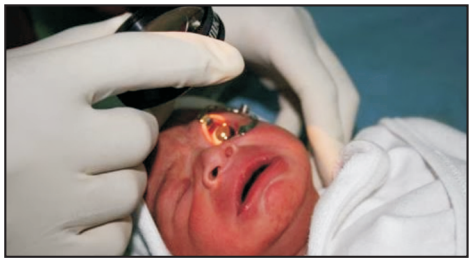

Figure 2: Examination with Indirect Ophthalmoscope

2. If a retcam is not available an indirect ophthalmoscope,a scleral depressor and a pediatric speculum is used.
3. Topical anaesthesia is given with 0.5% proparcaine eye drops.
4. Dilatation is done with half strength tropicamide plus eye drops,instilled not more than three times every 15 minutes,before the examination.Punctal occlusion may be done to avoid systemic absorption.[2]

Classification of Disease

Classification of disease is based on three clinical parameters:

» **Location of disease:**

- Zone 1-With disc as centre and twice the distance from disc to fovea , the circle formed is zone 1
- Zone 2-Extends from the peripheral border of zone 1 to nasal ora serrata and corresponding area temporally.
- Zone 3-Remaining temporal crescent of retina anterior to zone 2.

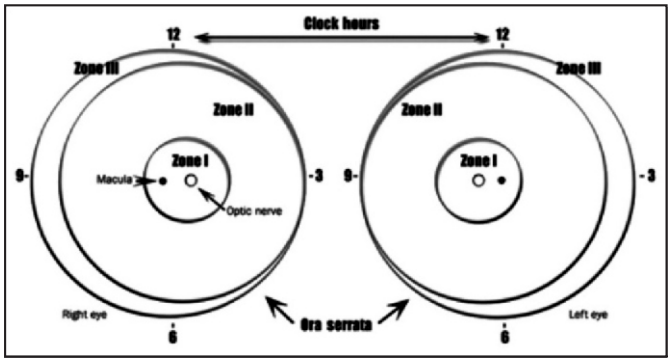

Figure 3: 3 zones of retinal involvement are recognized,each centered at the disc

» **Extent of disease:** This is defined by the number of clock hours of involvement.

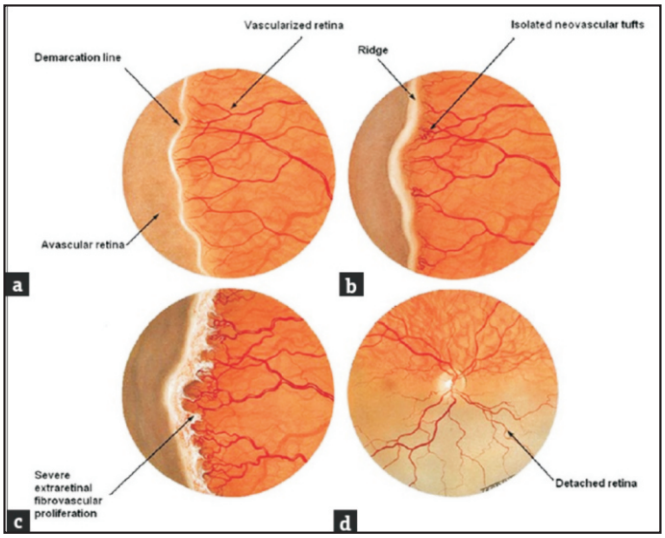

Figure 4 : Stages of ROP

Staging of Disease

Stage 1- Demarcation Line-It is a thin, flat white line within the plane of retina that separates a vascular retina anteriorly from vascularised retina posteriorly.

Stage 2- Ridge-It arises in the region of demarcation line, has a height and width and extends above the plane of retina.

Stage 3- Extra Retinal Fibrovascular Proliferation-It extends from the ridge into the vitreous.

Stage 4- Partial Retinal Detachment-Retinal detachment that may or may not involve the fovea.

Stage 5- Total Retinal Detachment-It is generally tractional and may occasionally be exudative.

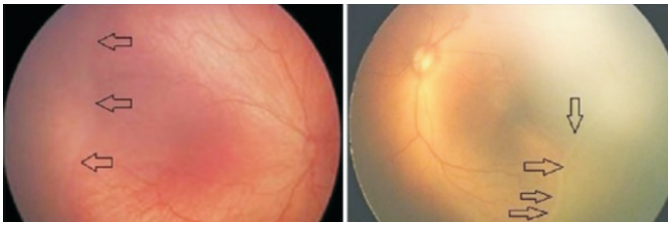

Figure 5: Stage 1-Demarcation line, Stage 2-Ridge

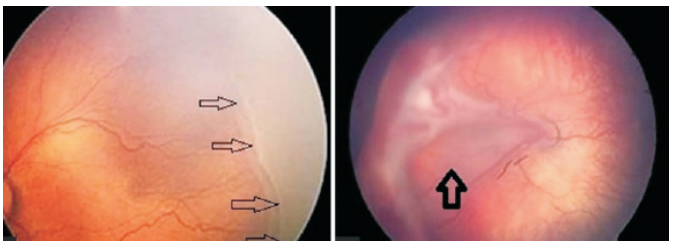

Figure 6 : Stage 3-Fibrovascular proliferation, Stage 4-Partial retinal detatchment

- **Aggressive posterior ROP-(AP-ROP)-**It is a rapidly progressing severe form of ROP.It is located posteriorly and has a prominence of plus disease.It is commonly seen in zone 1.
- **PLUS DISEASE-**There is increased venous dilatation and arteriolar tortuosity,and may include iris vascular engorgement and vitreous haze.
- **PRE-PLUS DISEASE-**This is defined as vascular abnormalities of posterior pole insufficient for the diagnosis of plus disease but demonstrate more arterial

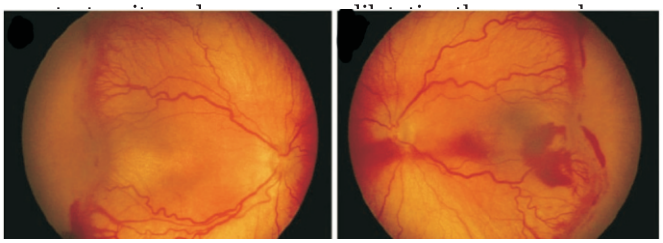

Figure 7 : Stage 3, Zone 2 with plus disease

When To Treat

Threshold disease: As per CRYO-ROP study,it is defined as stage 3 in zone 1 or 2 involving >5 contiguous or 8 cumulative clock hours with plus disease.

Pre-threshold disease: Early treatment ROP study has revised the treatment guidelines. The study proved that earlier treatment has a better outcome.

High risk pre-threshold

- Zone 1 any stage with plus disease
- Zone 1 stage 3 without plus disease
- Zone 2 stage 2 or 3 with plus disease.

Low risk pre-threshold

- Zone 1 stage 1 or 2 without plus disease
- Zone 2 stage 3 without plus disease

How To Treat

Different modalities of treatment are-

1. *Cryotherapy*- Thismodality of treatment is rarely used these days.

2. *Laser photocoagulation*- This the most widely used modality of treatment. Peripheral laser is done to stop neo vascularization. If done adequately and at the right time, the disease regresses and does not come back. The success rate has been quoted to beover 90%.[3] The peak incidence of treatment is usually 35-36 weeks, the child is followed upto 50 weeks. The long-term benefits of treatment are that it protects a against peripheral retinal tears. However there are certain risks, which should be kept in mind. Some institutes require laser to be done under general anaesthesia which has its own risks in a premature infant. It is usually done under topical anaesthesia in the presence of an anaesthetist, in NICU, with the monitors in place.

In roughly 5 percent of the cases treatable areas can be missed. In posterior disease, one can easily ablate two thirds of the retina ,which might lead to loss of peripheral field of vision[3] in some cases. The retina is ablated upto the ora serrata from the ridge. In severe cases laser may be done over the ridge also, to facilitate regression .[2] Follow-ups are done weekly, till the disease regresses completely and vascularization reaches the temporal ora.

3. *Anti -VEGF Therapy*- VEGF plays a significant role in both ischaemic and vasoproliferative phases of the disease, and anti -VEGFs play an important role in treatment of the disease. Its easy to use and has a rapid response, sometimes the result is evident within a day of injection whereas it usually takes a week to see the result of laser therapy .[3] Another advantage of anti -VEGF therapy is that it promotes near normal vascularization and hence preserves peripheral field of vision.

Two year follow up of BEAT-ROP study showed a lower incidence of myopia after anti VEGF therapy. In a study conducted at Bayer college of medicine, investigators found a mean incidence of myopia to be 0.9 d in anti VEGF group, while it was 4.4 d in the laser group .[3] However, in patients treated with anti VEGF, it took longer for the retina to develop normal vascularization. The retina remained a vascular for a long time and there was an increased chance of recurrence, sometimes even at 60 to 70 weeks .[10] A longer follow up of these infants was therefore required. VEGF is required for organogenesis and vasculogenesis. Systemic absorption of anti VEGFs may cause delayed vascular development in other organs. Hence it is not recommended as a first line of therapy. BEAT -ROP study showed promising results of Bevacizumab monotherapy in stage 3 disease in Zone 1. Laser treatment has been found to be

less effective in zone 1 disease. In all such cases bevacizumab injection followed by laser has shown to improve the efficacy of laser, with reduced need for extensive laser in the posterior pole. Anti VEGFs were found to be risky in children with comorbidities like Bronchopulmonary dysplasia. In fact four out of five deaths in BEAT -ROP study were pulmonary deaths. The optimal dosage of anti VEGF used in BEAT-ROP study was 0.625 mg .

4. *Surgery*- Indications for surgery are partial and total retinal detachment. Lens sparing vitrectomy has shown good results in stage 4.Bhende et.al have shown 82% success rate in stage 4A and 50 % success rate in stage 4B.[8] Stage 5 has been associated with poor surgical outcomes.

Sequelae

ROP babies have a strong association with development of myopia. About 65% develop myopia by 9 months of age. About 26% of babies treated for high risk pre threshold retinopathy ,have been found to develop more than 5 D of myopia in the ETROP study .[1] These patients also have a high incidence of amblyopia, strabismus and nystagmus. Parents of these babies should be explained the possibility of development of all these sequelae in their childhood years, hence the importance of regular eye checkups.

Examination Schedule

Following schedule should be followed for babies who do not need ablative treatment:

» One week or less follow up
  - Stage 1 or 2,zone 1 ROP
  - Stage 3,zone 2 ROP

» One to two week follow up—
  - Immature vascularization zone 1—No ROP
  - Stage 2, zone 2 ROP
  - Regressing ROP, zone 1

» Every two week follow up
  - Stage 1,zone 2 ROP
  - Regressing ROP zone 2

» Every two-three week follow up-
  - Immature vascularisation zone 2-No ROP
  - Stage 1or 2 zone 3ROP
  - Regressing ROP zone 3

Follow up examinations are done till complete retinal vascularisation.

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Can you find the answers to following Riddles?

1. Your hands have ten, and ten has two, and two has one, and that's your clue.
2. What's not a game, but can be played; is never seen, but often made?
3. I run but never walk, have a mouth but never talk, have a bed but never sleep, have a head but never weep. What am I?
4. The more there is, the less you see. What is it?
5. Say my name and I disappear. What am I?

Source: MSN

Surface Ablation – A Review

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Abstract: Excimer surface ablation techniques for refractive error correction have become popular, mainly in patients with a possible risk of complications after lamellar surgery. Improvements in the understanding of corneal biomechanics, wound healing modulation, laser technologyincluding ablation profiles and various methods of epithelial removal have expanded the scope for surface ablation. In this review, we describe the preoperative assessment, techniques (photorefractive keratectomy, laser assisted sub-epithelial keratectomy, epithelial laser-assisted in situ keratomileusis), outcomes, andcomplications of surface ablation techniques. Surface ablation techniques will continue to evolve, with potential improvements in results accompanying future sophisticated ablation profiles and advanced laser technology.

Keywords: excimer laser, PRK, epi-LASIK, LASEK, photo refractive keratectomy, surface ablation.

Introduction

Correction of refractive error using excimer laser energy was initially introduced in the form of photo refractive keratectomy (PRK).[1] Surface ablation is a term referring to the application of excimer laser directly on to the anterior stromal surface. The excimer laser is applied to the stroma after the epithelium is removed. There are various ways in which the epithelium can be separated from Bowmans layer and then the epithelium is either discarded or fashioned as a flap and replaced. Surface ablation does not require intra-stromalflap formation and therefore has no risk offlap - related complications, flap-induced higher order aberrations, diffuse lamellar keratitis and epithelialin growth. Also, there is minimal risk ofect asia than with other modes of refractive surgery. However, surface ablation is associated with haze formation, especially in corrections of higher refractive errors, and may need modulation of the wound healing. The main excimer surface ablation techniques include PRK, trans-epithelialPRK (t-PRK), laser-assisted sub-epithelial keratomileusis (LASEK) and epithelial laser-assisted in situ keratomileusis (epi-LASIK).[2]

Preoperative assessment, indications and contraindications

The preoperative assessment of a potential candidate for refractive surgery comprises a complete ophthalmic, medical and occupational history as well as a comprehensive ophthalmological examination including refraction, tonometry, slit-lamp examination, fundus examination, corneal topography, pachymetry, pupillometry and aberrometry.

Indications

(1) Correction of myopia (up to -10 dioptres [D]), hypermetropia (up to +6 D), and/orastigmatism (up to 4 D)[3] (although this differs between surgeon and laser)

(2) A better option in situations like treatment of patients (eg. army personnel, contact sport athletes, those involved in martial arts/boxing) with risk of LASIK-flap complications[4,5]

(3) Patients with relatively large pupils (who may suffer from glare and halos in the event of flap decentration and an abrupt border of their wider-than-the-flap-diameter ablation)[6,7]

(4) Patients with recurrent corneal erosions, anterior basement membrane dystrophy and corneal surface irregularities[5,8]

(5) Patients with laser-assisted in situ keratomileusis (LASIK) complications in fellow eye[5,8]

(6) Patients with very deep-set eyes, small palpebral fissures, or very prominent orbital roofs[8]

(7) Chronic blepharitis patients, mainly if lid massages are required[9]

(8) Patients with veryhigh or low keratometry readings, low pachymetry,and situations that may predispose to irregular, thin,or buttonholed flaps[10-12]

(9) Patients with previous surgery involving the conjunctiva (e.g. trabeculectomy bleb, scleral buckle)[5,8]

Contraindications

Absolute contraindications include keratoconus, active infection of cornea and conjunctiva, previous herpes zoster ophthalmicus infection and severe dry eye.[3] Relative contraindications include unstable progressive myopia, irregular astigmatism, herpes simplex keratitis, previous corneal surgery, active, recurrent or residual ocular disease, corneal scar, uveitis, retinopathies and significant lagophthalmos. Also, a risk of developing glaucoma later

shouldbe taken into consideration because of potential difficultieswith intraocular pressure measurements aftercorneal refractive surgery.[13]

Systemic diseases such as diabetes mellitus, atopy, pregnancy or lactation(hormonal effects could alter refractive errors), connective tissue diseases (systemic lupus erythematosus, rheumatoid arthritis) may be consider edrelative contraindications, if uncontrolled. Patients with uncontrolled diabetes may suffer from poor epithelialhealing and may have an unstable refractive error. Patients with autoimmune disease may also suffer poor or inadequate healing, activation of associated ocular disease and severe dry eye.[2,14]

SURFACE ABLATION TECHNIQUES

PRK

PRK is performed by complete removal of the corneal epithelium and basement membrane using mechanical debridement, alcohol-assistedremoval, laser-assisted removal (t-PRK) or a combination of these methods.

Mechanical epithelial debridement

The epithelium is removed either with a blade or with a brush such as an Amoil's rotary brush and then moistened by a damp polyvinyl acetate (PVA) sponge immediately before excimer laser treatment to equalize the distribution of fluid on the cornea .[15,16] The anterior cornea lstroma is then reshaped by photo ablation using a 193 nm or 213 nm argon-fluoride excimer laser.[17] A bandage contact lens (BCL)is applied until the epithelium is healed(typically after 3 to 5 days).[18] The outcome of this technique is influenced by the wound healing response as the central Bowman layer is ablated.[19] Sometimes, the wound-healing response leads to a regression of the desired effect over time and also the formation of subepithelialhaze.[20,21] Higher intended corrections may lead to less predictable outcomes, accompanied by an increased formation of subepithelial haze.[22]

Alcohol-assisted epithelial removal

18–20%ethanol is placed inside a 7–9.5 mm central corneal well (to avoid spillage on the untreated areas)for 20–40 seconds.[23] The alcohol is then absorbed with a dry PVA sponge and residual alcohol is washed away. After drying the surface, the loosened epithelium is then peeled off the surface (epitheliorhexis) using a dry sponge, blade or a specially designed epithelial scrape and discarded. Some refer to this technique as epithelium-off LASEK. Reports reveal that epithelial removal using alcohol is safe, fast, and easy to perform compared with mechanical debridement. Also, this technique can produce sharp wound edges with a clean, smooth Bowman layer and that the central epithelium can be translocated in part or en toto.[24,25]

Trans-epithelial PRK

The epithelium is removed using excimer laser. The cornea undergoes an epithelialablation within a fixed diameter. The lights of the operating room are turned off as blue fluorescent light is emitted to ablate the epithelium. Disappearance of the blue fluorescence indicates that the epithelium has been removed.[26]Accuracy of this technique depends upon regular epithelial thickness across the treatment zone and similar epithelial thicknesses between two eyes. This technique can provide variable outcomes when laser surface enhancement is proposed after previous refractive surgery due to areas of epithelial hyperplasia causing variable epithelial thickness.[2,26]

LASEK

This technique was described independently by Shah (who named this Epiflap), Azar and Camellin, who all performed this initially in 1996 .[27-29] The aim of LASEK is to preserve the epithelium so that visual rehabilitation can be accelerated and corneal haze can be reduced. Four primary techniques have been described. In the Azar flap technique, multiple marks are made around the corneal periphery.[30] Alcohol is applied to the corneal surface using a corne almarker and is absorb edusing a dry cellulose sponge after 30 seconds. One arm of a modified Vannas scissors is then insert edunder the epithelium and traced around the delineated margin of the epithelium, leaving a hinge of 2-3 clock hours of intact margin, preferably at the 12 o'clock position. The loosened epithelium is peeled as a single sheet using a PVA sponge, leaving it attached at its hinge. After performing stromal laser ablation, an anterior chamber cannula with balanced salt solution (BSS) is used to hydrate the stroma and epithelial flap. The epithelial flap is replaced on the stroma using the cannula under intermittent irrigation and care is taken to realign the flap using the previous marks without causing epithelial defects. The flap is then allowed todry for 2 to 3 minutes and a BCL is placed.

The Camellin technique uses a sharp, partial thickness trephination of the epithelium prior to the application of alcohol to allow better diffusion into the epithelium.[29] The Vinciguerra butterfly technique creates a thin para central epithelial line from 8-11 o'clock, whereby a spatula is used before application of alcohol.[31,32] The epithelium is separated from Bowman layer, proceeding from the center to the periphery on both sides. After drying the surface, excimer laser ablation is performed.

The McDonald technique is alcohol free: A round cataract blade is used to make a small linear abrasion through which a LASEK spatula is slipped. Using that hole as a fulcrum, a spatulating motion is made and the epithelium peeled off. A dedicated curved cannula is slipped under the epithelium and a tear substitute is injected to create a dome in the epithelium. The raised epithelium is bisected with a Vannasscissors and parted sideways before stromal ablation.[33]

Epi-LASIK

A mechanical deviceor epikeratome with a blunt blade is used to separate the epithelium.[34] However, it needs a vacuum suction ring. After irrigating with BSS, the corneal epithelium is dried using a sponge and the cornea is marked peripherally with a standard LASIK marker. The sub epithelial separator is applied to the eye and suction is activated by a foot pedal. The oscillatingblade separates the epithelium producing approximately a flap of 9 mm, leaving a 2–3 mm nasal hinge.[35] After removing the suction ring, the epithelial sheet is reflected nasally using a moistened sponge to expose the corneal stroma for ablation. After stromal ablation, the cornea is irrigated with BSS and the epithelial sheet is repositioned with the help ofthe markings and adhered for 2–3 min. ABCL is then placed. Many surgeons use epi-LASIK for definitive epithelial removal and the epithelial flap is not repositioned following excimer laser ablation .[36-38] This approachis a variant of PRK.

Epi-Bowman Keratectomy

Epi-Bowman keratectomy is a novel variant of PRK. Instead of a metallic blade, an instrument with a copolymer tip is used to remove the epithelium layer by layer. [39]

WOUND HEALING EFFECTS

Visual rehabilitation after surface ablation and subsequent haze formation depend upon re-epithelialization.Healing of the cornea is initiated by the release of inflammatory cytokines such as interleukin-1, tumour necrosis factor alpha and Fas ligand by the damaged corneal epithelium.[40] This in turn, leads to apoptosis of the underlyingstromal keratocytes at the damaged epithelium and also some distance into the stroma.[41] Reflex lacrimal gland secretionincreases both tear production and the concentration of various growth factors, which initiate and assist both epithelial and stromal healing responses.

After 12-24 hours of the initial injury, adjacent keratocytes start to migrate and proliferate within the anterior stroma, while inflammatory cells start to migrate into the region viatears and directly from limbal blood vessels.[42,43] Keratocytes, which migrate and proliferate within the anterior stroma, are prompted to transform into a myofibro blastic form through cytokines, such as hepatocyte growth factor released from the lacrimalgl and and transforming growth factor (TGF-b) from overlying epithelial cells. Migrating bonemarrow-derived monocytes may also transform into fibroblastic cells within the anterior stroma providing another potential source of cells to repopulate the anterior stroma.[44] Histologically, haze appears to be associated with highly reflective myofibroblastic cells and disorganized collagen deposition, which may be more responsive to treatment with anti-inflammatory agents.

The wound healing response is complex and subject to inter-individual variation, which can result in both delayed and excessive epithelial and/or stromal healing processes. The objective of refractive surgery is to produce a regular dependable healing process, which does not interfere with either the shape or clarity of the treated corneal surface.

Surface ablation techniques, which retain at least a partially intact epithelial basement membrane, might improve or regularize healing. Studies have shown efficacy in reducing the levels of TGF-b through the use of epithelial flap techniques when compared with PRK.[45] However, factors such as the retention of dead epithelial cells within the epithelial sheet, raise the potential to paradoxically prolong the immediate healing response, whereas transection and removal of the epithelial flap might allow relatively quick reconstitution of an epithelial surface with the regeneration of a new basement membrane; hence the use of epi-LASIK, which is aimed at the preservation of a healthy epithelial flap. The epithelial flap cleavage plane lies within the basement membrane between the lamina lucida and the lamina densa in LASEK, whereas the cleavage plane may lie under the basement membrane in epi-LASIK, depending on the device used .[38,46,47]

Adjunctive use of Mitomycin-C

Mitomycin-C (MMC) is a DNA alkylating agent, derived from Streptomyces caespitosus. It in hibits DNA/RNA replication, especially in rapidly dividing cells such as fibroblasts and can suppress wound healing. Its use as an adjunctive medication applied intraoperatively immediately after stromal laser ablation in PRK to suppress wound healing and there by reduce haze and regression of correction was first suggested by Talamo and colleagues over two decades ago.[48] Its efficacy has been proven both in experimental work and now through large-scale clinical usage. The advantages of low concentration, short duration of MMC (0.02%for 15–60 seconds) are evident, producing clear corneal stroma after the procedure whether used in conjunction with PRK, LASEK or Epi-LASIK. The resulting anterior corneal stroma, however, is significantly devoid of cellular repopulation even at 6 months after surgery.[49]

There is uncertainty regarding optimum concentrations and peri-operative application times. In a retrospective study, Thornton, Xu and Krueger reported less haze in eyes undergoing high myopic corrections, greater than -6.00 D and with an ablation depth deeper than 75 mm, treated with0.02% MMC compared to0.002%.[50] Concerning application times, Virasch and colleagues in a retrospective, comparative case series observed no significant difference in final visual acuity or haze with the application of MMC 0.02% for 12 seconds compared with 1 and 2 minutes.[51] In contrast, in a study of human eye bank eyes, Rajan and colleagues reported that the administration of MMC 0.02% for 60 seconds resulted in optimum modulation of corneal wound healing characterized by decrease dactivation of keratocytes and normal epithelial differentiation.[52]

Obviously, there are concerns regarding itsun known long-term

complications. A better understanding of both the corneal wound healing and its response to the various surgical and therapeutic interventions are required to enable development in this field both to improve visual outcomes and to reduce complications.

POSTOPERATIVE MANAGEMENT

The objective of immediate postoperative manage mentis to promote epithelial healing, preserve the epithelial flap following LASEK or Epi-LASIK, reduce postoperative pain and minimize the risk of complications such as inflammation and haze.

Contact lens

A BCL protects the de-epithelialized cornea, decreases pain and may result in faster re-epithelialization. It is placed over the cornea until epithelialization is complete, which is usually by postoperative day.[4] Patients with a BCL soaked in ketorolac0.45% solution had less pain immediately after the surgery than patients with a regular BCL.[53] The use of a BCL can cause corneal hypoxia, especially with low-oxygen trans missibility BCLs (low Dk). Also, extended wear non-silicone hydrogel lenses and lowDk lenses may be associated with higher ratesof infection.[54]

Topical corticosteroids

Topical corticosteroids, ranging from fluorometholone 0.1% to prednisolone acetate 1%, may be used for some weeks following surgery to modify the inflammatory response. The healing epithelial defect and the BCL may both lead to sterile infiltrates, which can also be treated by topical corticosteroids. There is a thought that topical corticosteroids delay the normal healing response and visual recovery and hence are not used in all treatment regimes.[55]

Topical non-steroidalanti-inflammatory agents (NSAIDs)

Topical NSAIDs inhibit cyclo-oxygenase activity in the arachidonic acid cascade and thus reduce inflammation without the side-effects of steroids. Alcohol application for epithelial removal for PRK and epithelial flap construction for LASEK may cause up regulation of COX-2, expression of vascular endothelial factor and other pro-inflammatory cytokines.[56] Topical corticosteroids and NSAIDs are useful in these situations. However, NSAIDs also decrease prostaglandinsynthes is, which is essential for protein and DNA synthesis in epidermal cells and hence could have adverse effects on the corneal epithelium on long term application.[2] NSAIDs are therefore, commonly used in the initial 3-5 days postoperatively until epithelialization is complete. Also, they are highly effective in relieving pain following surface ablation.

Topical antibiotics

Topical antibiotics, such as fourth generation quinolones, provides broad spectrum activity against both Gram-negative and Gram-positiveorganisms. There is an increased risk of infection with the use of a BCL over a healing epithelial defect, so antibiotic cover is mandatory with BCL use.[2]

Tear substitutes

Surface ablation damages fewer corneal nerves than LASIK and hence induces fewer dry-eyesymptoms.[57] However, there is a vast variation in dry-eye symptoms mainly due to decreased corneal sensitivity and blinking rate, which can also occur after surface ablation.[58] Additional mechanisms that can worsen dry eye include toxic conjunctivitis medicamentosa from postoperative drops and a flatten edcorneal surface with altered tear flow dynamics.[59] It is advisable to use preservative free tear substitutes for an extended period.

OUTCOMES

The primaryoutcome measures of any refractive surgery are predictability, uncorrected distance visual acuity (UDVA), the stability of visual outcomes, loss of corrected distance visual acuity (CDVA), retreatment, and safety. There has been much debate in the literature as to which surface ablation technique issuperior. Clinical studies comparing the different surface ablation techniques are summarized in Table 1 .[60-70]

PRK has the most long-termresults, as it is the oldest surface ablation procedure. Hyperopic PRK results are often less reported than myopic PRK results.[71-75] An initial myopic over-correction is described, after hyperopic PRK which occurs within the first month and resolves between 3 and 6 months postoperatively.[72-75] The results of hyperopic surface ablation correction remain less accurate than those of myopic correction but continue to evolve. Clinical studies comparing surface ablation to LASIK are summarized in Table 2. [76,11]

COMPLICATIONS

Corneal haze

Haze is a typical association with corneal wound healing, starting at 4–6 weeks and then resolving by 6-12 months. [77] The altered keratocytes are transformed into myofibroblasts that deposit collagen and cause the type of dense haze that is persistent and defined asscar tissue. Sub-epithelial haze after PRK is believed to result from light scattered by scar tissue and is more severe with increased ablation depth.[78] Haze is measured subjectively by forward light scattering and has been graded by Hanna on afive-point scale 0–4+, with grade 2+ or more being classed as clinically significant enough to distort vision.3 It is hypothesized that there is reduced corneal haze with the LASEK and epi-LASIK techniques because the surface stroma gets protected from exposure to inflammatory cells in the tear film by the epithelial flap. Less inflammatory cell invasion causes less inflammatory damage and less corneal haze. Intraoperative use of MMC 0.02 % for 15 to 60 seconds is found to be usefulto reduce haze formation.[79,80] Some surgeons

adviseoral vitamin C, 500 mg daily, in the postoperative period and others reserve MMC for the treatment of dense haze that is recalcitrant to topical corticosteroids. They first remove the epithelium, then scrape the underlying haze carefully before applying MMC with a sponge and finally, wash the eye thoroughly to avoid contact of other ocular structures with MMC. Another approach is cooling the ocular surface with an ice-chilled irrigation solution before and/orafter surface ablation to lessen the wound-healingresponse and thus haze formation and pain perception, though solid proof is unavailable.[59]

Pain

Early postoperative pain is the major limitation of PRK technique. The de-epithelialized cornea following PRK results in direct exposure of the nerve endings leading to pain.[81] It usually takes 3 to 5 days for the complete epithelialization of cornea. Various approaches to relieve early postoperative pain include the application of a BCL, use of a cold BCC, topical NSAIDs, topical cycloplegics, topical anaesthetics and oralanalgesics.[78,82] Topical NSAIDs have been associated with complications such as superficial punctate erosions, subepithelial infiltrates, epithelial defects and delayed corneal epithelial healing.[53] These complications are more often with diclofenac, which is no longer commonly used.[83,84] However, the safety of ketorolac ophthalmic solution has been well established by multiple studies.[85,86] Topical cycloplegics may reduce the pain over the first 2-3 days, although this has an effect on visual acuity monitoring.[2] Topical anaesthetics such as Tetracaine 1% used conservatively not more than 6 times for the first 24 hours postoperatively, can also help in relieving the pain.[78] Use ofa BCL soaked in Acuvail (a preservative-free solution containing carboxymethylcellulose and ketorolac tromethamine0.45%) has been shown to provide better analgesia for a longer time than conventional methods ofpain relief after trans epithelial PRK.[53] The adsorbed ketorolac on the BCL is released within the first hour after the concentration of drug is stable, thereby reducing the pain immediately after surgery.[53]

Infection

Infection after surface ablation is rare but potentially vision threatening. The risk for bacterial keratit is following surface ablation ranges from 0.01% to 1.0% and is likely significantly higher than after LASIK secondary to the creation of a large epithelial defect and the use of a BCL. Common organisms seen with keratit is include Staphylococcus aureus, coagulase negative Staphylococcus, and Streptococcus[11,87,88]. Antibiotic prophylaxis should exert adequate cover against these organisms. There have also been a few reports of fungal and my cobacterial keratitis after PRK and LASEK, implying that the size of epithelial defect is not the only factor[89,90].Viral keratitis has also been reported after PRK, though whether it is directly related is unknown.91,92Valacyclovir has been suggest edprophylaxis if there is a prior history of herpes simplex keratitis[93].

Ectasia

Ectasia is a rare condition in which the eye become sprogressively more myopic with irregular astigmatism, topographic steepening, corneal thinning and results in a loss of uncorrected and corrected distance visual acuity.[94] Iatrogenic ectasia occurring after refractive surgery has beendescribed as the most severe complication.3The risk for ectasia appears to be lower after surface ablation than after LASIK.[95] This complication is best avoided by careful patient selection.

Dry eye

The occurrence of dry eye following surface ablation is less compared to LASIK because surface ablation damages fewer corneal nerves than LASIK.[57] Reports show that there is faster rehabilitation of corneal sensitivity and tear function after surface ablation.[96,97] It is advisable to avoid topical medications with preservatives in the postoperative period. Permanent or temporary punctal occlusion may reduce severe dry-eye symptoms.[59]

Stromal incursion of the dull epitome blade

This complication is unique to epi-LASIK and may lead to a stromal defect resulting in irregular astigmatism with decreased visual acuity.[98] A flawless blade before epithelial flap preparation must be ensured to avoid this potentially severe complication. If the stroma is dissected as in LASIK, it is best repositioned and allowed to heal.

Incomplete epithelial removal

Incomplete removal of epithelium in PRK could be a cause for an irregular refractive result. Residual epithelium can be identified immediately as the epithelium fluoresces upon exposure to UV radiation. Delayed removal of the epithelium can lead to stromal hydration changes and unpredictive refractive results.[99]

Glare and haloes

Glare and haloes may be caused by the formation of corneal haze or may occur when the pupil diameter extends beyond the optical zone of excimer treatment. This usually occurs in low-light environments but may also occur in patients with large photopic pupils. Decentered ablation profiles may also lead to increased symptoms of glare and haloes. Decentrations less than1.0mm are likely to be visually insignificant, but tho semore than 1.0 mm can cause glare, halos, mono culardiplopia, and decreased vision.[100]

CONCLUSION

Surface ablation techniques appear to be useful for patients in need of refractive surgery, especially when the aim is to preserve 50-100 mm of corneal stroma. They may be indeed

useful in selected eyes where LASIK is contraindicated. Refractive and visual outcomes are excellent and comparable to those after LASIK. Also, there is evidence to suggest that there may be less induction of higher-order aberrations with surface techniques. Long-term stability and safety are found to be satisfactory. However, surface ablation techniques are associated with more inconvenience, discomfort, and slower recovery than LASIK.

Disclosures: None of the authors has a financial or proprietary interest in any material or method mentioned.

Table 1. Clinical studies comparing the different surface ablation techniques

Study	Number of eyes	Surface ablation technique	Follow-up period	UDVA	Dioptres with attempted correction	Remarks
Lee et al.[60]	27	PRK	1 week 3 months	37% with ⩾20/25 56% with ⩾ 20/25		UDVA higher with LASEK; no significant differences in spherical equivalent; more haze and pain with PRK
	27	LASEK	1 week 3 months	57% with ⩾ 20/25 63% with ⩾ 20/25		
Pirouzian et al.[61]	32	PRK	1 week 1 month	Mean, 20/27 Mean 20/21		No significant differences in UDVA
	32	LASEK	1 week 1 month	Mean 20/28 Mean, 20/20		
Cui et al.[62]	140	PRK	1 month 12 months	44-96% with ⩾ 20/20 (Mean, 73%) 67-79% with ⩾ 20/20 (Mean, 70%)	24-79% within ± 0.5 (Mean, 43%) 57-92% within ± 0.5 (Mean, 64%)	No significant differences
	140	LASEK	1 months 12 months	52-82% with ⩾ 20/20 (Mean, 71%) 73-82% with ⩾ 20/20 (Mean, 75%)	29-71% within ± 0.5 (Mean, 47%) 70-88% within ± 0.5 (Mean, 74%)	
Teus et al.[63]	47	LASEK	1 day 1 week 1 month 3 months	87% with ⩾ 20/40 89% with ⩾ 20/40 100% with ⩾ 20/40 79% with ⩾ 20/20	89% within ± 0.5 95% within ± 1.0	UDVA better on 1st day and 1st month in LASEK; larger proportion of eyes within ± 0.5 of attempted

		Epi-LASIK	1 day 1 week 1 month 3 months	64% with ⩾ 20/40 87% with ⩾ 20/40 96% with ⩾ 20/40 66% with ⩾ 20/20	77% within ± 0.5 93% within ± 1.0	correction in LASEK; safety index better in LASEK; 9% LASEK lost >1 line CDVA; 15% epi-LASIK lost > 1 line CDVA
Hondur et al.[64]	25	LASEK	1 month 3 months 6 months 12 months	72% with ⩾ 20/20 80% with ⩾ 20/20 92% with ⩾ 20/20 92% with ⩾ 20/20	84% within ± 0.5 92% within ± 1.0 92% within ± 0.5 96% within ± 1.0 92% within ± 0.5 96% within ± 1.0	No significant differences
	25	Epi-LASIK	1 month 3 months 6 months 12 months	60% with ⩾ 20/20 80% with ⩾ 20/20 92% with ⩾ 20/20 92% with ⩾ 20/20	88% within ± 0.5 92% within ± 1.0 92% within ± 0.5 96% within ± 1.0 92% within ± 0.5 96% within ± 1.0	
Ghanem et al.[65]	51	PRK	2 days 2 weeks 1 month 3 months 6 months 12 months	Mean UDVA 20/59 96% with ⩾ 20/40 Mean UDVA 20/33 43% with ⩾ 20/20 100% with ⩾ 20/40 89% with ⩾ 20/20 96% with ⩾ 20/20 94% with ⩾ 20/20	8% haze 14% haze 16% haze 94% within ± 0.5 100% within ± 1.0 8% haze	No significant differences; 2% LASEK lost >1 line CDVA; 0% PRK lost >1 line CDVA

	51	LASEK	2 days 2 weeks 1 month 3 months 6 months 12 months	Mean UDVA 20/72 92% with ⩾ 20/40 Mean UDVA 20/33 43% with ⩾ 20/20 100% with ⩾ 20/40 89% with ⩾ 20/20 96% with ⩾ 20/20 94% with ⩾ 20/20	14% haze 24% haze 26% haze 86% within ± 0.5 98% within ± 1.0 8% haze	
Kulkarni et al.[66]	163 361	Epi-LASIK (retained flap) LASEK (retained flap) Epi-LASIK	3 months 6 months 12 months 3 months 6 months 12 months	79% with ⩾ 20/20 86% with ⩾ 20/20 89% with ⩾ 20/20 88% with ⩾ 20/20 94% with ⩾ 20/20 93% with ⩾ 20/20		No significant differences; 8% Epi-LASIK lost > 1 line CDVA; 3% Epi-LASIK (flap off) lost >1 line CDVA;
	277 199	(discarded flap) LASEK (discarded flap)	3 months 6 months 12 months 3 months 6 months 12 months	89% with ⩾ 20/20 92% with ⩾ 20/20 94% with ⩾ 20/20 76% with ⩾ 20/20 86% with ⩾ 20/20 86% with ⩾ 20/20		4% LASEK lost >1 line CDVA; 7% LASEK (flap off) lost >1 line CDVA
Sia et al.[67] (contralateral eye study in moderate-high myopia)	84	PRK with MMC	1 month 3 months 6 months 1 year	44% with ⩾ 20/20 76.2% with ⩾ 20/20 93.5 % with ⩾ 20/20 97% with ⩾ 20/20	58.3% within ± 0.5 63.4 % within ± 0.5 81.8 % within ± 0.5 83.3 % within ± 0.5	1.3% PRK-MMC lost >1 line CDVA at 3 months 3.7 % PRK lost >1 line CDVA at 1

	84 83	PRK without MMC (fellow eye) LASEK 	1 month 3 months 6 months 1 year 1 month	59.5 % with ⩾20/20 86.6 % with ⩾20/20 89.6 % with ⩾20/20 96.9 % with ⩾20/20 63% with ⩾20/20	40.5 % within ± 0.5 63.4% within ± 0.5 72.7 % within ± 0.5 84.6 % within ± 0.5 48.8% within ± 0.5	month 1.4% LASEK lost >1 line CDVA at 3 months
Yuksel et al.[68]	22 20	LASEK Epi -LASIK	1 year 1 year	95% with ⩾20/25 95% with ⩾20/25		No significant differences
Reily et al.[69]	100 100	PRK LASEK	6 months 1 year 6 months 1 year			Epi -LASIK has a slight advantage over LASEK and PRK in the early postoperative period considering
	97	Epi -LASIK	6 months 1 year			pain; Epi - LASIK has less significant haze
Hansen et al.[70]	46 35	PRK with cooling LASEK	4.6 years (average) 6 years (average)		63% within ± 1.0 35% within ± 1.0	PRK with cooling was more effective than LASEK in decreasing initial significant haze

UDVA = uncorrected distance visual acuity, PRK = photorefractive keratectomy,
LASEK = laser-assisted subepithelial keratectomy, Epi-LASIK = epithelial laser in situ keratomileusis,
CDVA = corrected distance visual acuity, MMC = mitomycin-C
(Adapted from Azar DT, Gatinel D, Ghanem RC, Taneri S. Refractive Surgery3rd ed. Elseiver Inc.; 2019.)

Table 2. Clinical studies comparing surface ablation with LASIK

Study	Number of eyes	Technique	Follow -up period	UDVA	Dioptres with attempted correction	Remarks
Randleman et al.[76]	136	ASA	1 day 2 weeks 3 months	54% with ⩾ 20/10 29% with ⩾ 20/20 88% with ⩾ 20/40 82% with ⩾20/20 99% with ⩾ 20/20	86% within ± 0.5	LASIK had statistically better UDVA until 3 months, when a larger proportion of ASA eyes had ⩾ 20/20
	136	LASIK	1 day 2 weeks 3 months	90% with ⩾ 20/40 58% with ⩾ 20/20 96% with ⩾ 20/40 71% with ⩾20/20 97% with ⩾ 20/40	82% within ± 0.5	
Ghadhfan et al.[11] (low -moderate myopia with SE < -6.00 D)	323	LASIK	< 1 year	55 % with ⩾ 20/20 98% with ⩾ 20/40	91 % within ± 0.5	No significant differences
	67	LASEK	< 1 year	48% with ⩾ 20/20 94% with ⩾ 20/40	84% within ± 0.5	
	49	m-PRK	< 1 year	74 % with ⩾ 20/20 92% with ⩾ 20/40	92% within ± 0.5	
	37	t-PRK	< 1 year	65 % with ⩾ 20/20 100 % with ⩾ 20/40	95% within ± 0.5	
Ghadhfan et al.[11] (high myopia with SE -6.00 to -11.25 D)	141	LASIK	< 1 year	28% with ⩾ 20/20 85% with ⩾ 20/40	72 % within ± 0.5	t-PRK more likely to achieve > 20/30 CDVA; t-PRK more likely to achieve within ± 0.5
	37	LASEK	< 1 year	30% with ⩾ 20/20 84% with ⩾ 20/40	76 % within ± 0.5	

	20	m-PRK	< 1 year	25 % with ⩾ 20/20 80% with ⩾ 20/40	70 % within ± 0.5	D of attempted correction; 2.7% LASEK lost >1 line CDVA; 0.7% LASIK lost >1 line CDVA; 0% m -PRK, t-PRK lost >1 line CDVA
	22	t-PRK	< 1 year	36 % with ⩾ 20/20 95 % with ⩾ 20/40	95% within ± 0.5	

UDVA = uncorrected distance visual acuity, ASA = advanced surface ablation, LASIK = laser in situ keratomileusis, SE = spherical equivalent, D = dioptres, LASEK = laser-assisted subepithelial keratectomy, m-PRK = mechanical debridement photorefractive keratectomy, t-PRK = transepithelial photorefractive keratectomy, CDVA = corrected distance visual acuity
(Adapted from Azar DT, Gatinel D, Ghanem RC, Taneri S. Refractive Surgery3rd ed. Elseiver Inc.; 2019.)

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Amazing Eye Facts

1. The eye is the fastest muscle in your body – hence why when something happens quickly, we say 'in the blink of an eye!'
2. While a fingerprint has 40 unique characteristics, an iris has 256. This is why retina scans are increasingly being used for security purposes.
3. Geckos can see colours around 350 times better than a human, even in dim lighting.
4. Dolphins sleep with one eye open.
5. The largest eye on the planet belongs to the Colossal Squid, and measures around 27cm across.
6. Most hamsters only blink one eye at a time.
7. Guinea pigs are born with their eyes open!
8. A worm has no eyes at all.
9. Some people have a fear of eyes; it's called ommatophobia

Primary Bilateral Tubercular Dacryocystitis: A Case Report

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Abstract:

Tuberculosis is a communicable disease caused by Mycobacterium tuberculosis. It spreads mainly via air droplet infection and pulmonary tuberculosis is the most common form. Extra-pulmonary tuberculosis accounts for 15–20% cases.[1] The most common type of ocular tuberculosis is tubercular uveitis. Tubercular dacryocystitis is rare[2] with just 18 cases of tubercular dacrocystitis reported world-wide; and no published data was found on bilateral cases. Considering the rarity, high suspicion is required for its diagnosis. We report a case of primary bilateral nasolacrimal sac tuberculosis in a 17-year-old boy who presented with epiphora.

A 17-year-old boy presented with bilateral epiphora for one year. There were no other ocular or nasal complaints. Patient did not have any past and family history of prior surgery or any chronic illness. Regurgitation test was positive and syringing done from both upper and lower puncta showed nasolacrimal duct block on both sides. Nasal endoscopy was normal. Complete blood count, kidney, liver function tests and chest X-ray were normal. The diagnosis of chronic dacryocystitis was made and patient was taken up for left endoscopic dacryocystorhinostomy (DCR) surgery.

During surgery, after raising mucosal flap, part of frontal process of maxilla overlying the lacrimal sac was found partially eroded and lacrimal bone was friable, walls of the lacrimal sac were inflamed and granulations were present. On incising the lacrimal sac, it was filled with white cheesy necrotic material (Figure 1). Biopsy was taken from the sac and overlying eroded bone and further surgery was aborted.

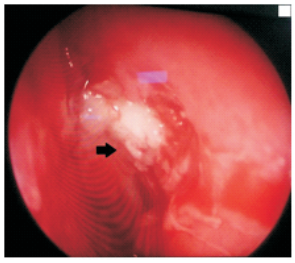

Figure 1 : Nasal endoscopic picture (left nostril) showing white caseous material inside lacrimal sac.

Histopathology showed multiple caseating granulomas with epithelioid cells suggestive of tuberculosis (Figure 2).

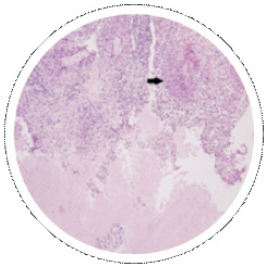

Figure 2 : Histopathologic picture showing caseating granulomas (arrow) H&E stain, 100×.

Patient was further investigated. Mantoux test was positive (15mm x 18mm induration). Erythrocyte sedimentation rate (ESR) was raised (54 mm). Category I anti-tubercular therapy (ATT) according to Revised National Tuberculosis Control Program (RNTCP), was started. The patient completed six months of therapy and responded well. Epiphora resolved and on syringing, patency was established on both sides. Tuberculosis of lacrimal sac was thus established retrospectively on the opposite side as well.

Discussion

Extra-pulmonary tuberculosis involves head and neck region in 10% of cases. The order of occurrence is tubercular lymphadenitis (73.3%), laryngeal tuberculosis (14.5%), tuberculous otitis media (2.4%), parotid (1.8%), oral cavity (5%), nose (1%) and temporo-mandibular joint (1%).[1] Ocular tuberculosis can affect uvea, sclera, cornea, choroid, lacrimal gland adnexa and periorbital cutaneous tissue having variable prevalence of 5.6–10.13% in India.[2] Tuberculosis of lacrimal sac is very rare. Review of English literature revealed 18 cases of tuberculosis of lacrimal sac to the best of our knowledge. Bilateral afflictions have not been yet reported.

Konstam and Meynell referred to tuberculosis of lacrimal sac as a primary tuberculous "chancre".[3] Tubercular infection may reach the lacrimal sac via haematogenous route, direct inoculation, and contiguous spread from nasal cavity, via skin or through tears in cases of conjunctival exposure. Tuberculosis of lacrimal apparatus may occur as primary form or in association with nasal/paranasal sinus tuberculosis, periorbital, and lupus vulgaris or with cervical lymphadenitis. Tubercular dacryocystitis can ensue at any age particularly in endemic countries. In our review of 18 cases, age group ranged from 14 months to 60 years. There were 11 females and 7 males.

Clinical attributes of dacryocystitis are epiphora and medial canthus swelling. It is essential to ask for any nasal complaints as 8 out of 18 reported cases were associated with nasal tuberculosis.[5–9,12,13] Two cases had associated cutaneous tuberculosis and one had peri-ocular tuberculosis.[12,16] Three patients had lacrimal fistula at presentation.[3,6,15] History of failed lacrimal surgeries should raise suspicion and patients need to be investigated for underlying cause. Six out of 18 cases had failed drainage procedures.[5,6,8,12,13,16] Family history of tuberculosis should be sought as a possible source of infection.[3]

Examination should comprise of regional lymph node evaluation, nasal endoscopy, and any local swelling or ulcer should be carefully examined apart from lacrimal apparatus. Lymph node tuberculosis was found to be associated with two cases in the review.[9,15] The importance of detecting an enlarged lymph node is that it may provide valuable clues for the cause of dacryocystitis on subsequent aspiration cytology.[15] Nasal endoscopy is an essential tool for detecting any suspicious lesion in nasal cavity. Any granulations or congested friable mucosa in inferior meatus or middle turbinate should prompt for pre-operative biopsy and confirming diagnosis.

The investigation includes fine needle aspiration cytology from medial canthus/facial swelling, or any suspicious lymph node. Routine blood investigations may detect lymphocytosis, raised ESR or positive tuberculin test. Chest X-ray is important in detecting any pulmonary tuberculosis. It is interesting that no case had associated pulmonary tuberculosis in the present study. Granulations in nasal cavity or skin lesion over the lacrimal sac should be sent for histopathology and culture. Histopathology may reveal caseating granulomas with epithelioid, Langerhans giant cells along with tubercular bacilli. Culture is gold standard for diagnosis. Other tests such as QuantiFERON, TbFERON, polymerase chain reaction (PCR) and nucleic acid amplification test (NAAT) help in detecting tuberculosis in shorter duration. Computed tomography is helpful in detecting soft tissue density in lacrimal sac and associated nasal and paranasal sinus involvement. Bone erosion or osteomyelitic changes in bones forming lacrimal fossa should prompt for further investigations. This is important for primary cases of tubercular dacryocystitis which accounted for 5 cases out of 18 apart from the present case.[4,10–12,14] Intra-operative findings such as thick inflamed lacrimal sac, granulations over sac, bone erosion and white caseous material should persuade surgeon to take tissue for biopsy and culture. Whitish caseous material and thinned bone were the only findings in the present case report which arose suspicion of tuberculosis. Treatment of tubercular dacryocystitis is ATT with surgery reserved for cases who remain epiphoric after medical treatment. Standard four drugs (isoniazid, rifampicin, pyrazinamide and ethambutol), Category I regimen according to RNTCP, India are applicable. However, defaulters and drug-resistant forms may require category II treatment. To summarise, primary lacrimal sac tuberculosis is very rare. History of failed surgeries, tubercular contact and lacrimal fistula are valuable clues. Nasal endoscopy is helpful in detecting cases of associated nasal tuberculosis. Regional lymph node examination is essential. ATT is mainstay of treatment. Endoscopic DCR should be reserved for persistent epiphora after ATT.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Retinal Haemorrhage in Neonate, Case Reports and Review of Literature

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Introduction

Retinal hemorrhages in infancy are not uncommon and were first described by Jaeger. In his study, the incidence of neonatal retinal haemorrhage varied from 2.6 to 50 %. Giles reported the incidence of neonatal retinal haemorrhage was 40% at 1hour post-delivery and significantly reduced to 20% at 72 hours. However, these haemorrhages are mostly self-limiting and resolve between the second and fourth week of life.

Herein, we report multiple retinal haemorrhages in twoneonates during routine retinopathy of prematurity (ROP) screening and related review of literature. Our observation gives us insight into ocular conditions that may affect premature infants, thereby emphasizing the need to have a high degree of clinical suspicion in all cases that undergo routine ROP screening.

Smartphone camera for capturing clinical photos and videos have been described in various literature. The fundus images of neonates screened for ROP can be captured by wide-field digital retinal imaging (Retcam II, Clarity medical system, Pleasanton, CA, USA) or more recently smartphone have been reported to be used for the same purpose. , In this case report, we have documented the fundus images of the cases using the android smartphone as described by Goyal A et al.[7]

Case reports-

Herein, we report two cases of neonatal retinal haemorrhages which were found coincidentally during ROP screening in a tertiary care hospital.

CASE 1-

A 28 weeks old male neonatewith birth weight 1500grams, appropriate for gestational age had a normal vaginal delivery at a private hospital. The mother had premature rupture of membranes and the baby had a breech presentation at the time of delivery. After 25 days of birth, parents noticed the child to be refusing feed and being lethargic for which they consulted a private practitioner who then referred the child to our hospital.

Herein, the baby was diagnosed withlate-onset sepsis and admitted in the neonatal intensive care unit (NICU). The patient under went routine retinopathy of prematurity (ROP) screening at the 4th week of age after birth as per standard ROP screening protocol at our hospital. On examination, there were multiple pre-retinal haemorr hages(>1disc diameter) in both eyes of the neonate but no signs of ROP (Photo 1A,1B).

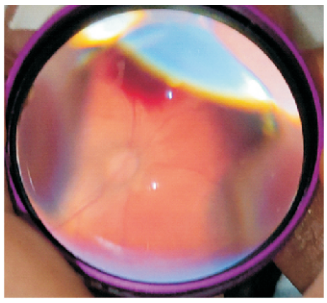

Figure : 1A

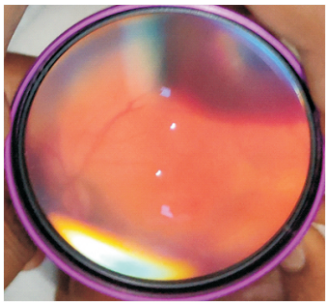

Figure: 1B

There was no maternal risk factor for retinal haemorrhages like hypertension, eclampsia or preeclampsia. Other risk factors were present, such as early age of the pregnancy, premature rupture of membrane and succeeding vaginal delivery. On investigation, the platelet count and total leucocyte count were low (0.2lac cells/mm^3 and 3800 cells/mm^3 respectively) at the time of admission. There was nocoagulation disorder or systemic disease as per blood reports. Patient's activated partial thromboplastin time(APTT) was 40 seconds and prothrombin time(PT) was 16.2 seconds. After packed cell and platelet transfusion, the platelet count improved to 2.11 lac cells/mm^3. There was no active ophthalmic intervention and the patient was kept under observation till spontaneous resolution of haemorrhages occurred as the blood parameters improved with treatment. The patient was reviewed 4 weeks after the initial examination and complete resolution of preretinal haemorrhages was found on fundoscopic examination(2A, 2B). The platelet counts were maintained at level of 4.5 lac cell/ mm^3 and there was no further dip in platelet count till the time of reporting.

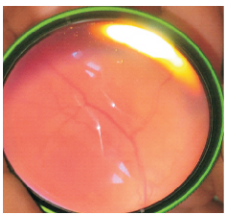

Figure : 2A

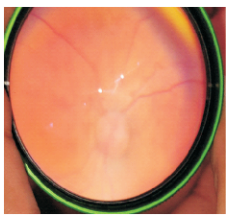

Figure : 2B

CASE 2-

A full-term (36 weeks of gestational age) male infant with a birth weight of 3300 grams, appropriate for gestational age had assisted vaginal delivery at a community health centre. The patient had a vertex presentation at the time of delivery. The baby did not cry immediately after birth and also had frequent episodes of seizures. Thereafter, the baby was referred to our hospital where he was diagnosedas perinatal asphyxia with meconium-stained liquor with hypoxic-ischemic encephalopathy and was admitted in NICU. The patient underwent ROP screening at 3 weeks of age as per the protocol. On examination, there were multiple small(1/4 to 1/2 disc diameter) pre retinal haemorrhages in both the eyes. In the right eye, haemorrhages also involved the macula. In both the eyes, Zone 1 and Zone 2 were vascularised and there was no sign of ROP (Photo 3A, 3B)

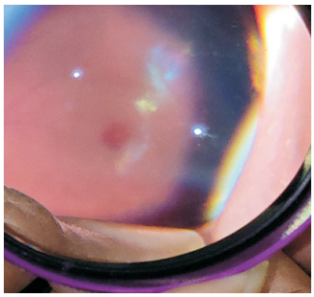

Figure: 3A

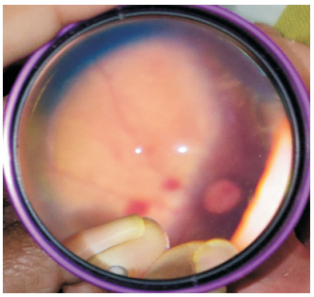

Figure: 3B

Maternal risk factors present in this case were early primiparity with assisted vaginal delivery. All blood investigations of the patient were in the normal range. The patient was kept on injection phenobarbitone in NICU for repeated episodes of seizures. There was no active ophthalmic intervention and the new born was re-examined weekly until the haemorrhages were completely resolved. All haemorrhages cleared within 3 weeks except macular haemorrhage in the right eye which had taken 2 more weeks to resolve completely after the initial examination (4A,4B).At the time of subsequent

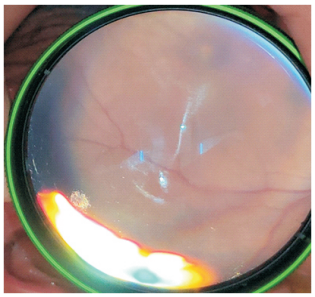

Figure: 4A

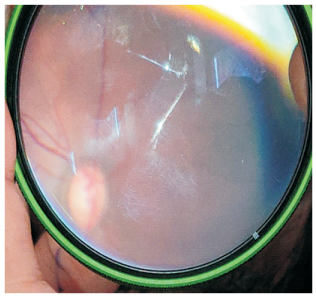

Figure: 4B

follow up, the retinal haemorrhages had cleared completely and there was no residual pathology seen.

Discussion

Retinal haemorrhagesare one of the most common neonatal abnormalities diagnosed on fundus examination.[6]

Table -1 : Showing risk factors for retinal haemorrhage in neonates based on previous studies

S.No.	RISK FACTORS	CAUSES
1.	Maternal	Preeclampsia, eclampsia, pregnancy-induced hypertension [8,9] Early age of pregnancy8 Primiparity[8] Multiparity[10]
2.	Birth process associated	Mode of delivery (common in spontaneous vaginal delivery than cesarean section[2,6,11] Method of delivery (more common in vacuum extraction)[12,13] Delivery time[10,14]
3.	Foetal	Prematurity,[15,16] neonatal asphyxia,[17] perinatal distress,[18] low birth weight[8]

The risk factors are known to cause retinal haemorrhages in neonates as listed in table 1 and are discussed below.

Mode of delivery-The rate of retinal haemorrhages is higher in spontaneous vaginal deliveries than caesarean section because extrusion of fetal head can result in increased intracranial pressure and increased pressure in ophthalmic artery.[2,6,11]

Instrumental delivery –The incidence is more in infants delivered by vacuum extraction.[12,13] It is probably due to the constant suction force resulting in increase in intra cranial pressure, which leads to stasis of blood flow in the central retinal vein. This further causes an increase in the pressure in ophthalmic artery and may thus precipitate the retinal bleeding.

Early primiparity- Some studies have also found early primipara as a risk factor associated with retinal haemorrhage because they have more resistance in the birth canal during delivery, uterine inertia and insufficient force of labour which can lead to perinatal distress.[8]

Delivery time-Another study showed that retinal haemorrhage were more commonly found during succeeding vaginal deliveries than first delivery because mothers delivering for the second time have birth canal looser than mothers delivering for the first time, their stages of labour are shorter, and rapid descent or rapid compression and decompression of foetal head may affect the rate of retinal haemorrhages.[10,14]

Perinatal distress and Neonatal asphyxia- Neonatal asphyxia and hypoxia causes increase the permeability of brain capillary endothelium. The increase in cerebrospinal fluid

pressure can lead to auto regulatory hypoxic cerebral vasodilatation which produces an increase in intracranial pressure, which in turn increases retinal venous pressure. Additionally, hypoxia-related vascular fragility also increases the risk for intraocular haemorrhages.[17,18]

In our first case, the maternal risk factors were early age of pregnancy, premature rupture of membrane and succeeding vaginal delivery and the risk in baby were prematurity, low birth weight, and throm bocytopenia.There has been only one case series that considered throm bocytopenia to be a possible etiological factor of retinal haemorrhage in neonates.[15] In our case, throm bocytopenia was one of the major risk factors for retinal haemorrhage. Although few studies state that throm bocytopenia associated with aggressive posterior ROP might cause retinal haemorrhage in the term infant. But in our case, there is no evidence of ROPand zone 3 was vascularised at the time of evaluation.

Possible maternal risk factors present in our second case were primiparity and assisted vaginal delivery. And foetal risk factors were perinatal distress and neonatal asphyxia.

We kept both the patients on regular follow up for monitoring of resolution of retinal haemorrhages. In both the cases, retinal haemorrhages underwent complete resolution within 4-6 weeks after initial examination with no morphological and functional sequelae.

Since both our patients were under critical care in NICU, so we adapted for smartphone retinal imaging for documentation of retinal haemorrhages. As smartphone fundus photography is a unique, simple and affordable technique that allows picture documentation of retinal changes.

Conclusion

This report exemplifies the uncommon occurrence of retinal haemorrhages in neonates as seen during routine ROP screening which can be associated with a multitude of maternal and foetal risk factors. However, these haemorrhages usually resolve within 4-6 weeks and have no morbidity as seen during the observed short clinical course. Long term effects on visual functions and other retinal insufficiencies that may occur with time will require longer longitudinal studies.

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Retinal Pigment Epithelium Alterations in Diabetic Macular Edema

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Introduction

Diabetes mellitus will be the seventh leading cause of death in 2030 as projected by WHO.[1] The prevalence of Diabetic Retinopathy (DR) is intimately linked to the upsurge in prevalence of diabetes.[2] DR is the leading cause of vision loss in adults aged 20–74 years.[3] Proliferative diabetic retinopathy (PDR) is the most common vision-threatening lesion particularly among patients with type 1 diabetes mellitus. However, diabetic macular edema (DME) is responsible for most of the visual loss experienced by patients with diabetes as it remains the major cause of vision loss in the highly prevalent type 2 diabetes.[4,5]

RETINAL PIGMENT EPITHELIUM

ROLE OF RPE IN DEVELOPMENT OF RETINA

Healthy RPE has functional intact tight-junctions which are required for the effective and controlled removal of fluid from the subretinal space.[6] A variety of growth factors secreted by RPE maintain the structural integrity of choriocapillaris endothelium and photoreceptors. These growth factors are essential for both endothelial cell differentiation and photoreceptor differentiation.[7-11] RPE is essential for the maintenance of photoreceptor excitability. This is achieved by various mechanisms: stabilizing ion composition in the subretinal space,[12-14] phagocytosis of shed photoreceptor outer segments [15-18] and rebuilding light-sensitive outer segments from the base of the photoreceptors. Hence, RPE is essential for both development of retinal structures and visual function.[19]

PATHOPHYSIOLOGICAL CHANGES TAKING PLACE IN RETINAL PIGMENT EPITHELIUM IN DME

EFFECT OF VEGF ON RPE AND ITS RELATION WITH SEVERITY OF DR

Vascular endothelial growth factor (VEGF) is part of a subfamily of growth factors involved in angiogenesis. VEGF is secreted from retinal pigment epithelium (RPE) cells, pericytes, astrocytes, muller cells, glial cells and endothelial cells .[20] VEGF causes retinal capillary endothelium damage due to basement membrane thickening, pericyte loss and decreased capillary perfusion. This leads to fluid leakage out of the capillaries resulting into DME.

Serum VEGF levels serve as a simple, reliable, physician-friendly, and easy to comprehend biomolecular bio-marker for severity of DR. Significantly elevated levels of VEGF come into play even before the evidence of DR. Estimation of serum VEGF is a useful laboratory test for predicting the onset of DR.

VEGF has been shown to induce functional changes in the RPE.[21,22] Damage to RPE leads to degeneration of the retinal layers and impaired visual function.

In our earlier study we discovered that severity of DR was associated with increase in topographic RPE alterations (RPE-A) on SD-OCT .[23]

Clinical and OCT parameters and RPE grade showed significant increase in severity of diabetic retinopathy with increase in levels of Serum VEGF

EFFECT OF OXIDATIVE AND NITROSATIVE STRESS ON RPE

Increased NO-mediated damage was demonstrated and proposed to be responsible for the RPE damage and thus breakdown of the BRB in diabetic animals.[24] NO has been shown to decrease rod outer segment phagocytosis by RPE cells.[25] Exogenous NO has also been shown to inhibit human RPE cell proliferation.[26] RPE has been found to be responsible for transport of ions, retinal proteins, growth factors and metabolism of the photo receptor layer.[27,28] In case of damage of the RPE, neuronal retina and photo receptors are the most affected tissues in theeye.[29]

In our previous study we found that, with increase dseverity of diabetic retinopathy, increased levels of plasma NO and LPO were found to be significantly

related to decrease in visual acuity, disruption of the photo receptor ellipsoid zone and topographic alterations in RPE. Increased plasma NO levels were associated with RPE alterations.

ASSOCIATION OF RPE ALTERATIONS WITH DAMAGE TO BLOOD VESSELS AND CHANGES IN RESISTIVE INDEX

Blood Supply of RPE: Choriocapillaries which in turn are supplied by Ophthalmic artery through short posterior ciliary arteries

The integrity of the choroidal capillaries is regulated by RPE. Increased severity of DR, an increase in RI of OA results in decrease in blood flow to RPE. This leads to RPE topographic alterations and resultant decrease in VA.

Retinal capillary endothelium damage in diabetes occurs

due to basement membrane thickening, pericyte loss, increased expression of intercellular adhesion molecule-1 (ICAM-1),[30] advanced glycation end products (AGEs),[31] oxidative and nitro sative stress[32]and decreased capillary perfusion. This in turn leads to fluid leakage out of the capillaries resulting into DME, capillary closure and decreased capillary blood flow. In addition, positive correlation of AGEs with grades of RPE alterations has been observed in diabetic retinopathy.[33] Blood supply to retina is decreased due to biochemical and biomolecular changes with resultant retinal ischemia and increased vascular endothelial growth factor (VEGF) release .[34-36]

Blood flow to adjacent retinal capillaries is increased due to retinal ischemia, resulting in increase in vessel wall shear stress.[37] Capillary closure and alterations in rheological properties of blood also results in increased shear stress. Locking of the vessel occurs due to increased glycation and thickening of the basement membrane.[38] Also in the presence of dilated vasculature the systemic blood pressure is more easily transmitted to the micro circulation resulting in increased capillary pressure. As a result shear stress in vessel wall increases as the vessel diameter is unable to change, leading to mechanical injury to the vascular endothelium. This circumferential stress resulting into mechanical damage to the endothelium is directly proportional to the perfusion pressure and radius and inversely proportional to the thickness of the vessel wall.[39] Hence, circumferential stress damage occurs more on vessel with larger diameter resulting into further dilatation of vessel. The tension resisting circumferential stress in the vessel wall has an inverse relationship with the radius of the vessel, as a result tension to counteract circumferential stress is not attained in a dilated vessel, and therefore there is a tendency towards dilatation with consequent hyperperfusion.

Additionally, several other factors resulting in hyperperfusion are abnormal autoregulation of the retinal circulation,[40] increased conductance as an autoregulatory response to retinal ischemia,[41] endothelin-1 resistance, inhibition of calcium influx channel in smooth muscle cells and increased activity of nitric oxide synthase. As these changes occur in retinal vasculature the resistive index increases. In the present study, we found an increase in RI of OA with severity of DR, grades of RPE alterations and EZ disruption.

CORRELATION OF VITAMIN D WITH RPE ALTERATIONS

Normal serum Vitamin D levels range from 25 to 50 ng/ml. In our earlier study we found that the mean Vitamin D levels decrease with severity of DR. Low Vitamin D levels have also been found to correlate with increase in RPE-A.[42]

RPE TOPOGRAPHY BY SD OCT

Retinal Pigment Epithelium (RPE), the outermost hyperreflective band on SD-OCT is located between light-sensitive outer segments of the photoreceptors and choriocapillary vessels. RPE- Alterations (RPE-A) was evaluated by single layer retinal pigment epithelial (SL-RPE) map. RPE-A was graded as, Grade 0: No alterations, Grade 1: Alteration in two quadrants, Grade 2: Alteration in more than two quadrants12.

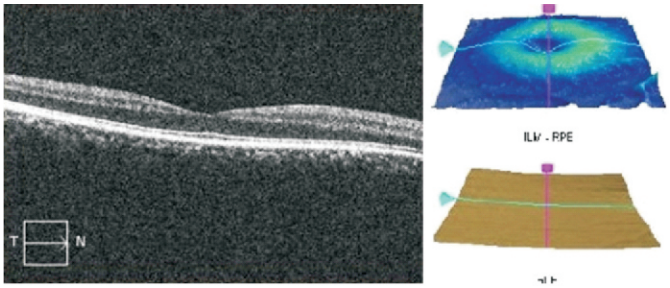

Figure 1a : SD-OCT showing normal RPE.

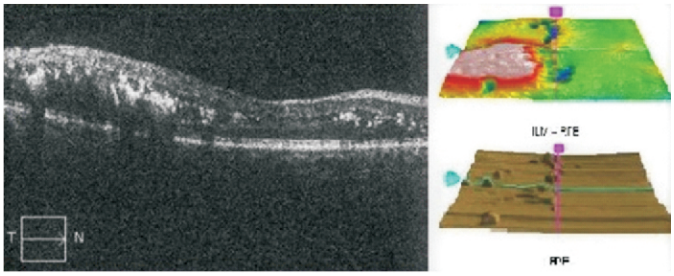

Figure 1b : SD-OCT showing DME on cross-sectional image, increased macular thickness on colour coded map and grade 2 RPE-A on RPE map.

TAKE HOME MESSAGE

1. **SD-OCT changes correlate significantly with severity of diabetic retinopathy and RPE-A. Hence must be performed at appropriate intervals for monitoring of the disease**
2. **There is positive correlation between VEGF levels and RPE-A.**
3. **Serum levels of Vitamin D correlate with increased severity of Diabetic retinopathy and RPE-A. Patients should be screened for Vitamin D deficiency.**

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An Approach to a Patient with Post-Operative Endophthalmitis

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Endophthalmitis is a condition in which the internal structures (inner layers) of the eye are invaded by replicating microorganisms, resulting in an inflammatory response. All the structures may get involved ultimately with resulting loss of function.

Only rarely do the organisms get across the intact cornea and sclera. Exogenous endophthalmitis (Post-operative and traumatic) occurs when the integrity of the outer wall is breached. We will focus our discussion on the post-operative endophthalmitis.

Cataract is the most common intra ocular procedure performed and hence the incidence of endophthalmitis is highest. Approximately 90% of post-operative endophthalmitis occur following cataract surgeries. Other causes are intra vitreal injections, trabeculectomies, penetrating keratoplasties and pars plan a vitrectomies.

Intravitreal injections of anti VEGF agents represented 8.5% of all cases of endophthalmitis. Cultures yielded positive results in 75% of cases, majority of them were aerobic coagulase negative staphylococcus.

In **Trabeculectomy** the overall incidence of endophthalmitis vary with the surgical technique and use of metabolites, in the range of 0.12 to 1.2 percent per year. Commonly isolated organisms are Streptococci (acute), Haemophilus influenzae (delayed). Gram negative organisms and fungus are also isolated in post trabeculectomy endophthalmitis. Use of mitomycin increased the risk of endophthalmitis. Glaucoma valve related endophthalmitis have similar isolates as in post cataract endophthalmitis.

After **Penetrating keratoplasty** the incidence of reported endophthalmitis ranged from 0.382 to 0.67%. Factors associated with endophthalmitis were donor cause of death (infection), high risk cases and indication for corneal transplantation (infections). In 60% donor buttons were the likely source of infection and the most common organisms were gram positive cocci.

Post **pars plana vitrectomy** the incidence of end ophthalmitis is 0.05%. The risk of end ophthalmitis was lesser in sutured sclerotomies and in tamponade agents other than BSS.

The type of operation, onset of symptoms, clinical presentation, duration, age of patient, geographic location and other co morbidities etc. may indicate, with reasonable accuracy towards the causative organism. Intuitively a broad spectrum therapy is initiated while awaiting the specific microbiological reports from the laboratory.

The normal conjunctiva harbours commensals, in conjunctival swab cultures most commonly isolated are aerobic coagulase negative Staph. epidermidis. Predominant anaerobic isolates were Propionibacterium. Children harbour less number of organisms and the predominant isolates were streptococcus species.

The culture positivity rates vary from 30% to 70%. The culture results in EVS (endophthalmitis vitrectomy study) showed 69% with confirmed bacterial growth, 18% with no growth and 13% with equivocal growth. 94.2% of culture positives were gram positive bacteria, of them 70% were gram positive coagulase negative, 9.9% Staph. aureus, 9% Streptococcus species, 2.2% Enterococcus and 3% others. Gram negative species were involved in 5.9% cases.

A survey in India reported 53% of post-operative endophthalmitis were gram positive and 26% were gram negative . In another study from the same institute in south India 60% culture positive cases were Nocardia.

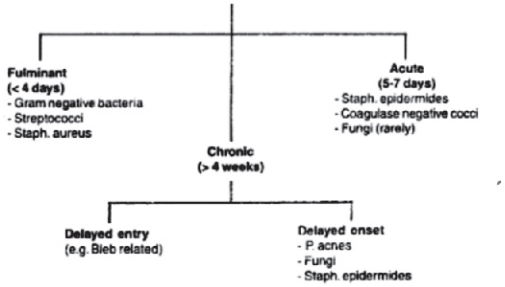
Among the gram negative, P. aeruginosa though reported as the most frequent organism has until never been reported as the single most common organism in studies. Other gram negative isolates are E. coli, Klebsiella, Sphingomonas paucimobilis etc.

Clinical features

The incidence of post-operative endophthalmitis though has sharply declined over the past 50 years, it is still the one of the most catastrophic complications of eye surgeries.

The presentation can be fulminant, acute or delayed as shown in the chart.

Chart-1
Post-Surgical Endophthalmitis



Blurred vision, sudden increase in pain 1 to 7 days after surgery, though absent in 25% of cases are the commonest presenting symptoms.

On examination the signs are lid edema, conjunctival chemosis, yellowish exudates in the cul de sac, corneal edema – infiltrate, AC cells, flare, hypopyon, exudates and fibrin membrane on either side of IOL.

Posterior segment examination shows vitreous exudates, retinal phlebitis (earliest sign). Sometimes only a red reflex is visible obscuring all the other details, poor dilatation and media opacity are major limitations to posterior segment evaluation.

Ultrasound B-scan is a useful tool for evaluation in such severe cases. Vitreous membranes filling the cavity and their density are indicative of severity. Status of retina, choroid and optic nerve head is very well defined in opaque media. Follow up USG is done at same gain settings to evaluate the response of treatment with reasonable accuracy.

Bacterial endophthalmitis

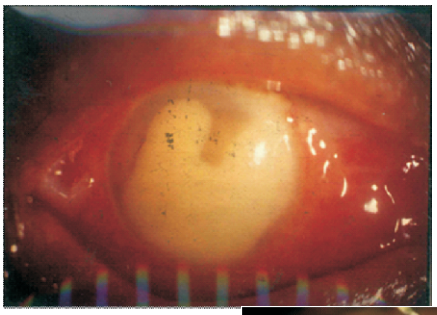


Figure 1 : Bacterial (gram negative)

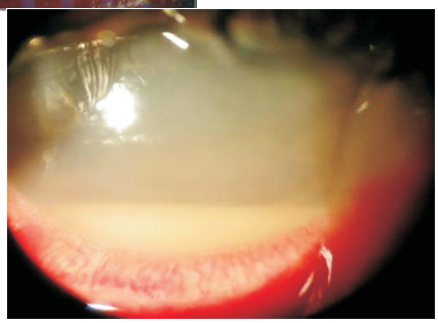


Figure 2: Bacterial (gram positive)

Onset is within 24 to 48 hours. There is marked visual loss and pain. On examination conjunctival hyperaemia and chemosis is noticed, there could be corneal edema and infiltrate with increasing AC reaction and hypopyon. There can be no red glow and the fundus details may be obscured. A rapid progression of signs usually occurs.

Fungal endophthalmitis

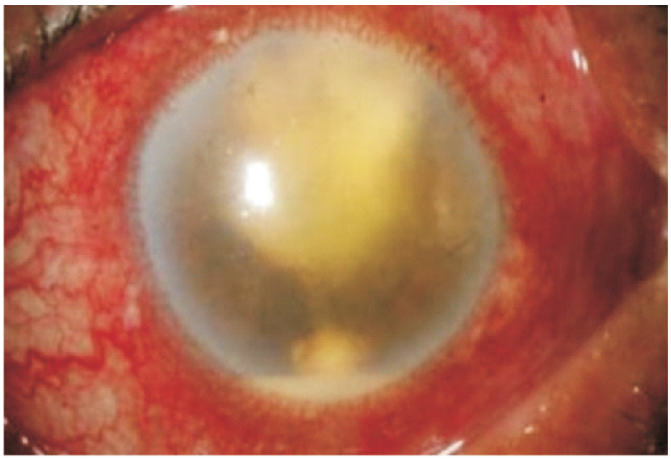


Figure 3: Fungal exudates

Presentation is usually late (after 4weeks) but can occur after one week. There are mild symptoms and minimal discomfort, visual discomfort may as well be minimal. Fibrinopurulent AC exudates, vitreous snow balls and vitreous abscess are suggestive of fungal infection. Most commonly isolated species are Candida albicans, Aspergillus and Fusarium.

Nocardia

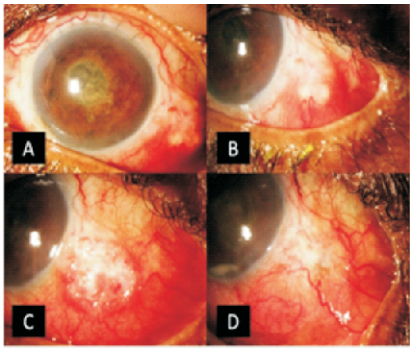


Figure 4a: Scleral exudates in Nocardia infection

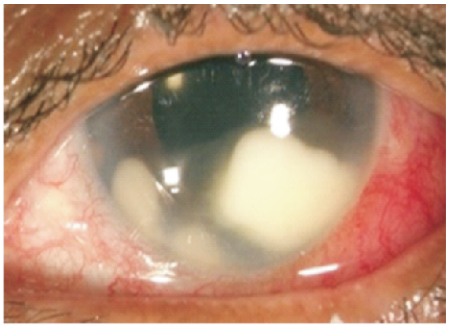


Figure 4b: Nodular exudates in Nocardia infection

The exogenous variant involves the anterior segment, since the vitreous is not a good medium for growth. The bare foot habits of the geographic location should be kept in mind while evaluating a case of post-operative endophthalmitis. Identifiable nodular exudates in AC are quite characteristic.

Propionibacterium acenes

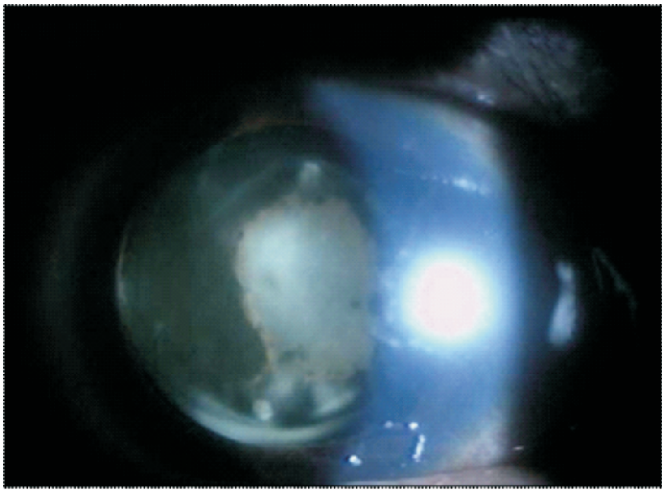


Figure 5: Posterior capsule plaque in P. acenes

A normal commensal of the conjunctival sac ,anaerobic gram positive bacillus, causes late post-operative endophthalmitis because of routine post-operative uses of steroids. Exacerbation of inflammation is noticed each time steroids are tapered. Presents as equatorial white plaques mimicking posterior capsular opacification. YAG capsulotomy exacerbates the reaction and can lead to vitreous reaction and full blown endophthalmitis.

Sterile post-operative endophthalmitis

Here the symptoms are less intense. Intra ocular drugs, gas, chemicals from sterilisation, mechanical irritation of iris ciliary body by IOL, autoimmunity to retained lens matter or excessive iris or vitreous manipulation are the usual causes of sterile endophthalmitis. Retained lens matter and endophthalmitis may occur concurrently and one should suspect infection in any post-operative ocular inflammation with retained lens material

Work up sheet

History

Visual acuity

Examination of lid and adnexa

Examination of specific area of interest (wound site, bleb etc)

IOP

Ocular movements

Anterior segment examination

Fundus examination

Systemic examination

Complete hemogram, blood sugar viral markers (optional with consent)

Informed consent for further management

The role of meticulous history taking and thorough systemic examination cannot be over emphasised. The co morbidities like diabetes, tuberculosis and other immuno compromised states due to disease or treatment must be addressed and managed simultaneously, one cannot wait until completion of the treatment and subsidence of signs of the co morbidity.

Examination of the periocular structures, lids, naso lacrimal system need be done to identify the possible source of infection.

Wound abnormalities like wound leak, vitreous wick, inadvertent filtering bleb, suture abscess etc should be looked for. Other surgical risk factors are vitreous disturbance, exteriorised haptics / sutures as in scleral fixated IOL.

Newer studies have not confirmed higher incidence of endophthalmitis following clear corneal incisions compared to scleral incisions.

Diagnosis

Confirmation of infective etiology depends upon the identification of microorganism. The best chance will have 70% isolation of organism, still 30% will remain unidentified. The samples from aqueous aspirates yield upon 36- 40% positive cultures whereas vitreous aspirates/ biopsy are positive in 56-70% cases.

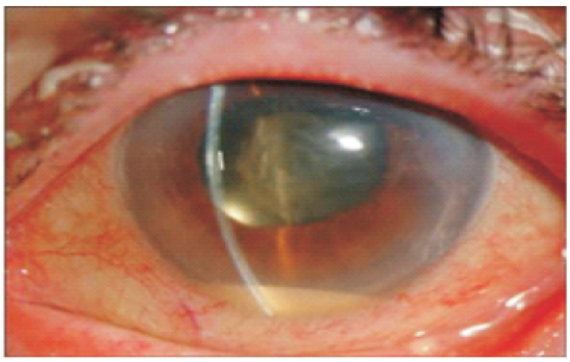


Figure 6: Post operative AC reaction

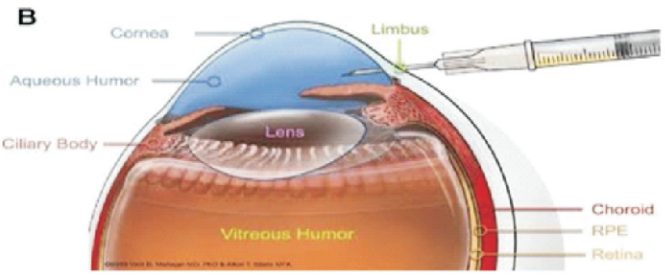


Figure 7: 26 G needle AC TAP

Aqueous fluid / hypopyon 0.1 – 0.2 ml is obtained by paracentesis using 23 g needle, 26 g needles are to fine to

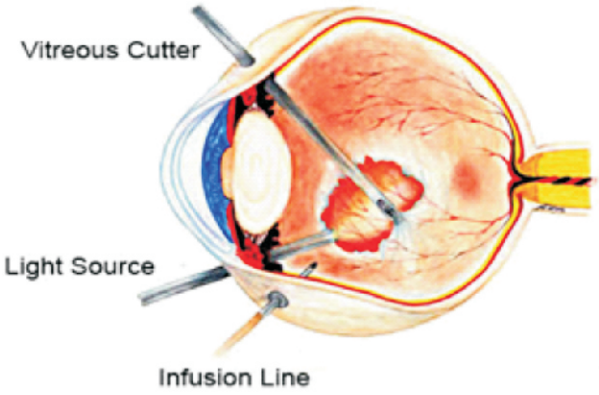


Figure 8: Vitreous biopsy

Vitreous samples of 0.2 – 0.3 ml are obtained by aspiration through pars plana with the help of 23 g needle. In most of the severe cases there is high probability of a dry tap, hence biopsy with the cutter has the highest probability of getting adequate sample and yield.

Biopsy can be performed with 2 pars plana ports, without opening the infusion vitreous sample is collected in a syringe connected to the aspiration tube. (alternately the infusion can be through a 26 g needle instead of a canula). The cutter is placed behind the lens/ IOL and tip should be visible though hazy. In case of IOL a piece of posterior capsule may be taken in the sample.

Other samples could be IOL, suture, abscised tissue etc.

Best is to inoculate immediately in the operation room, loss of precious time in transport of samples would have poor yield. First Gram and Giemsa stain is done, inoculations are done on blood agar, choclate agar, saburouds and Maconky agar for aerobic organisms and thioglycolate broth for anaerobic bacteria.

The reasons for a poor yield could be fastidious organisms, insufficient sample, sterile endophthalmitis or prior administration of antibiotics. Repeat cultures may be needed in poor response to treatment, presence of contaminants in the media or presence of fungi which are likely to be missed in the initial examination.

Newer microbial detection methods

FISH (florescent in situ hybridisation)

MICROARRAYS – large scale screening system for simultaneous diagnosis and detection of many pathogens

LAMP (loop mediated isothermal amplification)

DNA sequencing

MALDI-TOF MS (matrix assisted laser desorption ionisation time off light mass spectrometry)

PCR & MULTIPLEX PCR – it is a technique that has led the way into this new era by allowing rapid detection of microorganism that were previously difficult or impossible to detect by traditional microbiological methods. A quick, highly transport tolerant, highly sensitive and specific test. Unlike other tests which detect immune response, this detects pathogens. Valuable in detecting fastidious organisms, Mycobacterium, Bacillus cereus, Nocardia, Hemophilus etc.

Not without limitations though, false positive tests due to contaminants and dead organisms. The test is costly, has limited availability and cannot comment on antibiotic sensitivity as well.

Current perspective on endophthalmitis management

Endophthalmitis vitrectomy study (EVS 1995) guides us to the management of endophthalmitis, however re-evaluation of the EVS recommendations seem appropriate as treatment modalities have changed since then.

EVS recommends management on the basis of visual acuity and the media clarity, on the visibility of retinal structures. Recommends vitrectomy in eyes with severe media opacity and PL, PR vision. It also recommends that systemic antibiotics have no added benefit (excluding traumatic, bleb related and endogenous endophthalmitis).

On confirmation of endophthalmitis by clinical examination before confirmation of organism a broad spectrum antibiotic is chosen which is non-toxic to the ocular structure in the required doses. Unfortunately not a single agent is effective against gram positive, gram negative cocci and bacilli. The intra vitreal doses of commonly used drugs-

For **gram positive organisms**

Vancomycin- 1mg/0.1 ml

Cephazolin – 2.25 mg/ 0.1ml

Cefuroxime – 1mg/0.1 ml

Ceftriaxone – 2.25mg/0.1ml

For **gram negative organisms**

Amikacin - 400µg/0.1ml

Ceftazidime 2.25mg/0.1ml

Gentamicin 200µg/0.1ml

Role of intra vitreal vancomycin remains a standard choice for gram positive organisms though increasing number of resistant strains are emerging.

For gram negative organisms intra vitreal amikacin is the most effective of all but has toxic effects on the retina, ceftazidime is

safe but many organisms are resistant to the drug.

Dexamethasone 400µg/ 0.1 ml, is administered concurrently to minimise the inflammation caused.

Less commonly used intra vitreal drugs-

Piperacillin - tazobactam - 250µg/0.1ml – effective against P. aeruginosa, Enterobacter, klebsiella

Colistin – 0.1mg (1000IU)/0.1ml

Imipenem 50-100 µg/0.1 ml

Carbenicillin – 2000µg/0.1 ml

Ticarcillin - 3000µg/0.1 ml

Aztreonam -100µg/0.1 ml

Ciprofloxacin 100µg/0.05 ml

For **fungal infection** sintravitreal drugs used are

Amphotericin B - 5µg/0.1 ml

Voriconazole 100µg/0.1 ml

Intra vitreal drugs as per the culture/ sensitivity reports (if available) or the broad spectrum antibiotic combination are administered. The fungal filaments are seen on smears, and subsequently antifungal drugs are administered. Half the normal doses are administered in vitrectomised eyes.

Oral administration of moxifloxacin 400 mg once daily, linezolid 600 mg twice daily (for resistant organisms) have been found to be effective, wasn't studied in the EVS.

Every treating centre shall have a treatment protocol based on the scientific background and their own experiences as per the review of their results/ outcome. The decision to undertake a surgical procedure (core vitrectomy) is imperative to the prevailing conditions like severity, media clarity (corneal infiltrate, opacity are limitations to vitrectomy), accessibility etc.

Intra vitreal injection at the outset has advantages of improvement without further intervention, clarity of media and sometimes spontaneous induction of PVD.

Core vitrectomy is undertaken if the intravitreal injection is not effective or minimally effective in 24 to 48 hrs post injection. Sometimes also undertaken for removal of residual vitreous opacities after the control of infection. The debate between early vitrectomy vs deferred is still on. With the introduction of small gauge trocar canula system the incidence of peripheral retinal tears has come down significantly. Minimal efforts should be made to induce PVD, though PVD ensures near complete removal of vitreous. Posterior capsulectomy is generally performed for better capsular bag lavage, better drug penetration and media clarity.

Decision of repeat surgery depends upon poor response and persistence of infection. Removal of IOL and capsular bag with vitreous lavage is done in repeat procedures.

Use of silicone oil is not done frequently. Used in cases of retinal breaks and retinal detachments. It may prevent retinal detachment in untreated superior breaks for a while. To an extent prevents the growth of microorganism as well.

Retinal detachment is the most dreaded complication and once it happens visual outcome is severely compromised. Thorough examination of the retinal periphery must be done, a hazy media and opaque vitreous cuff hinders the peripheral view. A low infusion pressure allows easier indentation for a better visualisation.

Late complications

Although some of the problems resolve on its own in due course of treatment some may lead to fixed/ progressive visual loss and ocular morbidity. Delayed vitreo retinal pathologies are high risk factors for poor outcome.

Anterior segment complication are corneal opacification, posterior/ anterior synechia, subluxation/ dislocation of IOL, secondary glaucoma, bullous keratopathy etc. Ocular hypotony and band shaped keratopathy are ominous signs.

Posterior segment complications can involve macula, optic nerve, retina and the choroid- ciliary body. Inflammation, endotoxin and drugs are responsible for the deleterious effects.

Macular pathologies

Cystoid macular edema (CME) –A common cause of vision loss caused by inflammatory or mechanical factors. Persistent edema causes disruption of the neural networks leading to gliosis and atrophy resulting in permanent vision loss. Inflammatory process can be treated by systemic or periocular, supra choroidal, intra vitreal steroids. Epiretinal membranes are the cause for mechanical traction and persistent macular edema. Removal of the cause (ERM) treats such persistent edema.

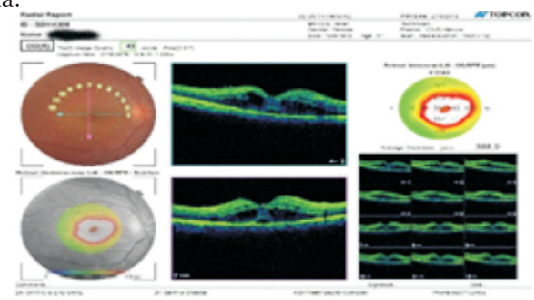


Figure 9: Macular edema

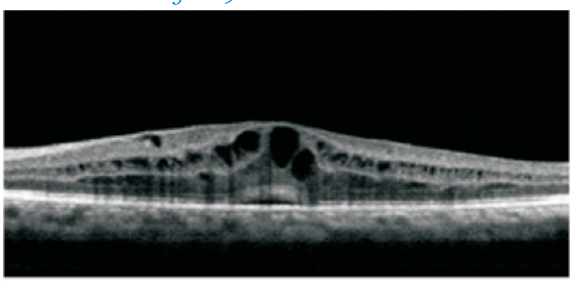


Figure 10: Cystoid Macular Edema

Retinal toxicity though not very common are due to drugs (aminoglycosides, amphotericin), seen as whitening of macular area with intra retinal haemorrhage at the posterior pole.

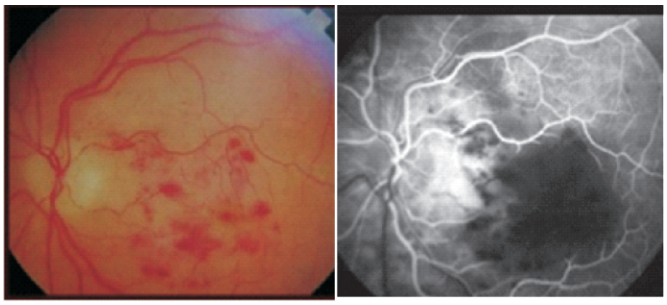


Figure 11: Drug Toxicity

Haemorrhagic occlusive retinal vasculitis (HORV) –a rare but devastating complication is due to delayed hypersensitivity to vancomycin. Early intensive steroid can salvage a few.

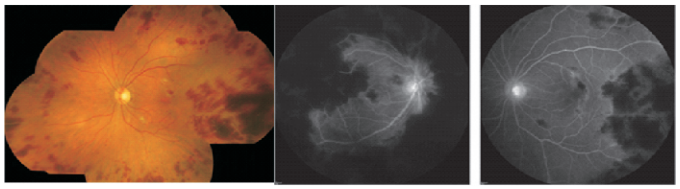


Figure 12 : Haemorrhagic occlusive retinal vasculitis (HORV)

Retinal detachment a feared complication has risk of 7.4 to 8.4 % after treatment of endophthalmitis. Usually encountered in infection by virulent organisms with poor presenting visual acuity. Anatomical success was reported in 78% in EVS, but the occurrence was correlated with poor visual outcome.

Prevention of endophthalmitis

Prevention of endophthalmitis is much cheaper than its management. Pre-operative instillation of antibiotics (moxifloxacin, gatifloxacin), application of 5% povidone iodine 3 minutes before surgery, intracameral moxifloxacin have been found to be effective.

The sterilisation of instruments and operation theatre, quality of consumables and clean practices are important aspects in prevention of endophthalmitis.

Documentation of each and every event and the advice to the patient should be meticulously done and kept in the records to safeguard practices.

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Micropulse Trans-Scleral Cyclophotocoagulation: A New Innovative Technology in Glaucoma Management

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Abstract : Glaucoma is a progressive optic neuropathy and is the leading cause of irreversible blindness worldwide.[1] The treatment of glaucoma aims to lower the intraocular pressure (IOP) by using medications, lasers and incisional surgery. Laser treatment in Glaucoma till now was in the form of YAG laser peripheral iridotomy, Laser trabeculoplasty and highly destructive cyclo photo coagulation using G probe.

Diode laser micro pulsing has been shown in previous clinical and experimental studies to be useful in achieving targeted tissue damage and minimizing collateral thermal injury to adjacent tissues.[2,3,4] Micropulse diode trans scleral cyclo photocoagulation (MP-TSCPC) has emerged as a new treatment option for glaucoma. The new **Cyclo G6,Glaucoma laser system** (Diode laser 810nm) is an innovative cyclo photocoagulation system **with unique patented Micro Pulse technology.** The Micro Pulse technology makes this laser safe and efficacious.[6]

This article would discuss mode of action,indications,procedural considerations and advantages of MP-TSCPC.Atlast,the results of our own prospective study would be mentioned.Ourstudy included 40 eyes of 38 patients who underwent MP-TSCPC with the new CycloG6,Glaucoma laser system.We included varied types of glaucoma.At 6 months follow up,the mean IOP reduced by 43.4% which was statistically significant with a P value of 0.0001.The mean no. of medication reduced from 3.2 at baseline to 1.94 at 6 months follow up which again was statistically significant(P value 0.001)

Thus, this newer **Cyclo G6, Glaucoma laser system with Micro Pulse technology** is a gentle,low risk option to control IOP and reduce the number of medication needed.As compared older G probe,MP3 provides a kinder,gentler approach with identical efficacy yet improved safety profile.

Introduction :

Glaucoma is a progressive optic neuropathy and is the leading cause of irreversible blindness worldwide.[1] The treatment of glaucoma aims to lower the intraocular pressure (IOP) by using medications, lasers and incisional surgery. Laser treatment in Glaucoma till now was in the form of YAG laser peripheral iridotomy, Laser trabeculoplasty and highly destructive cyclo photocoagulation using G probe.

Diode laser micro pulsing has been shown in previous clinical and experimental studies to be useful in achieving targeted tissue damage and minimizing collateral thermal injury to adjacent tissues.[2,3,4] In contrast to conventional laser delivery where a continuous train of high intensity energy is delivered, micropulse laser application delivers a series of repetitive short pulses of energy with rest periods in between pulses.[5] Micropulse diode trans scleral cyclo photocoagulation (MP-TSCPC) has emerged as a new treatment option for glaucoma. The new **Cyclo G6,Glaucoma laser system** (Diode laser 810nm) is an innovative cyclo photocoagulation system **with unique patented Micro Pulse technology.** The Micro Pulse technology makes this laser safe and efficacious.[6]

Figure 1 : Cyclo G6 Glaucoma Laser System

Micropulse trans scleral cyclophotocoagulation (MP-TSCPC) was **approved by FDA in January 2015.**

Mode of action

In **MP-TSCPC**, a fractionated continuous wave diode laser is

Figure 2 : Micro Pulse P3 (Pars Plana Probe)

employed which targets melanin in a non destructive way in ciliary body tissues thus reducing aqueous production. Also, possibly, it increases uveo scleral out flow. In MicroPulse technology 31.3% duty cycle signifies that the laser is off 68.7% of the time, thereby avoiding focal heating and burning of the tissue. The technique of gliding the MP3 device back and forth over 1 hemisphere of the ciliary body results in a slow, steady application of laser energy. Micropulse delivery allows energy to build up to the coagulative threshold in targeted pigmented tissues during the "on" cycles. Adjacent non-pigmented tissue cools during the "off" cycle and does not reach the coagulative threshold. Collateral tissue damage is therefore minimized, thus resulting in fewer complications without sacrificing efficacy.

Where can it be used ?

A wider range of patients can be treated with the MP-TSCPC procedure. This is used for **patients who are often on maximum medical therapy** or for whom other treatments have failed.[7] It can be used in place of traditional surgery and even together with cataract surgery. Those who are not good surgical candidates for one reason or another may do well with this procedure. Patients who may have bleeding problems or who would have a difficult time with care after traditional glaucoma surgery are also good candidates.

So, the **indications are :**

1. Complicatedglaucomas(Silicone oil induced, Uveitic, Post keratoplasty and neo vascular glaucoma). However, inneo vascular glaucoma, it doesn't seem to have promising results.
2. Patients who are not fit for surgical intervention/who refuse surgical intervention
3. Refractory glaucomas[8]
4. Patients with conjunctival scarring
5. Failedtrabeculectomy
6. May be a promising treatment for early glaucomas once more and more studies are available9,[10]

What are the advantages of this technology ?

1. Non-incisional
2. Non invasive laser procedure
3. Less of follow up
4. Repeatable
5. FDA approved

How to perform the procedure ?

Anaesthesia :Retrobulbaranaesthesia / Peribulbaranaesthesia

I prefer to perform the procedure in operating room. The laser settings used are 2000mw energy, 31.3% duty cycle which translates to 0.5 ms of on-time and 1.1 ms of off-time.The laser probe's fiber-optic tip is applied with steady pressure in a continuous sliding arc (painting) motion. The probe (Micropulse pars plana probe) is put perpendicular to the globe in such a way that probe notch is towards the limbus. The tip is designed in a way to fit and adhere to the ocular globe at 3mm posterior to the limbus. MP3 probe is applied in superior and inferior hemispheres for a total of 160 seconds that is 80 seconds in each hemisphere. The MP3 probe is applied directly posterior to the limbus and moved every 10 seconds. The voice countdown timer feature on the laser makes this process very easy and efficient. We have to be careful in **avoiding the laser treatment at 3 and 9 clock hours** as it could affect ciliary nerves and therefore leading to pain. During treatment areas of scleral thinning are avoided. At the conclusion of surgery, 1% atropine is administered. Post laser treatment regimen includes topical steroid in tapering dose for a month. Also, antiglaucoma treatment is to be continued and gradually withdrawn depending on IOP level.

Our experience :

We evaluated 6 month resultsin a prospective,non comparative interventional case study of 40 eyes of 39 patients of various types of moderate to advanced glaucoma who underwent **MP-TSCPC** at Rajas Eye & Retina Research Centre, INDORE (M.P.) between March 2018 and October 2018. The patients had either the uncontrolled IOP with maximum medical therapy or they were non compliant for multiple medication.We included Primary Open Angle Glaucoma (POAG), Developmental Glaucoma, Neovascular Glaucoma (NVG), Post Traumatic Glaucoma, Refractory Paediatric Glaucoma, Silicone Oil Induced Glaucoma, Post Keratoplasty Glaucoma, Co-existing Cataract and POAG, Failed Trabeculectomy and Chronic Angle Closure Glaucoma (CACG). The cases with thin sclera were excluded from the study.

The mean baseline IOP was 33.8 mmHg which reduced by 46%,52.4%,47.2%,42.5%,44.2%and 43.4% on follow up days

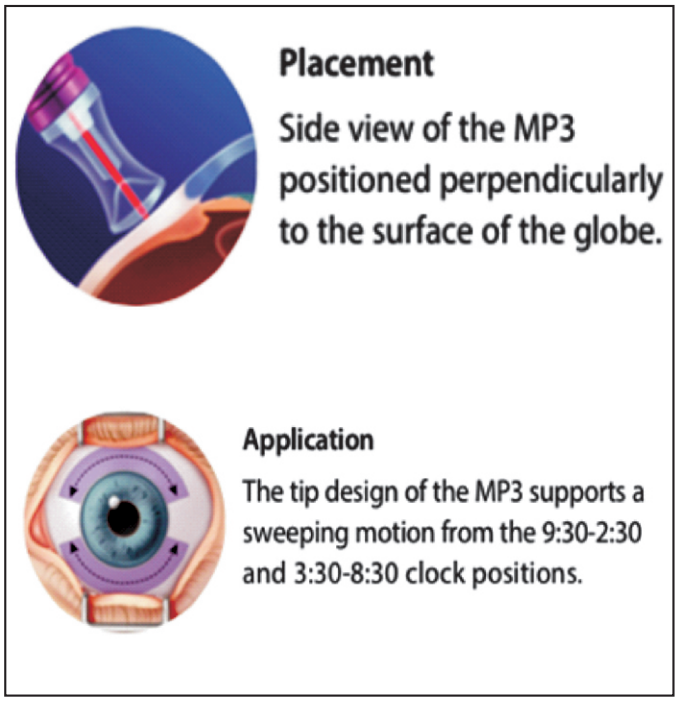

Figure 3 : Placement and Application of MicroPulse Pars Plana Probe

1,7,15,1month,3 months and 6 months respectively. The statistical analysis of observed IOP from baseline to follow up visits was done by computed Wilcoxon Signed rank test and the P value at all time points was less than 0.0001 meaning thereby that there was a significant reduction in IOP following **MP-TSCPC.**

The mean no. of medication reduced from 3.2 at baseline to 1.94 at 6 months follow up.(P value 0.001)

Thus in our study there was significant decrease in IOP and number of medication at variable follow-up periods. No major side effects were noted.

Conclusion :

Similar to continuous wave TSCPC, MP-TSCPC eliminates the need for a sterile operating room, provides less post-operative activity restriction, virtually no risk of infection and is a portable technology. **MP-TSCPC** is a non-invasive option for range of glaucoma patients and also it is a good alternative for managing co-existing cataract and glaucoma. **MP-TSCPC** using the MP3 probe and the new Cyclo G6 glaucoma laser system has been shown to have excellent safety and efficacy rates. **MP-TSCPC** is an effective modality of managing glaucoma cases(Especially refractory glaucoma) without significant side effects as used to be seen with age old continuous pattern trans scleral cyclophotocoagulation.[11] Thus, this newer **Cyclo G6, Glaucoma laser system with Micro Pulse technology** is a gentle, low risk option to control IOP and reduce the number of medication needed. As compared older G probe,MP3 provides a kinder, gentler approach with identical efficacy yet improved safety profile.

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Nurture Your Eyes with Autologous Serum

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Autologous serum eye drops (ASED) are many things: effective, well tolerated and full of substances that artificial tears can't replicate. Eye drops derived from a patient's own blood have gained therapeutic standing over the intervening decades, helping many dry-eye patients live better lives. Autologous serum (AS) was one of the fluids used in a 1975 study testing the ability of a perfusion pump to keep chemically burned eyes moist.[1]

The Production

Preparation protocols for ASED vary, but they all share these fundamental steps: This includes testing for hepatitis B (HBV) and C (HCV), syphilis, and HIV serology. The patient then donates blood; the blood is allowed to stand for 24–48 h at 4°C to allow clotting, and then centrifuged at 4000 rpm for 10 min. The serum is separated from the blood and diluted with in a laminar flow cabinet. Most drops are 20% serum, although some patients use 25%, 50%, or even 100% serum drops. Preservatives usually are not added to AS, thus reducing the risk of preservative induced toxicity associated with other dry eye treatments. However, lack of preservatives theoretically increases the risk of ocular infection. AS can be stored for less than one month at 4°C while in use, and for up to three months at 20°C.[2]

The Benefits

ASED are thought to alleviate dry eye by supplying tear components.

Serum contains bioactive agents that may promote healthy cell growth and healing of the ocular surface, including albumin, vitamin A, nerve and epidermal growth factors, and immunoglobulins, some in higher concentrations than in natural tears. These epitheliotrophic factors are thought to be responsible for the therapeutic effect of serum observed on ocular surface disorders.[3]

Fox was the first to use serum to treat human dry eyes.[4] However, the recent renaissance of this therapy began when Tsubota in 1999 described its successful use in eyes with persistent epithelial defects.[2]

Studies have concluded that the topical use of autologous platelet-rich plasma as monotherapy is an effective treatment to improve signs and symptoms in patients suffering from moderate to severe chronic dry eye disease. Improvements of the dry eye disease subjective symptoms, corneal fluorescein staining (CFS), and corrected distance visual acuity (BCVA) were evaluated.[5]

The Indications

ASED have been recommended for treatment of patients with several ocular surface disturbances, such as:

- Sjögren's syndrome related tear deficiency,
- Non-Sjögren's tear deficiency associated with graft versus host disease,
- Neurotrophic keratitis,
- Persistent epithelial defects,
- Superior limbic kerato conjunctivitis,
- Recurrent erosion syndrome,
- Chemical burns,
- and Postoperative dry eye induced by LASIK.

People treated with 20% to 50% AS four to eight times a day have reported subjective improvement in dry eye symptoms.

Recent studies identified selenium compounds, e.g., Selenoprotein P (SeP) and Se-lactoferrin as candidates for treatment of dry eye. Tear SeP is a key molecule to protect the ocular surface cells against environmental oxidative stress.[6]

Matsumoto showed that AS contains nerve growth factor and SP levels that are several times higher than the levels in tears and harbors IGF-1.[7] In neurotropic keratopathy in which neural factors such as acetylcholine or SP are depleted from the cornea, 20% AS drops are believed to suffice them.

The rationale of using AS in chemical burns derives from the fact that it contains antiproteases such as alpha 2 macroglobulin (which reduces collagenase) and vitamin A (which modulates the normal growth and differentiation of the epithelium).[8,9]

In localised tear film deficiency disorder like Superior limbal kerato conjunctivitis, a prospective cohort study in which 20% serum eye drops were used as additional therapy, showed improvement all patients. Tear break up time increased significantly and conjunctival squamous metaplasia was

reduced.[10]

The Add Ons

Among overall blood derived eye drops, both autologous (from the patients themselves) and homologous (from donors) products exist, with different advantages and disadvantages. Homologous sources including allogeneic serum obtained from healthy donors, and umbilical cord blood serum collected at the time of delivery, are efficient alternatives, especially when autologous serum therapy is contraindicated or not appropriate.[11]

Use of standardized and quality-controlled cord blood serum (CBS) eye drops represent a promising therapeutic approach in the healing of severely injured corneal epithelium and in subjective symptom relief. These drops can be obtained as readily available and quality-controlled blood derivative from cord blood banks on a routine basis.[12]

Mesenchymal stem cells from umbilical cord blood can be used to regenerate corneal tissue and retinal nerve cells, umbilical cord serum might be applied for tissue engineering and regenerative medicine in the future.[13]

Though blood derived products have come out as a pool of various epitheliotrophic factors they also contain TGF-β. It is known to have antiproliferative effects, and high concentrations of TGF-β may suppress wound healing of the ocular surface epithelium.[14] This observation contributed to use of a diluted solution of serum to maintain TGF-β levels that are comparable with those of tears.

Conclusion

Strict guidelines for good manufacturing, quality control and documentation must be established and maintained before and throughout the therapeutic use of autologous serum eye drops. Meanwhile, the use of serum eye drops remains an experimental approach. Therefore, all applicable legislative restrictions should be carefully considered and well documented and informed consent should be obtained from each patient.

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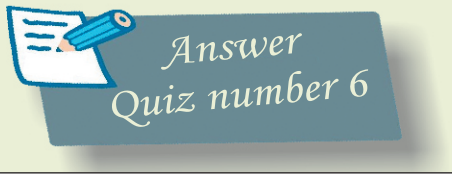

1. Digits 2. Music 3. River 4. Fog 5. Silence

Hermann Ludwig Ferdinand von Helmholtz

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1. **Hermann Ludwig Ferdinand von Helmholtz** (August 31, 1821 – September 8, 1894) was a German physician and physicist who made significant contributions in several scientific fields.
2. Helmholtz was born in Potsdam the son of the local Gymnasium headmaster, Ferdinand Helmholtz, who had studied classical philology and philosophy.
3. In physiology and psychology, he is known for his mathematics of the eye, theories of vision, ideas on the visual perception of space, colour vision research, and on the sensation of tone, perception of sound, and empiricism in the physiology of perception.
4. Trained primarily in physiology, Helmholtz wrote on many other topics, ranging from theoretical physics, to the age of the Earth, to the origin of the Solar System.
5. In physics, he is known for his theories on the conservation of energy, work in electrodynamics, chemical thermodynamics, and on a mechanical foundation of thermodynamics.
6. As a philosopher, he is known for his philosophy of science, ideas on the relation between the laws of perception and the laws of nature, the science of aesthetics, and ideas on the civilizing power of science.
7. Helmholtz revolutionized the field of ophthalmology with the invention of the direct ophthalmoscope; an instrument used to examine the inside of the human eye. Although some credit the invention of the ophthalmoscope to Charles Babbage in 1847, it was not until it was independently reinvented by Hermann von Helmholtz in 1851 that its usefulness was recognized.
8. In 1881, Helmholtz was elected Honorary Fellow of the Royal College of Surgeons in Ireland.
9. On 10 November 1881, he was awarded the Lėgiond'Honneur: au grade de Commandeur, or Level 3 - a senior grade. (No. 2173).
10. The largest German association of research institutions, the Helmholtz Association, is named after him. The asteroid 11573 Helmholtz and the lunar crater Helmholtz as well as the crater Helmholtz on Mars were named in his honour. In Charlotte burg, Berlin, the street Helmholtzstraße is named after von Helmholtz.