The IDOS

News & Views

Official Publication of Indore Divisional Ophthalmological Society

Website : idos.co.in Year : 2021-22 Volume 1 Issue 1

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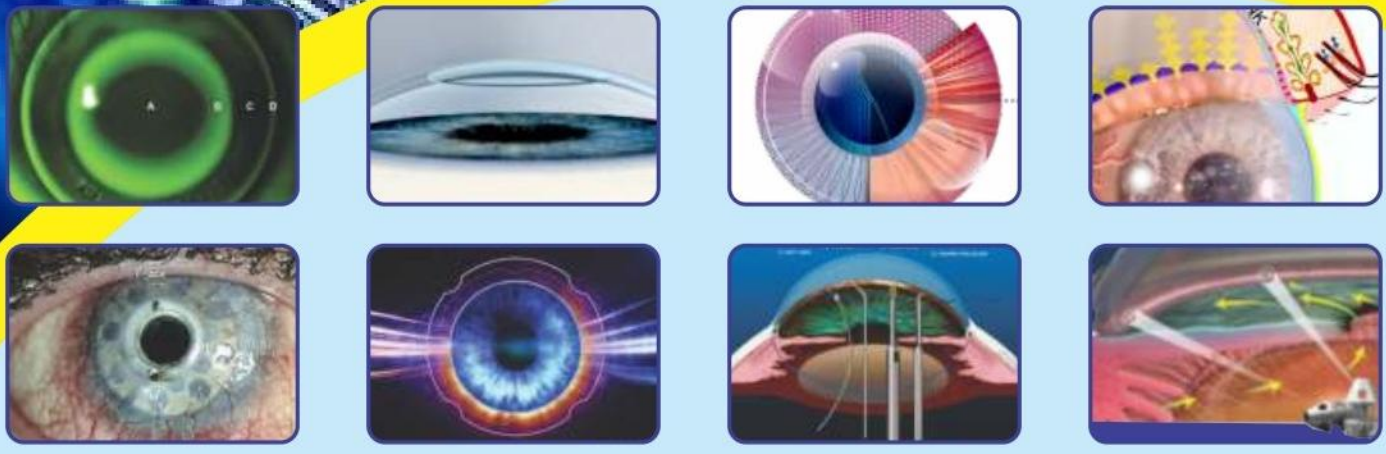

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1. Koercher T, Buchholz P, Kummich E. Clin Ophthalmol 2009; 3: 33-39. 2. Optive Prescribing information, India, 2020. 3. Hardten et.al; Current Medical Research and Opinion; Vol. 23, No., 2007, 2083–2091.

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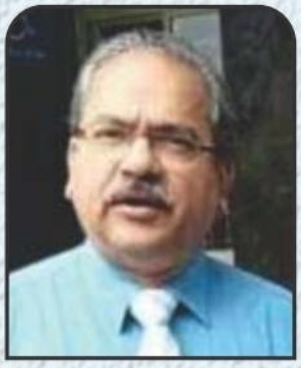

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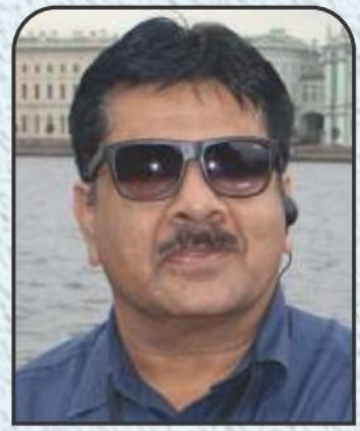

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THE IDOS - News & Views

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FROM THE EDITOR'S DESK.....

If you talk about it, it's a dream , if you envision it, it is possible, but if you schedule it, it's real.

TONY ROBBINS

It gives me an immense pleasure in presenting this new form of our previous news letter " News and views ".The new academic letter is in the process of taking the form of a journal.

Everything is possible if you desire it, you dedicatedly work on it. The IDOS family is known for its cohesiveness. This journal is an example of the same. The team worked together day and night to make the efforts fruitful.

We have tried to compile articles from different sub specialities so as to give a broad overview.

The burning topic of myopia control, the guest editorial on.

Similarly article on management strategies of Meibomian gland dysfunction Bowman's topography and synthetic cornea gives a new perspective of corneal technologies. Newer developments on medical and surgical strategies of glaucoma updates the reader on newer happenings. The gene therapy of retinal disorders is an eye opener. oculofacial aesthetics give a newer perspective to the practice.

Competency based MBBS curriculum is the need of the day. Overall I feel my team has worked hard to present this journal full of knowledge with updates. Your appreciation and contribution will give a boost in our efforts .

Dr. Vandana Telgote
Editor

Dr. Urvija Choudhary
Dr. Sumit Agrawal
Co-Editor

MYOPIC EPIDEMIC....

Dr. Sharadini Vyas

Myopia is sixth leading cause of visual impairment in children .The global incidence of myopia was 27% in 2010 out of which 2.8% had high myopia. Changes in lifestyle specially during Covid 19 pandemic with increased indoor and screen activity has led to a rapid increase in progression of its incidence and degree. It is expected that by 2050 the incidence will rise to 52% with around 10% of it being high myopia.This is like an epidemic of myopia being the adverse effect of recent pandemic.

Million dollar question is why myopia is an issue. Myopia not only affects the quality of life of the patient but also has an impact on social and emotional functioning of the patient. Uncorrected myopia also adds to economic burden to the society. The main issue of myopia is its progression with age, as high myopia is known to cause additional visual morbidity due to increased incidence of maculopathy, retinal detachment, cataract and glaucoma. The reported incidence of CNVM is around 5.2 % to 11.3%,macular holes being 6-8%.Axial length elongation leads to peripheral retinal degenerations and glaucoma due to peripapilary stretching. Each diopter of increase in myopia increase the risk of glaucoma by 20%.

All these factors call for a serious note on controlling myopic progression at the right age . Myopia is a mismatch between axial length and refractive components of the eye which leads to defocus of light before retina.The normal defocus is corrected by routine mono focal glasses or contact lenses .These modalities still leave a mid peripheral defocus on the retina which is supposed to be the strong factor for myopic progression.

All treatment modalities available today aim towards reducing or correcting this defocus.Executive bifocals, Progressive glasses, Defocus Incorporated Multiple Segment ,Highly Aspherical Lens have significant impact on controlling myopic progression.

Pharmacological control of progression can be used alone or can be combined with specialty spectacle, contact lenses. Orthokeratology a new upcoming treatment for controlling myopic progression is on horizon with promising results.

We need to face the upcoming epidemic of myopia and be prepared with new methods for understanding and controlling it so as to prevent significant morbidities.

Publishing in the Times of COVID-19.....

Rolika Bansal[1], Santosh G Honavar[2]

"Medicine is a science of uncertainty and an art of probability" **William Osler**

The COVID-19 pandemic came as a ball of fire for the medical fraternity as little was known about the etiology, disease presentation, management protocols and prognosis of the disease. The world of medicine and science for a moment came to a stall. But, indeed just for a moment. The medical practitioners, scientists, researchers and health organizations all over the world were quick off the mark in understanding the disease etiology, managing the cases actively even though it had a myriad of presentations, framing standard management protocols and figuring out the prognosis of the disease. The uncertainty of the disease left us all perplexed looking for answers and finding solutions for our patients and has hence the importance of expedited and targeted research and publications.

We are thankful to all the authors and the national and international journals for expediting the publication process of the most important articles related to SARS CoV-2. It created a virtual network of helping hands and we were able to fight it all together as a united medical fraternity. We have always been thankful to the pioneers in the field of medicine for working extensively and describingnovel treatment modalities, investigations, and management protocols. Little did we know that this pandemic will bring out the best in us and turn out to be a blessing in disguise by giving us an opportunity to explore our research potential and surface the extraordinary perceptive nature of all the contributors to this cause.

Chan et al have stated in their review that 3,827 papers were published in various journals in a span of mere 5 months. The articles included commentaries (1370), narrative reviews (982), editorials (738), observational studies (456), case reports (221), systematic reviews (55), randomized clinical trials (4) and bibliometric analyses (1) with maximum contribution from the public health sector (1346). This is an impressive surge in the number of publications worldwide. However, the disproportionate distribution of type of publications, uncertain quality and validity of the studies cannot be ignored.[1]

Ophthalmology being a field affected by COVID-19 in terms of marked increase in number of exenterations due to rhino-orbital-cerebral-mucormycosis[2] along with various other eye manifestations, required a major need for data and publications. Reitinger et al reported a whopping spike of 22.1% in the ophthalmology publications in 5 months as compared to 2019, mostly noted between May 2020 and August 2020.[3] Banu and Singh reported that a total of 434 articles were published related to ophthalmology in 5 months of their analysis.[4]

Indian researchers, from the field of ophthalmology, pitched in substantially and added a colossal number of publications to the pool of knowledge available for COVID-19. From January 2020 to March 2021, Indian

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Journal of Ophthalmology (IJO), a peer-reviewed open access monthly journal by the AllIndia Ophthalmological Society (AIOS), expedited COVID-19 related articles and published 182 articles (13.55% of all the articles published in that duration). This resulted in a hike in the number of articles, improvement in citations and impact factors of the journal.[5] A geographical variation and a regional difference in pandemic severity was also noted[6] which called for a need for publications from different corners of the world.

"The discipline involved in finishing a piece of creative work is something on which you can truly pride yourself." **J. K. Rowling**

We take pride in noting that the need to segregate COVID-19 related information led to the creation of LitCovid - a database of all the SARS-CoV-2 and COVID-19 related articles in PubMed, with the most systematic and categorized approach for the convenience of the readers.[7] As on February 1, 2022 the database provided access to a total of 2,18,005 articles.[8,9]At the same time, it is important for us to note that the expedited articles need to undergo a stronger review process. It is believed that considering the limited number of patients and random distribution of patients, there is a possibility of bias bringing down the quality of articles. It has been stated that the speed at which the articles were getting published had inverse relationship with the quality of articles.[10,11] We believe that it could be due to the sharp increase in inquisitiveness and urge to explore more about the disease and provide for the patients suffering as a consequence of the pandemic and a good check at the level of reviewers of the journals could lead to publication of hand-picked quality-controlled relevant articles.

A major panel of researchers went on exploring the possibility of vaccines for COVID-19. This enabled the researchers to go beyond their comfort zone and discover a way to bring down the severity of the pandemic. Clinicians were able to spare more time for research as a number of departments faced a decline in foot-fall in the clinics.[3] It is expected out of the clinicians and researchers to keep up the excellent work and the upsurge of publications as the clinical work has resumed.[12] The pandemic has taught us the importance of publishing and flourishing, so it is mandatory for us to keep up with the pace. It has brought out the best of our research potential and we must understand and cater to the need of publishing in our respective fields by providing our validated observations for the benefit of our peers. It duly hones our reading, writing, clinical and observational skills and speaks of our diligence leading to self-growth and evolution.

"Writing the perfect paper is a lot like a military operation. It takes discipline, foresight, research, strategy, and if done right, ends in total victory." **Ryan Holiday**

Prosthetic Cornea

Trushaa Agrawal

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Diseases affecting the cornea are a major cause of blindness worldwide with about 2 million new cases of corneal blindness being reported each year.[1]

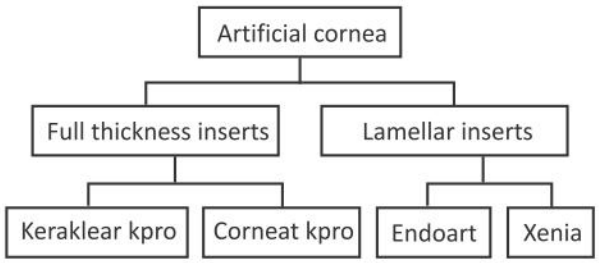
A recent study published in JAMA Ophthalmology assessed the shortage of cornea. There is only one available cornea for every 70 cases.[1]

Several attempts to develop an artificial cornea have failed in creating robust, scalable and reliable solutions.

Current keratoprosthetic devices have 2 major disadvantages:

1) They require a donor cornea for the procedure
2) High rate of secondary glaucoma

We have further classified prosthetic corneas into 2 categories



KERAKLEAR KPRO :

KeraKlear KPro (K3) is a foldable and injectable single-piece artificial cornea with no back plate or locking ring. It is made biocompatible acrylic material, similar to what is used in intraocular lenses . (Fig. 1)

The implant has a 7-mm overdiameter and has a 4-mm diameter central optic, and a perforated all peripheral skirt which allows fixation within a lamellar corneal pocket .

The KeraKlear is comes in six different models which are called KeraKlear XT. The number after XT indicates the amount of corneal tissue replaced in microns which also corresponds to the depth of the lamellar pocket. The six models are XT200, XT300, XT400, XT500, XT600, and XT700. It is recommended to leave approximately 100 μ of the corneal tissue posterior to the pocket.

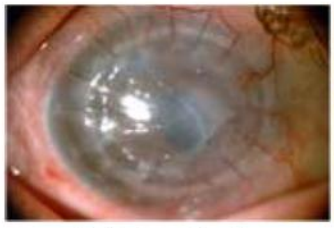
Indications- Non-inflammatory forms of corneal blindness (e.g. keratoconus, corneal dystrophies, corneal scars, and corneal edema).

Consultant, Cornea & Refractive
R.K. Eye & Retina Center, Indore

Surgical technique -

The KeraKlear artificial cornea is implanted into the cornea by using a femtosecond laser to create a uniform lamellar pocket within the cornea and to create a trephination incision 3.5mm in diameter. After preparation of the cornea, the KeraKlear is then inserted into the corneal pocket through the anterior opening in the cornea using non-toothed forceps. The rim of the device is then tucked into the pocket recesses. Postoperatively, these patients wear a bandage contact lens and receive prophylactic antibiotic eye drops.

Figure 1 : Keraklear KPRO



Failed graft with vascularisation

12 months post op Keraklear implantation

CORNEAT KPRO :

It is a dual member implant having a central PMMA optical member and an external integrating skirt formed by carbonated polyurethane fibers. (Fig. 2)

It integrates underneath the conjunctiva, a site rich with fibroblasts, which heals quickly and vigorously.

Indications - Failed keratoplasty

Not suitable for herpes keratitis, corneal degenerations, ICE syndrome, aniridia , SJS, OCP, alkali burns, vascularised cornea

The first-in-human (FIH) clinical trial for the CorNeatKPro took place in January 2021. The surgery was conducted by Prof.

IritBahar at Rabin Medical Center, Israel. It is expected to release for commercial use in market from 2023.

Surgical technique -

The PMMA lens provides a wide visual field and posterior side of the lens is designed to easily snap into the central trephined cornea and maintain the eye's integrity and as a result intraocular pressure remains normal post-surgery. The lens is then sutured to the eye using three non-degradable sutures. The lens is surrounded by a non-degradable porous integrating skirt, which is implanted subconjunctivally.

The skirt embeds itself into the sclera within weeks and stimulates anchoring cellular growth. Grooves on the circumference of the lens are filled with porous material and as a result are colonized with tissue. This novel integration method of biological stitching further secures the device coupled with long-term retention. The CorNeatKPro lens is designed to enable post-operative ophthalmic examinations and subsequent anterior and posterior segment surgeries (i.e. cataract and retinal surgeries). This is achieved with four openings or "ports," located on the rim of the lens, corresponding to the limbal zone. Four corresponding port indicators can be viewed through an ophthalmic microscope directing the surgeon to these port's locations.

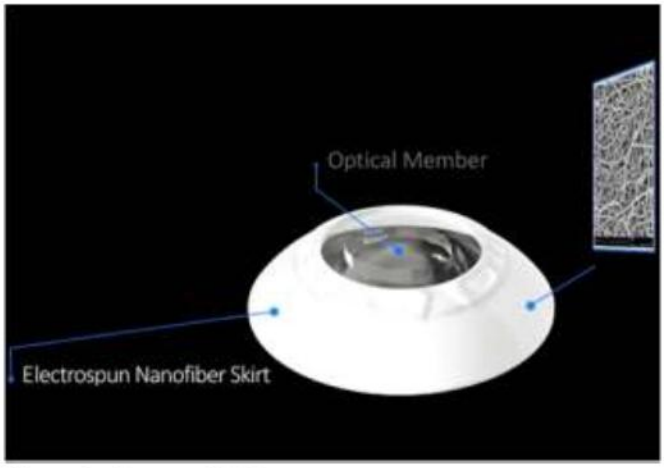


Figure 2 : Corneat KPRO

ENDOART artificial endothelial layer :

EndoArt is the world's first USFDA approved and only synthetic implant that replaces the human endothelium that the human body can never regenerate.

It attaches to the posterior corneal surface, to treat chronic corneal edema secondary to endothelial dysfunction

The EndoArt® implant is dome shaped, around 50 microns thick, with a curvature that resembles the posterior cornea. It is made of an optically clear, foldable, biocompatible co-polymer.

It is a strong, resilient graft that covers around 40 percent of the cornea's area, blocking excessive aqueous humour penetration from one side, while ensuring corneal nutrition from the other.

SURGICAL TECHNIQUE - The folded implant is inserted through a clear corneal incision around 2.2 mm in length. After insertion, EndoArt® unfolds itself and is attached to the posterior corneal surface using the air bubble technique, similar to a DSAEK or DMEK procedure.

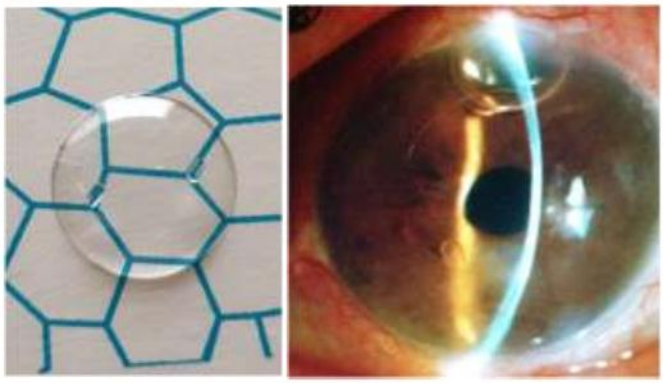


Figure 3 : EndoArt Implant

Xenia :

XENIA is a corneal implant made of natural corneal collagen of animal (porcine) origin. (Fig. 4)

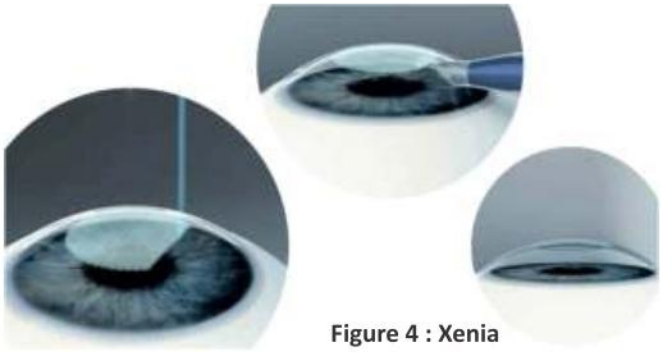


Figure 4 : Xenia

The XENIA material undergoes a special process to remove foreign cells including antigens. This special process is called decellularization. XENIA material is completely devoid of foreign cells and, hence much more tolerable.

Advantages -

1. Prevents corneal transplantation or defer corneal transplantation as long as possible.
2. Stablilization and vision improvement -The XENIA implant for keratoconus is crosslinked and therefore, significantly stronger as compared to the patient's own stroma and thus stabilizes the patient cornea.

At the same time the XENIA implant regularizes the patient corneal topography. It flattens the cornea, as well as reduces Higher Order Aberrations and therefore, improves the patient's visual acuity.

Surgical technique -

1. For keratoconus patients, a corneal stromal pocket with a small opening is created using femtosecond laser
2. The XENIA implant is inserted by means of an injector or forceps
3. After insertion, the XENIA implant is unfolded in the pocket.

All patients undergo Epithelium-off accelerated corneal cross-linking (CXL) 3 months after the Corneal Lenticular implantation

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PEEP INS

Liquid lens technology

The liquid lens technology is on the way for spectacles, contact lenses as well as intra ocular lens implantation.

Developed by university of utah, the liquid lens technology incorporates two membranes with liquid glycerin in between. The rear membrane has a mechanical actuator which adjust the curvature of the lens electronically with a infrared distance meter attached to the frame's bridge. With the change in gaze over different objects, the lens adjusts the curvature and therefore focus automatically in less than 14 milliseconds. The glasses are connected to the smart phone and the correction can be adjusted through the app wirelessly. Auto focusing smart contact lenses are also on the way. Fluid based intra ocular lenses will adjust focus with movement of ciliary muscle for distance and near vision.

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Advances in Meibomian Gland Dysfunction and Evaporative Dry Eye Management

Tushar Grover

Dry eye disease (DED) has come a long way, from the use of basic tear substitutes to advanced Vector Thermal Pulsation (VTP) treatments. With an improved understanding of the pathophysiology and manifestations of various types of dry eye, a plethora of new diagnostics and treatment modalities have become available. This is particularly true in the case of Meibomian gland dysfunction (MGD) associated evaporative dry eye.

Various innovations in diagnostic modalities such as meibography, interferometry, and tear film osmolarity measurement have helped quantify Meibomian Gland Dysfunction and tear film instability, which allows the clinician to take an informed decision on the treatment modalities most appropriate in each case.

This section will discuss a variety of treatments which have brought about a paradigm shift in dry eye care.

Need for advanced Therapies - Limitations of conventional warm compresses and manual lid expression:

Warm compresses with manual lid expression, or eyelid massage continues to be the first line of treatment for Meibomian Gland Dysfunction. However, due to the positioning of the Meibomian glands towards the inner surface of the eyelids and the requirement of a temperature of 32-45^{0}Celsius[1] to melt meibum, thereby consistently requiring more than 45^{0}C on the external surface of the eyelids. Retaining this heat with a dry or wet facecloth is often not possible. Additionally, it has been found that the pressure needed for the evacuation of expressible contents from the Meibomian glands ranges from 10 - 40 psi. Only 7 % patients are able to tolerate this degree of pressure over their eyes.[2] Due to the above reasons, compliance is a challenge, and even in the most compliant individuals, the desired results are often not achieved and patients are not always completely satisfied with this line of management.

Lipiflow:

Lipiflow, or Vector Thermal Pulsation (Johnson & Johnson Vision, USA) overcomes the limitations of conventional hot fomentation and lid massage by providing controlled outward directional heat and intermittent bidirectional pressure to the eyelids. This helps facilitate smooth release of lipids from the viable Meibomian glands. (Fig. 1)

Figure 1 : (a) Setup of Lipiflow Vector thermal pulsation system with (b) eyepiece activator

The lipiflow system is made of a sterile disposable eyepiece activator which connects to the main console. The activator itself comprises of 2 parts:

1) **Lid warmer** Composed of a heater, eye insulation and vaulted shield. This provides heat to the palpebral surface of the upper and lower eyelids directly at the level of the Meibomian glands (Fig. 2).

Figure 2 : Application of heat and pressure during treatment with lipiflow (arrows indicating direction of pressure)

2) **Eye Cup** Composed of an inflatable air bladder and rigid activator. This delivers graded pulsatile pressure to the outer eyelid

Various studies have looked at the clinical efficacy of Lipiflow and have found improvement in dry eye parameters such as Tear Breakup Time (TBUT), Lipid Layer Thickness (LLT), and reduction in OSDI (Ocular Surface Disease Index) and SPEED (Standard Patient Evaluation of Eye Dryness) Questionnaire scores indicating symptomatic improvement. The duration for which the effect lasts has been found to be between 6 months to 2 years. There are no defined parameters which determine

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how many sittings should be performed. Clinicians generally base this on symptomatic and clinical improvement.

Limitations:

1) The procedure is extremely expensive owing to the cost of the activator to the physician, thus most patients are unable to afford it.
2) Individuals with extensive Meibomian gland dropouts (as seen on meibography such as Lipiview) are usually refractory to any treatment and such patients may instead be managed using conventional measures with explanation of poor prognosis and alternative therapies.

MiboThermoflo:

The MiboThermoflo (Mibo Medical, USA, FDA approved) is a therapeutic device which supplies continuous heat to the external surface of the eyelids. The eyelids are gently massaged with the probe using an ultrasound gel which helps liquefy the contents of the Meibomian glands, following which they can be manually expressed to express the sebum (Fig. 3). This treatment is at present far more cost-effective compared to most other newer modalities.

Figure 3 : Mibo Thermoflo

Limitations :

1) Heat is applied from the external surface only.
2) No pressure pulsations are applied in the treatment. The glands need to be manually expressed after treatment.

Eyelid Heating masks:

Various heating masks such as MGDRx Eyebag®, EyeDoctor ®, Bruder®, Tranquileyes XR™, Thera°Pearl® are now available (Fig. 4). Comparative studies have shown stable heat retention throughout the treatment cycle, and have found all of these to be better than conventional warm compresses with facecloth.[3]

The modalities discussed above have also been compared in terms of heat achieved at the inner surface of eyelids, of which Lipiflow was found to be the most effective in attaining the surface temperatures of 40°C. (Fig. 5)

Limitation:

Manual massage is required to be performed in conjunction, to express the gland contents.

Figure 4 : USB-based heating mask

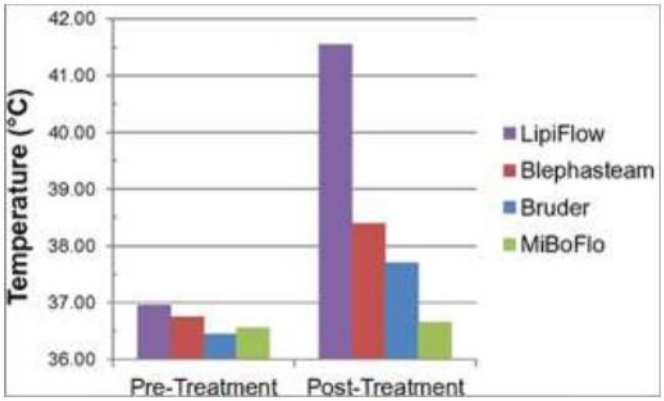

Figure 5 : Temperatures at the inner surface of eyelids (Source : Kenrick CJ et al, Case Rep Ophthalmol 2017)

Intense Pulsed Light (IPL):

Intense Pulsed Light, previously used extensively for Rosacea and other skin conditions is now gaining popularity in the treatment of Meibomian Gland Dysfunction. IPL is a polychromatic light source with a wavelength spectrum of 500-1200 nm, which can be filtered to allow only a range of wavelengths to be emitted.[5] The procedure involves

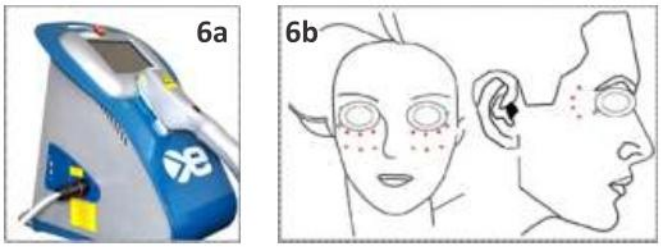

Figure 6a : Intense Pulsed Light console
Figure 6b : Intense Pulsed Light treatment zones

placement of a probe along with ultrasound gel on 10 -15 spots on either side of the face during the treatment cycle. Application is repeated for a total of two passes on each side. (Fig. 6)

The mechanism involves selective thrombosis of the vessels surrounding the Meibomian glands which leads to regression of telangiectatic vessels and reduction of the access of inflammatory mediators to the glands. In addition to this, the heat generated helps liquefy the contents of the glands.

Limitations:

1) The treatment is aimed at patients with Fitzpatrick skin type IV or lighter, as there is a greater risk of skin pigmentary changes in darker individuals.
2) Though the treatment is relatively safe, certain ocular complications such as uveitis, iris atrophy and pupillary defects have been documented . A case of corneal pigment deposition after IPL treatment in an individual wearing coloured contact lenses has also been reported.[7]

iLux:

The iLux MGD Treatment System (Alcon, USA) is a handheld device that provides light-based heat and compresses the meibomian glands to help express them. The sterile tip comprises an inner pad which slips behind the eyelid and the outer pad which work together to compresses the eyelid using a single-click button. Temperature sensors measure the inner and outer lid temperature to maintain a meibum melt temperature of 38-42^{0}C.(Fig. 7)

Figure 7 : iLUX device (Image Source : Tauber et al. Clinical Ophthalmology 2020)

A recent study comparing the iLux device and Lipiflow has found that both are comparable in terms of safety and efficacy, with no clinically meaningful or statistically significant differences between the two.[8]

Limitation:

A more recent device, there is limited literature on efficacy and safety. More controlled studies targeted on our population will help establish its role more clearly

Summary:

With a wide range of devices now available to treat Meibomian gland dysfunction and associated evaporative dry eye, clinicians are flooded with a plethora of options. It is important for each practitioner to take individual decisions on which modality/modalities are the most suitable in their practice, keeping in mind the nature of practice, the prevalence of dry eyes and the affordability of their patients. In a value-centric country like India, the perceived benefit from various treatments may vary depending on the affordability and that has to be kept in mind before choosing which treatment to administer. Additionally, a trial of warm compresses and manual lid expression, though less effective provide a reasonable starting point and also justifies the need for additional treatment if the patient is not improving symptomatically.

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Decoding Bowman's Topography

Shruti Maru

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Bowman's layer is an acellular interface between the epithelium and the stroma. The epithelium is a self-renewing layer, and constancy of epithelial thickness is essential for ocular refraction. The thickness of the epithelial layer is not constant over the entrance pupil, and its refractive index differs from the underlying corneal tissue.Reinstein et al [1] established the ability of the epithelium to reshape the anterior corneal surface, suggesting that the epithelium can remodel itself to compensate for stromal surface abnormalities caused by flap irregularities or irregular stromal ablation after lamellar refractive surgery. They found that changes in the epithelial thickness profile induced by myopic laser in situ keratomileusis (LASIK) result in a myopic shift called epithelial regression.[2]

Hence, the epithelial layer may induce subtle changes to the topography of the underlying corneal stroma. Simply removing the epithelium may alter the refractive and geometric properties of the cornea prior to photoablation.The topography of the Bowman membrane can bring relevant information regarding the properties of the corneal epithelium layer, by comparing the topographies obtained before and after epithelial removal.

Comparison of anterior corneal topography and Bowman topography in normal eyes

Gatinel et al in 2007 were the first to perform topographic analyses after epithelial removal.[3] Using an Orbscan II topography system, they studied normal eyes treated with PRK for myopia. They found a more prolate and flatter cornea at the centre after epithelial removal. They concluded that the epithelium affected the topographic properties of the cornea by significantly reducing corneal topographic astigmatism, asphericity and irregularity. In another study, Patel et al found that the corneal epithelium accounted for a mean of 1.03 D of the power at a central 2.0 mm zone in ex vivo normal eyes.[4] These studies of the epithelium's refractive function found very small keratometric and refractive reading changes after epithelial removal in normal eyes.

Comparison of anterior corneal topography and Bowman topography in keratoconus

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In 2012, Touboul et al[5] studied the contribution of the epithelium to topography in keratoconus. Specular topographies were performed before and immediately after epithelial removal during conventional CXL surgery in patients with keratoconus. Bowman topography revealed increase in corneal curvature and irregularity after epithelial removal (Figure 1). These findings are consistent with the hypothesis that in hyperprolate keratoconic corneas, the epithelium is thinner in the steepest area and thicker in the flattest areas and compensates for the negative asphericity and refractive asymmetry. However, the disadvantage with this method is that its invasive and intraoperative.

Newer non-invasive, noncontact quantification of topography with High-Speed OCT

OCT topography is a novel non-invasive method to analyse the Epithelium- Bowman's interface in normal and keratoconic eyes. Shetty et al[6] developed a proprietary algorithm for a non-invasive method of virtual de-epithelization using OCT, where no physical removal of epithelium is required.OCT device (RTVue, Optovue Inc., Irvine) captured 8 B-scans (16 meridians) of the cornea. Custom edge tracking of the anterior edge and epithelium-Bowman's layer interface were performed. Blue edge is the detected anterior surface, red edge is the detected Bowman's interface and green edge is the detected posterior Surface (Figure 2).Curvature and wavefront aberrations of the air-epithelium interface (A-E) and epithelium-Bowman's layer interface (E-B) were derived (Figure 3). This noncontact method to quantify the topography and aberrations of corneal surfaces with OCT, yielded greater curvature and aberrations than Pentacam in both normal and keratoconic eyes.

How good is the virtual OCT curvature and aberrations of the Bowman's in comparison with magnitudes on removal of the epithelium?

Khamar et al,[7] compared OCT and Scheimpflug curvature/ aberrations of the Bowman's layer before and after removal of the epithelium. Bowman's layer was mapped with OCT (Optovue) before and after removal of the epithelium in normal eyes undergoing PRK and keratoconic eyes undergoing corneal cross-linking. The anterior corneal surface before removal and the underlying Bowman's layer after removal of the epithelium were also mapped with Pentacam and the

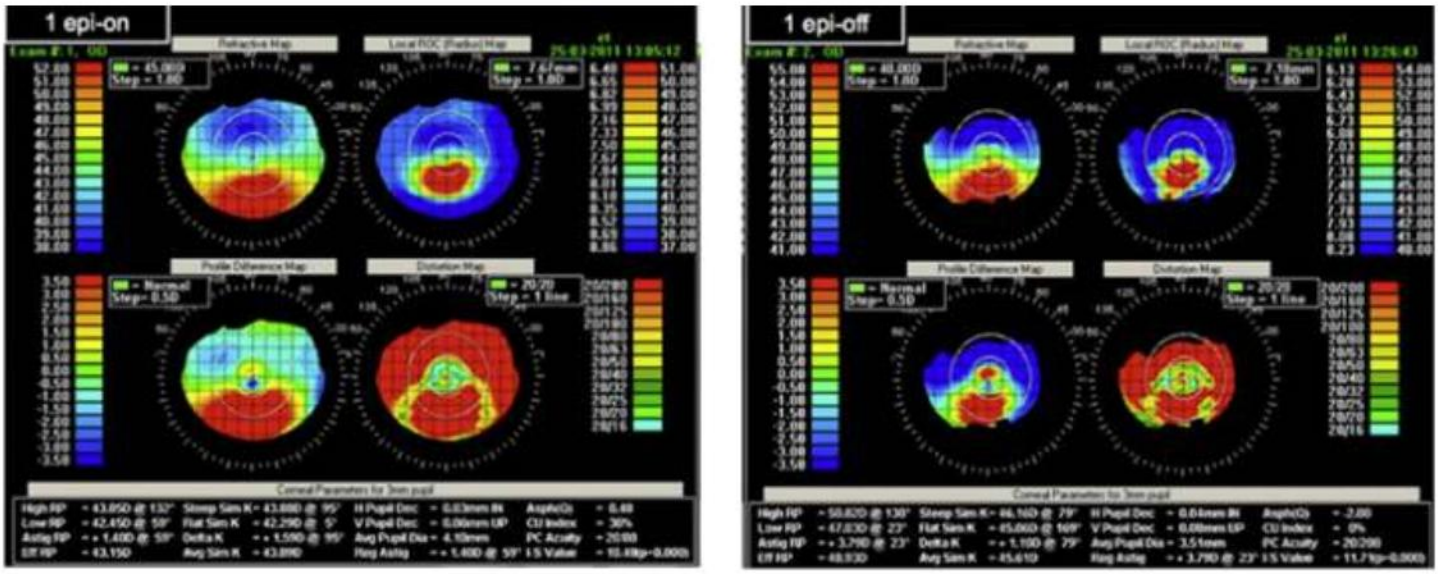

Figure 1: Difference in anterior surface Mean K(epi-on) and Bowman's layer mean K (epi-off)

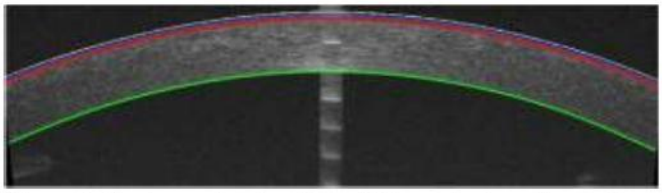

Figure 2: Custom edge tracking of the anterior edge and epithelium-Bowman's layer interface

surface aberrations with ray tracing were computed. The virtual OCT curvature and aberrations of the Bowman's layer agreed well with its actual magnitudes on removal of the epithelium in the keratoconic eyes. In normal eyes, the agreement was inferior for aberrations but not for curvature.

Bowman's topography for improved detection of early ectasia

In a study by Narayana Nethralaya group,[8] they evaluated the role of OCT topography of the Bowman's layer and artificial intelligence (AI) for better diagnosis of forme fruste (FFKC) and clinical keratoconus (KC). For KC eyes, both Scheimpflug and OCT performed equally. Thus, OCT Topography of Bowman's layer significantly improved the detection of FFKC eyes.

Further, Bowman's layer lay just above the stroma, which also underwent disease-related changes in KC. Thus, the topography of the Bowman's layer could be considered as a surrogate marker of early ectasia. Bowman's layer topography also showed differential surface features of post-refractive surgery ectasia, which could potentially improve the distinction between the surgery induced ectasia and natural progression of ectasia.

An example (Figure 4) of E-B topography (C) of a formefruste keratoconus eye. (A) and (B) are the corresponding topography from Pentacam and OCT A-E surface, respectively. Combining Tomography and OCT based indices increases sensitivity and specificity of FFKC detection.

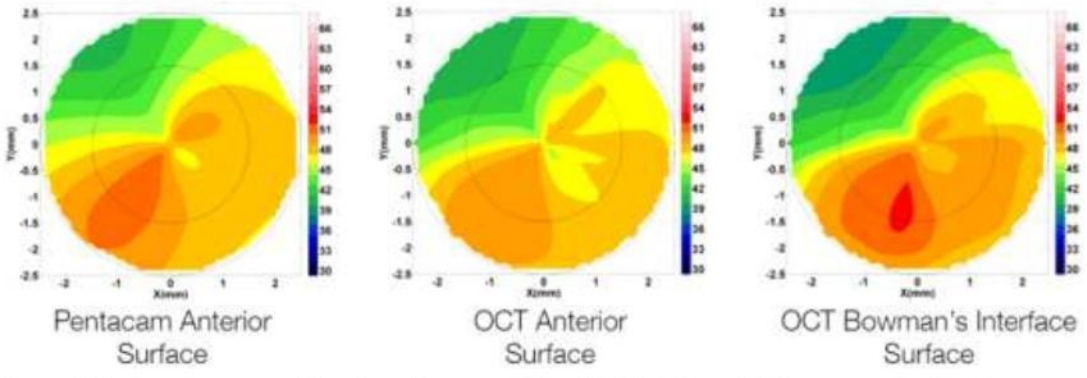

Figure 3 Non-contact quantification of topography with High-Speed OCT as compared to Pentacam

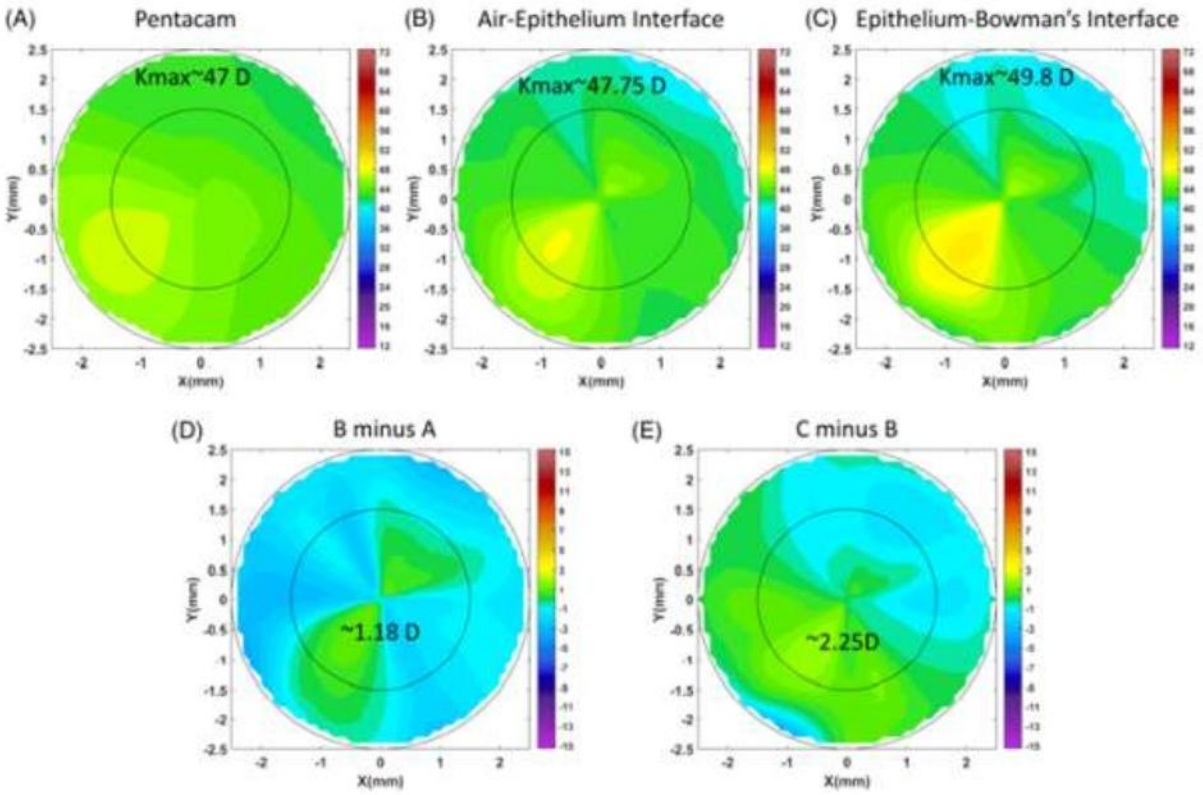

Figure 4 : Increase steepness of bowman's layer as compared to anterior corneal surface

New insights on remodeling after photorefractive keratectomy

Laser ablation nomograms consider the curvature of the anterior corneal surface. However, it is the sub-epithelial surface that receives the laser pulses and undergoes reshaping. Thus, epithelium remodeling can cause some offset in the intended curvature change. In a study conducted at Narayana Nethralaya[9] OCT of corneal layers was generated to analyse the remodeling of the epithelium and stroma after photorefractive keratectomy (PRK). Understanding the topographic remodeling of the A-E and E-B interfaces could be the missing piece in improving the accuracy of the procedure.

Role of bowman's topography in postrefractive surgery ectasia

In a recent study by Khamar et al[10], they investigated topographic features of five patients with post-surgery ectasia (three patients with post-LASIK and two patients with post-SMILE ectasia). OCT revealed a steeper and more aberrated E-B interface than A-E though correlation between them was inferior to the correlation for keratoconic eyes. Furthermore, the magnitude of differences between the A-E and E-B interfaces was greater in the ectasia eyes than the keratoconic eyes. OCT could possibly assist better in selecting appropriate treatment plan for post-refractive surgery ectasia eyes than conventional tomographers.

Conclusion

Current topographers help in detection of patients who are at risk of ectasia, however they cannot compensate for the masking effect of epithelium which tends to smoothen out irregularities and give a false impression that topography is normal than it is. Development of new tomography tools and software for detecting early ectatic disease and characterizing the predisposition for ectasia progression is an area of intense research. Epithelium- Bowman's interface is the level where the disease process starts. Imaging the Bowman's layer with OCT can be a biomarker to detect the onset of KC. Topography at the level of Epithelial Bowman interface may help in the early detection of disease and more accurate profile in patients undergoing cross-linking procedures and surface ablation, early detection of keratoconus and understand post refractive surgery ectasia better. New insights could be useful for refinement of surgical algorithms of various procedures.

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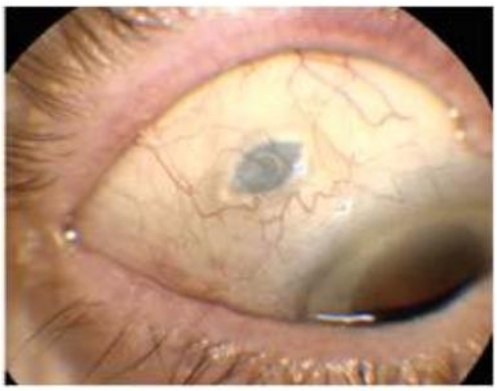
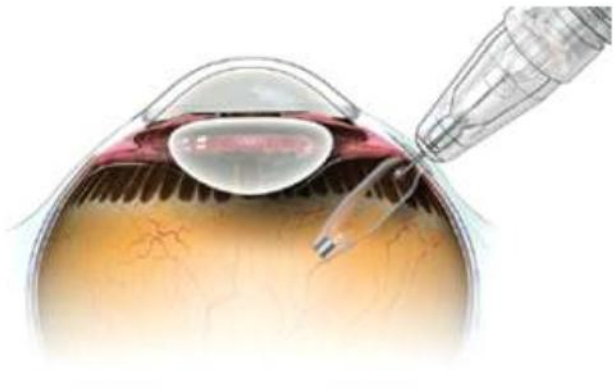
Peep in - Susvimo

First ever refillable, sustained release drug reservoir for Ranibizumab delivery gets FDA approval.





'Susvimo' (by Roche, previously known as Port Delivery System) is a permanent, reusable, surgically placed, refillable drug reservoir. Approximately the size of a grain of rice, it is placed through a 3.5-mm scleral incision at the pars plana. Composed of polysulfone, it has a silicone septum proximally that can be entered with a special needle many times to refill the device. At the distal end, there is a semipermeable titanium membrane that permits continuous passive diffusion of the drug from the higher concentration in the reservoir to the lower concentration in the vitreous body, a process that follows Fick's law of diffusion.

The device has 20 microliters of customized formulation of ranibizumab (100 mg/mL). It is refilled with a specialized refill needle that flushes out the device while at the same time recharging it with fresh ranibizumab.

The FDA approval is based on positive results from the phase III Archway study , which showed vision gains equivalent to monthly ranibizumab injections at weeks 36 and 40 of treatment in neovascular AMD patients. More than 98% patients could go six months before their first refill.

Most frequent adverse events included conjunctival haemorrhage, conjunctival hyperaemia, iritis and eye pain. 2% endophthalmitis rate has also been observed. The device will soon be available in the US and is under review with the European Medical Agency.

Orthokeratology : Nonsurgical Treatment of Anisometropia

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Sharadini Vyas

Anisometropia in children is a challenging situation. Spectacle correction leads either to diplopia or suppression. Diplopia results in child not wearing glasses and long term suppression leads to amblyopia, both of which affect binocular vision and stereopsis. Anisometropic eye can have myopia, hyperopia or high astigmatism.

Anisometropic eye is known to have a continuous progression of myopia at a pace much faster than a normal myopic eye. All these factors call for early treatment of anisometropic eye to arrest this progression. Surgical intervention is not possible due to unstable refraction. Glasses may not be possible due to anisometropic refraction affecting bionocular vision.

Orthokeratology is a branch of contact lens fitting which causes intentional and reversible flattening of cornea resulting in temporary reduction in the refractive error after overnight use of these speciality lens.[1] Orthokeratology has shown to reduce the progression of myopia in myopic eyes, more so with high myopia. [2] We hereby describe a case of a child who had anisometropia and amblyopia and was managed with orthokeratology lens in anisometropic eye.

Case :

A 10 year old boy presented to our clinic with history of poor vision in one eye. His best corrected visual acuity in right eye was 6/6 and the left eye was 6/12. The uncorrected visual acuity in right eye was - 6/60 and in the left eye was 2/60. His refraction in the right eye was - 2.00 D sphere with -1.5 D cylinder at 180. The left eye refraction was -10.00 D sphere with -1.5 D cylinder at 180 degree. With this anisometropia, he had suppression in his left eye.

An overnight Ortho K lens trial was done with the aim of matching the refraction of the anisometropic left eye with right eye so that the child can wear glasses during day time. The lenses were prescribed to him after giving training of insertion and removal of the contact lens and explaining the do's and don'ts with the lens. The child was seen at one week and one month interval.

At this time his left eye uncorrected visual acuity improved to 6/18 from pre treatment acuity of 2/60.The refraction done after the lens wear for one month was-1.5D sphere with -2.00 D of cylinder at 180 degree in the anisometropic eye, which comparable to his other eye refraction. The child is now using his ortho K lens at night and spectacle with balanced refraction in both eyes during the day, maintaining visual acuity of 6/9 and 6/6 in OD and OS respectively with improved vision. This way his binocularity is maintained and amblyopia is also prevented. (Figure 1)

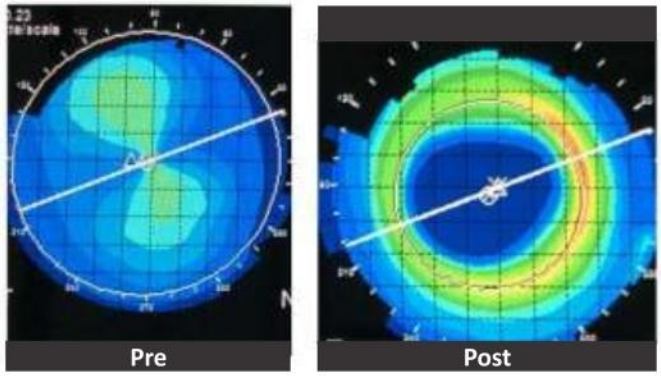

Figure 1 : Pre & Post Orthokeratology anterior surface topography. Post treatment picture resembling post lasik flattening

Discussion :

Though not a new modality, orthokeratology is often neglected due to apprehension by both parents and contact lens practitioner due to its overnight use. Its horizon if utility is increasing with knowledge about extended indication. Ortho k lens, also termed asreverse geometry rigid gas permeable lenses, act as abridge between regular optical correction and surgery. It causes an intentional flattening of central cornea just like photorefractive correction with the only difference that it is a reversible process and after discontinuation of the lens the refraction and the corneal surface goes back to its original state though after some time. Also, these lenses are used nowadays for prevention of myopia progression. Complications with these lenses are similar to any other RGP lens, and though the risk of infectious keratitis is rare with RGP lenses, one has to be vigilant about it and explain the parents and the child.[3] Acanthamoeba keratitis is known with overnight wear.[4] Mechanical complications such as lens binding may occur. [5]

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Conclusion :

Though challenging, orthokeratology once again is gaining popularity due to improved quality of lens material and increasing indications. Like any other treatment modality limitations and complications are known, but judicial use with proper indication makes it a popular modality to fill the bridge between spectacle corrections and surgery.

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Micropulse Trans-scleral Cyclophotocoagulation (MP-TSCPC): An innovative Technology in Glaucoma Management

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Tanuja Kate

Introduction :

Continuous wave transscleral diode cyclophotocoagulation (CW-TSCPC)has been widely used since its development in the 1990s.In this procedure, a diode laser targets and destroys the pigmented ciliary body epithelium,thereby decreasing production of aqueous humor. However, laser delivered at a continuous dose frequently results in significant collateral tissue damage, contributing to serious complications, such as uveitis,vision loss, chronic hypotony, choroidal detachment, and more rarely, phthisis bulbi and sympathetic ophthalmia. Micropulse diode transscleral cyclophotocoagulation (MP-TSCPC) has therefore been developed over recent years as an alternative, potentially safer approach to cyclodestruction. 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 transscleral cyclophotocoagulation (MP-TSCPC) has emerged as a new treatment option for glaucoma. Two devices in use are the Iridex cyclo G6 glaucoma laser system (Mountain View, California, USA) with the P3 probe

Figure 1 : Cyclo G6 Glaucoma Laser System

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(Figure 2) and the Supra 810 nm Subliminal Quantel Medical laser (Cournon d'Auvergne Cedex France) with the subcyclo probe. The Iridex cyclo G6 (Figure 1) is more commonly used. The new Cyclo G6, Glaucoma laser system (Diode laser 810nm) is an innovative cyclophotocoagulation system with unique patented Micro Pulse technology.The Micro Pulse technology makes this laser safe and efficacious.[6]

Figure 2 : MicroPulseP3 (Pars Plana Probe)

Micropulse transscleral cyclophotocoagulation (MP-TSCPC) was approved by FDA in January 2015.

Mode of action :

In MP-TSCPC,a fractionated continuous wave diode laser is employed which targets melanin in a non destructive way in ciliary body tissues thus reducing aqueous production. Also, possibly, it increases uveoscleral outflow. 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.

More than its photocoagulative effect, MPTSCPC is hypothesised to increase uveoscleral outflow by an ill-understood mechanism and, so far, it is unclear what role is played by ocular pigmentation, impacting on the total energy used. As it is a relatively new technique, there is still no clarity

on the guidelines for the ideal laser parameters that balances efficacy with side effects.

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[12] 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.

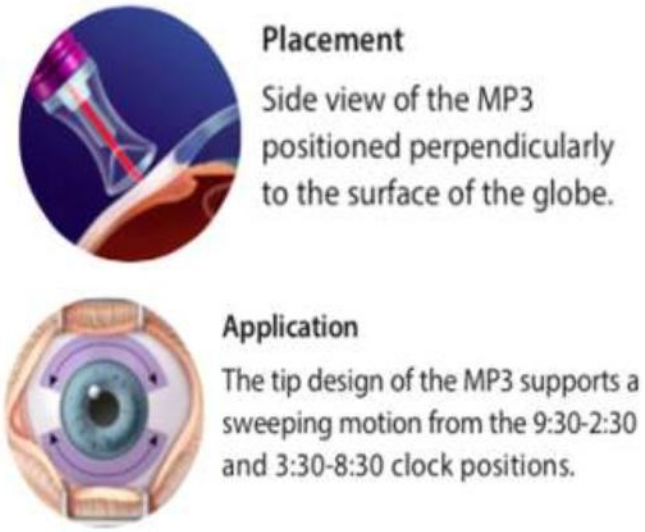

Figure 3a : Placement and Application of MicroPulse Pars Plana Probe

So,the indications are :

1. Complicated glaucomas (Silicone oil induced, Uveitic, Post keratoplasty and neovascular glaucoma). However, in neovascular 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. Failed trabeculectomy
6. May be a promising treatment for early glaucomas once more and more studies are available[9,10,13]

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 : Retrobulbar anaesthesia/Peribulbar anaesthesia

- 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. Although 2000 mW has been the power most commonly used, various studies have reported settings ranging from 1600 mW to 2500 mW. The laser probe's fiber-optic tip is applied with steady pressure in a continuous sliding arc (painting) motion (Figure 3b). The MP3 (Micropulse pars plana probe)probe is put perpendicular to the globe (Figure 3a) 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 with steady pressure (while maintaining firm contact at all times) while sweeping it back and forth 8 times (each sweep in one direction is 10 seconds) over 180 degrees for a total of 80 seconds in the superior hemisphere, and then repeated in the inferior hemisphere. 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, staphyloma,and cystic blebs are avoided.The voice countdown timer feature on the laser makes this process very easy and efficient. At the conclusion of surgery, a drop of atropine and steroid is instilled. 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.

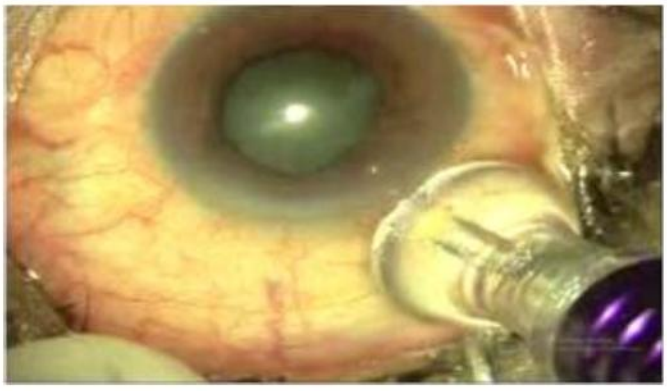

Figure 3b : Placement and Application of MicroPulse Pars Plana Probe

To repeat or not to repeat ?

If the patient has not responded to MP-TSCPC initially, procedure is not repeted.

If the patient has responded to treatment but greater effect is desired, another application is made after 90 days

Many patients will experience waning effects over time.This is not failure and reapplication is the first course of action.

Studies have shown that between 6% and 47% of eyes required retreatment with MP-TSCPC. To date, there is a lack of long-term data on repeated MP-TSCPC treatment.

Complications :

The reported complications in literature include a drop in visual acuity, hyphema, hypotony, prolonged anterior chamber inflammation and cystoid macular edema. Neurotrophic keratitis with a persistent epithelial defect with difficulty in healing and recurrence has also been reported. Drop in visual acuity by two or more lines has been reported to vary from 0% to 35.1%.Increase in total energy (power and or duration) and a varying technique like the stop and go where the probe is held in place for 10s at a time before moving to an adjacent site are seen in studies reporting higher rates of drop in acuity.

Real Time Case Scenarios :

Case 1 : 53 year old patient,a case of post keratoplasty graft failure and secondary glaucoma had a visual acuity of HM+ and IOP of 34mmHg on 2 drugs. I planned this patient for MP-TSCPC.The follow up visual acuity and IOP were as under:

Follow up period	Visual acuity	IOP	No. of medication
1st day	HM	6 mmHg	0
15th day	HM	16 mmHg	0
1 month	HM	17 mmHg	0
6 months	PL PR	10 mmHg	2

Thus, we can see in this case that following MP-TSCPC,IOP was controlled and number of medication reduced from 2 to nil till 1month but then at 6 month follow up 2 antiglaucoma drugs were required for control of IOP.The visual acuity reduced due to opaque graft.

Case 2 : A 71 year old patient,a case of Advanced Primary Open Angle Glaucoma(POAG) had a visual acuity of 6/12 and IOP of 26mmHg with 3 drugs.This case was taken up for MP-TSCPC. The follow up visual acuity and IOP were as under :

Follow up period	Visual acuity	IOP	No. of medication
1st day	6/24	6mmHg	0
7th day	6/18P	6mmHg	2
15th day	6/18	10mmHg	1
1 month	6/18	9mmHg	1
6 months	6/12	10mmHg	1

Thus this case showed a significant reduction in IOP and number of medication even at 6 months follow up. However, there was semidialated pupil till 3months follow up and hence proportionate drop in visual acuity by 1-2 lines which restored to pre laser level at 6 months follow up.

Case 3 :

A 70 year old patient,a case of neovascular glaucoma with a visual acuity of 6/60 and IOP of 43 on 4 drugs was taken up for MP-TSCPC.

The follow up visual acuity and IOP were as under :

Follow up period	Visual acuity	IOP	No. of medication
1st day	5/60	18 mmHg	0
7th day	2/60	30 mmHg	3
15th day	2/60	15 mmHg	3
1 month	2/60	20 mmHg	3
3 months	2/60	26 mmHg	3

In this case, IOP was high at 7th follow up day & at this point of time pan retinal photocoagulation (PRP) was done. Following PRP, IOP was controlled with 3 drugs on 15th day but it again raised. The reduction in visual acuity during follow up period is attributed to vitreous hemorrhage. So, this case did not respond to MP-TSCPC and at 3 months follow up period, the patient was advised Ahmed Glaucoma Implantation (AGV).

Our Experience :

We evaluated 6 month results in 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 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 number of medication reduced from 3.2 at baseline to 1.94 at 6 months follow up (P value 0.001). In regards of complications, in our study visual acuity decrease of 1 line was seen in 3 cases (8.57%), mydriasis was seen in 2 (5%) cases and corneal bullae were seen in 1 (2.5%) case.

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 CW-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.

But, this comes at a substantial cost to the patient. Therefore, the relative advantages of the laser may become obscure in low-to-middle income countries, where cost is a major concern.

The potential for rare but reported sight threatening complications should be kept in mind, especially before using this in non refractory cases of glaucoma when other time tested options are available.

Further research is needed to elucidate the role of MP-TSCPC as an early glaucoma treatment and in glaucoma suspects.

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Eyeball Cluster on Stalks

White baneberry (Actaea pachypoda) is known as doll's eye as the black stigmas in the white berries make it look like a cluster of eyeballs on stalks. Doll's eye is poisonous to humans but delectable to birds.

Minimally Invasive Glaucoma Surgery

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Ankush Mahajan

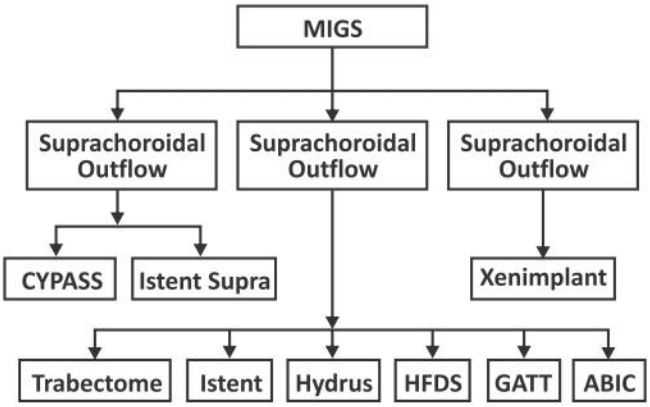
By Current definition, MIGS is the term applied to a variety of surgical procedures employing techniques or implants to lower the intra ocular pressure.

By definition MIGS procedures should be -

1. Minimally invasive (use small incisions) with Ab Interno approach
2. Minimal tissue dissection
3. High safety profile
4. Rapid visual recovery
5. IOP lowering to physiological levels

Some of these procedures have been around since more than 5 years now and some are pretty new. Enough evidence in form of randomized control trial is available for XEN implant , I stent , Trabectome [2,3,4]

CLASSIFICATION: MIGS procedures are usually classified depending on the outflow pathway targeted. [5]



WHY MIGS SURGERY?

The need for MIGS has been felt since long as a Safer alternative to conventional filtering procedures. Though MIGS procedures in their current form cannot hope to achieve IOP levels achievable at present with filtering procedures, but MIGS is much safer and hence can be offered to patients with early glaucoma who might not be happy with their eye drops.

MODE OF ACTION :

1. Cypass[5,6,] and Istent[8] supra create pathway for aqueous into suprachoroidal space. The problem with these is that most procedures with suprachoroidal aqueous drainage tend to fail over time due to scarring.
2. XEN[4] implant drains the aqueous into subconjunctival space. Though this has been categorized as an MIGS procedure but it does involve a lot of dissection initially and later on patients may need needling similar to as done for other subconjunctival procedures. Xen gel trials report around a 20% reduction in IOP from baseline but do also report need for secondary needling procedures in significant patients.
3. Trabectome[2] is a device that's used ab interno to cut the trabecular meshwork using electro cautery and simultaneously suck the debris with vacuum. The issue with it is that it can only work on nasal angle for 90 to 120 degree at most, leaving the rest of Schlemm's canal blocked.
4. Kahook dual blade[7] is a device that functions similar to trabectome (removing trabecular meshwork) used to do trabeculectomy Ab Interno. It's a one-time use device but with same limitation as the trabectome i.e. cannot be used in areas other than the nasal angle.
5. Istent[8] allows aqueous to bypass trabecular meshwork and drain into Schlemm's canal. It's a small metal stent with perforation that creates a communication between Schlemm's canal and anterior chamber, allowing aqueous to enter unhindered in Schlemm's canal. Most studies agree that a single I-stent does not lower IOP much and 2 or 3 of these are needed to get a reasonable IOP drop. Moreover the cost of these stents are very high.
6. Hydrus[9] implant also allows aqueous to bypass trabecular meshwork. In addition it also dilates the Schlemm's canal. It's an 8 mm, 295 micron thick stent-like curved device with perforations to allow for free flow of aqueous into the Schlemm's canal.
7. HFDS (High Frequency Deep Sclerotomy) [10]: By creating micro perforations, HFDS also allows aqueous to bypass the trabecular meshwork. It's tip attaches to the OERTLI phaco machine. Problems include scarring and closure of perforations created and inability to treat full 360 degree of trabecular meshwork.
8. GATT[11] uses an illuminated microcatheter to create a 360 degree Ab Interno trabeculotomy. This procedure can also

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be accomplished using a 5-0 prolene suture (SUTURE GATT) as a low cost alternative. BANG (Bent Angle Needle Goniotomy) is another low cost alternative.

9. Abic (Ab Interno Canaloplasty)[12] uses an illuminated micro catheter with a central drug delivery channel to deliver highly cohesive viscoelastic to the entire 360 degree of Schlemm's canal in order to dilate the **Schlemm's canal** as well as post trabecular collector channels. It's not very clear though, as to how this flushing of the collector channels with viscoelastics provide a long lasting IOP drop.

Of the above, most devices and implants are not available in India. What is being practiced is Suture GATT, BANG, Abic, Ab interno trabeculectomy (Kahook) and HFDS.

INDICATIONS OF MIGS PROCEDURES :

In India, since most patients have narrow or borderline narrow angles , hence it is best to combine MIGS with cataract surgery in phakic patients or use conventional filtration surgery in case patient is phakic but with no cataract.

1) Mild to moderate (open or closed angle) glaucoma requiring cataract surgery
2) Mild to moderate (phakic) open angle glaucoma not compliant with medication or progressing despite medical management
3) Mild to moderate (pseudophakic) open or closed angle patients interested in decreasing the number of eye drops being used to control IOP
4) Any glaucoma patient who is at high risk of failure or complications with traditional surgery- high myopes, one-eyed patients, uveitic glaucoma
5) Pseudophakic patients with previous failed trabeculectomy with open or closed angles
6) Phakic patients with previous failed trabeculectomy but with completely open angles
7) Congenital or juvenile glaucoma requiring surgery
8) Steroid induced glaucoma

HOW TO ASSESS FOR SUITABILITY FOR AN MIGS PROCEDURE :

- GONIOSCOPY is a MUST for deciding about any MIGS procedure
- If scleral spur is visible all around WITHOUT indentation -- any MIGS procedure can be attempted alone regardless of lens status.

CONTRAINDICATIONS FOR MIGS PROCEDURES :

1) Phakic patient with no cataract and a closed angle
2) Patients with raised episcleral venous pressure
3) Patients with any kind of vitreous bleed or vascular event in retina like CRVO, BRVO, proliferative diabetic retinopathy --- they have very high failure rates .
4) Patients where angle structures cannot be visualized like corneal opacity etc.
5) Neovascular glaucoma
6) Glaucoma secondary to silicon oil

Which is the BEST MIGS procedure?

There is no single best procedure at present but learning more than one MIGS procedure and its nuances and using the same in clinical practice can benefit your patients a lot.

MIGS in INDIA :

Currently the MIGS procedures being tried in INDIA include:

1) Gonioscopy assisted transluminal trabeculotomy with a suture (suture GATT)
2) KAHOOK dual blade assisted trabeculotomy
3) Trabectome assisted trabeculotomy
4) Bent needle assisted goniotomy (BANG)
5) Abic Interno Canaloplasty (Abic)

Let's take up the nuances of these one by one ---

1) **Suture GATT -** this is a 360 degree ab interno trabeculotomy technique, where in a 5-0 prolene suture with a slightly heat morphed tip is inserted ab interno into the Schlemm's canal. The view is assisted by a surgical goniolens. The suture is fed progressively into the Schlemm's canal and once the suture tip has traversed 360 degree of the canal and returned to the insertion point , the tip is held by a forceps and another forceps is used to pull on the distal suture lying outside the eye . This manoeuvre causes the suture to cheese-wire through the trabecular meshwork in its 360 degrees , hence removing the resistance to aqueous outflow . Some issues with the technique are that the cut trabecular meshwork tissue (cut as a hinge) may fall back and scar to close down the opening, resulting in IOP increase after a year or so. At our

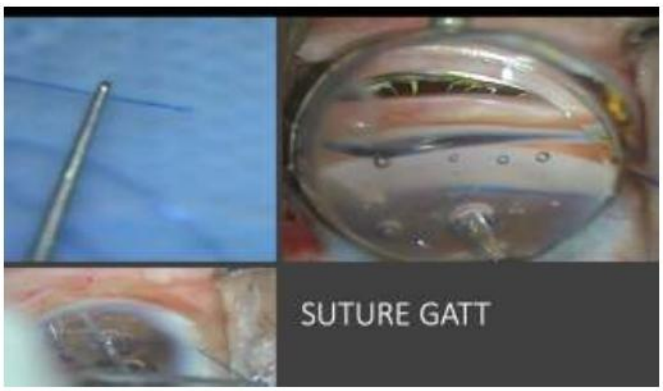

Fig. 1 : Suture GATT Technique

center we have found this technique to be much better if used with cataract surgery or alone in a pseudophakic patient or in a patient of narrow angle glaucoma with peripheral anterior synechiae. Reason being that the PAS will keep the trabecular meshwork flap from falling back onto the opened Schlemms canal(fig 1)

2) **KAHOOK** dual blade assisted trabeculotomy. This is an ab interno trabeculectomy technique where in a blade (230 micron thick) (fig 2) with a base and two cutting edges on the side is used to enter the Schlemms canal . The blade is then moved to left and right for 90 to 120 degree (as much as is possible) to remove a strip of trabecular meshwork from 90 120 degree . Problem with this device is that it will remove a strip less than 200 microns thick leaving edges of trabecular meshwork superiorly and inferiorly and these edges can scar down later. Also it does not treat the full 360 degree of trabecular meshwork.

3) **Trabectome assisted trabeculotomy -** the technique is similar to Kahook blade . The difference being that it uses an electroablative tip that is moved in an arc of 90 120 degree to remove as much of trabecular meshwork as possible . The problem with this is that it does not treat the whole 360 degree meshwork and various studies have shown closure of opening created later on in some cases.

Fig. 2 : KAHOOK BLADE

4) **Bent needle assisted goniotomy (BANG)** this is a cheaper alternative to above techniques , uses a bent 30G needle tip to create an trabeculotomy in an arc of 90- 120 degree . This technique is very unpredictable and can cause damage to outer wall of Schlemm's canal. Scarring and closure of the opening is likely to be highest in this, though sufficient data is not available at present.

5) **ABiC -** Ab Interno Canaloplasty (fig 3) -- this technique uses a hollow 250 micron catheter with an illuminated tip . The catheter is fed into the canal for 360 degree and then

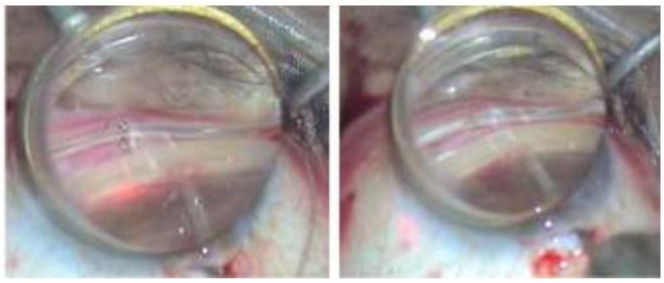

Fig. 3 : AB Interno Canaloplasty

slowly withdrawn while injecting healon GV through the catheter every 2 clock hours .The aim is to use healon GV to pressure flush and dilate the collector channels, and also to create micro fractures in trabecular meshwork, leading to increased aqueous outflow. This is an easy and fast technique. Problems include costly catheter, ill sustained IOP drop and in many cases IOP may rise after 6 to 12 months .

THE FUTURE OF MIGS :

MIGS is an upcoming surgical technique in glaucoma which can provide a safer alternative to traditional filtration procedures in mild to moderate glaucoma , leaving the conjunctiva untouched for future filtration surgery if and when required .

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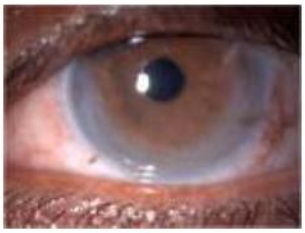
PHOTO ESSAY - Brown McLean Syndrome

Urvija Choudhary, *Cornea Cataract & Refractive surgeon, Rajas Eye Hospital, Indore*

A 52 year old male with complain of foreign body sensation and watering in righteye. Had history of both eye cataract surgery with IOL 4 years. On Examination had peripheral corneal edema progressing circumferentially more in right eye.

This condition presents with peripheral corneal edema progressing circumferentially, central cornea commonly remains uninvolved. Pathophysiology is not known, but patient usually has a history of cataract extraction or other ocular surgeries and are mostly asymptomatic. Specular microscopy studies reveal that central corneal endothelial count and morphology remain normal. Most cases of brown McLean syndrome are responsive to hypertonic saline and topical steroids. Surgical management with amniotic membrane grafting or anterior stromal puncture is an option for cases unresponsive to medical management.



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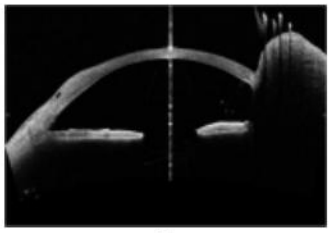

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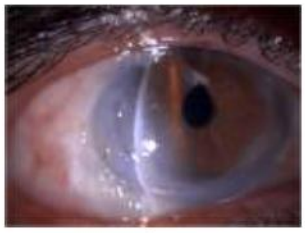

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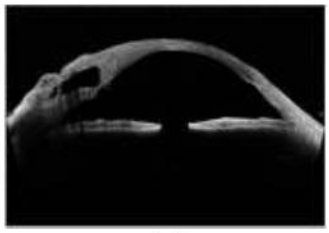

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Figure 1a: Left eye showing early peripheral epithelial edema in pseudophakic eye and clear central cornea
Figure 1b: Anterior segment OCT of left eye showing epithelial edema in peripheral cornea and limbus
Figure 1c: Right eye showing advanced peripheral edema in pseudophakic eye involving the inferior part
Figure 1d: Anterior segment OCT of right eye with severe cystic edema in peripheral cornea.

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RHO Kinase Inhibitors : New Kid in block for management of Glaucoma

Prateep Vyas

1) What are Rho Kinase Inhibitors ?

The Rho family (RhoA, RhoB, RhoC) are small G-proteins. They are activated by a number of secreted cytokines, including endothelin-1 (ET-1), thrombin, angiotensin II, lysophosphatidic acid, and transforming growth factor (TGF)-â, or via integrin activation.

They issue regulate cell morphology, proliferation, adhesion, cytokinesis and apoptosis along with smooth muscle contraction and neurite elongation.

The effectors of the Rho family are the Rho kinases, ROCK1 and ROCK2. These 2 serine/threonine kinase isoforms are Rho guanosine triphosphate binding proteins.

ROCK1 and ROCK2 are present throu out the body in various organs like Lungs, Kidney, Heart, Brain, Liver Eye etc to exhibits their action.

Rho kinase inhibitors have a variety of effects. They can increase blood flow by causing vascular smooth muscle relaxation leading to vasodilation.

On the ocular surface, this can lead to conjunctival hyperemia.

Rho kinase inhibitors also have antitumor activity, acting to inhibit tumor cell invasion and metastasis, presumably by decreasing cell motility and cell division.

Rho kinase inhibitors prevent axonal degeneration and promote axon regeneration.

Rock inhibitors like Fasudil (HA-1077), approved for treatment of cerebral vasospasm and pulmonary hypertension.

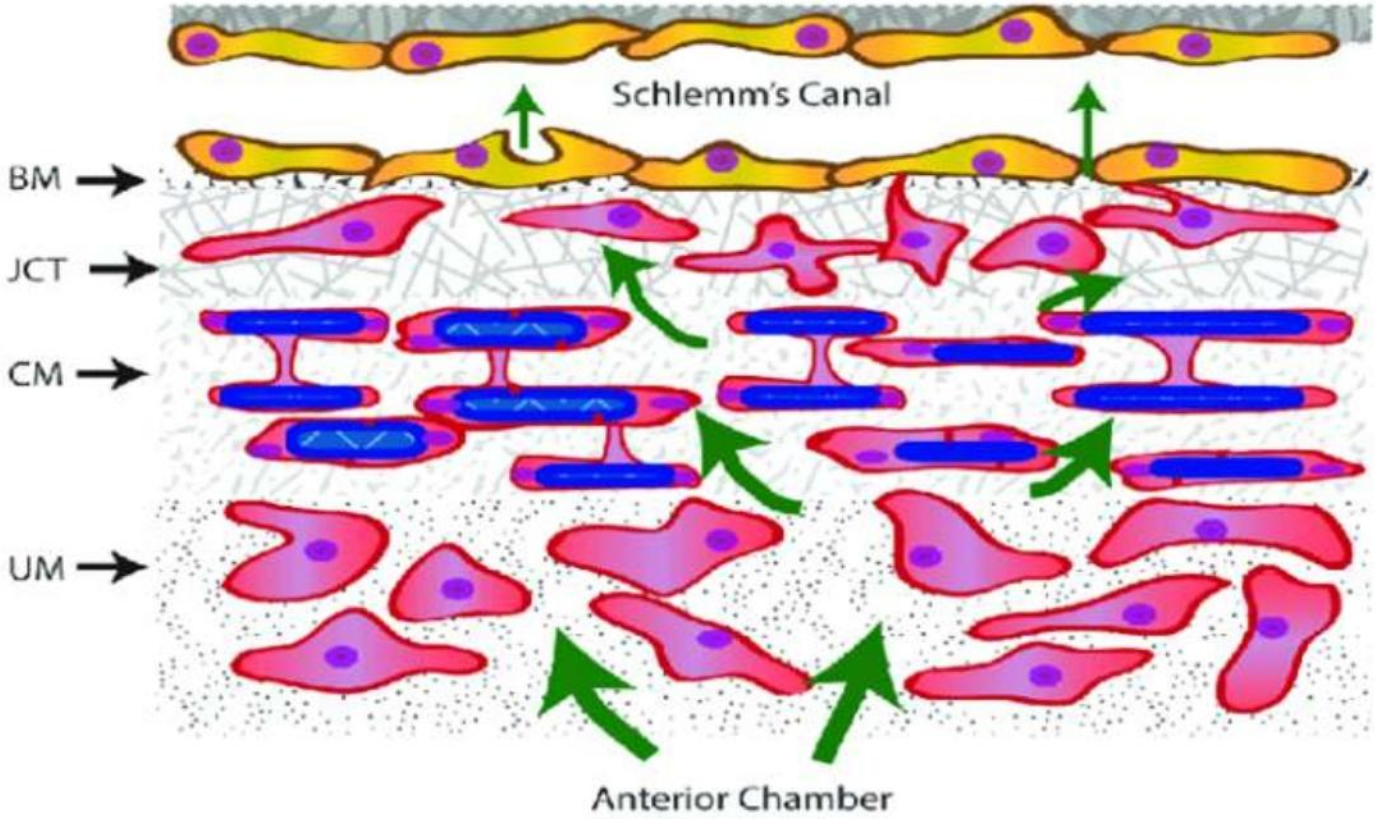

Figure 1 : ROCK inhibitors effects on Extra Cellular Matrix and Juxta Canalicular tissue to enhance aqueous eggression out of anterior chamberUM:Uveal meshwork, CM:Corneal meshwork, JCT: Juxta Canalicular tissue, BM:Basement membrane

Medical Director
Glaucoma Services
Center For Sight,
Indore

2) How Rho Kinase Inhibitors lowers IOP ?

Two Rho kinase inhibitors currently approved for treatment of glaucoma: Ripasudil 0.4% first was approved in Japan in 2017

and now more potent Netarsudil 0.02% approved for use in glaucoma.

In 1977, Kaufman et al showed that cytochalasin B, an actin depolymerizing agent, reversibly decreased outflow resistance suggesting a possible role of the cytoskeleton in determining aqueous humour outflow resistance(Fig 1). The decreased outflow resistance was attributed to increased density of pores in Schlemm's canal cells along with breaks between cells.

Although the pores in the inner wall endothelium are thought to be too large and numerous to generate significant flow resistance themselves, a hydrodynamic interaction known as the "funnelling" between these pores and the extracellular matrix in the juxtacanalicular connective tissue (JCT) makes inner wall pore density an important determinant of outflow resistance.

ROCK inhibitors also reduces IOP through reducing Episcleral Venous Pressure (EVP), being a potent vaso-dilators they dilate Episcleral vein there by reducing EVP and enhancing aqueous outflow to low pressure area via conventional pathways (Fig 2).

ROCK Inhibitors are aqueous suppressant also through their inhibition of Nor Epinephrine Transporter (NET), which is present in pigmented part of ciliary epithelium.

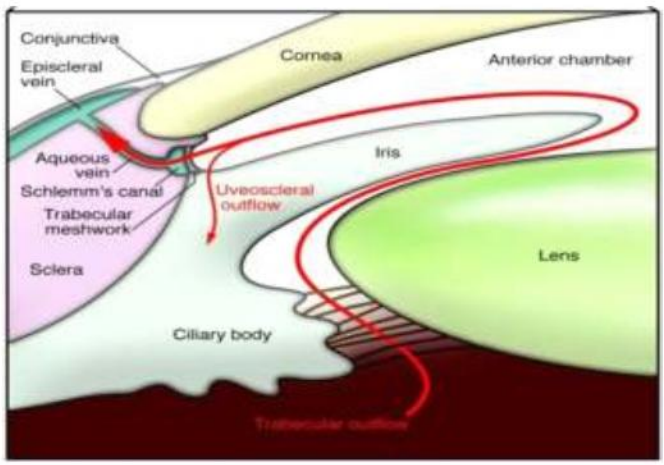

Figure 2 : Diagram showing production of aqueous and its out flow, ROCK inhibitors increases outflow through Trabecular pathways by decreasing EVP

3) Rho kinase Inhibitors in POAG and OH -

ROCK Inhibitors provide novel mechanism to reduce IOP in Ocular Hypertension and POAG. It is the first anti glaucoma medication which mostly reduces IOP through conventional aqueous pathway.

Both Ripasudil and Nitarsudil lowers IOP significantly in these patients, Nitarsudil has shown non inferiority to beta blockers in several clinical trials and reduces IOP by 4-6 mm of Hg from base line.

However Ripasudil is not as potent as Nitarsudil but it also reduces IOP 3-4 mm of Hg from base line.

Nitarsudil 0.02% given once a day .

Ripasudil 0.4% given twice a day.

4) Rho Kinase in ACD -

Though there is not enough data available which suggest role of ROCK I in lowering IOP in angle closure disease, However EVP and NET mechanism looks to work in ACD.

5) Rho Kinase Inhibitors in secondary Glaucoma -

ROCK acts through cytokines an inflammatory mediators hence ROCK inhibitors theoretically should be beneficial in inflammatory secondary glaucomas like uveitic glaucoma, post surgical glaucoma etc

6) Other effect of Rho kinase Inhibitors in Eye -

1) Protection to Corneal Endothelium

   ROCK I are extensively studied as corneal endothelial protective agents, they prevent apoptosis of corneal endothelium and also helps in expanding endothelial cells to fill the gaps of lost cells.Post surgical bullous keratopathy and Fuch's endothelial dystrophy may benefit by this. Ripasudil is tried more than Nitarsudil.

2) Neuro protection of retinal ganglion cell through its non apoptotic activity

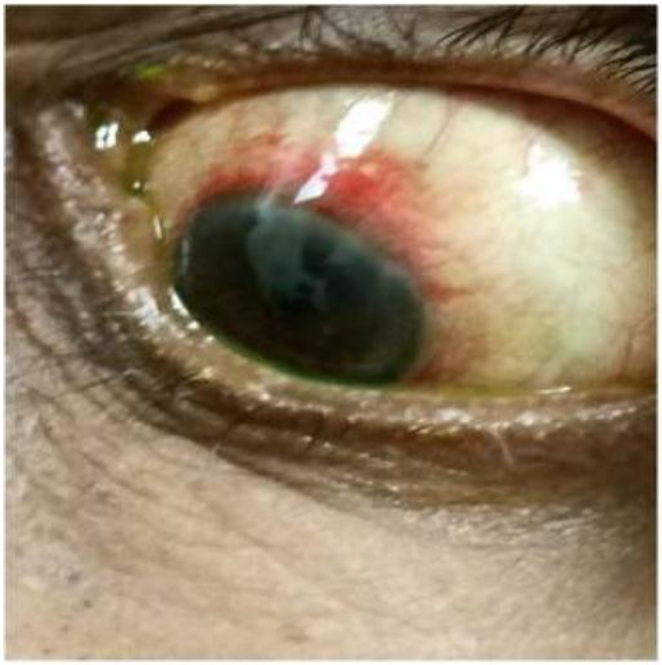

Figure 3 : Conjuctival hyperemia and hemorrhage following instillation of Nitarsudil

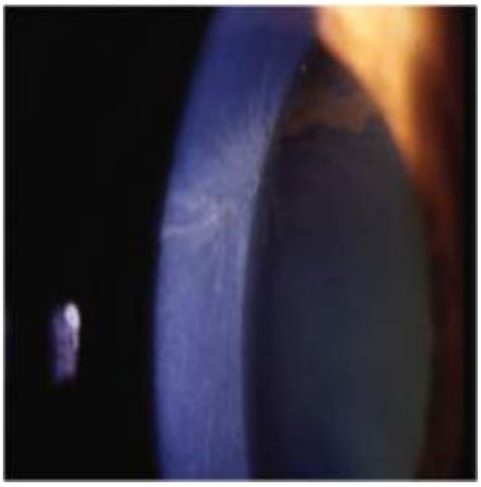

Figure 4: Corneal Verticillata following instillation of Ripasudil

3) Post trabeculectomy enhancement of survival of bleb through its anti inflammatory activity
4) Protection in diabetic retinopathy through its vaso protective activity (Vaso dilatation)

7) Side effect and tolerability of Rho Kinase Inhibitors -

Conjuctival hyperemia (Fig 3)
Conjuctival hemorrhage (Fig 3)
Corneal Verticillatta (Fig 4)
Corneal Guttata like changes
Itching
Punctate keratitis
Blurred vision

Are very important ocular side effects of which conjunctival hyperemia is seen in up to 35% patients

8) Fixed drug combination

Rocklatan is new fixed drug combination having ROCK Inhibitor Nitarsudil 0.02% with Latanoprost 0.005% is instilled once a day and presumed to be most potent anti glaucoma drug. Not yet available in our market.

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Gene therapy for inherited retinal disorder An update

Ekta Singh Sahu[1], Arun Bhargava[2]

The inherited retinal degenerative dystrophies (IRDs) are a heterogeneous group of genetic disorders that are characterized by dysfunction and degeneration of photo-receptors, retinal pigment epithelium, or the choroid leading to concomitant loss of functional vision. The clinical manifestation includes color or night blindness, peripheral visual defects and irreversible vision loss of variable extent. IRDs can be sporadic or familial, stationary or progressive, non-syndromic disease or syndromic diseases. Some of the important photoreceptor IRDs are retinitis pigmentosa and Leber congenital amaurosis whereas common macular dystrophies include Stargardt and Best disease. IRD can propagate through all modes of inheritance: autosomal dominant (AD), autosomal recessive (AR), X-linked (XL), and mitochondrial.[1] Given that many IRDs are progressive and irreversible,long-term vision outcomes can be improved with prompt diagnosis and genetic assessment. Nearly 2 million people worldwide are affected by IRDs.[2] The identification of pathogenic genes, mutations and gene editing technologies has opened up IRD to therapeutic development. To date around 260 genes associated with IRD have been identified.[3]

RETINA, THE IDEAL PLAYGROUND :

Eye is an ideal target for in vivo gene therapy as a small relatively immune-privileged organ, displaying unique compartmentalized anatomy, presence of the blood retina barrier, direct visibility and stable populations of target cells.[4] Eye immunologic privilege environment makes sustained transgene expression with minimal risk of systemic effects. The gene therapy landscape is evolving rapidly and the genes evaluated in each panel are updated periodically. It is important to educate pediatric patients and their families about the availability and potential benefits of genetic testing at time of IRD diagnosis. More than 30 middle- and late-stage gene therapy clinical trials are in vogue for different IRD indications.[5] Many of these trials are limited to patients 18 years of age or older, however, pediatric patients are being recruited for clinical trials evaluating gene therapy for XLRP and for CNGA3- or CNGB3- associated achromatopsia after favorable safety profiles have been established.[6]

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COMPONENTS OF OCULAR GENE THERAPY :

IRD's are segregated into simple (mono-, di-, and tri-genetic) and multifactorial where most IRDs are monogenic in nature. The vital components of ocular gene therapy are (1) the genetic material, which consists of the codon-optimized therapeutic transgene (2) the delivery vehicle to introduce the genetic material and (3) the route of administration, either via intravitreal or subretinal injection to form bleb with or without intraoperative OCT guided.[7]

GENE THERAPY THREE WAYS :

The approach to gene therapy is broadly strategized into gene augmentation, gene inactivation and gene editing depending on its underlying cause.[8] In gene augmentation therapies a functioning copy of a gene to restore expression of a mutated gene is introduced; gene inactivation involves blockage of harmful gene expression and gene editing aims to directly edit and correct the mutation.

The functioning copy of a gene is delivered as DNA, or alternatively as mRNA or mRNA analog. The DNA platform used for delivering functioning copy of a gene is the preferred choice for gene therapy for its less immunogenicity and more sustainability than RNA counterpart.[9] A functional copy of a gene introduced via engineered viruses does not alter a patient's native DNA but is expressed to produce normal protein to treat a genetic defect. Viral vectors used as gene delivery vehicle have been optimized by removing pathogenic elements and impeding the viruses' ability to replicate. Common delivery vectors include adeno-associated virus (AAV) and lentivirus. Among the various AAV serotypes identified AAV2, AAV5, and AAV8 have been most extensively studied in ocular gene therapy.[10] Gene augmentation strategy is an effective treatment for AR IRDs, XL conditions and AD disorders with haploinsufficiency.[11] A notable example of the gene augmentation strategy and gene editing system is Voretigene neparvovec-ryzl (Luxturna, Spark Therapeutics) and the clustered regularly interspaced short palindromic repeats (CRISPR) and CRISPR-associated-9 (Cas9) system respectively.[12]

GENE THERAPY FOR IRD :

RPE65-MEDIATED DISEASE

RPE65 gene encodes a carotenoid oxygenase enzyme important in visual pigment regeneration. Mutations in RPE65

have been associated with LCA type 2 (LCA2) and RP (RP20). Voretigene neparvovec-rzyl (Luxturna) is a breakthrough gene therapy commercially approved December 2017 for IRD related to biallelic mutations in the RPE65 gene. Voretigene is the first AAV-vector based US FDA approved gene therapy. It is a normal copy of the RPE65 gene delivered into subretinal space after pars plana vitrectomy to produce the functioning RPE65 protein in photoreceptor cells. Results are promising showing continued improvement and durability; more so in paediatric age group where treatment is started in early stage of disease.[13] However, in some recent studies, atrophy in inferior perifoveal distribution and chorioretinal atrophy has been reported. MeiraGTx is also developing an AAV-RPE65 gene supposedly 100 to 1,000 times more potent than the first-gengeneration therapy. [14]

CHOROIDEREMIA :

CHM gene encodes for Rab escort protein 1 (REP1). REP1 function loss leads to cell death and progressive loss of choroid, RPE, and photoreceptors cell death. SPK-7001 (Spark Therapeutics) and NSR-REP1 (Nightstar Therapeutics) are ongoing prospective clinical trial NSR-REP1.[15] Among 32 participants included in phase 1/2 clinical trials, NSR-REP1 had encouraging results with maintenance or improved visual acuity in more than 90% of patients. An interim analysis of SPK-7001 phase 1/2 open-label clinical trial had no product-related serious adverse events though late stage enrolled participant showed nonstatistically significant indications of efficacy on one or more endpoints.

X-LINKED RETINITIS PIGMENTOSA :

RPGR is involved in the transport of RP GTPase regulator protein (RPGR) responsible for maintenance of photoreceptor health. Mutations in RPGR gene causes progressive death of rods and cones and has been associated with approximately 70% of X-linked RP (XLRP). Several gene therapy trials in XLRP are in progress. NSR-RPGR Nightstar Therapeutics utilize an AAV vector with a codon-optimized RPGR gene (NSRRPGR) to produce the RPGR configuration(RPGR-ORF15) expressed in the retina.AAV-RPGR MeiraGTx is conducting a dose escalation phase in [18] adult with XLRP to later implement in 12 pediatric patients as well.[16] In a dose escalation phase, up to 18 adults will receive one of three escalating doses. Applied Genetic Technologies Corporation (AGTC), in collaboration with Biogen, enrolled the first patient in a phase 1/2 open-label, dose escalation study of subretinal administration of an AAV-based gene therapy.

X-LINKED RETINOSCHISIS :

RS1 gene encodes a protein, retinoschisin protein secreted by the outer retina is involved in cell to cell adhesions and retinal intracellular matrix development. Mutation in RS1 gene causes retinoschisin abnormality and expression of XLRS abnormality. A single-center, dose escalating, prospective clinical trial administered intravitreal vector AAV8-RS1 with pathogenic RS1 gene mutations in nine patients with pathogenic RS1 gene mutations.[17] AAV8- RS1 Dose-related increases in systemic AAV8 antibodies was noted. The retinal cavities closed transiently in one treated patient in the higher dose group. However other regimens are being explored. In has been another clinical trial of rAAV2tYF-CB-hRS1, in collaboration with Biogen, 27 patient in four group of sequential dose-escalating groups were enrolled.[18] Also a group of pediatric patients receiving the middle dose was enrolled. Results are being evaluated based on safety, visual function, retinal structure and quality-of-life

ACHROMATOPSIA :

Congenital achromatopsia is an autosomal recessive disorder characterized by loss of cone function. Mutation in gene encoding cyclic nucleotide-gated channel beta 3 (CNGB3/ ACHM3) proteins and four other genes has been identified which are required for critical steps of the phototransduction pathway in cones. A dose escalating, phase 1/2 open-label clinical trial administered one of three doses of AAV-CNGB3 subretinallyin adult patients.[19] Pediatric patients will be treated once an acceptable dose is established among 18 adult patients receiving AAV-CNGB3.

STARGARDT DISEASE :

ABCA4 gene encodes the protein needed for clearance of extra all-trans-retinal. Mutations in ABCA4 gene hamper clearance of excess all trans-retinal after photoexcitation, leading to Stargardt disease where excess of all-trans-retinal accumulate and deposits in photoreceptors and retinal pigment epithelium (RPE) cells. Sanofi conducted a phase 1/2 open-label dose-escalation clinical trial SAR422459, formerly known as StarGen (NCT01367444). The trial evaluated the safety and tolerability of a subretinal injection of a lentiviral vector over a 48-week follow-up period. The trial was terminated in 2019 as serious adverse events increased intraocular pressure in one and uveitis in another were listed. All patients suffered one or more trivial adverse events. No conclusions can be drawn until the study is peer-reviewed. With early termination of this study all patients have been transferred to a 15-year follow-up (NCT01736592).[20]

The biotech company Alkeus is conducting a multi-center Phase II clinical trial for the oral once-daily C20-D3-vitamin A molecule drug (ALK-001) that targets the toxic build-up in the retina.

HOPE IS NEAR :

Treatment options for IRDs continue to expand, as number of clinical trials is ever-growing.The encouraging experience with monogenetic IRDs has provided pathway for more precise molecular diagnosis of retinal degenerations and highlighted its increasing importance among patients and practitioners.

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RLRL for myopia control

Repeated low red light therapy

Too much of near activity is one of the important factor for myopia progression. Increasing outdoor activity is known to have a protective role in preventing this progression.Considering this in mind a device is developed to deliver light to the retina at repeated short durations. This device use red light at a wavelength of 650 nm. The therapy is a home treatment done under parental control , 3 minutes per day , twice a day, with minimum 4 hours gap ,5 days a week.One year follow up showed significant slowdown in myopic progression (0.26 mm) showing 69.4% slowing in axial length elongation. No structural or functional damage was seen in any of the studies.

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Spectrum of Botulinum Toxin Utilization in Oculoplasty and Aesthetics

Bhagyesh B. Pore

Botulinum toxin, which is an exotoxin produced by the naturally ubiquitous bacterium Clostridium botulinum, a gram-positive, spore-forming, anaerobic rod commonly found on plants, in soil, water and the intestinal tracts of animals and fish.[1] BOTULISM may develop hours to days (usually 18-36 h) after ingestion of toxin, the symptoms consist of progressive weakness, dizziness, blurred vision, difficulty in speech and swallowing, and finally respiratory distress.

Botulinum toxin, once thought as the 'most poisonous poison' is now one of the most frequently used medications in ophthalmic plastic surgery. The organism C. botulinum was originally isolated by Professor E Van Ermengem in 1895. Over the subsequent 30 years, botulinum toxins have been used to treat a host of other conditions, and are currently used in almost every sub-specialty of medicine.[2, 7]

Pharmacology :

Types of Botulinum Toxin -

C. botulinum elaborates eight antigenically distinguishable exotoxins (A, B, C1, C2, D, E, F and G), Type A is the most potent toxin.

Mechanism of Action -

Intramuscular administration of botulinum toxin acts at the neuromuscular junction to cause muscle paralysis by inhibiting the release of Acetycholine (Ach) from presynaptic motor neurons [Fig. 1].[18]

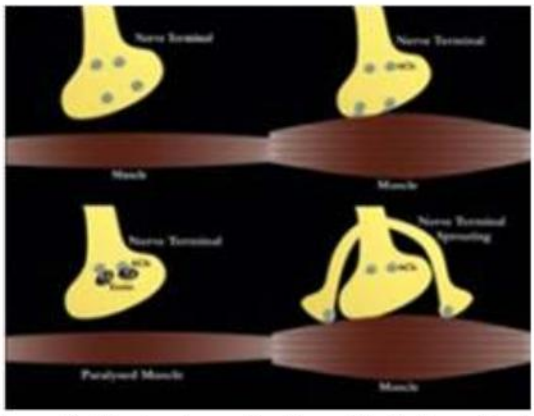

Figure 1 : Mechanism of action of botulinum toxin.

Normally, skeletal muscle contracts due to Ach vescicles released into the synaptic cleft (Fig. 1 top left and right). When botulinum toxin is injected into the muscle, it binds to the nerve terminal, gets internalised and prevents release of Ach vesicles, thereby paralysing the muscle (Fig. 1-bottom left). The muscle action however recovers due to sprouting of nerve terminals, which re-innervate the muscle (Fig. 1 -bottom right)

Commercial Preparations :

Three preparations of botulinum toxin are commercially available at present. Botox® (Allergan Inc., Irvine, CA, USA) and DysportÒ (Ipsen Pharmaceuticals, France) are the type A toxins. MyoblocÒ (Elan Pharmaceuticals, San Diego, CA, USA) is the type B toxin. Type A toxin is easily producible in culture in a highly purified, stable and crystalline form. Type A toxin also has the longest duration of action, sterile vacuum-dried purified extract of botulinum toxin type A, produced from fermentation of the Hall strain of C. botulinum type A.[3]

CONTRAINDICATIONS TO THE USE OF BOTULINUM TOXIN -

- Ø Peripheral motor neuropathies like Amyotrophic lateral sclerosis
- Ø N-M junction disorders like Myaesthenia gravis, Eaton-Lambert syndrome
- Ø Pregnancy
- Ø Areas of active infection
- Ø Known hypersensitivity to any ingredient of the formula

Toxin Reconstitution -

The type A toxin has to be reconstituted with sterile, nonpreserved 0.9% saline prior to injection. The toxin concentration per 0.1 ml of diluent is dependent on the volume of diluent used [Table 1].[3] The reconstituted solution should be clear, colourless and free of particulate matter, and should be stored in a refrigerator at 40°C until use. The dose recommendations for common therapeutic indications of botulinum toxin are given in [Table 2]. The reconstituted toxin is drawn into a tuberculin syringe via a fine gauge needle (30G or 32G) for final injection. The manufacturer recommends Botox® to be used within 4 hours of reconstitution.[3]

Diluant added in [ml]	Botox dose [U/0.1 ml]
01	05
02	2.5
04	1.25

Table 1 : Effective botulinum toxin concentration (units per ml) of Botox® with various amounts of diluent used.

Director, Shakuntala Netralaya,
Indore

Clinical Entity	Approximate Dose Of Botox In [U]
Benign essential blepharospasm	30-40
Hemifacial spasm	15-20
Chemo-tarsorraphy	05-10
Upper eyelid retraction	2.5-05
Lower eyelid retraction	10-20
Injection in lacrimal gland	2.5-05

Table 2 : Dose recommendations for common therapeutic indications of botulinum toxin in oculoplasty

Facial dystonias -

Botulinum toxins have revolutionised the treatment of patients with facial dystonias. The success rate is reported to be over 90%.[4]

Facial dyskinesias presenting to the ophthalmologist include Benign Essential Blepharospasm (BEB), Hemifacial spasms (HFS), Orbicularis myokimia, Meige syndrome and Apraxia of lid opening (ALO).

BEB is an involuntary and repetitive bilateral spasmodic contraction of the orbicularis oculi muscle [Fig. 2], and is often progressive. It usually presents in the fourth to sixth decade with an increase in the blink rate, which increases in 1 or 2 years to forceful involuntary closure of eyelids. Symptoms are often exacerbated by environmental conditions like bright light, dusty air or optokinetic stimulus. The aetiology of blepharospasm is considered to be an organic dysfunction of the rostral brainstem. Treatments that have been tried for BEB include central nervous system depressants (diazepam and clonazepam), orbicularis myectomy and selective facial nerve neurectomy. However, patient acceptance is highest with botulinum toxin chemodenervation.[5, 13]

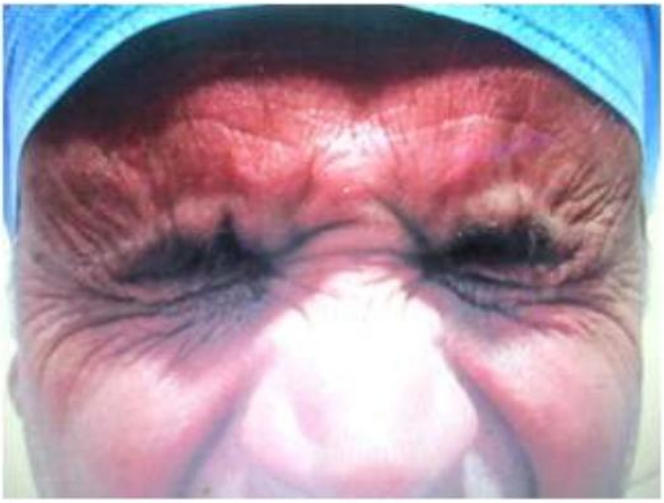

FIGURE 2 : Patient of BEB with bilateral spasmodic contraction of the orbicularis oculi

Reflex blepharospasm, caused by dry eye or ocular surface pathology can mimic BEB. It can be associated with spastic lower eyelid entropion that in turn induces ocular surface damage and the vicious cycle continues. It is typically relieved by instillation of topical anaesthetic. Botulinum toxin injection helps to break the vicious cycle, by inducing temporary paralysis of orbicularis oculi.[5]

Meige Syndrome was first described in 1910 by Henry Meige, as 'spasm facial median'. It is a form of cranial dystonia characterised by the presence of bilateral blepharospasm with concurrent dystonia of the lower face, in the form of lip pursing, chewing, or jaw opening movements. Dysarthria and dysphonia may also be seen.

HFS is characterised by repetitive unilateral periodic tonic contractions of ipsilateral facial muscles. It begins in middle age and is more common in females. It generally results from mechanical-vascular compression of the seventh cranial nerve root in the cerebello-pontine angle. Less than 1% are caused by posterior fossa tumours, therefore a magnetic resonance imaging may be indicated in patients with HFS. Although neurosurgical microvascular decompression procedure may be the definitive form of treatment, Botulinum toxin injections are effective in controlling HFS.[20]

Orbicularis myokimia generally occurs in younger individuals, and involves involuntary twitching of the upper or lower eyelid, resulting from spasm of individual bundles of muscle fibres. It is related to stress, fatigue, use of alcohol or excess caffeine.

For chemodenervation of facial dystonias, a pre-injection evaluation involves examination of the muscles involved in the spasms, and assessment of the muscle mass. Videography of spasms before and after injection may allow identification of the involved muscles, and help in planning future treatment. Patients with BEB typically require repeat injections every 3-4 months, whereas those with HFS have a longer spasm-free interval of 4-6 months. [17]

Common complications of botulinum toxin chemodenervation for facial spasms

- Ptosis
- Lagophthlamos
- Ectropion or entropion of the eyelid
- Functional epiphora due to lacrimal pump failure
- Diplopia
- Eyelid hematoma

We commonly use Botox® (Allergan, Irvine, CA, USA) by diluting 50 U vial to obtain a dilution of 2.5 or 5 U per 0.1 ml. For the treatment of BEB, subcutaneous injection of

botulinum toxin is given into the orbicularis oculi of upper and lower eyelids as well as the eyebrows [Fig. 3]. The sites injected vary for each patient and subsequent injections are modified based on patient's response to treatment. For HFS, the periocular injection sites and dosage remains similar to that of BEB. Additional injections into the involved lower facial muscles may be required in HFS.

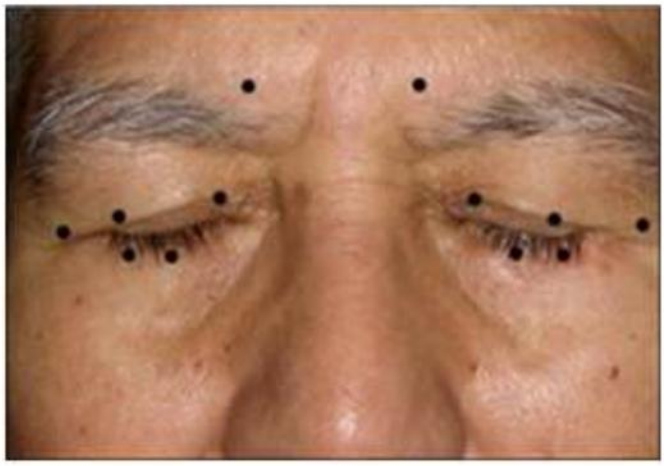

Figure 3 : Injection sites for BOTOX in BEB.

Patients with HFS demonstrate a longer duration of action than BEB, because HFS demonstrates less of nerve and muscle hyperactivity. Moreover, the facial nerve progressively degenerates in HFS, leading to a longer spasm free interval. Injection into the pretarsal muscle has been shown to produce a significantly better response compared to preseptal injection in blepharospasm and HFS patients.[5] Meige syndrome is more difficult to control than BEB, requires a higher total toxin dose, and has a shorter spasm free interval. Orbicularis myokimia if persistent, requires focal toxin injection into the involved muscle bundle.

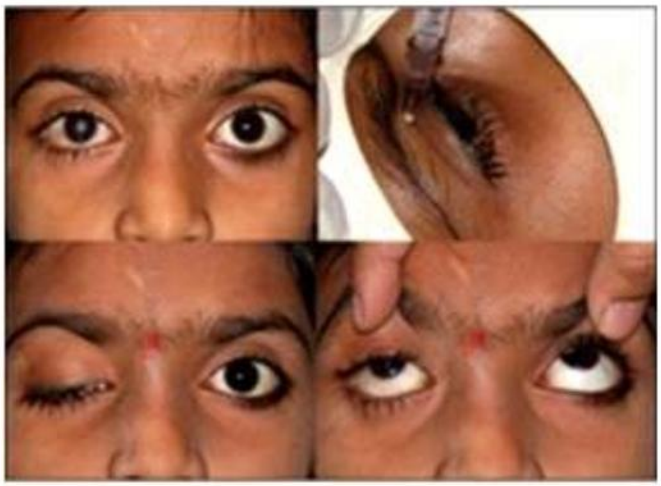

FIGURE 4 : Transcutaneous chemodenervation of the levator muscle (top right). Same patient 1 week after botulinum toxin chemodenervation (bottom left) demonstrating complete ptosis

Chemo-tarsorrhaphy -

Traditionally, tarsorrhaphy has been used in cases of corneal exposure due to facial nerve palsy, persistent epithelial defects, and indolent corneal ulcers.[8] Botulinum toxin chemodenervation of levator muscle is a quick and easy procedure for induction of temporary ptosis for corneal protection, thereby avoiding surgical tarsorrhaphy and subsequent scarring of eyelid margin. (Fig. 4)[4]

Upper eyelid retraction -

Botulinum toxin injection into the levator can be an effective treatment for upper eyelid retraction associated with thyroid eye disease [Fig. 5]. Though the amount of resultant ptosis is unpredictable.

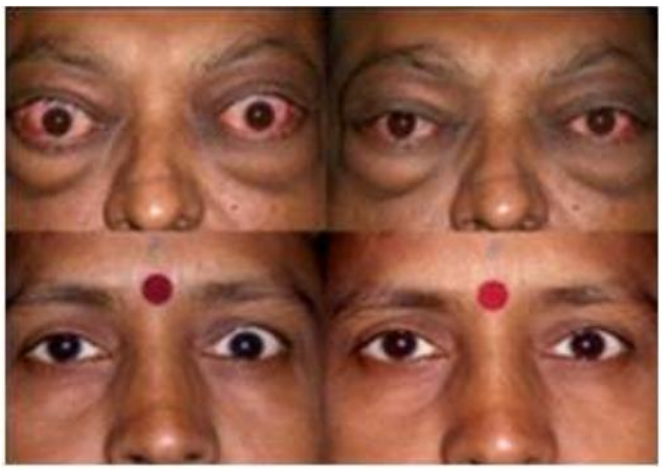

FIGURE 5 : Patient with bilateral (top, left and right) and unilateral (bottom, left and right) eyelid retraction due to thyroid ophthalmopathy, before and 1 week after trans-conjunctival botulinum toxin chemodenervation

Lower eyelid senile entropion -

One of the aetiologies of lower eyelid senile entropion is the overriding of preseptal orbicularis muscle over pretarsal orbicularis muscle. Surgical treatment of senile lower eyelid entropion is definitive and persistent. However, botulinum toxin chemodenervation is a quick outpatient procedure

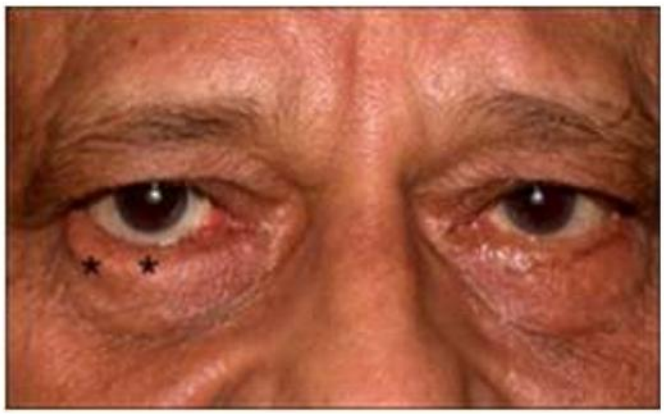

Figure 6 : Injection Sites for BOTOX in Senile entropion

[Fig. 6] for patients who are unfit or waiting for surgery. The mean duration of action has been reported to range from 12 to 15 weeks,approximately 10-20 U of Botox® is required for the desired effect.[6]

Facial nerve palsy and aberrant regeneration -

Aberrant regeneration of facial nerve can lead either to 'crocodile tears' (gustatory epiphora), Frey's syndrome (gustatory sweating) or abnormal facial movements.[14] These late effects of facial nerve regeneration can be treated effectively with botulinum toxin.

Gustatory epiphora -

Gustatory epiphora, is characterised by excessive lacrimation while eating or smelling food. This usually follows a Bell's palsy or stroke, involving the proximal facial nerve or its nucleus. Abnormal lacrimation in gustatory epiphora can be treated with intraglandular injection of botulinum toxin [Fig. 7]. Ptosis and superior rectus underaction are common side effects.[16]

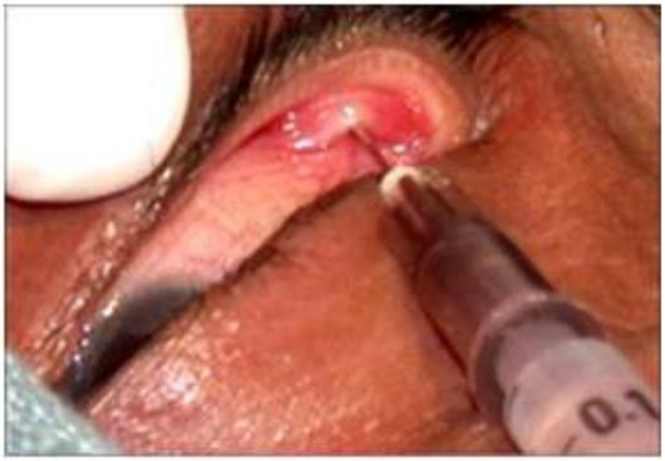

FIGURE 7 : Trans-conjunctival intraglandular injection of botulinum toxin into the left lacrimal gland

Lacrimal gland hypersecretion and dry eye -

Injection of botulinum toxin into the lacrimal gland [FIGURE 10] has been described for the treatment of gustatory epiphora. However, it can also be used for primary lacrimal gland hypersecretion, and secondary causes such as functional epiphora.

FIGURE 8 : Glabellar frown (left). Wrinkles around the lateral canthus (periocular crow's feet), (right)

Injection of botulinum toxin into the medial eyelid decreases lacrimal drainage by paralysing the lacrimal pump mechanism. This can prove to be a useful adjunct in the management of dry eye patients.

Cosmetic oculoplasty -

Facial wrinkles or rhytides may be categorised as static or dynamic. Dynamic wrinkles are the result of activity of underlying muscles. On the other hand, static wrinkles result from thinning of the dermis due to age, sun exposure, and smoking.[12]

Glabellar frown lines: the glabellar wrinkles [Fig. 8] are caused by the actions of corrugator supercilli, depressor supercilli and procerus muscles. Injection into these areas has been shown to cause temporary paralysis that lasts up to 6 months [Fig. 9], thereby eliminating these wrinkles. For treatment, 2.5-5 U of botulinum toxin type A (Botox®) are injected at five to seven sites into both corrugators and into the procerus muscle.

Horizontal forehead wrinkles: the action of the frontalis muscle may, over years, lead to the development of horizontal forehead wrinkles. Injection of botulinum toxin type A (Botox) in four to eight sites spaced evenly over the forehead may relax the muscle and soften these lines. The injections are typically given 2-3 cm above the orbital rim using 2.5-5 U per injection sites [Fig. 9].[12]

Periocular crow's feet: the contraction of the lateral orbicularis fibres, zygomaticus and risorius muscles gives rise to dynamic wrinkles spreading out from the lateral canthus, known as the crow's feet [Fig. 8]. Three to four injections of 2.5-5 U of Botox into lateral orbicularis oculi are required for effective treatment of crow's feet [Fig. 9].

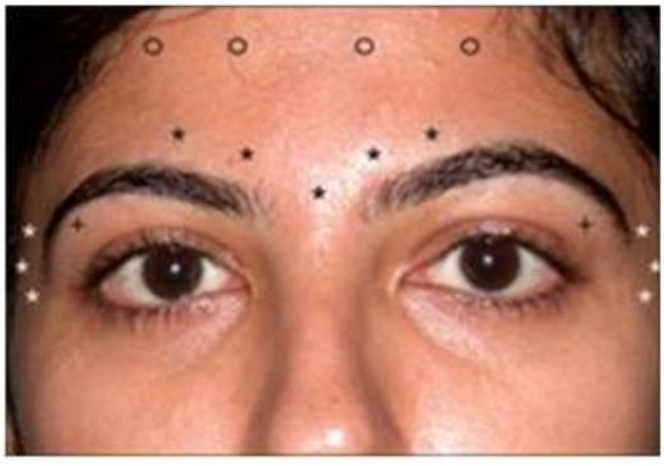

FIGURE 9 : Photograph demonstrating placement of injections for treatment of horizontal forehead wrinkles (open circles), glabellar furrows (black asterix), crow's feet (white asterix) and chemical brow lift (cross sign). Each site is injected subcutaneously with 2.5-5 U

Chemical brow lift: botulinum toxin can be used to create a chemical brow lift by selectively paralysing the depressors of the eyebrow. Botulinum toxin injections are given into the glabellar area (as described earlier) and lateral orbital orbicularis muscle [Fig. 9] below the eyebrow.[15]

Other aesthetic facial applications of botulinum toxin include 'bunny lines', peri-oral treatment, dimpled chin, 'marionette lines' and platysmal bands.

Botulinum toxin has also been found to be useful in the management of Migraine, and Tension type headache. When injected into the neck or facial muscles (temporalis, frontalis, corrugator-procerus complex and occipitalis), it is believed to block the release of nociceptive neuropeptides involved in the chronic inflammatory pain response.

A LONG WAY AHEAD.....

Type A botulinum toxin has widened its clinical range of applications, but the risk of developing antibodies limits the repeated use of high-dose injection. Other serotypes of botulinum toxin are being investigated as useful alternatives to botulinum toxin type A. Botulinum toxin type F differs from type A, mainly by its lower potency, efficacy and shorter duration of action. Botulinum toxin type F blocks a different SNARE protein as compared to type A toxin. Therefore, a combination of toxins A and F has been suggested to reduce the total units required, and therefore the overall antigenic dose.

Conclusion :

The use of Botulinum toxins has revolutionised the treatment of various ophthalmic plastic disorders from facial dystonias to periocular wrinkles. In future, we are likely to see the development of new potent toxins with increasing effectiveness and duration of effect. The ophthalmologist should be aware of this expanding and interesting field of chemodenervation, and use it to the fullest potential.

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Oculofacial Aesthetics in Ophthalmology

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Introduction :

An ophthalmic plastic surgeon most commonly deals with lacrimal conditions, orbital surgeries and ocular oncology. However, along with eyelid procedures, more and more oculoplastic surgeons are opting to practice aesthetics. Now that the periocular region has come into focus from an aesthetics perspective, it is imperative that practicing oculoplastic surgeons equip themselves with the know-how to manage these patients. It is also important to create awareness amongst the general public that as surgeons, we are well equipped to handle eye related as well as most facial procedures safely.

Paradigm shift :

Aesthetic treatments are not only limited to the aging face namely "facelifts" that were traditionally performed by plastic surgeons, but are also open the younger population to enhance their facial features or correct any preexisting undesirable flaws. Another paradigm shift has been that of patients opting for less and less invasive procedures rather than "going under the knife". The global survey done by the International Society Of Aesthetic Plastic Surgery in December 2020, shows that face and head procedures have increased by 14.5%, with men increasingly opting of aesthetic surgeries[1]. India has one of the largest groups of Oculopalstic surgeons in the world and is now ranked within the top 10 countries where aesthetic procedures are being performed[1].

Training :

Oculofacial procedures must be done by a qualified surgeon after completing training in either ophthalmic plastic surgery or training pertinent to any other surgical field. Improper methods or untrained surgeons performing these techniques may result in complications and lead to litigation. In our country, there are various institutes that conduct fellowships and short-term instruction courses in aesthetic procedures. International observerships and fellowship programmes such as those offered by the International Council of Ophthalmology (ICO) give candidates an opportunity to learn from reputed colleges and mentors.

Set-up :

To start in the journey of providing aesthetic and cosmetic services to the patients, it is important to modify practice to cater the clientele. It is extremely important to gain confidence of the patient in the result of these procedures. And to do the same, efficient scheduling and well informed communications by doctors and counsellors are very important. The design of the clinic should be appealing and comforting to the patients. In today's time, where patients do a lot of research before choosing a particular doctor, social media handles of the clinic should have appropriate data in forms of images and videos.

Anatomical Changes :

The aging face shows changes in bone, fat and other soft tissues, facial muscles and connective tissue. Midfacial aging is thus an interplay of several factor and a 3-D process that involves volume loss, descent, and surface alterations[2]. Due to accelerated bony resorption, the orbital rim enlarges, the maxilla shortens and length and height of mandible decreases[3]. There is associated deepening of nasolabial fold (NLF) and atrophic changes resulting in hollowing of cheeks. Dermal thinning, decreasing skin elasticity and fat atrophy coupled with muscular traction and bony volume loss result in rhytids and the formation of creases, NLFs, jowls, and the aged appearance of facial skin[4].

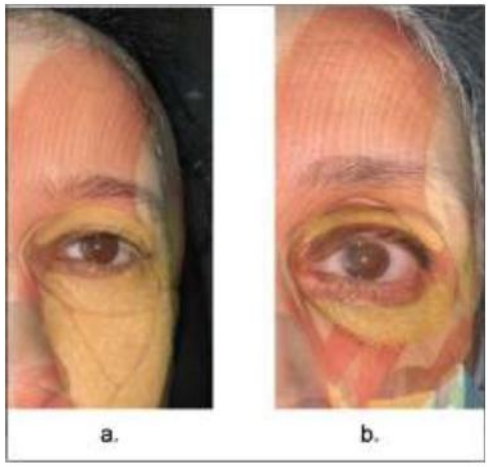

Fig.1 Interplay between fat and facial muscles changing with age: a. In a 26 year old lady and b. In a 65 year old lady

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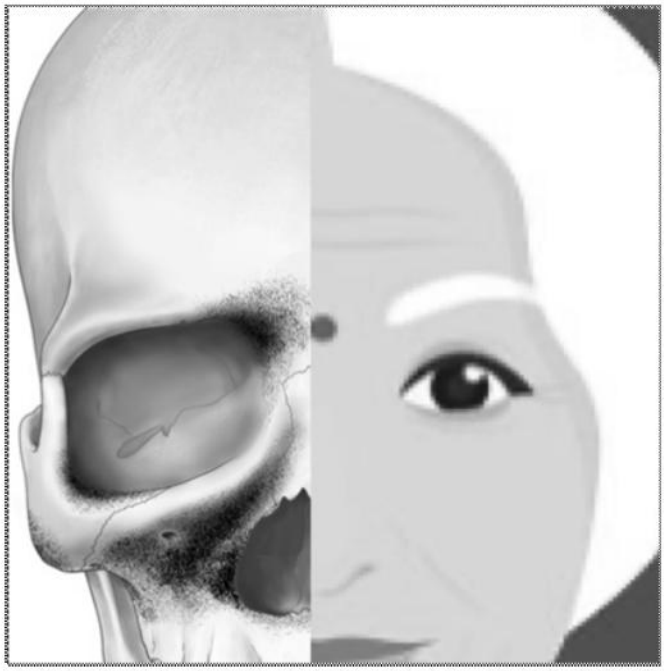

Fig.2 Bony aging: The maximum resorption of bone takes place in the superomedial and inferotemporal orbit. This results in elevation of the medial aspect of the brow and lengthening of the lid-cheek junction

Patient selection :

Deciding whether or not a patient is an ideal candidate for a procedure is of utmost importance. It is important to assess the patient's expectations and proceed only once both client and doctor are on the same page. Counselling prior to the procedure, regarding realistic and achievable results, can make the difference between satisfied and unsatisfied patients.

Procedures should be avoided or done under caution in patients who have :

- Pre-existing dry eye disease
- Known bleeding or clotting disorders
- Patients on antiplatelets and anticoagulants
- Neuromuscular disorders
- History of blepharochalasis
- Unreasonable expectations

Patient evaluation :

- Skin diseases, eg. Rosacea, Acne
- Facial symmetry and bone structure
- Shape and position of the brow
- Upper lid
  1. Excess skin
  2. Ptosis, Lid retraction
  3. Position and symmetry of lid crease
  4. Prolapsed orbital fat
  5. Xanthalesma
  6. Dermatitis
  7. Prolapsed lacrimal glands
- Lower lid

1. Tear trough deformity/hollowness
2. Abnormal lid position entropion/ectropion/lid retraction
3. Excess skin, rhytids
4. Protruding orbital fat
5. Eyelid laxity
6. Lateral canthal rounding
7. Hypertrophied orbicularis muscle
8. Malar bags or festoons

- **Rhytids**

1. Nasolabial folds (NLF)
2. Smoker's lines
3. Marionette lines
4. Glabellar lines, forehead creases
5. Crow's feet

Treatments :

1. Non-surgical :

- **Cosmoceuticals** Acne treatment, Depigmentation, Sunscreens, Emollients
- **Dermabrasion -** The most common indications for dermabrasion are in the treatment of acne scars, vitiligo, traumatic or surgical scars, photo damage, few benign tumors, actinic keratoses, and perioral rhytides. Also, melasma, tattoos, or postinflammatory hyper pigmentation can be lightened with dermabrasion. It gives 35-50% improvement. Patients should be told that the maximal effect is usually observed 6 months after surgery.
- **Facial peels** they can be superficial, medium depth and deep peels, based on the indication.
- **Laser resurfacing-**bypulsed carbon dioxide (CO_2) and Erbium : Yttrium-Aluminum-Garnet (Er:YAG) or combination of these two.
- **Botulinum toxin injections-** They are used to smoothen out static and dynamic wrinkles. It is also useful in patients who have a prominent orbicularis roll below the lashes. They can also be combined in solutions used for microneedling along with hyaluronic acid as 'mesobotox' to give a good glow to the skin.

Fig.3 Procedure of Hyaluronic acid injections for tear trough

- **Filler injections-** to improve scars, fine wrinkles, grooves and folds, as well as to address periorbital hollows. Permanent fillers are PMMA and silicon, their use is no longer preferred. Autologous fat, hyaluronic acid, PLLA, collagen are temporary fillers. Temporary fillers are most commonly preferred due to their safety and reversibility.
- **Thread lifts** cogged/barbed threads are inserted under the skin and tightened by engaging soft tissue and muscle, thereby lifting tissues as well as stimulating collagen production. They can be made of PDO (Polydiaxanone), PLLA (Poly L-Lactic Acids) and PCL (Poly Caprolactone).

2. Surgical :

- BLEPHAROPLASTY :

- Upper lid blepharoplasty- to address hooding and bulging fat pads. It can be done for both functional and cosmetic purposes. Brow ptosis should be addressed prior to proceeding with upper lid blepharoplasty.

  Achieving symmetry requires accurate measurements of skin and muscle to be excised. The marking should be done in the sitting position when the tissues are in their normal gravitational relationship. First, skin crease incision should be marked which is precisely at the crease in younger patients and 1 mm caudal to existing crease for older patients. The amount of skin left after excision should be at least 20mm between eyebrow and eyelashes to ensure proper lid closure.

  After skin and muscle excision, septum is identified, and it is opened throughout its length. At this point pre aponeurotic fat is seen and is dissected off the levator towards the superior orbital rim. The central and medial fat pad are excised.5 Crease forming sutures may be passed from skin to the aponeurosis with 6-0 Vicryl. Skin is closed with 6-0 Prolene.

- **Lower lid blepharoplasty-** Mainly to address fat prolapse and skin laxity. It is most commonly performed viathe inferior transconjunctival approach.Transconjunctival approach is preferred in cases where there is no excess skin and muscle. Incision is given along inferior edge of the tarsus. Septum is opened and excess fat lying anterior to the inferior orbital rim is excised or re-draped as needed. Conjunctival incision is closed using 6-0 Vicryl sutures.

In the transcutaneous approach, a sub-ciliary incision is made below the lashes from the punctum to about 5mm lateral to lateral canthus. Traction sutures are passed and dissection is carried out till the inferior orbital rim is reached. The orbital septum is identified, incised and the underlying fat is exposed. Excess fat from the three fat pads, namely, nasal, central and lateral fat pads are excised. The lateral fat pad is covered with more septae and thus may not spring forward easily, necessitating dissection. The medial fat compartment is the most difficult to locate. The medial fat pad appears different from the central and lateral fat pads, as it is white and membranous. Excision should be done judiciously, as excessive fat removal posterior to inferior orbital rim would result in a hollow look. The end point of the fat excision is when the anterior border of the fat lies flush with the inferior orbital rim when light pressure is applied on the globe as in upright posture. The skin and muscle are excised conservatively as excess removal may result in ectropion. Skin is incision is closed with 6-0 Prolene.

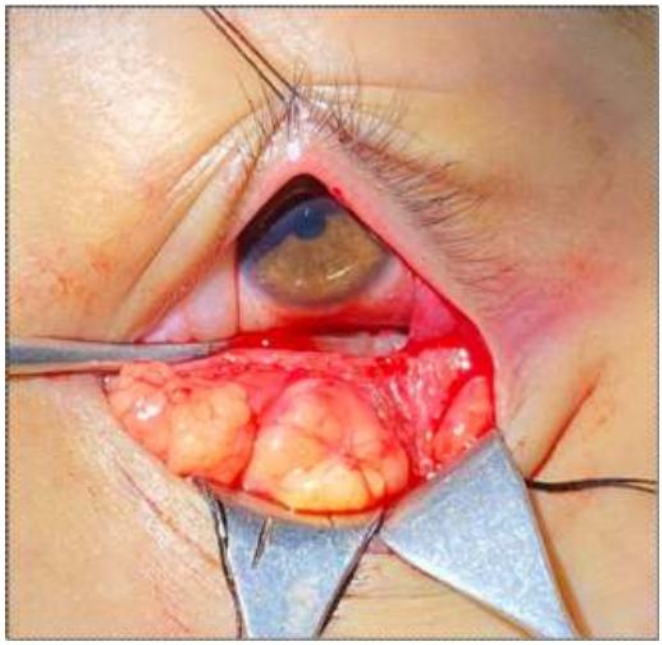

Fig.4 Image showing the medial, central and lateral fat pads dissected at the time of lower lid transconjunctival blepharoplasty

- BROWPLASTY :

It is used to correct fullness due to abundance of retro-orbicularis oculi brow fat (ROOF).

- BROW LIFT :

To address brow ptosis

- Supra brow lift- open (traditional) brow lift with incisions just above the eyebrows
- Temporal brow- lift- in the mid forehead region
- Frontal brow lift- in the hairline
- Coronal brow lift

The approaches can be subperiosteal, subgaleal, or subcutaneous. The most common is a subgaleal approach through a hairline or coronal incision. The most important step is assessment and marking of the skin. The brow is lifted to the desired position and a ruler is placed next to inferior brow hair. The eyebrow is allowed to drop and this distance is measured and multiplied by factor of 1-1.5 to calculate the height of final incision. Ellipse is drawn above the eyebrow. Skin and muscle are excised in one layer. Supra orbital nerve medially and frontal nerve laterally should be preserved. Wound is closed in 2 layers with 4-0 vicryl and 6-0 non absorbable interrupted sutures.

- Endoscopic-Brow elevation may be achieved to a predictable degree, but fixation remains a concern with the endoscopic lift. Multiple techniques have been described which includes suture suspension, screw and K wire fixation. Endoscopic techniques, due to limited incisions, proves to be desirable to patients and considered as a "minimally invasive procedure"[7].

- PTOSIS :

The choice of the surgery is determined on the basis of following

1. Whether the ptosis is unilateral or bilateral
2. Severity of Ptosis
3. Levator action
4. Simple ptosis or associated anomalies

Depending upon the above criteria, commonly performed procedures are

1. Fasanella servat
2. Muller muscle conjunctivo resection
3. Levator resection
4. Brow suspension ptosis repair commonly known as Frontalis sling surgery

- EYELID MALPOSITIONS :

Other eyelid conditions include ectropion, entropion and lid retraction. Lid retraction can be non-surgically corrected by botulinum toxin injections. Surgically it can be managed with single or combination of procedures such as retractor release, levator disinsertion, spacer grafts (eg. Hard palate graft), lower lid tightening, etc.

- MID FACE LIFT :

It is also known as midface suspension, and mainly aims at elevation and tightening of the soft tissues like fat and muscle of the cheek area. It restores a more youthful lower eyelid-cheek "continuum", by lifting the nasolabial fold and partial softening of the "tear trough deformity" and improving the appearance of the malar bags ("cheek bags"). It is usually performed under general anaesthesia due to extensive dissection of facial.

COMMON COMPLICATIONS OF AESTHETIC PROCEDURES :

- Hematoma
- Infection
- Eyelid retraction
- Lagophthalmos
- Ectropion/symblepharon
- Ocular motility problems
- Blindness

Conclusion :

A plethora of new and emerging aesthetic procedures have entered the market, which are gradually being applied to Ophthalmic practice with the help of Oculoplastic surgeons. It is important that we learn to cross-specialize in this era, specifically with reference to Dermatology as this can help surgeons to deliver holistic care to their clients.

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An Insight into New Competency Based MBBS Curriculum

Nitin Nema[1], Romi Srivastava[2], Sukhwant Bose[3]

Introduction :

Competency-based medical education (CBME) has generated a huge amount of interest in medical educators all over the world as well as in India.[1] Past few years have witnessed many medical schools adopting competency framework as the basis of training.[2],[3],[4] It is a harsh truth that the traditional medical education system did not ensure skill development in students eroding trust between patient and doctor and denting patient-physician relationship.[5] To address this challenge, National Medical Commission(NMC, erstwhile Medical Council of India, MCI) decided to introduce CBME in all medical colleges across the country from the year 2019.[6] The much awaited reform replaced the more than two decades old traditional curriculum by CBME driven curriculum. This article will give the readers an overview of CBME curriculum excerpted from the Graduate Medical Education Regulation, Amendment 2019 (GMER 2019).[7]

CBME is an outcome-oriented approach which is learner centric wherein students take responsibility for acquisition of competency.[1] It promises greater flexibility and accountability that make learners identify their learning needs.[8] It lays emphasis on attainment of competencies, self-directed learning (where students take charge of one's own learning), reflection and active learning.[9]

The traditional curriculum, on the other hand, was subject-centered and time-based (Table 1). The teaching-learning activities and the assessment methods focused more on knowledge rather than on attitude and skills. Therefore, graduates used to have extraordinary knowledge, but lacked basic clinical skills required in practice. Moreover, they were also deficient in soft skills, communication skills, doctor-patient relationship, ethics and professionalism.[10]

Competency is defined as the ability to do something successfully and efficiently, and CBME is an approach to ensure that the graduates develop the competencies required to fulfill the patient's needs.[11] CBME curriculum focuses on the desired and observable ability of learners in real life situations. Furthermore, it helps Bachelor of Medicine and Bachelor of Surgery (MBBS) students attain the goal of medical education.

The undergraduate medical education program is designed with a goal to create an "Indian Medical Graduate" (IMG) possessing requisite knowledge, skills, attitudes, values and responsiveness, so that he or she may function appropriately and effectively as a doctor of first contact of the community while being globally relevant. The goal of MBBS training program can be fulfilled if the medical graduate is able to function in the following roles appropriately and effectively:

1. **Clinician** who understands and provides preventive, promotive, curative, palliative and holistic care with compassion.
2. **Leader** and member of the health care team and system with capabilities to collect analyze, synthesize and communicate health data appropriately.
3. **Communicator** with patients, families, colleagues and community.
4. **Lifelong learner** committed to continuous improvement of skills and knowledge.
5. **Professional** who is committed to excellence, is ethical, responsive and accountable to patients, community and profession.

The training during the MBBS course should be in alignment with the goals and competencies and, therefore, the following changes were made in the curriculum:

Foundation course :

In India, the criteria of selection of students in medical colleges do not take into consideration their non-scholastic abilities. They, therefore, need to adapt to the challenging atmosphere of medical colleges.[12] To overcome this challenge, a methodically planned foundation course is introduced in MBBS curriculum for the freshers.

The prime goal of foundation course is to prepare the student to study medicine effectively. It is a one-month duration program just after admission in a medical college. It will equip

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Table 1: Showing salient differences between traditional and competency-based curriculum

Features	Traditional Curriculum	CBME Curriculum
Goal	Attainment of knowledge	Application of knowledge
Driving force	Course content (subject-based)	Outcome (competency-based)
Responsibility of teaching	Teacher	Student and teacher
Teaching	Fragmented	Integrated
Teaching-learning	Teacher-centered	Learner-centered
Learning	Assumed to be 'one size fits all'	Individualized, allowing learner to focus on enhancing learning
Path of learning	Hierarchical (teacher to learner)	Non-hierarchical (teacher=learner)
Reflection and self-monitoring	Limited opportunities	Regular and frequent
Assessment	Norm referenced#, mostly summative	Criterion-referenced$, continuous and formative
Feedback	'No feedback' culture	Feedback culture
Professional development	Difficult to monitor	Easily monitored
Program completion	Fixed time	Variable time

#Comparing students' performances to one another, $Comparing students' performances against set criteria

the students with required knowledge and skills that assist them to get acclimatized to the new professional environment. Moreover, it will give the learner a strong platform for lifelong career in medical profession.

The main objectives of foundation course are to: (i) Orient students to MBBS program, medical profession and explain them the role of physician in society, (ii) equip with basic important skills required for patient care like language, communication, computer and learning skills, and (iii) provide an opportunity for peer and faculty interactions and an overall sensitization to various learning methodologies.[13] Sports and extracurricular activities are also planned during this period. One parent-teacher meeting will be held during this month long course. Time dedicated for foundation course cannot be used for any curricular activity. The students must have at least 75% attendance in foundation course which will be certified by Dean of the college.

Early clinical exposure :

Early clinical exposure (ECE) is a teaching-learning methodology which fosters exposure of medical students to patients as early as the first year of medical college via classroom, hospital or community settings. The objective of ECE is to enable the first professional medical students recognize the relevance of basic science subjects in context to diagnosis and treatment of disease and patient care. It generates interest in the learner and dispels monotony.[14] Furthermore, the students learn professional behavior, ethics, communication skills and correct attitude needed for appropriate doctor-patient relationship. It will help the student correlate basic science with clinical science and understand socioeconomic and cultural factors involved in delivery of health care via the study of humanities and social sciences. ECE is a form of vertical integration between preclinical subjects and clinical subjects that helps to develop professional behavior in students.

Attitude, Ethics and Communication skills :

In recent times, there has been immense dissatisfaction of society with doctor's attitude and behavior. It is mainly due to lack of professionalism and empathy of the treating doctor towards the patient and relatives. Professional development program, hence, has been introduced in the new curriculum. It is a new teaching-learning element which includes Attitude, Ethics and Communication (AETCOM) module developed by Medical Council of India. It is a longitudinal program that begins during the foundation course (1st Professional) and runs through Internship. Herein, soft skills, behavior, communication, respect to the cadaver and ethics will be taught in the classroom just like teaching other subjects.[15]

The objective of professional development program is to understand and apply principles of bioethics, empathy and other human values to the care of patient, communicate effectively with patients, families, colleagues and health care professionals, and understand alternative systems of medicine.

A minimum of 75% attendance is required in AETCOM teaching to appear for final examination of each professional year. AETCOM module will be taught explicitly and assessed mainly in internal assessment; however, at least one question

pertaining to the cognitive domain of AETCOM will be asked in each paper of clinical specialties in the University examination whereas skill competencies of AETCOM are tested during the clinical, practical and viva voce.

Alignment and Integration :

Alignment is defined as the grouping together of related topics (under an organ system or a disease) in subjects of same phase at the same time in the time table. It allows similar topics in different subjects to be taught separately butduring the same time frame.

Integration is the organization of concepts in a topic or an organ system, that are similar or redundant, in a single teaching session. It interrelates or unifies the subjects and discards discipline-based demarcation. Integration can be either horizontal (subjects in same phase are taught together) or vertical (subjects from across phases come together),and practiced for the purpose of introduction or reinforcement of a topic. It makes the teaching-learning more interesting and meaningful.[16]

In traditional curriculum subjects were taught in isolation (silo teaching) without much effort to integrate the preclinical/ paraclinical subjects with the clinical subjects. Integration, thus, bridges the gap. It makes the learning contextual and relevant to the students. Subject-based teaching although gives a broad and deep knowledge of discipline, but interconnectedness between subjects and application of knowledge is provided by integration ensuring deep learning. Learning theory of 'constructivism' states that medical students need to understand the concepts in basic sciences and make connections with their applicability in clinical sciences.[17]Integrated teaching decompartmentalizes the disciplines facilitating a holistic approach to the problem as well as removing both fragmented learning and repetitions.

Teaching methodology :

The average attention span of students during a lecture class is around 20 minutes following which it rapidly declines. Interactive lectures have been suggested to heighten attention and promote learning. Interactive teaching actively engages students, encourages them to take responsibility for their own learning and makes the classroom environment lively.[18] In the revised curriculum, lectures are more or less replaced with interactive teaching-learning methods.[19]

Didactic lectures shall not exceed one third of the schedule while rest of the time is devoted to interactive sessions, hands-on training and problem-based discussions. The role of teacher, therefore, in CBME curriculum has shifted from 'sage on the stage' to 'guide by the side'. In Ophthalmology, the allotted 100 teaching hours are split into didactic lectures (30 hours), tutorials, small group discussions, seminars, symposia and integrated teaching (60 hours) and remaining 10 hours for self-directed learning.

Student-Doctor program :

Student-doctor method of clinical training or clinical clerkship is designed to provide immersive learning experience to medical students by allowing them to take care of patients in a supervised environment.No learner is given an independent charge of the patient. The goals of learner-doctor program are to provide MBBS students clinical exposure with longitudinal patient care, working as a part of health care team and hands on care of patients in inpatient and outpatient settings. The students are supposed to maintain a logbook and document the case record. Submission of logbook to the department is required for eligibility to appear in the final examination of the subject. The clinical clerkship will commence right in the first professional year and continue till Phase III part 2.

Electives :

Electives contribute to both professional development and personal development of medical students in specific areas of interest outside the standard curriculum.[20] It will help learners gain exposure and pursue their individual academic interests.[21] The objectives of electives in CBME curriculum are to provide diverse learning experiences and to do research or community projects in order to stimulate lateral thinking.

Two elective blocks of one month each are offered to the students of their personal interests after the completion of MBBS Phase III part 1 examination and before the commencement of Phase III part 2. Block 1 has to be completed in a pre-selected preclinical or paraclinical science while Block 2 shall be done in a clinical department. The elective choices are made available to the learners in the beginning of academic year and each institution will develop its own mechanism for allocation of electives. Minimum 75% attendance and submission of logbook maintained during electives are mandatory for eligibility to appear in final MBBS examination.

Skill training :

Teaching clinical and practical skills to undergraduate medical students is not only essential to cope up with changing educational trends (CBME curriculum) but also to reduce adverse events during practice.[22] Skill is defined as ability to perform a specialized task with defined expertise and usually denotes procedural skills; however, it also includes clinical reasoning skills, decision making, team work and communication skills.

There are certain certifiable procedural skills that are desirable for MBBS students which they have to independently perform,

observe or demonstrate on patientsunder supervision or in a skill lab on simulation. In ophthalmology, visual acuity testing, instillation of eye drops, bandaging of eye and ocular irrigation are to be independently performed by an undergraduate student whereas indirect ophthalmoscopy and epilation shall be observed being performed in patients. The method of digital tonometry has to be demonstrated to them. These skills can be acquired and assessed through experiences in patient care, diagnostic and skill lab. 'Skill lab' is an abbreviation for skill laboratory that refers to specifically equipped rooms functioning as training facilities in a fault-forgiving environment for the practice of clinical skills prior to their real life application.[23] It is compulsory for every medical college in India to have a basic skill lab for training, practice and proper acquisition and certification of skills. Students must maintain the logbook of skill-based training.

Assessment and Feedback :

Assessment is the backbone of CBME curriculum, so it has to be robust and multifaceted. The purpose of assessment is to drive learning and, hence, considered indispensable to the learning practice.[24],[25],[26] It provides information to improve instruction (formative assessment) and to measure achievement of students (summative assessment).[27] The formative assessment improves academic excellence.[28] It also has the potential to provide feedback and give direction for further development.

Regular periodic examinations shall be conducted throughout the course in the new curriculum. Student's performance has to be assessed on day-to-day basis. Learners securing 50% or more marks (combined in theory and practical/clinical and not less than 40% marks in theory and practical separately) assigned for internal assessment in a particular subject are eligible for appearing for University examination. It is mandatory to complete the required certifiable competencies for that phase of training and the logbook before sitting in University examination of that subject. Moreover, the students who have minimum 75% attendance in theory and 80% in practical/clinical are allowed to appear for the final examination.

The University examination theory question paper will include multiple choice questions (not more than 20% of total theory marks), structured essay questions and short answer questions with marks for each part indicated separately. In ophthalmology the theory paper and clinical examination will be of 100 marks each. A student who secures 50% marks separately in theory and clinical (including viva voce) will be declared pass. According to the CBME curriculum, supplementary examination for those who fail shall not be conducted later than 90 days from the date of declaration of the result of main examination. A student who passes the supplementary examination joins the main batch for progression and the one who can't would appear in the examination with the junior batch.

A rider has been added on the total number of attempts for the completion of MBBS course. No more than 4 attempts are allowed for a candidate to pass the first professional and the total period for its successful completion should not exceed 4 years. A learner shall not be entitled to graduate after 10 years of joining the MBBS course.

Logbook and Portfolio :

Logbook is a verified written recordof clinical and academic activities documenting learning experiences pertaining to knowledge, skills and AETCOM competencies. Portfolio is a longitudinal description of learning journey. It includes both the learning experience and learner's reflection. The critical self-reflection component forms the heart of portfolio and differentiates it from the logbook. Therefore, portfolio is the evidence of course and process of learning and can be used effectively as an assessment tool. In addition, it promotes reflective practices and by looking at the portfolio of a student, the teacher can assess the needs of the trainee and can provide the required help.[29] Logbook forms the integral component of formative assessment and maintaining subject wise and phase wise logbooks is compulsory in CBME curriculum for keeping track of student's progress.

Internship :

Internship is a phase of training wherein a graduate acquires skills and competencies for independent practice. Interns will be entrusted with clinical responsibility under direct supervision of faculty with a goal to fulfill their role as doctors of first contact in the community. They should not work independently. They will have 15 days posting in ophthalmology with the aim to gain knowledge and skills to enable them to diagnose and treat common ophthalmological conditions. The objective of 12-month rotating internship program is to train the medical graduate possess all competencies (namely clinician, leader, communicator, lifelong learner and professional) required of an Indian Medical Graduate('five-star doctor').

Implementation of CMBE curriculum :

Members of Academic committee and Academic cell of NMC have meticulously designed the CBME curriculum. They have also minutely planned the strategyfor its implementation. In the new curriculum, thetotal duration of MBBS course remains 4 1/2 years, divided in 3 phases, followed by 1 year of rotating internship (Fig.1). Each academic year will have at least 240 teaching days of minimum 8 hours. The 3 phases

(preclinical, paraclinical and clinical) have same subjects with slight modification. The time duration of forensic medicine is increased and the students will write its examination with Phase III part 1 subjects. Moreover, AETCOM is a new introduction that will be taught longitudinally right from the beginning i.e., foundation course to phase III part 2.

The stakeholders have framed subject wise competencies to be taught in the MBBS course and suggested their methods of teaching, integration and assessment (available on NMC website).[6] These competencies are attained gradually and longitudinally across the phases (milestones i.e., gradual acquisition of competency). AETCOM module, self-directed learning and slot for internal assessment are embedded in the time-table of teaching program of each discipline and each phase. Ideal implementation strategy includes alignment of competencies, teaching-learning methods and assessment methods.[30]

John Dewey wrote:if we teach today's students as we taught yesterday's, we rob them of tomorrow's. Faculty development program is, therefore, a prerequisite for successful implementation of CBME curriculum.[31] As a part of capacity building all qualified medical teachers must undergo training in revised Basic Course Workshop in Medical Education Technologies (MET) either at Nodal/Regional Centers of MET or in Medical Education Unit of their college. Proper implementation of curriculum is the joint responsibility of Dean, Heads of Departments and Faculty members while Curriculum Committee is the overall in-charge of curricular delivery. Alignment and Integration team will coordinate with different departments for effective conduction of integrated teaching sessions.

In short, the NMC has done a tremendous job by successfully rolling outthe competency driven MBBS curriculum. There may be few operational and logistics challenges but this new concept looks promising for creating competent IMGs who can cater to thehealth needs of the society.

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*1 month time is fixed at the end of each phase for professional examination and declaration of result

Fig. 1: Time distribution and examination schedule of CBME curriculum

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Efficient Management of Case of Double Elevator Palsy & Congenital Synkinetic Ptosis

Shweta Walia

Double elevator palsy (DEP) also called monocular elevation deficiency, is characterized by restricted elevation in abduction and adduction due to hypofunction of the superior rectus (SR) and inferior oblique muscle. There are different opinions regarding the etiology of DEP. Jampel and Fells suggested a unilateral supranuclear lesion in the pretectal area near or inside the third cranial nerve nucleus in some cases.[1] Scott and Jackson stressed the importance of concomitant restriction caused by a tight inferior rectus (IR) muscle as the cause or sequel of DEP.[2] Ziffer et al classified DEP into three subgroups of IR restriction, complete or incomplete SR paralysis and supranuclear palsy.[3]

There are different surgical methods for treatment of DEP .Dunlop believed that muscle transposition is justified only when no restriction is detected on forced duction test (FDT).[4] Knapp recommended transposition of the horizontal rectus muscles to the SR insertion.[5] Scott and Jackson found that IR restriction plays a role in some cases based on FDT findings.[6] In such cases they recommended IR weakening and release of the retractor ligament without transposition of the horizontal recti to avoid the risk of anterior segment ischemia.

Fig.1: Childhood photograph & present photograph of patient

We report a case of 13 year child who presented with Right Double Elevator Palsy with Congenital Synkinetic Ptosis who was managed with Knapps Procedure followed by levator muscle disinsertion with Frontalis sling procedure.

Case Report A 13 year old boy presented with complains of drooping of right upper eyelid since birth which was non progressive, painless and improved with jaw movement. He was born at 40 weeks of pregnancy, with normal delivery. There was no history of trauma or any systemic illness.

Ophthalmological examination revealed right eye congenital synkinetic ptosis with fair levator function (8mm by Burke's method) and 45 PD hypotropia in primary position .Elevation of right eye was restricted in both adduction and abduction indicating hypofunction of superior rectus and inferior oblique. Force duction test was negative for all muscles. Bells Phenomena was good. Pupillary examination was normal on both eyes. Visual acuity in right eye was 6/36 and left eye 6/6 on a Snellen chart. Cycloplegic refraction revealed right eye having mixed astigmatism -1.5ds /+4 DC @ 90° and was amblyopic.

Figure 2 : Ocular movements in 9 diagnostic position of gazes depicting limited elevation both in adduction and abduction

Laboratory investigations and Brain MRI of the patient were normal. Patient underwent right eye Knapp's Procedure followed by levator muscle disinsertion with frontalis sling in next step after 6 weeks . Patient was prescribed glasses along with occlusion therapy for amblyopia.

Discussion :

Double Elevator Palsy is associated with limitation of elevation of the affected eye in both adduction and abduction. DEP is one of the causes of hypotropia and can be associated with

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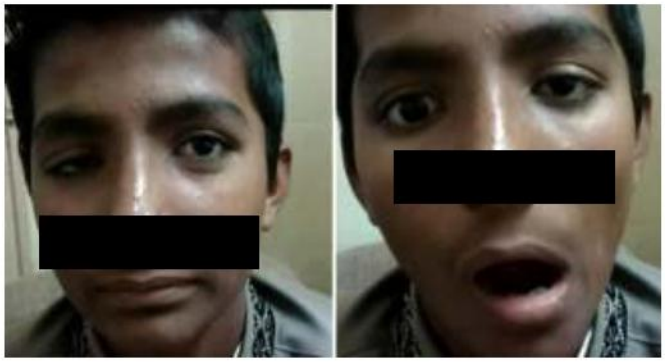

Figure 3 : Jaw Winking Phenomena - Improvement in ptosis with opening of mouth

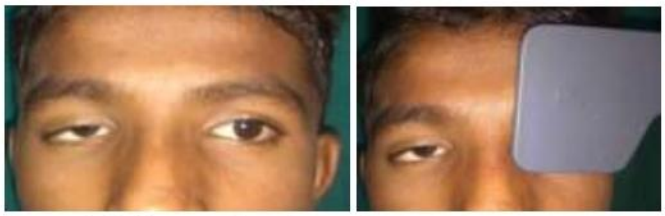

Figure 4 : Ruling out Pseudoptosis

Figure 5 : After Knapp's Procedure

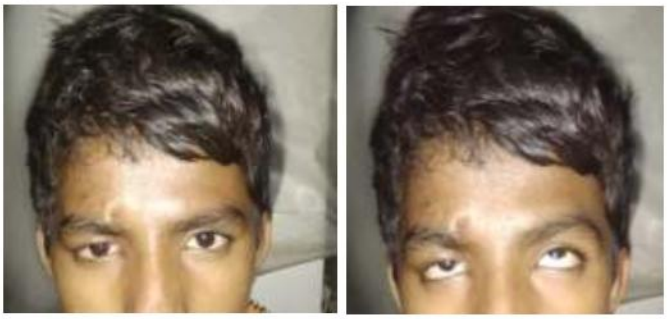

Figure 6 : After Levator muscle disinsertion and frontalis sling surgery for correction of synkinetic ptosis

ptosis/pseudoptosis. A predilection to right side involvement has been reported in DEP. [7,8] Our patient also had Right sided DEP associated with ptosis. The concomitant congenital Synkinetic ptosis and DEP represent a congenital misdirection syndrome that involves oculomotor nerve.[9] Marcus Gunn Jaw Winking (MGJW) is a nerve dysfunction syndrome that involves simultaneous retraction of the upper eyelid with the pterygoid muscles movement. It is accompanied by varying degrees of ptosis of the upper eyelid.[10] There are only few cases in the literature on MGJW synkinesis and DEP. Saemeh Nuzhat Ziffer et al. performed a study on 22 patients with DEP, nine (40.9%) of them had MGJW.[8] Ilaria Biagini et al. reported that more than half (59%) of the patients with MGJW and ptosis had amblyopia.[10] Our patient also had amblyopia which was managed by occlusion therapy.

Conclusion

MGJW & DEP can be 2 extremes of one disease spectrum ie congenital cranial dysinnervation disorders with variable severity. The management generally depends upon the amount of ptosis and the degree of jaw winking. It is a challenging task .Our case was efficiently managed in step wise manner.

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Is it Really Disc Edema ? The Answer Lies in Imaging

Dhaivat Shah

ABSTRACT :

Optic nerve head drusen (ONHD) are benign congenital anomalies of the optic nerve characterized by calcified hyaline globular bodies. They can be either buried or at the surface of the optic nerve head. They are associated with a variety of ocular and systemic diseases, such as retinitis pigmentosa, Alagille syndrome and pseudoxanthoma elasticum. It is proposed that congenitally small disc and scleral channels may cause axoplasmic flow stasis and ganglion cell axon death leading to their formation. While superficial drusen can be diagnosed easily during fundus examination via slit lamp biomicroscopy, detecting buried drusen necessitates the use of multimodal imaging modalities such as B-scan ultrasonography, optical coherence tomography, fundus fluorescein angiography and fundus auto fluorescence. Although impairment of visual acuity due to ONHD is rare, visual field and RNFL defects have been reported. Buried ONHD produce elevation of the disc and blurring of its margin, thereby mimicking optic nerve head edema. Herein we describe a case of a 19 year old myopic young male, who was diagnosed unilateral papillitis and advised treatment from elsewhere, which on multimodal imaging at our centre turned out to be buried ONHD.

INTRODUCTION :

Optic nerve head drusen are relatively benign globular calcified lesions which may occasionally mimic disc edema on routine fundoscopic examination. This report highlights the remarkable images of buried ONHD on multimodal imaging, which are not evident on slit lamp biomicroscopic fundus examination or conventional colour fundus photography.

Keywords : Optic nerve head drusen; multimodal imaging.

CASE REPORT :

A 19 year old male presented to us with complain of floaters in right eye since 1 month. The patient had consulted a local hospital, where he was diagnosed as unilateral (right eye) papillitis and was advised intravenous steroid pulse dose therapy. The patient was here to seek a second opinion. There was history of wearing glasses for distance since 10 years, and trauma to right eye before 2 years while playing football, which was treated in the sports centre clinic there. The BCVA is right and left eye were 6/9 N6 and 6/6 N6. The IOP were 16 and 14mm Hg. The colour vision and contrast sensitivity were within normal limits. Anterior segment examination was unremarkable. On dilated fundus examination, the right eye disc margins appeared blurry, but the vessels were clearly visible, and there were no surface micro vascular abnormalities noticed (Fig 1a). Left eye disc appeared normal. The right eye showed few vitreous floaters, and the foveal reflex in both eyes was normal. Multimodal imaging was advised henceforth.

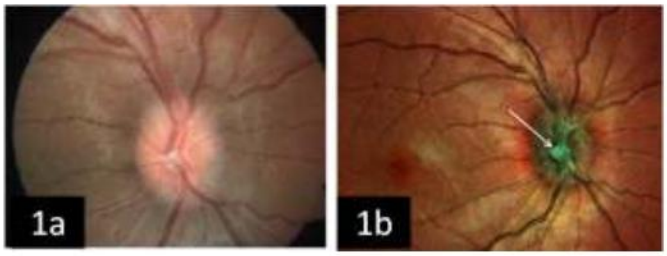

Figure 1 : Fig. 1a is the dilated disc photo of the right eye showing blurry disc margins; and no evident surface micro vascular abnormalities. Fig. 1b is the multicolour composite image of the right eye disc revealing a greenish hue at the area from the centre to the infero-temporal edge of the disc (white arrow).

The multicolour composite image revealed a greenish hue at the area from the centre to the infero-temporal edge of the disc (Fig 1b, white arrow). The right eye Humphrey's visual field 24-2 showed enlargement of blind spot, while the left eye was normal (Fig 2). The red free fundus photograph and

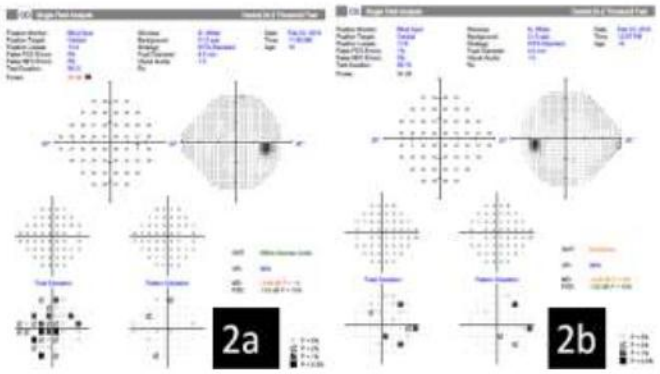

Figure 2 : Fig. 2a shows right eye Humphrey's visual field 24-2 showing enlargement of blind spot, while the left eye Fig. 2b shows a normal visual field.

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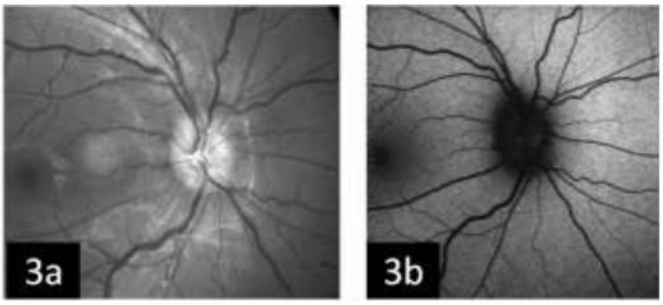

Figure 3 : Fig. 3a shows the red free fundus photograph and Fig. 3b shows Fundus Auto Fluorescence (FAF) revealing no Specific abnormalities.

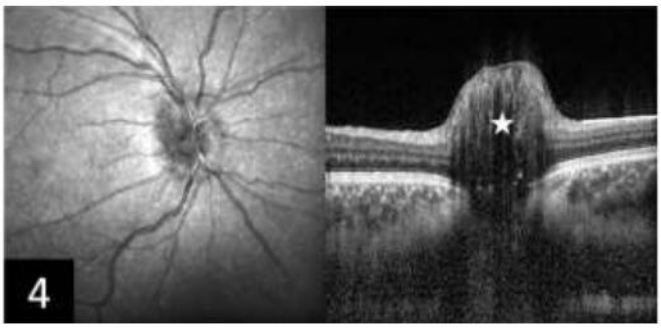

Figure 4 : Fig. 4 shows the OCT line scan through the centre of optic disc showed a hyper reflective elevation with a lumpy internal contour and a hypo reflective internal lumen (white star).

Fundus Auto Fluorescence (FAF) showed no specific evidence (Fig 3). The OCT line scan through the centre of optic disc showed a hyper reflective elevation with a lumpy internal contour and a hypo reflective internal lumen (Fig 4, white star). The B scan ultrasonography (USG) revealed an area of hyper reflective echo at the ONH, which showed a corresponding spike on the A scan, and persisted even on low gain (Fig 5, white arrow). On the basis of all these investigation modalities, a diagnosis of ONH Drusen (ONHD) was made, and the patient was reassured regarding the benign nature of this condition.

DISCUSSION :

ONHD are congenital anomalies of the optic nerve characterized by calcified hyaline bodies.[1] They are either buried or at the surface of the optic disc.[2] Although the mechanism of drusen formation has not been fully determined, it is believed that congenitally small disc and scleral channels may cause axoplasmic flow stasis and ganglion cell axon death.[3] They can be associated with a variety of ocular and systemic diseases, such as retinitis pigmentosa, Alagille syndrome, and pseudoxanthoma elasticum, or occur as an isolated entity.[4] They are rarely associated with visual field loss defects and RNFL thinning.[1] While superficial drusen can be diagnosed easily during

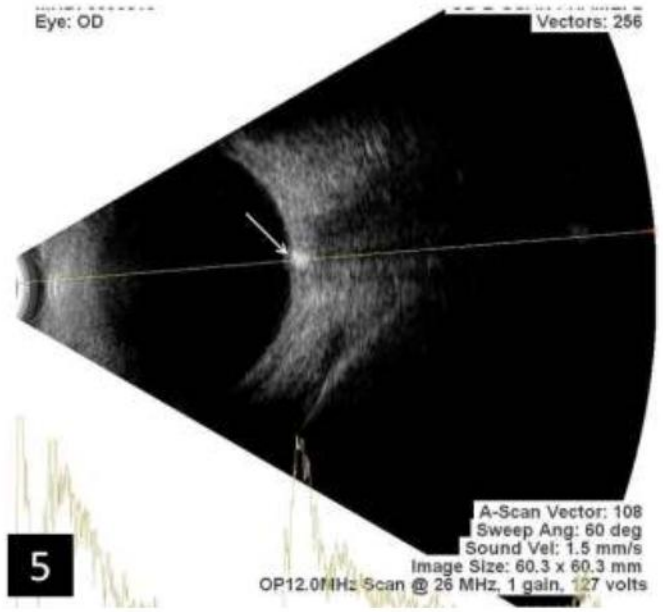

Figure 5 : Fig. 5 shows the B scan ultrasonography (USG) revealing an area of hyper reflective echo at the ONH, which showed a corresponding spike on the A scan and persisted even on low gain (white arrow).

fundus examination, detecting buried drusen requires the use of additional multimodal imaging techniques. Methods for detecting and imaging disc drusen include FAF, USG, OCT and HVF 24-2.

The SPECTRALIS MultiColor Module is a newer imaging modality which utilizes confocal scanning laser technology with light of discrete wavelengths instead of standard optics and white light to visualize the retina. MultiColor is able to achieve such sensitivity and specificity due to its confocal scanning laser imaging technology, which uses three laser wavelengths (blue, green and infrared) simultaneously to provide diagnostic images that show distinct structures at different depths within the retina. As a result, the high-resolution MultiColor images can be used to detect and delineate structures and pathologies not visible on ophthalmoscopy and fundus photography.[5] The buried drusen, which is not seen on conventional colour fundus photography, is evident as an area of greenish hue in multicolour image.

Although FAF is a convenient method of visualizing more superficial drusen, it is insufficient for detecting buried drusen. Deeply buried drusen do not appear on FAF because the overlying tissue prevents autofluorescence.

The electron microscopic contents of ONHD show aggregates of mitochondria that seemingly function as a nidus for overlying calcification embedded in a fibrillary protein matrix, which would have a higher superficial reflectivity in OCT scan images, as was noted in our case.[6] The RNFL was noted to be

within normal limits.

B Scan USG is an imperative tool for diagnosis of ONHD. The degree of hyper reflectivity and acoustic shadowing is proportional to the size of the echogenic focus.[7] The scan revealed an area of hyper reflective echo at the ONH, which showed a corresponding spike on the A scan, persisting on low gain.

This report highlights the remarkable images of buried ONHD on multimodal imaging, which are not evident on conventional colour fundus photography. It also helps the clinician to rule out conditions mimicking ONHD, which can be routinely misdiagnosed and mistreated with routine fundus examination techniques.

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