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Do we need to start Microinvasive glaucoma surgery (MIGS) in Bangladesh?

M N Islam[1]

In this issue of the JBGS a review article has been published on Micro Invasive Glaucoma Surgery (MIGS) by Dr. Mohammed Arifur Rahman. It is true that Glaucoma surgery has been a paradigm shift in the developed world but in the developing country including Bangladesh we could not start the procedures.

The reason behind is nonavailability of these devices and most important its cost. Though some of our Bangladeshi doctor has some kind of training on the MIGS procedure none can start it in practice. We believe we should not be behind the current glaucoma surgery procedures and I am trying to to highlight more on this issue.

Even in USA, several shifts in practice patterns have emerged as thesurgical management of glaucoma . Fornixbasedconjunctival flaps with diffuse application of lowerdoses of mitomycin C (MMC), pre operative low conc. MMC are commonly employed andassociated with more favorable bleb morphology and lowerrates of late bleb-related complications.Although trabeculectomyremains the most frequently performed glaucoma surgery around the world , glaucoma drainage

device (GDD) use has increased.Many new minimallyinvasive or microinvasive glaucoma surgeries (MIGS) haverecently been introduced into clinical practice.

We know that gaucoma is a leading cause of vision loss throughout the world, andintraocular pressure (IOP) is the single proven modifiablerisk factor for the development and progression ofglaucoma.In early stages of the disease, ocular hypotensivedrugs have traditionally been considered the firstlinetreatment. However, due to issues related to tolerabilityand/or drug administration, pharmacotherapy can bechallenging for glaucoma patients and result in poor compliance.

In addition, traditional incisional glaucomasurgeries (trabeculectomy, tube shunts, etc.) carry significant complication and risks. Thus, microinvasive glaucoma surgery(MIGS) procedures have emerged as a low-risk option forglaucoma management and are altering the glaucoma surgicalprofile.Earlier intervention with a safe and effectivesurgical procedure could reduce patients' medication burdenand enhance their quality of life.

The MIGS procedures are performed ab interno andmicroincisional through the clear cornea free of conjunctival incisions. The procedures are minimally traumatic and veryadaptable.The iStent (Glaukos Corp., Laguna Hills, CA),the first US Food and Drug Administration-approved abinterno MIGS device, is a device designed to serve as a

bypass through the trabecular meshwork to improvephysiological aqueous outflow and lower IOP. The Lshapedstent is 1.0mm in length and 0.33mm in height andis the smallest medical device ever approved by the USFood and Drug Administration. The iStent, typicallymplanted concurrently with cataract surgery, is implantedthrough the trabecular meshwork, and into Schlemm canalwith the assistance of a surgical gonioscope.

Cataract surgery alone has been demonstrated toproduce a reduction in IOP.Consequently, it remains asafe and effective treatment option for those in the earlystages of the disease, but may not lower pressure adequately.Prior work has demonstrated iStent implantationin conjunction with cataract surgery to be significantlymore effective than cataract surgery alone in reducing IOPlevels and use of glaucoma medications.So, glaucoma surgical therapy has entereda new and exciting era with the introduction of micro invasive glaucoma surgeries (MIGS) that offer clinically meaningful lowering of IOP with far fewer complications than existing alternatives of trabeculectomy or aqueous shunts

To date in the USA, only the Trabectome has FDA approval as either a stand alone procedure or combined with cataract extraction for treatment of pediatric and adult POAG. Glaukos' iStent also has FDA approval limited to combination surgery with adult cataract procedures. Besides these two, other devices are in the pipeline in the MIGS category including the

- Kahook Dual Blade (KDB) designed to remove a strip of meshwork
- CyPass designed to shunt aqueous into the suprachoroidal space – Recently withdrawn from world marketbased on an analysis of five-year post-surgery data from the COMPASS-XT long-term safety study – experienced statistically significant endothelial cell loss compared to the group who underwent cataract surgery alone
- Hydrus by Ivantis a trans trabecular shunt.
- Gonioscopy-assisted Transluminal Trabeculotomy (GATT):Circumferential 360-degree suture trabeculotomy is a well-established surgical technique for the treatment of primary and secondary open-angle glaucomas
- The XEN gel stent (Allergan, Dublin, Ireland) is a recently developed,permanent, ab interno collagen implant that reduces IOP bydraining aqueous fluid from the anterior chamber into the subconjunctivalspace. The stent is a hydrophilic tube that is 6-mm long, andit is composed of porcine gelatin crosslinked with glutaraldehyde. The stent comes in three sizes, and 140 m, all possessingdifferent inner diameters. The XEN45 gel stent is CE-marked in the EuropeanUnion, and it is indicated for the treatment of refractory glaucomathat has proven resistant to previous surgical treatment andfor patients with primary open angle glaucoma (POAG), pseudoexfoliative glaucoma, or pigmentary glaucoma that cannot be controlledwith maximum tolerated medical therapy. It is also licensedfor use in Canada, Switzerland, and Turkey.

Although all these devices can achieve clinically desirable IOP lowering with far fewer risks than trabeculectomy or tube shunts, none has yet completed gold standard randomized clinical trials including the comparison of one to another.

General advantages of these MIGS procedures compared with traditional filtering surgery and aqueous shunts include simpler safer surgeries, no bleb development, less anaesthesia, no requirement for antifibrotic medication and less lengthy and complex follow up than traditional glaucoma surgeries and we expect to start these novel devices in the glaucoma treatment in the people of our country and in the developing world too.

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Original Article

Efficacy and Safety of Tacrolimus 0.03% Ointment to Treat Moderate to Severe Vernal Keratoconjunctivitisin Patients with Steroid Induced Glaucoma

U Kawser[1], N Kamal[2], S Rahman[3]

Purpose : To determine efficacy and safety of Tacrolimus 0.03% ointment in the treatment of moderate to severe Vernal Keratoconjuctivitis (VKC) in patients with Open-Angle Glaucoma those who respond well to steroid.

Material and Methods : A prospective clinical trial was conducted at the Department of Ophthalmology, MH Samorita Medical College, Dhaka; Department of Ophthalmology, Ad-Din Sakina Medical College, Jashore and Glaucoma and Cornea Department of Vision Eye Hospital Dhaka from February 2017 – January 2018. In this regard, 32 consecutive cases (64 eyes) with moderate to severe VKC. There were 10 newly diagnosed cases and 22 recurrent. After discontinuing their previous medications, they were treated with Tacrolimus ointment, 0.03% applied into the lower conjunctival fornix twice a day along with lubricants for a period of 4 – 8 months. Clinical signs and symptoms were recorded at the beginning of the treatment and at all follow-ups which were conducted weekly for one month and then every month for one year.

Results : The duration of therapy was 4 – 8 months (mean 6 months). The patients were followed-up for a mean duration 10 ± 1.5 months. There was marked subjective as well as objective improvement in all cases within one month of therapy. There was no need for any additional therapy. No toxic effects of Tacrolimus were observed in any case. There was no evidence of elevated IOP beyond normal range in any cases.

Conclusion : It can be concluded that Tacrolimus ointment (0.03%) is an effective therapy to treat moderate to severe cases of vernal keratoconjuctivitis. It acts as a safe alternative to topical steroids in case of patients with steroid induced glaucoma.

Key words : Tacrolimus, Vernal Keratoconjunctivitis (VKC), Allergy, Steroid Induced Glaucoma.

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Introduction

Vernal keratoconjunctivitis (VKC)is an acute -chronic inflammatory disease of the conjunctiva and cornea,[1,2]. The patients are visually handicapped because of severe burning and itching along with lacrimation, stringy mucoid discharge, photophobia and heaviness of eyelids due to involvement of the tarsal conjunctiva. The symptoms are more noticeablein a warm, humid environment like Bangladesh. Mild cases of VKC show improvement with non-specific, supportive therapy. But severe cases show frequent remissions and relapses, run a protracted course, and if not treated properly, usually result in sight–threatening complications[3] over a period of time.

Treatment of vernal keratoconjunctivitis (VKC) is complicated because typical mast-cell stabilizersor anti-histamines are not as effective as it should be. Steroid can be an option to choose. But in case of patients with open-angle glaucoma steroid is a matter of concern. Elevated IOP is one the major drawbacks of steroid.

VKC starts as a Type I (immediate) hypersensitivity reaction[4] (histamine mediated). This occurs when a sensitized individual comes into contact with a specific antigen resulting in degranulation of mast cells in the conjunctiva and the release of histamine. Histamine binds with its receptor and causes watery, red eyes with intense itching in children; later there is super-imposed involvement of T lymphocytes[2,4] which results in chronicity of the disease, corneal and tarsal conjunctival signs. There is involvement of both eyes which may be asymmetrical. The disease is notorious for recurrence when the treatment is stopped. It needs to be differentiated from Seasonal Allergic Conjunctivitis which is an acute Type 1 hypersensitivity reaction and involves only the conjunctiva. In comparison to VKC, it shows marked

chemosis, conjunctival injection and eyelid edema due to the release of histamine from conjunctival mast cells resulting in increased vascular permeability. Patients with VKC exhibit large amounts of circulating Immunoglobulin E (IgE); the cross-linking of 2 adjacent IgE molecules by the antigen triggers mast cell degranulation. This releases various preformed mediators of the inflammatory cascade like histamine, prostaglandins, leukotrienes, tryptase, chymase, heparin and chondroitin sulfate. These mediators cause increase vascular permeability with migration of eosinophils, polymorphs, T and B lymphocytes and proliferation of fibroblasts which lay down of exuberant amounts of collagen in conjunctival tissue. Hence the ocular tissues exhibit the following changes:

Conjunctiva shows cellular infiltration with hyperplasia of epithelium and dilatation of conjunctival vessels along with increased permeability. The upper Tarsus is typically affected by the proliferation of fibrous layer of conjunctiva and its hyalinization resulting in the formation of giant papilla, more than 0.3 mm in diameter, giving the classic 'cobble – stone' appearance. In severe cases, these papillae may hypertrophy producing cauliflower-like excrescences (giant papillae) which may produce mechanical ptosis. These giant papillae are randomly distributed over the whole tarsus while those resulting from wearing of hard contact lenses are present only at the edge of the tarsus.

The limbal involvement comprises ofpapillae which are thick, gelatinous along with multiple white spots which are collections of degenerated epithelial cells and eosinophils called Horner – Trantas dots. They do not last longer than a week from their initial presentation as they undergo rapid dissolution.

The corneal involvement is variable. It may show Punctate Epithelial Keratopathy (PEK) due to toxic effect of inflammatory mediators released from the conjunctiva. These fine punctate erosions coalesce, resulting in larger erosions or a shield ulcer, which is typically shallow with white irregular epithelial borders. The giant tarsal papillae are a major contributing factor in its development by causing chronic mechanical irritation. Vernal pseudogerontoxon, a degenerative lesion in the peripheral cornea resembling corneal arcus, may be seen. Keratoconusis a frequent complication in chronic cases, due to chronic eye rubbing and superimposed corneal thinning by injudicious use of topical steroids. Corneal vascularizuation or pannus formation may also be seen.

In the acute but milder form of VKC, topical antihistamines, mast cell stabilizers, mucolytics, NSAID and lubricants are used as the first line of therapy. However, in the severe and chronic disease, corticosteroids [5] have to be added and they have to be used for a long term to control the symptoms; corticosteroid withdrawal leads to clinical worsening while their long term use is associated with side-effects like cataract, glaucoma, corneal thinning, corneal ectasia / keratoconus. Hence a marked ocular morbidity results from the prolonged use of steroids topically.

Immuno-modulators have been introduced for the past two decades into the armamentarium of drugs for the management of VKC[6]. They are mainly used as steroid – sparing drugs. Tacrolimus[7,8] is one such immunomodulating drug, the other being Cyclosporine eye drops. Tacrolimus is known to be 10–100 times more potent than Cyclosporine. It is a macrolide, discovered in 1984 from the bacteria streptomyces tsukubaensis. It is very affective in suppressing the activation and proliferation of B & T lymphocytes and formation of inflammatory mediators like cytokines, especially interleukin$_2$.

At first Tacrolimus was used as an immuno-suppressant in liver transplants and subsequently in other solid – organ transplants. For more than 10 years it has been used in the treatment of skin disorders such as vitiligo and atopic dermatitis etc. It is available as a skin cream 0.03% and 0.1% for the treatment of moderate to severe atopic dermatitis (eczema), vitiligo. It suppresses inflammation as affectively as topical steroids, with the major advantage for not causing skin thinning (atrophy) and other steroid related side-effects. On initial applications, it can produce mild burning or itching sensation, with increased sensitivity to sunlight and heat, no other side effects have been reported. Patients should minimize or avoid exposure to natural or artificial light. There may be an increased risk of

activation of skin infections which should be cleared up prior to its application.

According to numerous clinical studies[9-12], Tacrolimus has been successfully used in the treatment of autoimmune diseases of the ocular surface such as dry eyes, mooren's ulcer, scleritis, cicatricial conjunctivitis atopic and VKC. Its ophthalmic preparation is not available in Bangladesh so we conducted this study to find out the efficacy and safety of Tacrolimus ointment 0.03% applied in the lower conjunctival fornix in treating moderate to severe VKC in patients with open-angle glaucoma (steroid responder).

Material And Methods

A prospective clinical trial was conducted at the Department of Ophthalmology, MH Samorita Medical College, Dhaka; Department of Ophthalmology, Ad-Din Sakina Medical College, Jashore and Glaucoma and Cornea Department of Vision Eye Hospital Dhaka, from February 2017 – January 2018. 32 consecutive cases with moderate to severe VKC (64 eyes). The male to female ratio was 2:1. There were 10 newly diagnosed cases and 22 recurrent, being refractory to their previous therapy consisting of topical antihistamines, mast cell stabilizers and steroids. The study inclusion criteria was moderate to severe cases of VKC presenting with the symptoms of chronic, recurrent, bilateral red eyes with itching, redness, watering and mucus discharge with papillae found on the upper tarsal conjunctiva, along with limbal changes those who shows dissatisfactory response to mast cell stabilizer but well response to steroid (this steroid response can causeocular hypertension specially in patients with open angle glaucoma). Study exclusion criteria were cases of seasonal allergic conjunctivitis (histamine mediated) and mild VKC with only palpebral conjunctivitis; patients who had received systemic or sub-conjunctival corticosteroids, due to previous therapy, developmental cataract or any systemic illness.

Before starting the trial, all patients were given a questionnaire to grade the severity of their symptoms of itching, redness, watering, mucus discharge, photophobia and a foreign body sensation (Table 1), as 0 (none), 1 for mild (occasional symptoms), 2 for moderate (frequent symptoms), and 3 for severe (constant symptoms). They all underwent a thorough ophthalmic examination including the measurement of Best Spectacle-Corrected Visual Acuity (BSCVA), slit-lamp biomicroscopy, conjunctival/corneal fluorescein staining and applanation tonometry. The clinical signs like conjunctival injection, limbitis, papillary hypertrophy or giant papillae, punctate corneal erosions, corneal pannus formation were graded (Table 2 and 3) as 0 (none), 1 (mild), 2 (moderate), 3 (severe). The patients and / or their parents were fully explained the advantages and disadvantages of the treatment and a verbal consent was obtained.

After discontinuing the previous medications in recurrent cases, all were treated with Tacrolimus ointment, 0.03% applied into the lower conjunctival fornix twice a day along with lubricants (AquafreshLiquigel 4times/ day and Lacrilube eye ointment at night) for a period of 4 - 8 months (mean of 6 months). Efficacy of treatment was evaluated subjectively by assessing patient's symptoms and objectively by noting an improvement in the clinical signs. The need for any additional therapy was noted. Any side effects of the treatment particularly ocular discomfort werespecifically asked and possible complications such as intraocular pressure, lens opacification, secondary bacterial infections were noted. All these findings were recorded at the beginning of the treatment and at all follow-ups conducted weekly for the first month and then after every month, for 1 year. Any recurrence of symptoms and / or signs after stopping all therapy was also noted during the follow-up period.

Results

In all 32cases (64 eyes) included in the study, the commonest presenting symptom was itching and watering of eyes in addition to other symptoms shown in Table1. Papillary hypertrophy was noted in all cases while giant papillae were found only in 14 recurrent cases (moderate = 10 eyes and severe = 18 eyes), Table 2. Limbitis was found in all cases (mild = 8,moderate = 22, severe = 34 eyes), corneal involvement in the form of punctate erosions was seen in all cases (mild = 6, moderate = 34, severe = 24 eyes), corneal pannus in 26 cases (52eyes) and shield ulcer, unilateral,in 4 cases.

Table 1: Grading of symptoms of VKC patients before and after 1 month's therapy with 0.03% Tacrolimus Ointment

Symptoms	Grade Prior to Rx				Grade after 1 Month Rx				Improvement %
	0	1	2	3	0	1	2	3	
Itching	0	-	n=12	n=52			-	-	100.00
Redness	-	-	n=24	n=40	58	6	-	-	90.62
Watering	-	-	n=34	n=30	64	-	-	-	100.00
Photophobia	-	-	n=28	n=36	60	4	-	-	93.75
Grittiness	-	n= 36	n= 22	n= 6	62	2	-	-	96.87
Discharge	-	n= 18	n= 46	-	64	-	-	-	100.00

Grade 0= None, 1=Mild, 2= Moderate, 3=Severe

Table 2: Grading of clinical signs of VKC patients prior to therapy and after 1 month's therapy with 0.03% Tacrolimus Ointment

Signs	Score	Definition
Conjunctivitis	3	Impossible to distinguish individual blood vessels
	2	Dilatation of many vessels
	1	Dilatation of several vessels
	0	None
Limbitis	3	7 or more limbal papillae
	2	4 - 6 limbal papillae
	1	1 - 3 limbal papillae
	0	none
SPK	3	Diffusely scattered on whole cornea
	2	Half of cornea spared
	1	Only a few punctae erosions
	0	None
Giant papillae (Size 1 mm)	3	Elevated papillae in ½ or more of the upper palpebral conjunctiva
	2	Elevated papillae in ½ of the upper palpebral conjunctiva

Grade 0= None, 1=Mild, 2= Moderate, 3=Severe

Table 3 : Grading scales for objective clinical signs

Signs	Grade Prior to Rx				Grade after 1 Month Rx				Improvement %
	0	1	2	3	0	1	2	3	
Conj. injection	-	-	n=16	n=48	58	6	-	-	90.62
PEK	-	n=6	n=34	n=24	64	-	-	-	100
Limbitis	-	n= 8	n= 22	n= 34	64	-	-	-	100
Corneal Pannus	-	-	n=52	-	64	-	-	-	100
GPC	-	-	n=10	n=18	64	-	-	-	100
Shield Ulcer	-	-	n=4	-	64	-	-	-	100

After starting 0.03% Tacrolimus ointment, the patients were followed up for 8 - 12 months (mean duration 10 ± 1.5 months). All symptoms significantly improved after treatment though itching was the first to be relieved. Percentage improvement of symptoms after treatment has been shown in Table 1. By 1 month after treatment, the residual symptoms only included mild redness in 6 eyes (90.62% improvement), mild photosensitivity in 4 eyes and mild foreign body sensation in 2 eyes which disappeared after a further one month's therapy. The patients remained mostly symptom-free during the remaining period of therapy. However, when Tacrolimus was stopped after 2 - 3 months of continuous use, almost all of them had a recurrence of the disease though in a milder form. Hence it was continued for a further 2 months and then tapered gradually over another one month. After stopping all treatment, 6 cases developed mild recurrence after 3 - 4 months during the follow-up period which was of mild severity and was managed with anti-histamine eye drops only. While during treatment with Tacrolimus, none of the cases needed additional medications like topical steroids, anti-histamines or mast-cell stabilizers, for symptomatic relief.

Marked improvement was noted objectively, Table 2; conjunctival injection was the first sign to show improvement in all cases within two weeks of therapy. In addition, conjunctival papillary hyper-trophy showed improvement in all eyes. All 14 cases (28 eyes) with moderate to severe giant papillae, all showed reduction in size of the papillae as early as 2 weeks of therapy which flattened by1 month and disappeared by the end of 4 months of therapy. There was improvement in limbitis (limbal papillary hypertrophy) in all 32 cases (64 eyes), corneal punctate epithelial erosions in 64eyes (mild = 6 moderate = 34, severe = 24 eyes), and corneal pannus in 52 eyes after one month treatment which cleared fully after 2 months of therapy. All cases (4 eyes) with a shield ulcer healed after two months therapy. All cases showed improvement in visual acuity by two Snellen's lines.

Only two cases complained of mild discomfort on instillation of the cream; the remaining 30 cases did not complain of any discomfort or burning sensation when asked specifically. Intraocular pressure (IOP) remained normal in all cases and no other ocular complication related to Tacrolimus ointment was seen in any case. No patient had to discontinue the medication due to any adverse effect.

Discussion

Since VKC is an immune – mediated disease with marked ocular morbidity, the use of an immuno-modulating drug to control the debilitating symptoms of itching and watering in children becomes necessary in moderate to severe cases. The disease is known for its recurrence when therapy is stopped, hence the medications have to be used on a long – term basis. Topical steroids have been the preferred choice to – date to control symptoms in such cases, but their prolonged use results in vision-threatening complications like glaucoma, cataracts, corneal thinning and ectasia. Hence Tacrolimus has emerged as a very safe and effective steroid-sparing option which inhibits all immune reactions responsible for the pathogenesis of VKC.[9-12] Though an ophthalmic preparation is not available in Bangladesh; this study confirms that Tacrolimus ointment (0.03%) in such a mild concentration is a safe and effective therapeutic alternative to topical steroids for moderate to severe VKC in patients with open-angle glaucoma.

We opted for Tacrolimus after its effectiveness in VKC has been demonstrated in other studies. Tacrolimus 0.1% 'skin' cream applied to the skin of lower eyelid in previous studies[13,14] had effectively controlled VKC. Sengoku et al[15] used 0.01 – 1% eye drops in an animal study for ocular allergy while Ohashi et al[16] used an 0.1% ophthalmic suspension in another clinical study.

This study shows that not only there was an effective control of patient's symptoms in all cases (Table 1) but a subjective improvement was also noted soon after starting the treatment (Table 2). Conjunctival injection was the first sign to show improvement within 2 weeks of therapy while conjunctival papillary hypertrophy also improved in all eyes within one month of therapy. A similar improvement was noted in giant papillae which started regressing after one month of therapy and disappeared after 4 months in all case. Corneal signs like punctate epithelial erosions, pannus, and to some degrees, the opacities in corneal stromal showed improvement. Similar results have been shown in a study by Ohashi et al[16] Kymionis et al[17] who used an ophthalmic preparation.

4 cases in our series had a shield ulcer which also resolved after treatment with Tacrolimus and lubricants as has been reported previously[18]. However, the 2 cases which did not show improvement in VA had keratoconus which was confirmed by an Orbscan (due to constant rubbing of eyes and a thinned cornea due to previous use of

topical steroids).

In our study, an attempt to discontinue Tacrolimus after 2 – 3 months of continuous use resulted in recurrence of a milder form of VKC hence they were asked to use it for at least 4 – 5 months and then gradually taper it over a further one month. In other studies, topical Tacrolimus has been stopped after 4 weeks in VKC and no recurrence was documented.[15,16] In a study by Miyazaki et al,18 topical Tacrolimus was continued for 7 months while in another study, in patients with AKC,1[3,18] it was used for up to 42 months and no side effects were reported. In our study, none of our cases needed additional medications like anti-histamines or mast cell stabilizers. Since its long-term use has been shown to be safe, it can be used as a prophylactic drug in less severe disease as well to prevent its aggravation during the hot, humid season of the year.

Upon initial application of Tacrolimus, a local burning sensation has been reported,1[6-18] it was seen in only 4cases in our study and it disappeared after one week of therapy. During the follow-up period of 8 – 12 months (mean duration 10 ± 1.5 months), none of the cases developed any other side effects. However, because of its local immunosuppressive effect, it may result in activation of viral infections. Hence we excluded patients from our study who gave a history of previous herpes infection.

Conclusion

The use of Tacrolimus eye drops / ointment in the treatment of VKC has been a topic of extensive research. Consistent with previous reports, we found out that Tacrolimus ointment 0.03% used twice daily in the lower conjunctival fornix shows marked improvement in VKC in patients with open-angle glaucoma; all patients had an effective relief of their symptoms within one month of therapy. Since the nature of the disease requires long term usage, it was safe and easy to taper off the dosage and eventually stop it after 6 months with no adverse effects.There was no need to add additional medications like antihistamines or steroids in any case during the study. It seems Tacrolimus 0.03% will bea new dimension in the treatment approach of VKC in patients with steroid induced glaucoma (steroid responder).

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Correlation of Central Corneal Thickness (CCT) with Intra Ocular Pressure (IOP) in Ocular Hypertension (OHT), POAG and Normal Tension Glaucoma (NTG) among Bangladeshi Population

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Abstract

Objective : To evaluate the correlation between CCT and IOP.

Type of Study : Prospective, controlled, observational.

Methods : This observational non-interventional study included 100 people who attended at indoor and out-patient department of CMH Dhaka and NIO in the period of June 2014 to July 2015. Primary Open Angle Glaucoma (POAG), Ocular Hypertensive (OHT) and Normal Tension Glaucoma (NTG) were included in this study.

Results and Conclusion : The study was conducted on 100 cases including 60 males and 40 female subjects with mean age of 53±15 (range 19-80) years. Mean age in male and female subjects were 50±19 and 51±17 years respectively (P=0.184). Mean CCT was 540 ±15 μm overall, and 539 ±16 μm and 541 ±13 μm in male and female subjects respectively (P=0.11). In this study either eye of the subject is considered. Study shows a moderate positive correlation between IOP and CCT (Pearson correlation coefficient r= 0.50). IOP measurement in different groups are, control 15±2 SD mm Hg, POAG 23±3 mm Hg, OHT 25±2 mm Hg, NTG 18±2 mm Hg. CCT in normal population-539 ±11 m, POAG- 538 ±8 m, OHT-560±20 m, NTG-531±11 m. The study confirms that CCT can be a confounding factor while recording IOP. A patient may be labeled as ocular hypertensive just because of the error in measuring his applanation IOP, leading to unnecessary prolonged treatment and/ or follow up. The CCT measurement would go a long way in helping us make a clinically relevant decision.

Key Words : CCT, IOP, POAG, OHT, NTG.

Introduction

Glaucoma is the leading cause of irreversible blindness.[1] Glaucoma blindness affects over 6.7 million people, ranking only second to cataract (19.3 million) as a cause of blindness worldwide.[2] Unless detected at an early stage the prognosis for sight will be poor.[10] Once detected, effective delivery of care still presents dilemmas that are specific to the individuals and their social environment.

A population based study found 30% of adult blindness was attributable to cataract, while glaucoma accounted for 12%.[11] Report published in British Journal of Ophthalmology in Dec 2000 Prevalence of glaucoma in Bangladesh above 35 years = 3.1%

Prevalence of glaucoma suspect in Bangladesh above 35 years = 10%

Awareness about glaucoma amongst population= 4%

Early diagnosis and initiation of treatment are important factors in minimizing the progression of disease and reducing its burden. Intraocular pressure is an important risk factor for glaucoma and the only one that can be manipulated to alter the course of the disease. It is therefore important that it is measured accurately. Direct manometric measurement of IOP is possible but not practical; for clinical use we have to rely on indirect measurements. Goldmann applanation tonometry (GAT) has become the international "gold standard" for IOP measurements.

Thin central corneal thickness (CCT) has been shown to be a powerful risk factor for the progression of ocular hypertension (OHT) and preperimetric glaucoma to primary open-angle glaucoma (POAG). It varies amongst racial subpopulations, with thinner CCT found in African-American groups and is associated with more severe glaucoma progression. Patients with a CCT of less than 555µm in the ocular hypertension treatment study (OHTS) had a 3-fold increase in the risk of glaucoma development compared with those having CCT of less than 588µm. CCT is positively related to IOP with thinner corneas requiring less force than expected to achieve applanation by Goldmann applanation tonometry

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(GAT). [12]The effect of central corneal thickness (CCT) on IOP readings using GAT has become a topic of much interest. [3-9]A thick cornea would overestimate IOP and a thin one would underestimate it.[5]

Rationale of the Study

In recent clinical practice glaucoma patients are increasing. There is a strong correlation of CCT with IOP. CCT is seldom measured in routine case. Knowledge of CCT can help to attribute the likelihood of disease progression and assigning the risk can change clinical management decisions to reach a personalized target pressure.

Research Question

What is the correlation between IOP and CCT in POAG, OHT and NTG?

Objectives of the study

General objective

To evaluate the correlation between CCT and IOP.

Specific objectives

To assess CCT and IOP of POAG,OHT and NTG.

To compare with control groups.

To search for consistent findings to recognize the relationship between CCT and IOP.

Materials and Methods

Study design

Prospective, controlled, observational.

Place of study

Combined Military Hospital Dhaka and National Institute of Ophthalmology (NIO).

Study period

June2014 to July 2015

Sampling and Sample size

This observational non-interventional experiment studied of 100 people who attended at indoors and out-patient department in CMH Dhaka and NIO.

Selection criteria

1) Inclusion criteria

Either sex

Either eye

POAG, OHT &NTG.

2) Exclusion criteria

Extreme of age group.

Persons having corneal pathology.

Evidence of other anterior segment pathology including corneal opacities / oedema.

Previous intraocular or corneal surgery.

Diabetes mellitus

Use of contact lens

Secondary Glaucoma

Ethical measures

Informed written consent was taken from all study subjects after full explanation of the nature, purpose and potential risk of all procedures needed for the study. The tenets of the declaration of Helsinki were observed

Instrumentation and procedure

After determination of the best corrected visual acuity, a complete ocular examination was performed. As a normal procedure in clinic IOP was measured using the GAT with topical anaesthesia and fluorescein. The CCT measurements were recorded from a seated patient using a hand held ultrasonic pachymeter probe (Reichert IOPac Handheld Pachymeter Standard 16010 USA) gently placed in the mid-pupillary axis of the cornea in the undilated eye. The IOPac gives a mean value of CCT taken from 10 separate measurements.

All pachymetry readings were taken in similar manner by a single observer who was masked to the diagnosis. In order to minimize effects of diurnal variation on thickness, all measurements were taken between 09 AM and 02 PM. The CCT values of the three groups were compared using the student's t-test.

Data analysis

Data was analyzed and processed as frequency and percentage in tables using Micro-Soft Excel statistical program & IBM SPSS(Statistical Package for Social Sciences) program.

Result

The study was conducted on 100 cases including 60 male and 40 female subjects with mean age of 53±15 (range 19-80) years. Mean age in male and female subjects were 50±19 and 51±17 years, respectively (P=0.184). Mean CCT was 540 ±15 µm overall, and 539 ±16 µm and 541 ±13 µm in male and female subjects respectively (P=0.11). In this study either eye of the subject is considered.

	CCT(µm)		IOP(mm of Hg)		Average Age (Years)	
	Male	Female	Male	Female	Male	Female
Cohort	540	541	19	20	52	53
Control	538	540	15	14	45	53
POAG	539	537	25	23	62	64
OHT	568	553	26	23	38	30
NTG	527	539	17	21	64	61

Fig. 1 : Mean CCT , IOP in different types of glaucoma

Study shows a moderate positive correlation between IOP and CCT (Pearson correlation coefficient r = 0.50) in Fig -2

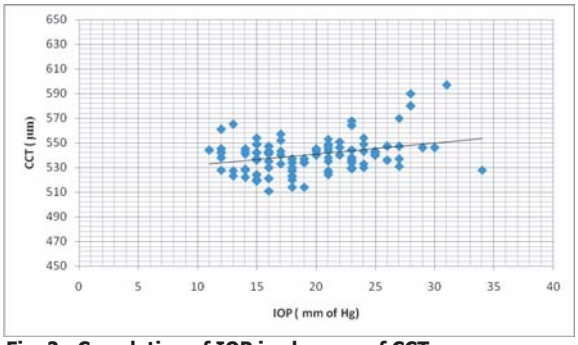

Fig. 2 : Correlation of IOP in changes of CCT

CCT was found in different study group, control 539 ± 11 SD µm, POAG 538 ± 9 m, OHT 560 ± 20 µm, NTG 531 ± 12 µm.

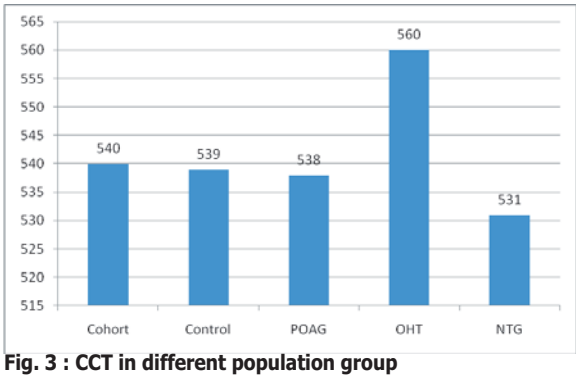

Fig. 3 : CCT in different population group

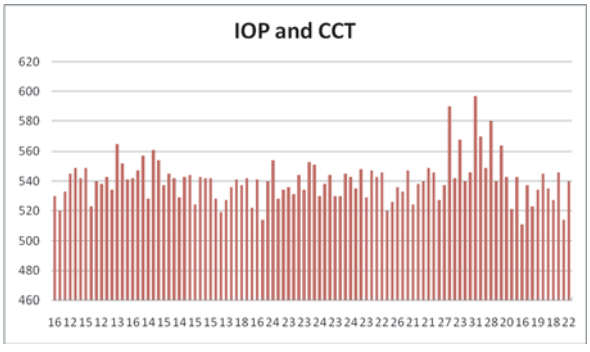

Fig. 4 : Relationships between CCT and IOP

Discussion

CCT measurement can be affected by several factors: technique of measurement, age, diurnal variation, contact lens wearer, ocular disease, and previous ophthalmic surgery. The knowledge of the average CCT in a particular population is required in order to predict the risk of glaucoma in that population.

Gordon et al.[13] made clear that individuals with CCT of 555 µm or less had a 3 times greater risk of developing glaucoma compared with patients with CCT of greater than 588 µm.[14] The average CCT (539± 11 µm) in our population was not significantly different from CCT in POAG group (538± 8), which is analogous with the findings of Maya Natarajan and et al.[15]

Average CCT of our population (539 ± 11 µm) closely matches that of the African Americans (531.0 ± 36.3 µm),[16] the Japanese (531.7 µm),[17] the Indians (537 ± 34 µm)[18] but is significantly different from that of the Caucasian population (558 ± 34.5 µm).The implications of this difference in average CCT are significant in terms of the correct determination of elevated IOP in our population.

The diagnosis of ocular hypertension, primary glaucoma and normal tension glaucoma is made on the basis of an arbitrary IOP cutoff point of 21 mmHg.[19]This cutoff is based on statistical grounds, primarily for screening purposes rather than as a diagnostic criterion.

It is obvious from the results that many patients with increased IOP without other glaucomatous features might merely have thicker corneas, but not be at higher risk for glaucoma. That is, there is a certain proportion of perfectly normal people who are labeled as glaucoma suspects or ocular hypertensive.

The cohort of glaucoma patients chosen for this study were patients with IOP controlled on medication, in most cases topical timolol maleate 0.5%. The effect of topical drops on corneal thickness is a genuine concern. However, it has been shown in Lass JHet al study that topical drops (timolol maleate 0.5% twice daily, betaxolol hydrochloride 0.5% twice daily) do not have any significant effect on corneal thickness after 12 months of therapy in patients with a baseline endothelial cell density greater than 1500 cells/ mm^2 and a CCT less than 680 µm.[20]

12 patients with normal tension glaucoma (NTG) were included in this study. The mean corneal thickness in this group was found 531µm ± 11. In this group of patients the IOP (18 mm of Hg ± 2 SD) recording may actually be an underestimation of the true IOP. Others have reported similar findings for low tension glaucoma.[21,22]Brubaker has suggested that while adjustment of IOP for corneal thickness could result in reclassification of borderline cases, it would rarely alter the decision to treat or not to treat a given case.[23]

Diagnosed glaucoma patients were included in this study if their IOP was stable and controlled with medications. This was done to avoid any physiological changes in CCT as a response to the widely fluctuating pressures known to occur in this population of patients. For the same reason, patients with angle closure glaucoma were excluded, as they are prone to intermittent closure with acute rise in IOP.

The study confirms that CCT can be a confounding factor while recording IOP. A patient may be labeled an ocular hypertensive just because of the error in measuring his applanation IOP, leading to unnecessary prolonged treatment and/ or follow up. The CCT measurement would go a long way in helping us make a clinically relevant decision.

Conclusion

The measurement of central corneal thickness is the factor to improve clinical decision making, especially if the other clinical findings do not seem to correlate with the IOP. Actual IOP may be underestimated in patients with thinner CCT and overestimated in patients with thicker CCT. This will help to prevent the erroneous labeling of normal patients as "ocular hypertensive" and primary open angle glaucoma patients as "normal tension glaucoma".

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Steroid Induced Glaucoma: A glaucoma that can be avoided

S Parvin[1]

Abstract

Corticosteroids are group of anti inflammatory drugs commonly use in many ocular and systemic conditions. Unmonitored use of steroids can cause cataract and potential irreversible sight threatening complication like steroid induced glaucoma. It is more likely when eye drops such as steroids are easily available over the counter.

The purpose of this review article is to describe the etiology, epidemiology, clinical features and management of steroid induced glaucoma and familiarize the clinicians with the potential sight threatening side effects of unmonitored use of steroids. The purpose also to make sure to counsel the patients discouraging self medication specially the children.

Introduction

Corticosteroids are a group of anti-inflammatory drugs commonly used to treat various ocular and systemic conditions. The use of steroids can lead to significant ocular side effects. Rise of Intra ocular pressure (IOP) and Cataract are among them. Steroid can induce ocular hypertension or glaucoma when administer irrespective of any route like topical, Peri-ocular, systemic or inhalational. Steroid induced glaucoma can be avoided with use of non steroidal anti inflammatory drugs where ever possible or IOP should be regularly monitored in case of steroid use specially in children to avoid the vision threatening complications.

Etiology

Steroid-induced glaucoma is a form of open angle glaucoma. The precise mechanism for IOP elevation is not very clear, but primarily it occurs due to reduced facility of aqueous outflow. The following are proposed theories for steroid-induced raised IOP:

- Steroid causes stabilization of lysosomal membranes and accumulation of polymerized glycosamino-glycans (GAGs) in the trabecular meshwork. These polymerized GAGs become hydrated, producing "biologic edema" and increased outflow resistance.

  Glucocorticoids also increases the expression of extracellular matrix protein fibronectin, GAGs, elastin, and laminin within the trabecular meshwork cells which leads to increased trabecular meshwork resistance Ultrastructurally, in steroid-induced glaucoma, there is accumulation of basement membrane like material staining for type IV collagen.

  Corticosteroids cause inhibition of phagocytotic properties of endothelial cells lining the trabecular meshwork which leads to accumulation of aqueous debris.[9].

- Recent case series has shown that trabecular outflow obstruction can occur due to crystalline steroid particles after receiving intravitreal triamcinolone ace-tonide (IVTA) injections for diabetic macular edema.
- Glucocorticoid decreases the synthesis of prostaglandin, which regulates the aqueous outflow.
- Several genes have been found to be associated with both protective and damaging glucocorticoid-treated trabecular meshwork cells. Glucocorticoids may exert their effect by increased expression of MYOC [Trabecular meshwork-induced glucocorticoid response (TIGR)] gene at locus GLC1A.

Epidemiology

It is stated that 5%-6% healthy population is developed marked rise of IOP after 4-6 weeks of steroid use specially topical betamethasone or dexamethasoe. Rise of IOP is related to frequency and duration of use.

Steroid-induced IOP elevation can occur in any age group. Children are also known to have a severe ocular hypertensive response to topical steroids when compared to adults and significant IOP elevation has also been reported in infants treated with nasal and inhalational steroids.

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Increasing trends of steroid-induced glaucoma in children over the last few years have been reported, probably signifying increasing use of unmonitored steroid use.

Risk factors

Although partially understood, several numbers of risk factors have identified for cortico-steroid induced glaucoma or ocular hypertension.

A. History of glaucoma/glaucoma suspect

In 1963, Becker and Mills demonstrated that patients who had glaucoma, or had been diagnosed as glaucoma suspects, had marked IOP rises in response to several weeks' exposure to topical corticosteroids. The IOP for the glaucoma group rose from a mean of 16.9 to 32.1-mmHg and that for the glaucoma suspect group rose from a mean of 17.1 to 28.3-mmHg. However, in the normal group the IOP rose much less, from a mean of 13.6 to only 18.2-mmHg.The IOP for all the patients studied returned to their baseline or to a normal level after cessation of the steroid treatment.

Approximately 30% of glaucoma suspects and 90% of POAG might have an ocular hypertensive response to a 4-week course of topical dexametha-sone 0.1%. Normal individuals classified as high steroid responders are more likely to develop POAG. First degree relatives of POAG patients are also considered to have a higher risk of being a steroid responder.

Incidence of Steroid responsiveness (in %)

Population	High responder	Moderate responder	Non responder
General Population	05	35	60
Patients with POAG	90	10	0
Siblings of POAG	30	50	20
Offspring of POAG	25	70	05

B. Age

In the year (1963), Armaly showed that the ocular hypertensive response to topical dexamethasone was due to a reduction in aqueous outflow, this outweighing a smaller reduction in aqueous production. Very young (<10 years of age) and older adults (bimodal distribution) are in greater risks.

C. Other factors

It has been reported that there is a greater risk of cortico-steroid response in patients with certain types of connective tissue disease specially rheumatoid arthritis, type I diabetes. High myopia or eyes with history of penetrating keratoplasty or refractive surgeries like photorefractive keratectomy, laser in situ keratomileusis (LASIK), and Descement's Stripping Endothelial Keratoplasty (DSEK). Steroid-induced glaucoma after refractive surgery is masked by falsely low IOP measurement due to thin central corneal thickness, ocular rigidity changes, corneal edema, and fluid accumulation beneath the LASIK flap. T raumatic angle recession, pigment dispersion syndrome, endogenous hypercortisolism.

Types of Steroids & Average time taken for IOP rise:

Route	Average dose	Time taken for IOP rise
Oral	25 mg Hydrocortisone /day	1 year
Oral	50 mg prednisolone/day	2-15 months
Inhalational	Most of steroid inhalers	3 months
Pulse Steroid	140 mg repeated 4 weekly	6 months
Dermatological	Betamethasone cream 0.1%	3 months
Topical	QID doses potent steroid	2-6 weeks
IVTA	4 mg	4-8 weeks
Post sub tenon	40 mg TA	4-9 weeks

In steroid responsive patients, IOP elevation usually develops within the first few weeks of steroid administration. However, it can be elevated within an hour or many years after chronic steroid use. After steroid is discontinued, IOP usually normalizes within 1 to 4 weeks.

IOP rise in different Steroids

Type of steroid	Mean IOP rise in mmhg
Dexamethasone 0.1%	22
Prednisolone 1%	10
Dexamethasone 0.005%	08
Fluromethalone 0.1%	06
Hydrocortisone 0.5%	03
Tetrahydrotriamcinolone 0.25%	02

Clinical Features

Patients usually presents with the features like Primary Open Angle glaucoma(POAG). Always there is history of steroid use. Children may present like congenital glaucoma with photophobia, watering and blepharospasm. Rise of IOP, incrised C:D, open angle on gonioscopy and visual field defects are the common features. In case of Vernal Kerato Conjunctivitis(VKC), there is always a history of long

continued steroid use due to relief of sign symptoms in children.

Differential Diagnosis

1. Primary Open Angle Glaucoma
2. Normal Tension Glaucoma
3. Juvenile Glaucoma
4. Uveitic Glaucoma
5. Glucomato cyclitic crisis

Management and treatment

D. The first line of treatment is to stop the steroid therapy. Most of the time IOP will be reduced within 1-4 weeks.

E. In some occasions topical or systemic steroids is to be continued. In that cases, potent corticosteroids like dexamethasone, betamethasone or prednisolone can be substituted by adrenal steroids like loteprednol etabonate, fluoromethalone or medrysone which are less likely to increase IOP.

F. In case of strong responders, steroid sparing agents and topical nonsteroidal anti inflammatory drugs (NSAID) like- flurbiprofen, bromofenac, ketorolac, nepafenac can be instituted.

G.In depot posterior sub tenon's steroid injections, excision of depot steroid can be done.

H. In IVTA, vitrectomy may give good control of IOP

I. Antiglaucoma medication can be started if needed. If IOP not controlled by antiglaucoma medication, SLT or ALT can be done where ever possible.

J. Trabeculectomy with or without anti metabolites may be the surgery of choice. Incase of intractable glaucoma, glaucoma drainage device or valve implant may be done.

Conclusion

Steroid induced Glaucoma is a preventable condition. Generous use of steroids and strict monitoring of IOP is essential in case of long time use specially in children to avoid the vision threatening complications. Doctors should talk with Patients and their associates about the potential complications and warned them about over the counter use of steroids specially in children. Easily available over the counter use of steroid is one of the most common cause of Steroid induced Galucoma in VKC and anterior uveitis as they cause rapid relief of symptoms.

So, prevention of steroid induced glaucoma can be achieved by some simple precautions in case of any form of steroid use:

1. Identifications of risk factors
2. Careful monitoring of IOP
3. Counseling of patients and associates with potential sight threatening side effects
4. Discourage self medication and over the counter use of steroids
5. Prompt treatment where ever necessary.

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Review Report

Neuroprotective Agents - A New Potential Treatment in the Glaucoma Management

K R Agaz[1]

Abstract : Neuroprotection in the field of glaucoma is defined as any treatment, independent of IOP reduction, which prevents RGC death. Glutamate antagonists, ginkgo biloba extract, neurotrophic factors, antioxidants, calcium channel blockers, brimonidine, glaucoma medications with blood regulatory effect and nitric oxide synthase inhibitors are among compounds with possible neuroprotective activity in preclinical studies. A few agents (such as brimonidine or memantine) with neuroprotective effects in experimental studies have advanced to clinical trials. Nevertheless, lack of compelling clinical evidence has not prevented the off label use of some of these compounds in glaucoma practice. Stem cell transplantation has been reported to halt experimental neurodegenerative disease processes in the absence of cell replacement. The advantage of this approach is a prolonged and targeted effect. Neuroprotection in glaucoma, pharmacologically or by stem cell transplantation, is an interesting subject waiting for broad and multidisciplinary collaborative studies to better clarify its role in clinical practice.

Key words : Brimonidine; Ginkgo Biloba Extract; Glaucoma; Memantine; Neuroprotection; retinal ganglion cells , Stem Cell therapy.

Objective : This article is a review to understand the pathophysiology of RGC damage and potential role of neuroprotective agents in glaucoma .This review, highlights some of the ocular pharmacological approaches that are being used and/or tested to reduce neurodegeneration and provide some form of neuroprotection.

Methodology : This systematic review is based on an extensive literature search of publications in PubMed, Google Scholar and Cochrane. The keywords used for the literature search included glaucoma, stem cells, Brimonidine; Glaucoma; Memantine; Neuroprotection; Retinal ganglion cells , Stem Cell therapy and therapeutics. Inclusion criteria were English language publications, all study designs, and publications from 2000 to 2018. A comparative evaluation of the results of each study was also made. Meta- analysis could not be done due to the heterogeneity of settings, interventions and outcomes. A synthesis of the included studies was performed.

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Introduction

Glaucoma is a multifactorial disease with well-described risk factors such as IOP, age, race, family history and myopia[15]. The exact mechanism(s) of RGC damage in glaucoma is complex and unknown. Glaucoma represents share certain clinical characteristics, including excavation of the optic disc and loss of the RGC with resultant visual field loss, with or without elevated IOP.

Globally, glaucoma is the most common optic neuropathy, the second most common cause of blindness and the most common cause of preventable visual disability[1]. It encompasses a spectrum of progressive optic neuropathies characterized by pathological degeneration of nonmyelinated retinal ganglion cells (RGCs), with structural damage at the optic nerve head. Irrespective of the multitude of potential initiating insults, the common theme in the pathogenesis of glaucoma is the triggering of a cascade that results in accelerated apoptosis of the RGCs.[2-4] This process of cellular death occurs in the absence of inflammation, and is characterized by DNA fragmentation, chromosome clumping, cell shrinkage and membrane blebbing. As a consequence of neuronal death within the central visual pathway, clinical signs of glaucoma include retinal nerve fiber layer defects, neuroretinal rim thinning with excavation of the optic nerve head ('cupping') and irreversible visual field loss. Neural degeneration in glaucoma is not limited to the retina; it also affects neurons in the lateral geniculate nucleus and visual cortex.[5,6]

Although intraocular pressure (IOP) is no longer part of the definition of glaucoma, it is the most easily modifiable risk factor to decrease both risk of disease onset and disease progression. IOP reduction by medical, laser surgical means remains the only clinically proven treatment for glaucoma,[7-9] but it is not entirely effective for all patients, as exemplified in

the Collaborative Normal Tension Glaucoma Study: despite IOP reduction, glaucomatous optic degeneration continued, albeit more slowly and in a smaller proportion of patients.[8] Sufficient IOP reduction to arrest the disease process entirely may be difficult, or may provoke significant adverse side effects. These inadequacies in current treatment paradigm have prompted research into neuroprotection as an alternative strategy for glaucoma. The processes of killing neurons in glaucoma: hypoxia, trophic insufficiency, oxidative stress, excitotoxicity, immune related attack and apoptotic death. Agents that benefit these neurodegenerative disorders may also assist in glaucoma.[10-12] Summary of causes of retinal ganglion cell injury and potential sites for neuroprotection shown in Table 1.

Mechanisms of RGC Damage

S2-Evidence indicates that apoptosis may be the final common pathway for RGC death in glaucoma. Apoptosis is a programmed cell death pathway that occurs without eliciting an inflammatory response.. Markers of apoptosis have also been observed in the human glaucomatous retina[15,16]. Several mechanisms that may initiate RGC apoptosis in glaucoma have been proposed (Fig. 1). These include neurotrophic factor deprivation, hypoperfusion/ischemia, glial cell activation, glutamate excitotoxicity and abnormal immune response.

Table 1 : Summary of causes of retinal ganglion cell injury and potential sites for neuroprotection

Mechanism of RGC loss	Potential neuroprotective class	Examples
Neurotrophin deprivation	Exogenous neurotrophins Neurotrophin receptor agonists	BDNF, NGF TrkA receptor agonist, TrkB receptor agonist
Ischemia	Vasodilators Calcium-channel blockers	Ginkgo biloba, vitamin E Nifedipine, verapamil, diltiazem, nilvadipine
Mitochondrial dysfunction	Antioxidants Vasodilators	Coenzyme Q10, vitamin E, melatonin, ginkgo biloba
Excitotoxicity	NMDA antagonists Calcium-channel blockers	Memantine, riluzole, flupirtine, dextromethorphan Flunarizine, lomerizine
Oxidative stress	Antioxidants/free-radical scavengers Nitric oxide synthase inhibitors	Coenzyme Q10, vitamin E, melatonin, ginkgo biloba Aminoguanidine
Protein misfolding	Vaccines and other immune mediators Heat-shock proteins	Glatiramer acetate, amyloid β antibodies Geranylgeraylacterone
Glial cell modulation	Growth factors	TGF, CNTF
Apoptotic pathways	Caspase inhibitors Calpain inhibitors TNF-α inhibitors	GLC756

BDNF: Brain-derived neurotrophic factor; CNTF : Ciliary neurotrophic factor; NMDA: N-methyl-D-aspartate; RGC: Retinal ganglion cell.

Neurotrophic Factors deprivation

A major destructive effect of increased or fluctuating IOP is deformation of the lamina cribrosa, mechanically compressing RGC axons. This reduces or blocks retrograde transport of essential neurotrophic factors such as brain-derived neurotrophic factor (BDNF), NGF, neurotrophin (NT)-3, NT-4 and NT-5, glial cell-derived neurotrophic factor, ciliary neurotrophic factor, and FGF-2, liberated by the superior colliculus and lateral geniculate body and transported to the RGC body by its axons.[17-19]

Ischemia

Another major theory in the etiology of glaucoma is vascular insufficiency at the optic nerve head.[19,20] Arising from systemic hypotension, vasospasm or even mechanical compression of the microvasculature at the lamina cribrosa, low perfusion of the optic nerve head may cause RGC ischemia. This ischemic insult may reduce essential nutrients and substrates available for energy production in metabolically highly active neurons. Antivasospastic drugs such as calcium-channel blockers and some adrenergic antagonists have potential as neuroprotectants.

Mitochondrial Dysfunction

Increasingly, mitochondrial dysfunction is believed to contribute to the pathogenesis of neurodegenerative disorders, including glaucoma.[22] Mitochondrial dysfunction induces the intrinsic apoptotic pathway by upregulation of NF-B and proapoptotic genes. As mitochondrial dysfunction may be triggered by aging, ischemia and/or oxidative stress, novel methods such as caloric restriction (to try to retard aging[23]), increasing optic head flow dynamics (with vasodilators) and decreasing oxidative stress (with antioxidants) may prove to be useful neuroprotective strategies.

Glutamate Excitotoxicity

Any hypoxic environment critically drops ATP production with failure of the vital sodium–potassium pump of both neurons and their supporting glia. excessive levels of glutamate are toxic not only to RGCs, but also to neighbouring healthy neurons causes calcium influx through hyperactivation of the N-methyl-D-aspartate (NMDA) receptor in a process termed excitotoxicity. Overstimulation of NMDA receptors also activates nitric oxide synthase (NOS), resulting in nitric oxide (NO) production. NO is a neuronal messenger critical for normal retinal neurotransmission and phototransduction. Unregulated, it has the potential to react with the superoxide anion to form peroxynitrite, a highly

reactive oxidant species.[24]

Oxidative Stress

A number of investigations have supported the role of oxidative stress in the pathogenesis of glaucoma.[25] These mainly demonstrated lower levels of antioxidants[26,27] and elevated oxidative stress markers in the aqueous humor of eyes with glaucoma,[27] antibodies against glutathione-S-transferase,[28] decreased plasma levels of glutathione[29] and increased lipid peroxidation products in the plasma of glaucoma patients.[30] Furthermore, tissue analysis studies comparing cultured human trabecular meshwork (TM) from eyes with POAG to that of non glaucomatous eyes have revealed higher concentrations of reactive oxygen species, decreased cell membrane potentials and reduced ATP production in the TM of eyes with POAG.[31] Oxidative free radicals have been implicated in human TM degeneration and subsequent IOP increase and glaucoma.[35]

Misfolded proteins

Misfolded proteins such as amyloid β (Aβ) are a prominent feature of many neurodegenerative diseases, including Alzheimer's, Huntington's and Parkinson's, with an accumulation of abnormal protein plaques in the brain. As Aβ has been linked to glaucomatous RGC apoptosis in a dose- and time-dependent manner,[30] targeting different components of the Aβ formation and aggregation pathways (e.g., using Aβ antibodies) may effectively reduce glaucomatous RGC apoptosis.[31]

Glial Cell Modulation

Retinal ganglion cells are not the only cells damaged in glaucoma: Müller glial cells, amacrine and bipolar cells are also injured. In the nonmyelinated region of the optic nerve head, astrocytes are the major glial cells to provide support to neuronal axons, as well as interface between connective tissue and blood vessels. To try to maintain homeostasis, quiescent astrocytes are transformed into a reactive state by liberated cytokines such as TGF,[34] ciliary neurotrophic factor,[35] FGF[36] and PDGF.[37] Reactive astrocytes exhibit altered intercellular communication, migration, growth factor signaling, oxidative species buffering capacity and connective tissue properties at the optic nerve head.[38]

Apoptotic Death Pathways

The final common pathway for any neuronal injury is necrosis or apoptosis, the latter playing a major role in RGC death in glaucoma. Apoptosis can be initiated by extrinsic or intrinsic pathways. Triggers for the extrinsic pathway include TNF-α, Fas ligand and TNF-relatedapoptosis-inducing ligand. The intrinsic pathway involves mitochondrial-mediated events. The exact processes of apoptosis and neuronal cell death are well described.[41] Regardless of the initiating injury, there is activation of the caspase cascade,[42] increased expression of proapoptotic genes such as Bax/Bid[43] and downregulation of antiapoptotic genes such as Bcl-2/Bcl-xl,[44] leading to noninflammatory programmed cell death.[45] Taking a lead from viruses that use caspase inhibition to prevent apoptosis of infected cells, pharmacological interventions that block the caspase cascade may be neuroprotective.

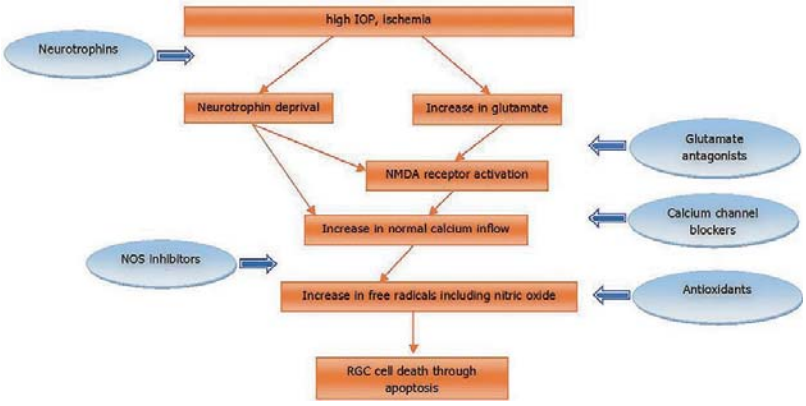

Figure 1 : Simplified pathway of RGC death and assumed mechanisms of neuroprotective agents. IOP, intraocular pressure; NMDA, n-methyl-D- aspartate; NOS, nitric oxide synthase; RGC, retinal ganglion cell.

One of the areas of great interest in glaucoma is how RGC death occurs.[46] The molecular basis of RGC death stems from investigations on animal models of glaucoma. Deprivation of neurotrophic factors,[47] elevated concentrations of excitatory aminoacids such as glutamate,[48] and oxidative stress[49] may contribute to RGC apoptosis [Figure 2].

Neuroprotective Compounds In The Treatment Of Glaucoma

IOP reduction per se can prevent or delay RCG death in glaucomas and therefore is indirectly neuroprotective. However, neuroprotection in glaucoma is defined as any intervention, independent of IOP reduction, that can prevent RGC death. Several natural and synthetic compounds, have been reported to possess neuroprotective properties. Neuroprotection can affect glaucoma by direct protection of RGCs or neutralization of the deleterious effects of toxic factors. The present article reviews current evidence on neuroprotective compounds in the treatment of glaucoma.

Drugs with dual pharmacophoric activities

At present two recently FDA-approved novel drugs, namely netarsudil 0.02%[52] and latanoprostene bunod 0.024%.[53] Netarsudil inhibits rho kinase and norepinephrine transporter it relaxes the TM and Schlemm's canal (SC) cells (thereby helping aquous humor (AQH) to drain via the conventional pathway), and it inhibits Na+/K +-ATPase in the ciliary epithelial cells thereby inhibiting AQH production and lowering IOP. In a similar vein, latanoprostene bunod releases latanoprost free acid (LFA) and nitric oxide (NO) the FP-receptors in ciliary muscle and TM are activated by LFA to cause local release of MMPs that digest extracellular matrix (ECM) to create/enlarge the UVS outflow pathway and promote AQH drainage from both the UVS and TM/SC pathways, while the NO activates soluble guanylate cyclase in TM/SC cells (Dismuke et al., 2009, 2010) that produces cGMP that relaxes TM/SC cells and enhances conventional outflow of AQH. Indeed, such studies have been conducted in POAG/OHT patients and the results are encouraging for this novel formulation containing both netarsudil and latanoprost.[54]

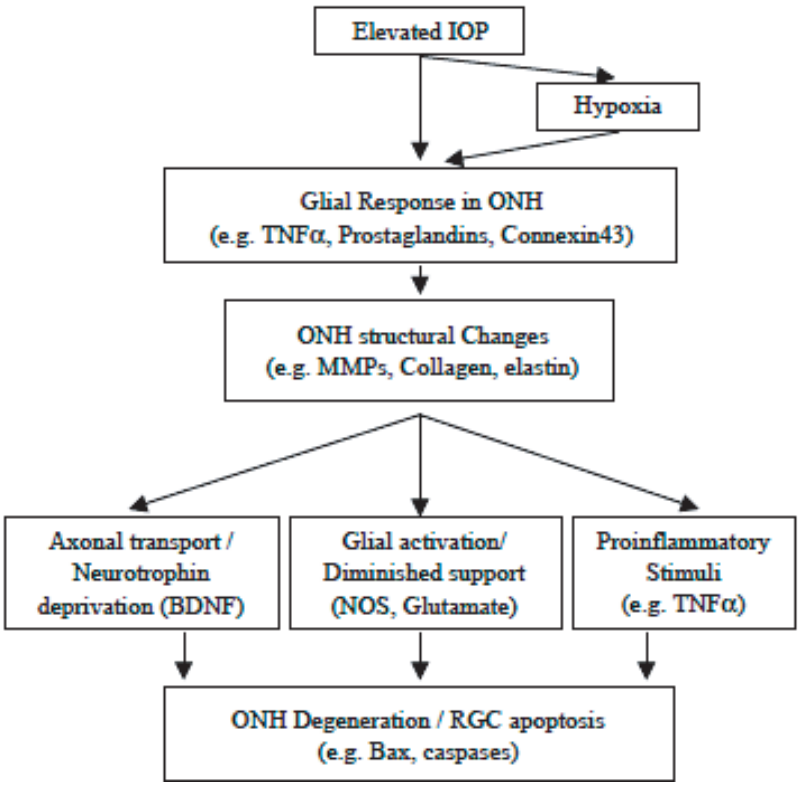

Figure 2 : Proposed mechanism leading to retinal ganglion cell death in glaucoma. MMP, matrix metalloproteinase. Ophthalmol Clin N Am 18 (2005) 383 – 395

Ginkgo Biloba Extract

Ginkgo is an ancient species of tree similar to plants which were living 270 million years ago. This tree is widely grown in China and was introduced early in traditional Eastern medicine to treat a variety of problems such as asthma, vertigo, fatigue and tinnitus or circulatory disorders. In modern medical science, the extract from the leaves of ginkgo biloba, named as ginkgo biloba extract 761 (EGb761), has been shown to be beneficial for cognitive impairment and dementia.[43]

This is the only antioxidants capable of penetrating into the mitochondria can be of benefit as neuroprotective agents. Ginkgo contains certain substances, including polyphenolic flavonoids which may theoretically prevent oxidative stress in the mitochondria and thereby protect RGCs.[46-48]

In a crossover randomized clinical trial, ginkgo biloba extract (GBE) improve significantly in visual field indices in NTG patients. Some glaucomatologists have been prescribing GBE for their patients as adjuvant therapy for several years.[52] However, increasing risk of bleeding during surgery has been a cause of concern in patients using ginkgo.[53] Efficacy and safety reports have recommended a daily dose of 120 mg of GBE.[51]

Neurotrophic Factors

Among a variety of candidate growth and trophic factors for RGCs, brainderived neurotrophic factor (BDNF), appears to be of particular importance to RGC function and survival.[60-64] BDNF has been shown to undergo both anterograde and retrograde axonal transport,[65] Quigley et al suggested the optimal dose of BDNF to be 0.01 mg per milliliter of vitreous volume for intravitreal injections and found that higher intravitreal doses decrease the protective effect of BDNF on RGCs possibly due to down regulation of Trk B, the BDNF receptor.[56]

Another trophic factor undergoing preclinical investigation is the human ciliary neurotrophic factor (CNTF). Pease et al assessed virally mediated over expression of CNTF and BDNF in an experimental model. Loss of RGC axons was 15% lower in CNTF treated retinas than in controls; however, neither the combined CNTF BDNF group nor the BDNF over expression group showed any significant improvement in RGC survival.[63] Artemin,[64] basic fibroblast growth factor,[65] interleukin-6[66] and erythropoietin[67] are other trophic factors or cytokines for which a neuroprotective effect has been proposed.

Purified Recombinant Trophic Factors

The blood retina barrier impedes such large proteins from reaching the retina with systemic administration. Intravitreal injection is an alternative route to deliver purified recombinant trophic factors to the retina. Valproate, phenytoin; anti inflammatory agents like ibudilast, aspirin and meloxicam) could be synthesized, formulated and delivered intravitreally to slow down the death of RGCs and their axons.[64]

Alpha 2 Adrenergic Agonists Including Brimonidine

The presence of alpha adrenergic receptors in human, bovine and porcine retinas, particularly in RGCs and the inner nuclear layer has been demonstrated.[69,70]

It has been suggested that brimonidine may prevent RGC death by direct interaction with alpha-2 adrenergic receptors, leading to reduced accumulation of extracellular glutamate and blockade of NMDA receptors; this protective effect is thought to be independent of IOP reducing mechanisms attributed to this agent.[71-73] Elimination of the protective effect of brimonidine by coadministration of an alpha 2 antagonist confirms that the mentioned effect is secondary to alpha-2 receptor activation.[71,74]

In another study, brimonidine treatment also preserved morphology, density and the total number of axons in the optic nerve subjected to high IOP.[75]

Nitric Oxide Synthase Inhibitors

Evidence in the literature points to a possible role for NO in RGC degeneration.[76-78] There are three forms of nitric oxide synthase (NOS): NOS-1 (neuronal NOS) and NOS-3 (constitutive NOS) act as vasodilators or neurotransmitters in normal retinal tissue, however NOS-2 (inducible NOS) contributes to RGC neurotoxicity.[80] An increased expression of NOS has been shown in optic nerve head (ONH) of glaucoma patients.[81,82] The possibility that NOS-2 inhibition could be neuroprotective in glaucoma was strengthened by reports showing that another NOS-2 inhibitor (N-nitro-L-arginine) delayed RGC degeneration.[83] The non-psychotropic component of

marijuana, cannabidiol (CBD), and the synthetic cannabinoids, tetrahydrocannabinol and HU-211 have been demonstrated to possess protective actions in part due to an effect on reducing formation of lipid peroxides, nitrite/nitrate and nitrotyrosine.[86,84,85] These data suggest that activation of NOS, especially NOS-2, may play a significant role in glaucomatous optic neuropathy and that nitric oxide synthase inhibitors could halt neurodegeneration.

Calcium Channel Blockers

The neurotoxic effect of NMDA is mediated by calcium influx into neural cells, followed by apoptosis and cell death.[86] Thus, calcium channel blockers (CCBs) seem to be a rational alternative for neuroprotection in glaucoma. CCBs theoretically rescue RGCs by prevention of cell death mediated by calcium influx and by improving local blood flow in ischemic tissues by inducing vasodilation.[87]

Different calcium channel blockers such as iganidipine, nimodipine and lomerizine have been shown to significantly increase purified rat RGC viability under hypoxia.[88] The effect of 2% topical flunarizine reduced IOP and attenuated injury to the retina, including RGCs.[82]

Other members of this family, brovincamine and nilvadipine, have high blood brain barrier permeability and are expected to induce favorable effects in the optic nerve or retina with minimal influence on systemic blood pressure.[83] They were shown to improve visual field defects and ocular circulation in NTG patients and diminished the rate of deterioration in visual field sensitivity of NTG patients in randomized clinical trials.[91-93]

Antioxidants

Theoretically, inhibition of ROS and upregulation of cell defense systems may enhance RGC survival.[94-97] Cell defense mechanisms against oxidative stress include the superoxide dismutase, glutathione (GSH) and thioredoxin (TRX) systems.[95] The TRX system mitigates oxidative damage by scavenging intracellular ROS. The reaction leads to TRX oxidation, which is returned to its reduced form by TRX reductase in the presence of NADPH.

Anti-Glaucoma Medications With Blood Regulation Effect

Vascular dysregulation has been implicated in the pathogenesis of glaucoma,[98] therefore a neuroprotective effect has been suggested for agents which can improve regulation of ocular blood perfusion.[99] Some antiglaucoma medications have additional ocular blood perfusion effects. For instance, carbonic anhydrase inhibitors increase ocular perfusion.[100] Improvement of ocular blood has also been reported with latanoprost.[101,102] Betaxolol is a putative selective B1-adrenoceptor blocker.[103,104] Some studies have suggested that betaxolol reduces the NMDA stimulated influx of calcium into isolated cells of rat retinas by direct interaction with voltage-dependent calcium channels or sodium channels.[105]

Stem Cell Transplantation For Rgc Neuroprotection

A systematic review to determine whether stem cell therapy had the potential to treat glaucoma. Nine studies were selected based on the predetermined inclusion and exclusion criteria. Of these nine studies, eight focused on neuroprotection conferred by stem cells, and the remaining one on neuroregeneration. Results from these studies showed that there was a potential in stem cell based therapy in treating glaucoma, especially regarding neuroprotection via neurotrophic factors. The studies revealed that a brain-derived neurotrophic factor expressed by stem cells promoted the survival of retinal ganglion cells in murine glaucoma models. The transplanted cells survived without any side effects. While these studies proved that stem cells provided neuroprotection in glaucoma, improvement of vision could not be determined. Clinical studies would be required to determine whether the protection of RGC correlated with improvement in visual function. Furthermore, these murine studies could not be translated into clinical therapy due to the heterogeneity of the experimental methods and the use of different cell lines. In conclusion, the use of stem cells in the clinical therapy of glaucoma will be an important step in the future as it will transform present-day treatment with the hope of restoring sight to patients with glaucoma.[106]

Summary

Over the past 30 years, numerous pharmacologic agents have been advocated as neuroprotective agents in glaucoma, however few of them such as brimonidine or memantine have advanced to clinical

trials.

Glaucoma is a chronic heterogenous group of disorders, and no animal model can fully mimic the course of human disease. Furthermore, considerable disease variability exists in human clinical trials; these include the presence of comorbidities, polypharmacy in elderly glaucoma patients, and minimal control over a myriad of physiologic factors.

Successful clinical application of one or more neuroprotective strategies depends on several factors: (1) the strategy has to have a rational scientific basis; (2) the neuroprotective agent must be delivered safely and efficiently to the site of damage; and (3) the efficacy and safety profile of the neuroprotective agent must be demonstrated in a randomized prospective clinical trial. For a chronic, slowly progressive disease such as glaucoma, proving clinical efficacy remains a challenge because it may take many years to detect significant benefit. Nonetheless, the goal of clinically significant optic nerve protection in glaucoma seems within reach.

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Micro Invasive Glaucoma Surgery (MIGS)

M A Rahman[1]

Introduction

- Traditionally initial treatment of Open angle glaucoma (OAG) are with medications.
- Laser Trabeculoplasty or SLT may be the other options.
- Trabeculectomy or other drainage procedure is reserved for moderate to advanced glaucoma.
- Those Procedures are delayed due its invasiveness and possible complications.
- MIGS may be the new option for those who do not meet the criteria for trabeculectomy.

MIGS Devices

- Each MIGS procedure involves implanting a tiny device to allow fluid to drain from the eye, reducing internal pressure.
- Some MIGS devices (iStent and CyPass) are implanted during cataract surgery.
- Another MIGS devices (Xen Gel Stent) is implanted as a single procedure for people without cataracts or who have already had cataract surgery.

  If someone needs more aggressive glaucoma treatment later on, a previous MIGS procedure does not affect it

Why MIGS?

1. Ab interno conjunctiva-sparing approach.
2. Minimal trauma to the target tissue.
3. Greater efficiency, high safety profile, and rapid recovery.
4. The clear corneal incision spares the conjunctiva for future surgeries if necessary.
5. Ab Interno incision allows direct visualization of the angle, optimizing placement of the stents.
6. Schlemm's canal procedures enhance physiologic outflow pathways.
7. Minimizes risks of serious and visually threatening complications associated with other glaucoma surgeries.

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Criteria for MIGS

- Currently, MIGS act in the
  - Schlemm's canal,
  - supra-choroidal space, or
  - subconjunctival space.

Indications

- Patients with mild-moderate glaucoma

–Primary open-angle glaucoma, pseudoexfoliation glaucoma, or pigmentary dispersion glaucoma

- If Glaucoma is uncontrolled with maximum pharmacologic treatment or there are barriers preventing adequate medication dosing.
- Age greater than 18 years.
- Patients with clinically significant cataract, as surgery may be performed simultaneously.

MIGS procedure	MIGS device
1. A b Interno	
i. Trabecular micro bypass	iStent
ii. Trabeculotomy	Trabectome
iii. Suprachoroidal stent	Cypass
iv. Subconjunctival Implant	Xen
v. Intracanalicular scaffold	Hydrus
vi. Endocyclophotocoagulation	ECP
2.A b- Externo	
i. Suprachoroidal gold microshunt	SOLX
ii. Canaloplasty	iTrack 250-A
iii. Modified trabeculectomy	Ex-press shunt

Trabecular micro bypass (iStent)

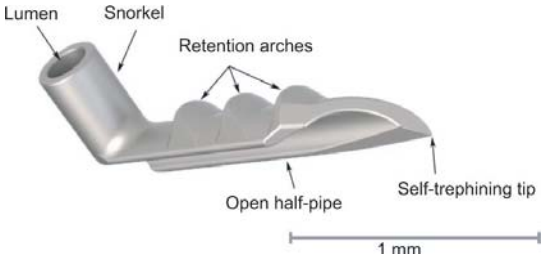
- iStent, A type of Micro-Invasive Glaucoma Surgery (MIGS)

- Became a preferred approach to glaucoma management for many eye care professionals
- Usually patients with mild-to-moderate glaucoma.
- Performed at the time of cataract surgery,

  Minimally traumatic to delicate eye tissue

Design

- The iStent is a first-generation trabecular micro-bypass product.
- It is a heparin-coated non-ferromagnetic, titanium stent connecting the anterior chamber directly to Schlemm's canal.
- Usually 1 mm in length and 0.3 mm in height ,
- The iStent is the smallest implantable medical device
- Using gonioscopy, the device can be visualized within Schlemm's canal and in the anterior chamber,
- Allowing aqueous to flow between these two spaces.

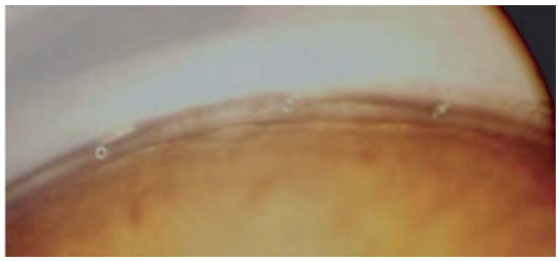


First-generation iStent.

- Perpendicular to the inlet, the longer pointed end facilitates entry into Schlemm's canal,
- The three retention arches secure its position.
- The half-cylinder profile with an open posterior wall prevents blockage or fibrosis over the tip.

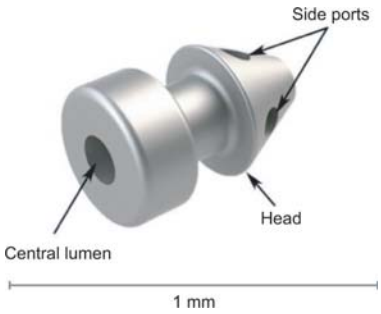
INSERTER OF 1ST GENERATION iStent

- The inserter consists of 26-gauge tubing and four finger extensions.
- This design facilitates device implantation via a clear corneal incision and ab interno approach under gonioscopy.
- These extensions also allow re-grasping of the device if further manipulation or repositioning is necessary.



Gonioscopic view of the angle with three implanted iStents into the trabecular meshwork.

A second-generation model, the iStent



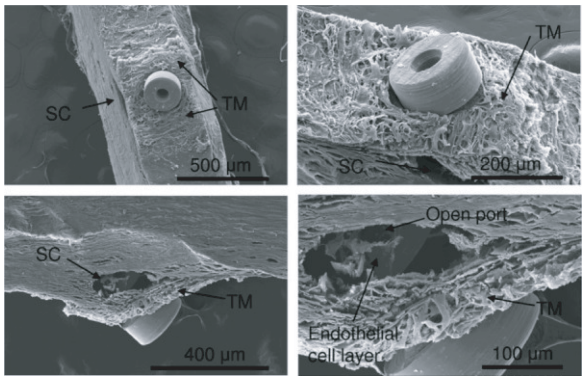
- Composed of titanium
- Smaller in size (360 microns)
- Its shape is characterized by an apical head, containing four inlets (passage of aqueous)
- The narrow body contains the lumen sits within the trabecular meshwork.
- A flange secures the device on the inner wall of the meshwork,
- A 23-gauge stainless steel insertion sleeve covers the injector, which comes preloaded with two stents.

Advantages

- Easier surgical technique
- No sideways sliding of the stent is required for positioning
- Two devices can be implanted with a single inserter at a time.

Mechanism of action :

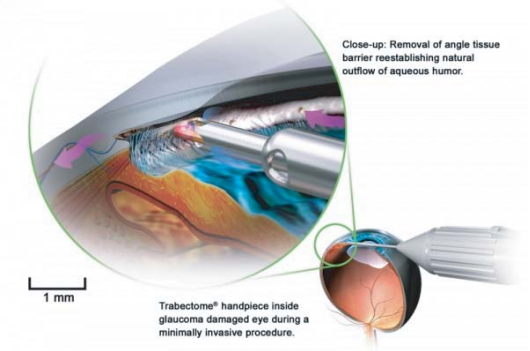
- Creating and maintaining a channel between the aqueous in the anterior chamber and Schlemm's canal,
- The iStent bypasses the site of highest resistance to aqueous outflow: the juxtacanalicular trabecular meshwork.



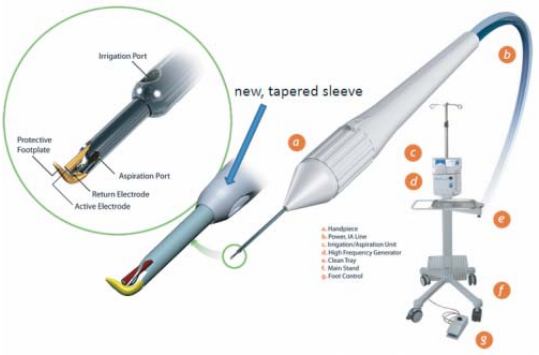
Various scanning electron microscope views of the iStent inject positioned within the trabecular meshwork (TM) and Schlemm's canal (SC) in human anterior segment culture.

Trabectome

- Trabectome is an electrosurgical form of ab interno trabeculectomy
- Trabectome surgery molecularizes the primary barrier to outflow the trabecular meshwork (TM)
- Insertion of the Trabectome tip through a 1.6 mm clear-corneal incision
- The conjunctiva remains undisturbed
- The TM is engaged with the instrument at the level of the scleral spur and begin ablation
- The target is to ablate 90° in each direction for a total of 180° per incision



Trabectome Surgery



Trbectome Machine

Use only in conjunction with cataract surgery

Cypass microstent

- The device is a fenestrated micro-stent
- Comprised of biocompatible polyimide material
- Designed to be inserted into the supraciliary space
- Creating a permanent conduit between the anterior chamber and the supraciliary space.

Design

- Flexible polyimide material curves along the applier's guidewire during insertion and straightens once placed
- This creates a tenting effect that promotes drainage of aqueous fluid through the device
- 64 fenestrations help to maximize aqueous outflow
- A series of retention rings keeps the device in place and guides proper depth of insertion

Surgical Procedure

- Flexible polyimide material curves along the applier's guidewire during insertion and straightens once placed
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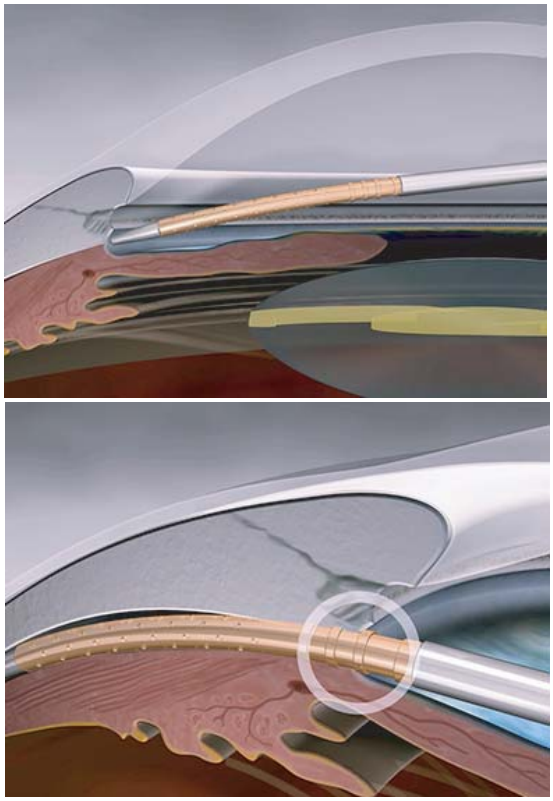


Cypass Micro stent

• **XEN Gel Stent**

• The XEN Gel Stent is tiny—about the length of an eyelash—and it's placed just under the conjunctiva

• It is a surgical implant

• Designed to lower high eye pressure in open-angle glaucoma

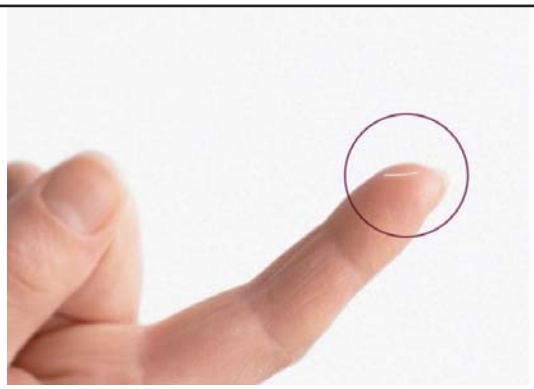
• It's a small tube that, when inserted into the eye, becomes soft and flexible.

• The advantages there are it will accommodate to the tissue and this should limit the erosion.

• The stent composed of collagen-derived non-inflammatory gelatin .

• This material allows it to conform to the ocular tissue.

• Minimizing many of the issues seen with synthetic materials such as migration, erosion and corneal endothelial damage.



XEN Gel stent

Surgical Procedure

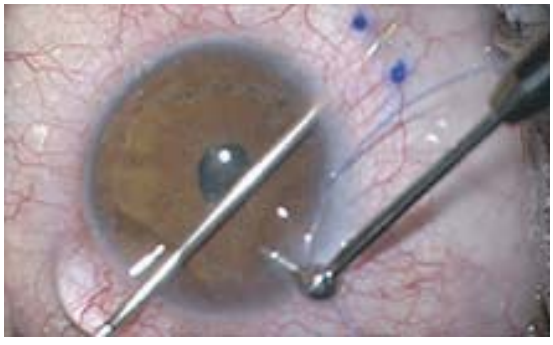
• Clear corneal ab interno incision

• The implant is injected with a pre-loaded, single-use injector with a 27-gauge needle.

• It is positioned with about 2 mm in the subconjunctival space,

• 3 mm left intrasclerally

• 1 mm in the anterior chamber.



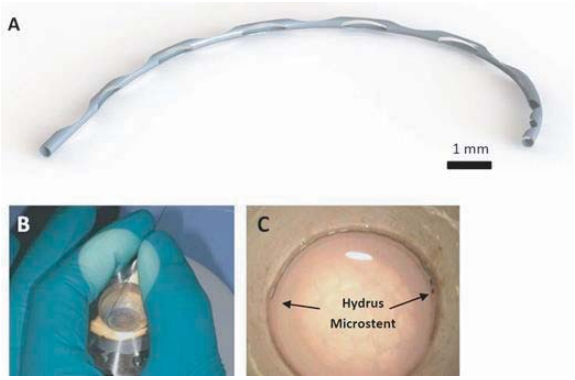
Surgical insertion of XEN Gel implant

Placement of XEN Gel implant

Indications

- Refractory glaucoma patients with failed previous surgical treatment
- Primary open-angle glaucoma (POAG)
- Pseudoexfoliative glaucoma
- Pigmentary glaucoma with open angles

--not responsive to the maximum tolerated medical therapy.



Hydrus Microstents

- The world's first intracanalicular scaffold for the treatment of POAG
- Procedure is less invasive than traditional glaucoma surgery .
- Can be performed during cataract surgery using the same microsurgical incisions.
- Roughly the size of an eyelash,

Made from a super-elastic, biocompatible alloy (nitinol), a well-proven biomaterial.

Design and Placement

(A) The Microstent design consists of a flexible Nitinol scaffold with windows along its walls to dilate Schlemm"s Canal (SC) and allow aqueous humor to flow through.

(B) Insertion of the Microstent into SC of an ocular anterior segment using a custom designed delivery system.

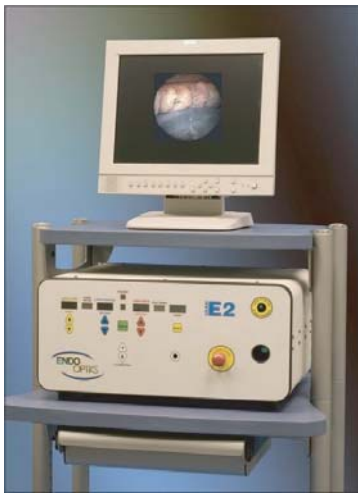
(C) Final placement of Microstent in SC.

Mechanism of action

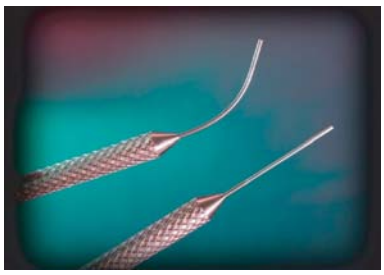
- The device opens a bypass through the trabecular meshwork.
- Dilates and scaffolds Schlemm canal to augment outflow.
- Spans 90° of the canal to provide expanded access to the eye's fluid collector channels.

Endocyclophotocoagulation (ECP)

- ECP involves the use of an endoscopic probe that allows the surgeon to visualize the ciliary processes and to coagulate or burn via the probe with a laser.
- ECP is an effective procedure for IOP-lowering in a variety of glaucomas.
- For most practitioners, the most likely use of ECP is as an adjunct to cataract surgery in the face of moderately uncontrolled glaucoma.
- It remains controversial as a primary procedure.



Endoscopic photocoagulation unit.



Curved and straight probes

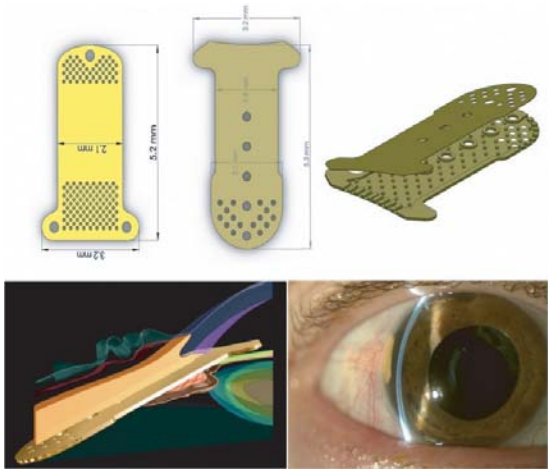
The SOLX gold shunt

The SOLX gold shunt is designed to :

- Transmit aqueous from the anterior chamber to the suprachoroidal space
- It will ultimately be redistributed and/or reabsorbed by the scleral channels or the choriocapillaris.

Composition

- The device is composed of two leaflets fused together vertically.
- Concealing microchannels within its body that connect the anterior inflow channels to the posterior outflow openings.
- The unit is fabricated from 24-kt medical grade (99.95%) pure gold, which is known for being inert and biocompatible.
- The original GMS was 3.2 mm wide, 5.2 mm long and weighed 6.2 mg.

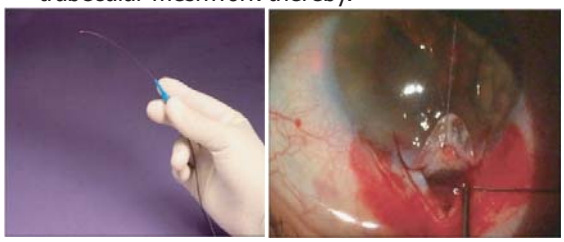


Surgical Procedure

- The gold shunt can be inserted in any quadrant.
- Creation of a conjunctival peritomy,
- 3–4 mm, full thickness scleral incision is created 2–3 mm posterior to the limbus to expose the supraciliary space.
- A scleral pocket at 95% depth, using a crescent knife to extend all of the way to the scleral spur.
- The dissection is to be continued posteriorly into the suprachoroidal space
- the anterior chamber is entered after the anterior chamber is stabilized with viscoelastic or by anterior chamber maintainer.
- The GMS is then delicately positioned with the proximal end in the anterior chamber and the distal end in the suprachoroidal space .
- Finally, the scleral incision is closed with multiple 10–0 nylon sutures and the conjunctiva is reapproximated with a 10–0 vicryl suture

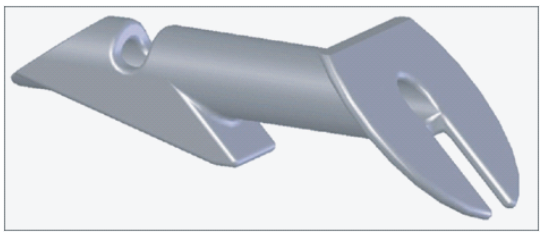
CANALOPLASTY- itrack 250

- The iTrack 250 is a flexible microcatheter.
- Enabled to perform 360 degrees of canaloplasty under the direct visualization of a beacon lighted tip.
- Allows for circumferential viscodilation of the entire length of SC.
- Subsequent suture placement may be performed through the canal.
- The suture allows for tension to be transmitted to the inner wall of Schlemm's canal and trabecular meshwork thereby.



Ex-PRESS shunt

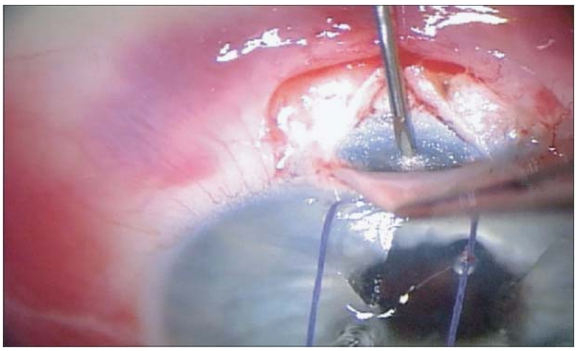
- The Ex-PRESS shunt was developed to shunt fluid from inside the eye to under the conjunctiva.
- Ex-PRESS shunt is placed under a partial-thickness scleral flap as a modification of trabeculectomy.
- The Ex-PRESS device is a stainless steel shunt .
- shown excellent biocompatibility with human tissue



Ex-PRESS shunt

Surgical Procedure

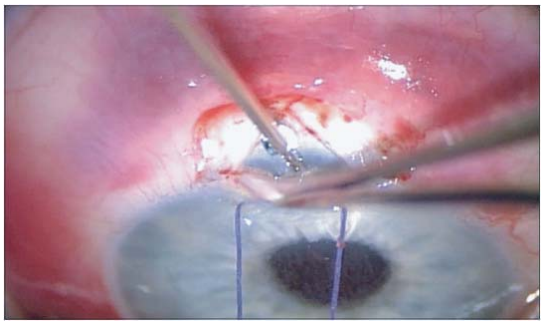
- A standard fornix or limbal-based conjunctival flap.
- Gentle cautery is performed in this area.
- Trabeculectomy type scleral flap
- Anti-fibrotic agents can be applied
- Identify the center of the "blue line" adjacent to clear cornea which corresponds to the location of the trabecular meshwork
- A 26 gauge needle is inserted into the anterior chamber through the center of the "blue line"



Creation of the wound for the Ex-Press Mini Glaucoma Shunt using a 26 Gauge Needle

- The Ex-Press shunt is preloaded on an injector.
- Fitted into the lumen of the shunt is a metal rod that is attached to the end of the injector

- The shunt is then placed in the anterior chamber through the ostium created with the needle.
- The angle of entry with the shunt is the same as the angle used to make the ostium .
- The shunt is inserted all the way into the wound making the plate flush with the scleral bed
- The scleral flap is then sutured
- One to three sutures are typically required
- The conjunctiva is then meticulously closed
- A fluorescein strip is used to make certain the wound is water tight.



The Ex-PRESS shunt under a scleral flap, postop day one. The bleb is elevated but fairly diffuse, the chamber is deep, and there is little inflammation

Conclusion

Modification, innovation and research are ongoing for better management of glaucoma specially on drainage surgeries. None of the surgeries are absolutely satisfactory or complication free. None is universal for all types of glaucoma. MIGS may be an improved version of glaucoma drainage surgery, specially in terms of bleb related & other complications. However, there is still a lack of absolute consensus, even among clinical trials, as to what constitutes a MIGS device, which patients are most appropriately suited for these procedures, which MIGS device is the best to use in any particular patient and what constitutes surgical success.

MIG surgeries currently appear unlikely to supplant traditional incisional glaucoma surgeries, they fill an important gap between medical therapy and incisional surgery for mild to moderate glaucoma, and can often mitigate medication burden. Costing, nonavailability of implants, learning curve or lack of expertise training may be the obstacles that MIGS is not yet so popular and familial among the Ophthalmologists. However it is promising and exciting for the field of glaucoma as these new technologies develop and come to the market.

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ICE Syndrome- management challenge: A case Report

SM Noman[1], **F Khan**[2]

Abstract

Purpose : To describe management challenge in a case of ICE syndrome

Method : A 38 years old lady came to this hospital with the complaints of severe headache and pain in the left eye for last few months. Ocular examination revealed reduced visual acuity as well as increased IOP in the left eye. Abnormal iris texture as wel as shallow anterior chamber indicated the case as ICE syndrome and the patient was medically treated .Filtration surgery with mitomycin –C was done while medical treatment failed to control IOP.

Result : Even after filtration surgery & anlimetabolites, patient repeatedly came with a very high rise of IOP in successive follow ups which was managed by repeated soft digital massage.

Conclusion : Trabeculectomy even when combined with adjunctive antimetabolites is frequently unsuccessful.Repeated bleb formation with soft digital massage in every frequent follow up is helpful to maintain a successful bleb

Case History

A 38 yrs old lady from Bakalia came to CEITC with the complaints of: Severe headache, Pain, Redness, Dimness of vision in her left eye for last 15 days. She had repeated episodes of headache in last few months. She went to an ophthalmologist who advised her anti-glaucoma medications like Brimonidine+ timolol maleate eye drop (2 times daily) and Tab. Acetazolamide 250mg (3 times daily) with potassium supplements.

He referred her to CEITC for further management. Her ocular examination revealed and 6/24 vision in the left eye (no improvement with pinhole), mild congested conjunctiva, oedematous cornea, irregular anterior chamber, vertically elongated people with peripheral anterior synechia. Intraocular pressure 12 mm hg. in the right eye and 40 mm hg. in the left eye. No abnormality was detected in the right eye.

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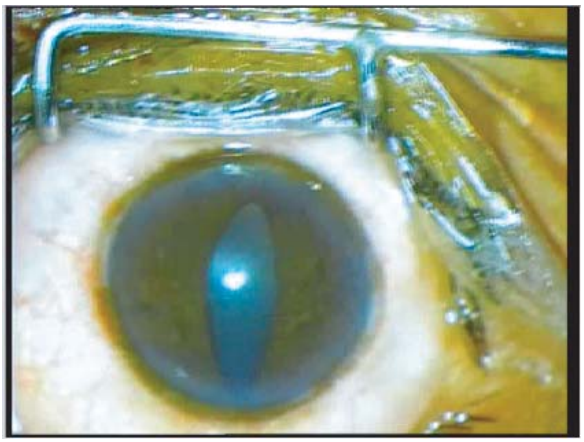

Figure-1 : ICE syndrome

She was treated with Brimonidine .2% & timololmaleate .5% eye drops (2 times daily). Dexamethasone eye drops (6 times daily). Brinzolamide eye drop 2% (3 times daily). Tab. Acetazolamide 250mg (4 times daily) with Potasium Supplement Patient was advised to come after 7 days.

After 7 days her visual acuity was improved (6/12), intraocular pressure was slightly reduced (35 mm of hg). Fundus was visible due to decrease corneal oedema. C.D. ratio was .8:1 Patient was advised Left Trabeculectomy + MMC $^{-}$ L/A

Operation was uneventful. Thin sclera, Inflamed eye, very high intraocular pressure, vertically oriented pupil were the challenges in the operation. As there were no space for superior peripheral iridectomy, Superior– nasal Trabeculectomy was done. Post operatively the patient was doing well. Intraocular pressure was 12mm of hg. and there was defuse filtering bleb observed in two successive follow ups. (1^{st} & 7^{th} post operative day)

After 14 days Patient came with the complaints of pain, redness, dimness of vision in left eye for last 2 days, Ocular examination revealed flat bleb, reduced visual acuity of 6/60, increased IOP of32 mm Hg. IOP was reduced to 12 mm Hg after a soft digital massage. Atropine 1% was added to deepen the AC.

8 days later patient came with the same complaints with same ocular finding with flat bleb, The bleb was again formed with soft digital massage. The same thing was happened in 2 successive followups and the patient was managed with same method. Gentle digital massage was taught to the patient and patient had been doing that 10 strokes 3 times a day.

After 3 months, patient came with a quite & settle eye with non-congested defuse filtering bleb and 16 mm of hg. intraocular pressure. Patient came with same ocular condition after 4 months also.

Figure : 2 : Filtering bleb after trabeculectomy.

Introduction

Iridocorneal endothelial (ICE) syndrome is typically a unilateral condition characterized by a corneal endothelial abnormality that is variably associated with corneal oedema, anterior chamber angle changes, alterations in the iris and secondary glaucoma. The disorder is usually diagnosed in early adulthood and is more common in females than in males. The spectrum of ICE syndrome is divided into Chandler's syndrome, essential (progressive) iris atrophy, and the Cogan–Reese (iris naevus) syndrome based primarily on the changes in the iris. Although clinically the distinction may be important, the three sub-types of ICE syndrome may more accurately be regarded as different manifestations of the same disease process. The subtypes of ICE syndrome are linked by the presence of an abnormal corneal endothelial cell layer. These cells have the capacity to migrate across the trabecular meshwork and onto the surface of the iris. Contracture of this layer results in iris changes, peripheral anterior synechiae (PAS) and glaucoma. The glaucoma is presumed to be secondary to angle closure or a membrane covering the trabecular meshwork. The rate of glaucoma associated with ICE syndrome has been reported to range from 46% to 82%.[1-4] Previous studies have suggested that essential iris atrophy has a more refractory glaucoma than Chandler's syndrome.

The glaucoma associated with ICE syndrome often is difficult to treat.[1,4-5] Medical therapy is usually limited to aqueous suppressants and often becomes ineffective.[4] Laser trabeculoplasty is ineffective. The success rate of filtering surgery is also believed to be lower than with most other forms of glaucoma.[6-7] A few smaller studies on secondary glaucoma in ICE patients have looked at the outcomes since the introduction of antifibrotic agents and glaucoma drainage implant (GDI) surgery, but these studies have had limited follow-up.[6-7]

Discussion

Iridocorneal endothelial (ICE) syndrome is a spectrum of conditions affecting the eye. Iris naevus (Cogan-Reese) syndrome, Chandler's syndrome and essential iris atrophy are all manifestations of the disease spectrum. Associated ocular pathology includes glaucoma as well as corneal and iris changes. Iris changes may manifest as stromal atrophy, corectopia, pseudopolycoria and the induced nodular irregularity of iris naevus syndrome, created by evaginations of iris stroma through holes in the multilaminar membrane that covers the iris in this condition. In any case in which the pupil is displaced or enlarged or if the stroma is insufficient to block light, glare and other unwanted optical phenomena may occur.

Diagnosis of ICE syndrome is based on abnormalities in the corneal endothelium, distortion of the pupil with ectropion uveae, thickening of the iris stroma with increased pigmentation, iris atrophy, peripheral anterior synechiae, glaucoma and unilaterality of disease[8].

In our case she had iris abnormalities like corectopia, peripheral anterior synechiae, iris atrophy, diffuse iris naevus and iris atrophy which are predominant a noted in nother study.[8] Among the three clinical variants, Cogan-Reese syndrome and progressive iris atrophy have been suggested to induce more severe glaucoma[9]. In our case , patient presented with high IOP and mild glaucomatous disc and field changes

were associated with multiple iris abnormalities, both atrophic and pigmentary (Figure 3).

ICE syndrome has been suggested to affect primarily one eye[12]. However bilateral cases have also been reported.[12,13] In recent years there is growing evidence about the sub clinical abnormalities of the fellow eye.[14] Our case is unilateral and no abnormalities were detected in the other eye.

Poor vision in patients with ICE syndrome might be related to corneal edema, glaucomatous optic nerve damage, cataract formation or due to a combination of these factors.[16-17] In our case, decrease visual acuity was due to similar causes. Raised IOP and Chandler's syndrome (Corneal edema) was present in our case and thus visual acuity was poor. Teekhasaenee and Ritch[18] reported that Cogan-Reese syndrome was the most common form in Asian patients, while Chandler's syndrome was more common in white patients. Both were present in our case.

Sherrard[9] described that, "the typical patient is a woman". Our patient is also an woman. Specular microscopy is a good tool for visualizing endothelial abnormalities directly and for assisting in differential diagnosis.[20]. Focal and specular microscopic examination reveals ICE cells and subtotal ICE (+) tissue in ICE syndrome.[20] It would have been better to perform specular microscopy on our ICE syndrome case.

Many investigations have been done to investigate the causative agent or stimulus for abnormal endothelial growth in ICE syndrome. No definitive proof has been established but a relationship may exist with the herpes simplex and Epstein –Bar viruses.[24] In our case we did not attempt to investigate causative factors.

Glaucoma due to ICE syndrome is difficult to treat.[5] Medical therapy is usually ineffective.[4] Filtration surgery is needed to control intraocular pressure.[4] The success rate of filtration surgery is also believed to be lower than that with most other forms of glaucoma.[6-7] Few studies have described the success rate of filtration surgery which can be improved by using antifibrotics and glaucoma drainage implants.[7] In our patient IOP was not controlled by even 3 antiglaucoma medications at the end the 10 months needed filtration surgery with mitomycin C to control intraocular pressure. Post operatively IOP was nicely controlled with a diffuse filtration bleb. .After 2 weeks patient developed severe pain and decrease visual acuity. On examination we observed a failing congested bleb, with raised IOP. We gave digital massage to the patient and IOP became come down with formation of the bleb again. The same thing occurred several times and was managed in the same ways. Now after 2 months there is sustain diffuse bleb with well control IOP with out medication. We taught patient to do slight digital massage 3 times a day over the lower tarsus. Patient is now habituated with this massage and doing well.

We can not define a final success due to short term follow-up. Further long term follow-up is needed to determine the success.

Conclusion

As ICE syndrome is an established cause of refractory glaucoma, medical control of intraocular pressure can not be achieved. Early diagnosis with proper examinations and investigations are needed. Explanation to the patients, proper counseling and strict follow-up is mandatory to achieve proper treatment outcomes. Glaucoma filtration surgery with antimetabolites is usually successful when done early and failure can be prevented by regular optimum digital massage of the filtration site.

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Choroidal Effusion with Exudative Retinal Detachment Following Ahmed Valve Implant in Sturge Weber Syndrome - A Case Report

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Abstract

Background : Ahmed glaucoma valve implant appears to be a relatively useful drainage device in eyes with Sturge Weber Glaucoma, however early postoperative choroidal detachment can occur from a rapid expansion of the choroidalhemangioma with effusion of fluid into the suprachoroidal and subretinal spaces. Surgeon needs to anticipate and reduce sudden hypotony during surgery. This report describes our clinical experience with the Ahmed Glaucoma Valve implant in Sturge-weber glaucoma in a 10- year old boy that was refractory to conventional medical and surgical treatment. In our case, choriodal detachment and exudative retinal detachment occurred postoperatively. Patient responded to conservative management and sclerotomy was not required.

Key words : Ahmed glaucoma valve, Sturge-Weber syndrome, choroidal hemangioma, Choriodal detachment

Introduction

Sturge-Weber glaucoma is present when the facial hemangioma involves the lids or conjunctiva.[1] The onset of glaucoma may present from infancy to early adulthood. In older children, the elevated IOP is due to an elevation of episcleral venous pressure that occurs as a result of arteriovenous shunts through the episcleralhemangiomas.[2,3]

Choroidalhemangiomas and episcleralhemangiomas are commonly seen, and leakage from the choroidalhemangioma may cause retinal edema. In approximately 20% of procedures which penetrate the anterior chamber, intraoperative or early postoperative choroidal detachment can occur from a rapid expansion of the choroidalhemangioma with effusion of fluid into the suprachoroidal and subretinal spaces[4]

In older children, medical therapy may be better tolerated and effective, with fewer side effects. If medical therapy is unsuccessful, filtration surgery can be used. However, the results of trabeculectomy without anti-metabolites are poor,[5,6] but adjunctive anti-metabolites can cause postoperative hypotony and other risks.[7,8] Hence the Ahmed Glaucoma Valve implant with a unidirectional valve that is designed to open at a pressure of 8 mm Hg, potentially decreasing the risk of postoperative hypotony may be a better surgical option for recalcitrant glaucoma in patients with Sturge-weber syndrome.

This report describes our clinical experience with the Ahmed Glaucoma Valve implant in Sturge-weber glaucoma that was refractory to conventional medical and surgical treatment.

Case Presentation

A 10-year old male child with Sturge Weber Syndrome(SWS) and glaucoma presented to the glaucoma department with raised intraocular pressure(IOP) in the left eye. He had undergone trabeculectomy in the right eye with mitomycin C before presentation. On Examination, his best correctedVisual acuity on the right eye was 6/6 and on the left was 6/9. His Intraocular pressure was 15mmHg on the right eye and 37mmHg on the left eye.

Slitlamp examination of the right eye was within normal limit while that of the left eye showed a diffuse superior bleb with a patent superior peripheral iridectomy. Cornea was clear and peripheral anterior chamber depth was equal to cornea thickness.

Fundoscopy revealed a cup disc ratio of 0.7 and was confirmed with a Colour fundus photograph (fig1a). B-scan ultrasonography revealed a diffuse

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choroidalhemangioma with no choroidal neovascularization or exudative detachment seen in the left eye (fig 1b).

Patient was placed on antiglaucomamedications (cosopt) eight hourly, travast once daily at night and acemox tablets 125mg twice daily for fifteen days. Follow up of this patient revealed progression of optic nerve damage and persistently raised intraocular pressure of 23mmHg despite antiglaucoma medication.

He underwent Ahmed glaucoma valve implantation in the left eye under general anaesthesia.

Post- operatively patient was placed on antibiotics (optimox) four hourly daily, steroid (cortan) two hourly daily, homatropine eight hourly daily, and steroid ointment (sonexa) at night. On the first postoperative day,the visual acuity was 3/60, the anterior chamber was shallow with choroidal detachment and exudative retinal detarchment.(fig 2a and 2b) Patient was then placed on conservative management.

On the fifth postoperative day, visual acuity improved to 6/60, slit lamp examination showed a peripheral anterior chamber depth of ½ central corneal thickness. Intraocular pressure was 9mmHg. Patient was continued on post-operative medications and follow up visits. Subsequent visit at one month postoperatively revealed visual acuity of 6/24 and intraocular pressure of 12mmHg. B-scan ultrasonography showed no choroidal effusion and no serous retinal detarchment. (fig 3)

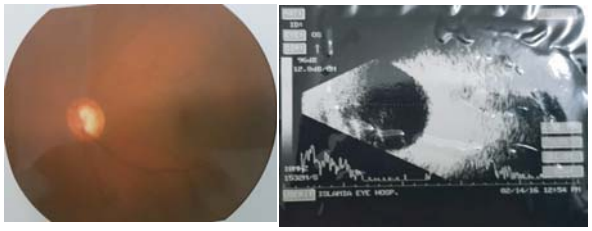

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Figure 1 : (a) Fundus photograph showed no choroidal neovascularization or exudative detachment. (b) B-scan ultrasonography revealed a diffuse choridalhemangioma with no choroidal neovascularization or exudative detachment.

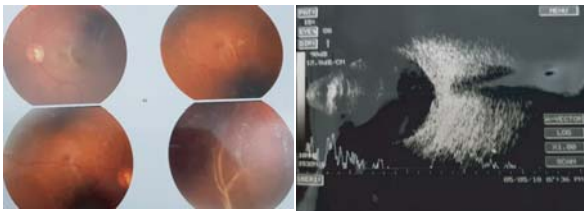

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Figure 2 : (a) Postoperative fundus photograph showing choroidal neovascularization or exudative detachment. (b) postoperative B-scan ultrasonography revealed a diffuse choroidalhemangioma with choroidal neovascularization or exudative detachment.

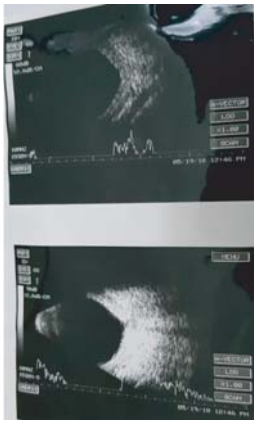

Figure 3 : B-scan ultrasonography showed no choroidal effusion and no serous retinal detarchment at one month postoperative period.

Discussion

Our study shows that Ahmed glaucoma valve is effective in the control of intraocular pressure in patients with Sturge-weber glaucoma. Previous studies have equally demonstrated the efficacy of Ahmmed valve implant in patients with sturge-weber glaucoma.[1,9] The major surgical concern in this case was the presence of a diffuse choroidalhemangioma. There is a higher risk of massive haemorrhage with a fragile choroidalhemangioma during surgery.

The best surgical modality would be one that produces the least hypotony during the procedure. Patients withSWS receiving Ahmedglaucomavalve implantation still have the potential of developing sight-threatening complications of choroidal effusion and haemorrhage when IOP suddenly decreases.[10,11,12,13]

In our index case, patient hadchoroidal effusion and retinal detarchment, which responded to conservative management.

Previous studies reported complication of choroidal detachment following Ahmed glaucoma valve.[14,15] Another study had no complication like in our study.[1] This may be because Ahmed glaucoma valve was primarily implanted in the latter while in the former studies there was a previous history of glaucoma surgeries. Our patient also had a previous history of trabeculectomy before receiving Ahmed glaucoma valve. Ligatation of the valved glaucoma drainage implants, as is done for the non valved implants has been suggested. Oral propanalol has also recently been used to treat patients with diffuse choroidal haemangioma prior to glaucoma surgery.[15]

Conclusion

Ahmed glaucoma valve offers safety and efficacy in controlling glaucoma in pediatric Sturge-Weber syndrome with choroidalhemangioma. However surgeons should anticipate and prevent sudden hypotony.

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Pattern of Axenfeld Rieger Syndrome with Secondary Glaucoma in a Tertiary Eye Hospital

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Abstract

Anterior segment dysgenesis is a failure of normal development of the anterior segment of the eye. The structural anomalies of the mature anterior segment are associated with increased risk of glaucoma1,2. Axenfeld-Rieger syndrome (ARS) is a rare, autosomal dominant condition characterized by ocular, craniofacial, dental (hypodontia, microdontia, enamel hypoplasia, conical-shaped teeth) and periumbilical abnormalities. Axenfeld Rieger syndrome (ARS) has been recognized for more than hundred years with its rare incidence of 1: 200000 live births.

Key words : Axanfeld Rieger Syadrome, Anterior segment dysgenesis, secondary glaucoma.

Introduction

Axenfeld-Rieger syndrome is primarily an eye disorder, although it can also affect other parts of the body. This condition is characterized by abnormalities of the front part of the eye, an area known as the anterior segment.

In this article we are presenting 3 cases of ARS, all were boys of age range from 10 to 17 years, were examined in between 2017-2018 at Ispahani Islamia Eye Institute and Hospital, Farmgate, Dhaka.

Case 1: A 13 years boy presented with dimness of vision in his RE since childhood and in LE for 2 years associated with photophobia. His eldest brother has also the same ocular problem. On examination we found his IOP was 41mmHg in RE and 40mmHg in LE. BCVA was PL, PR(+) in RE and FC-1.5m In LE. Gonioscopy revealed closed angle with peripheral anterior Synechea in 4 quadrants. On slit lamp examination cornea was clear in both eyes. Pupil in RE was dilated, sluggish reaction. Pupil in LE was mid dilated, sluggish reaction with corectopia. In both eyes there were ectopion uveae, iris atrophy around pupil, and multiple full thickness iris defects with irregular AC depth. On fundus examination RE revealed glaucomatous optic atrophy and in LE C:D was 0.9:1. General and systemic examination was normal.

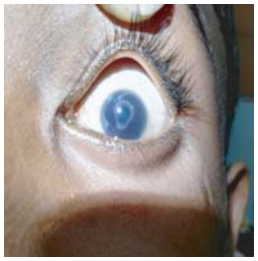
We diagnosed the case as Axenfeld Rieger anomaly with secondary glaucoma in both eyes. We treated this patient with oral Acetazolamide tablet, Brimonidine and Timolol combination eye drop and Brinzolamide eyedrop in both eye.

After 20 days of topical anti- glaucoma medication we performed Trabeculectomy with 0.2% MMC under GA in LE. After one week of surgery his IOP was 08 mmHg in LE and vision was 3/60.

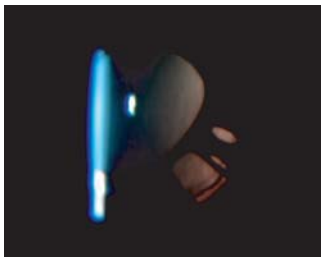
Figure : 1

a. No extra ocular feature

b. RE showing iris atrophy



c. LE showing iris atrophy & ectropion uveae



d. Full thickness iris defects

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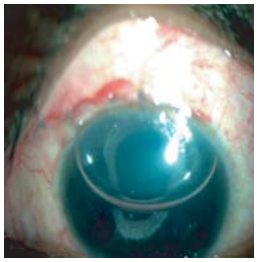


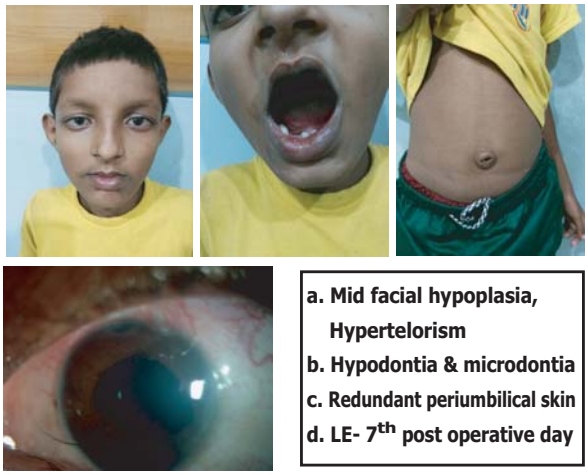
e. LE- 1st post operative day

Case 2: A 10 years boy was presented with dimness of vision in his both eyes since after birth. His IOP was 30mmHg in both eyes and visual acuity was FC-1m in RE and FC-2m in LE. Gonioscopy revealed closed angle. On SLE posterior embryotoxon, corectopia and iris atrophy was present in both eyes. Fundus could not be evaluated with nystagmus. On general examination he was founded as hypertelorism, maxillary hypoplasia, hypodontia and rudimentary paraumbilical skin.

We treated the patient with Brimonidine and Timolol combination eye drop and Brinzolamide eye drop in both eyes.

We have done Trabeculectomy with MMC under GA in his LE. After two weeks of surgery his IOP was 06mmHg. And visual acuity was 6/60.

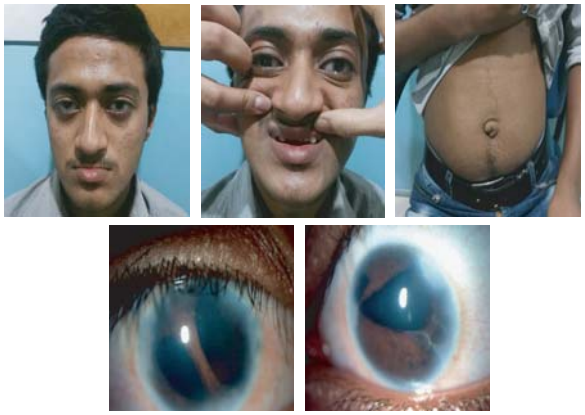
Figure: 2



a. Mid facial hypoplasia, Hypertelorism
b. Hypodontia & microdontia
c. Redundant periumbilical skin
d. LE- 7th post operative day

Case 3 : A 17 years old boy presented with dimness of vision in RE since childhood and in LE for 1 year. His IOP was 48mmHg in RE and 30mmHg in LE and his visual acuity was hand movement in RE and 6/18 in LE. Gonioscopy revealed closed angle in RE and open up to posterior trabeculum in LE. On slit lamp examination there was posterior embryotoxon in both cornea, corectopia with irregular pupil, large full thickness iris defect in RE and iris defect and iris atrophy in LE, and peripheral anterior synechea was in both eyes. On fundoscopy RE revealed glaucomatous optic atrophy and C:D of LE was 0.9:1. Patient was treated with topical anti-glaucoma drugs but not came for follow up.

Figure: 3



a. Maxillary hypoplasia, hypertelorism, prominent nasal breeze
b. Hypodontia & microdontia
c. Redundant periumbilical skin
d. RE- large iris defect, corectopia
e. Post. embryotoxon, peripheral ant. synechea

Discussion

Anterior segment dysgenesis is a group of rare autosomal dominant conditions including posterior embryotoxon, Axenfeld-Rieger syndrome, Peter's anomaly and aniridia. Several different gene mutations, encoding for transcriptional regulators have been described. These specify migration and differentiation of mesenchymal progenital cells of neural crest origin into distinct anterior segment tissues. Interplay between PITX2 and FOXC1 explains phenotypic variability and genetic heterogeneity of anterior segment dysgenesis[1]. Main features are bilateral developmental ocular abnormalities which may be asymmetrical, umbilical cord anomalies, agenesis of certain teeth (usually maxillary incisors) and a hypoplastic mid-face. Alagille syndrome is associated with posterior embryotoxon in 95% of cases and is characterized by paucity of intrahepatic bile ducts, cardiopulmonary malformations and vertebral defects[3]. Posterior embryotoxon may be

absent in Axenfeld-Rieger syndrome[4].

Ocular manifestations of Axenfeld-Rieger syndrome include iris stromal hypoplasia, ectropion uveae, corectopia, full-thickness iris defects, severe iris atrophy and extensive peripheral anterior synechiae. In our all three cases iris atrophy and full thickness iris defects and corectopia were present. Ectropion uveae was present in one case [Fig 1:C]. Posterior embryotoxon were present in two cases (case 2&3) [Fig 3:d,e]

Glaucoma develops in 50% of cases, usually during early childhood or early adulthood, due to an associated angle anomaly or secondary synechial angle closure. Schlemm's canal may be small or absent, development of trabecular meshwork is aberrant and extracellular matrix is altered[2]. Our all three cases were associated with secondary angle closer glaucoma.

Elevation of intraocular pressure is initially managed medically, although surgery may be required subsequently. In our two cases (one eye of each patient) we have done trabeculectomy with MMC and IOP is well controlled.

The signs and symptoms of ARS can also affect other parts of the body. Many affected individuals have distinctive facial features such as widely spaced eyes (hypertelorism); a flattened mid-face with a broad, flat nasal bridge; and a prominent forehead. The condition is also associated with dental abnormalities including unusually small teeth (microdontia) or fewer than normal teeth (oligodontia). Some people with ARS have extra folds of skin around their belly button (redundant periumbilical skin). In this presentation case 1 [Fig 1:a] was free from any systemic association but case 2 and 3 [Fig 2 & 3] were associated with hypertelorism, maxillary hypoplasia, oligodontia and microdontia, and with redundant periumbilical skin. Case 3 has mild mental retardation. Other, less common features can include heart defects, the opening of the urethra on the underside of the penis (hypospadias), narrowing of the anus (anal stenosis) and abnormalities of the pituitary gland that can result in slow growth. WE did not found any of these problems in any of our patients.

Conclusion

The ocular and systemic features of Axenfeld-Rieger syndrome are well-described in literature. The condition can lead to gradual and irreversible visual loss and needs specialist care and careful monitoring. Long-term follow up is important in cases of abnormal ocular findings noted at birth or early life, as these may only be a part manifestation of a potentially blinding syndrome.

The knowledge of early diagnosis of the dental, cranio-facial and systemic presentation of ARS to the dental practitioner could prevent the devastating ocular effects of infantile glaucoma.

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4th Asia-Pacific Glaucoma Congress

On behalf of the Asia-Pacific Glaucoma Society, The Korean Glaucoma Society we invite you to attend the 4th Asia-Pacific Glaucoma Congress (APGC) at the Busan Exhibition and Convention Centre (BEXCO) Korea, from 13-15 April 2018.

The APGC is the region's premier glaucoma congress. The three day event allows experienced and young professionals from across the field to come together to share knowledge and experiences, strengthening research, development, skills and collaboration in the Asia-Pacific region. Visit the congress website for more information. Prof. M. Nazrul Islam will present as a board Member.

The 9th International Congress on Glaucoma Surgery (ICGS), to be held at the Palais des Congrès, Montréal - Canada on September 6-8, 2018. Over the last 15 years, the ICGS has emerged as the key scientific meeting in the field of Glaucoma with the highest scientific calibre and offers an opportunity for immediate skill transfer from some of the most gifted glaucoma surgeons across the globe. This unique scientific meeting generates great enthusiasm and is renowned for garnering widespread interest and enrolment.

The world of glaucoma surgery is fast evolving and requires keen cooperation and harmonization between research, device innovations, and technical refinements in the surgical management of glaucoma. The prime focus of the ICGS is glaucoma lasers and surgery; however it endeavours to incorporate all aspects of glaucoma care, including epidemiology, diagnostics and medical therapy in order to be increasingly relevant to the glaucoma practitioner.