

## Open Angle Glaucoma-Trends in Management.

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**Abstract:** POAG is a chronic, progressive optic neuropathy characterised by morphological changes at the optic nerve head and retinal nerve fibre layer in the absence of other ocular disease or congenital anomalies (with / without a raised IOP). With an expected increase in the population and longevity, POAG is likely to become a major cause of ocular morbidity in the developing world. POAG patients have few symptoms in the early stages. Rarely a high IOP may cause a browache. Transient corneal edema from a raised IOP may cause coloured haloes. Patients with advanced damage often have altered vision. However a careful determination of history and physical findings often helps in timely diagnosis.

The goal of treatment is to preserve visual function. The decision to treat is individualized depending on whether the level of IOP will lead to progressive nerve damage. Available treatment algorithms rely on medical management to achieve the target IOP, failing which filtering surgery can be resorted to. In the Indian context, early filtering surgery to achieve the desired target pressure is a viable alternative. Laser trabeculoplasty is an intermediate step. The role of neuroprotection is not yet established clinically.

Glaucoma is the second leading cause of blindness worldwide accounting for 67 million suffer. Primary Open Angle Glaucoma (POAG) is estimated to affect 33 million people worldwide, majority of whom (about 26 million) reside in developing countries. Almost 90-100% of those affected in developing countries are unaware that they have the disease. Visual impairment is also more severe<sup>2</sup>. The estimated risk of blindness (over 12-20 years) from POAG ranges from 14.5% to 27% (unilateral) and from 7-9% (bilateral). With an expected increase in the population and longevity, POAG is likely to become a major cause of ocular morbidity in the developing world.

12 million people in India are affected by glaucoma accounting for 12.8% of the blindness in the country. Early population based studies reported a prevalence of glaucoma between 2% and 13%. The Vellore Eye Survey (VES) reported a prevalence of POAG as 0.41%, OHT 3.08 and 4.32% for PACG. The Andhra Pradesh Eye Disease Survey (APEDS) reported a prevalence of 1.62% for POAG, 0.32% for OHT. The Aravind Comprehensive Eye Survey (ACES) reported a prevalence of 1.7% for POAG, (95% CI 1.3-2.1) and 0.5% PACG (95% CI 0.3-0.7)<sup>3</sup>.

### PRIMARY OPEN ANGLE GLAUCOMA

Traditionally, Primary Open Angle Glaucoma (POAG) was characterised by the classical triad of a raised IOP, optic nerve head damage and corresponding visual field defects in the presence of open angles on gonioscopy. Today POAG is a chronic, progressive optic neuropathy characterised by morphological changes at the optic nerve head and retinal nerve fibre layer in the absence of other ocular disease or congenital anomalies (with/without a raised IOP).

#### Risk factors

Risk factors are factors, the presence of which increases the possibility of having glaucoma. (Table 1)

**Table 1:** Risk factors in Primary Open Angle Glaucoma

■ IOP	■ Thin Central Corneas
■ Optic head cupping	■ Diabetes
■ Age	■ Systemic Hypertension
■ Race	■ Myopia
■ Family History	■ Migraine
■ Steroid usage	

**IOP:** With an elevated IOP, the prevalence of POAG increases. Several population based studies have shown a consistent association between the level of IOP and POAG. Vascular ischemia, decrease perfusion of the optic nerve head, mechanical compression of the

lamina cribrosa and decrease axoplasmic flow are all important features of glaucomatous optic nerve damage which can be caused by a raised IOP.

**Steroid usage:** POAG has a strong association with steroids. The strength of the association is reinforced by the strong tendency to have a steroid induced rise in IOP amongst POAG patients as also the connection between the glaucoma gene, MYOC (GLCIA, TIGR), and its glucocorticoid induction in the trabecular meshwork.

**Family history:** Population based studies have supported an association between a positive family history for glaucoma and POAG. In the Barbados Eye Study undiagnosed subjects were more likely to develop glaucoma if they had a history of glaucoma in one or more siblings (odds ratio=4.5). In Rotterdam the population based familial aggregation study showed that the life time risk of glaucoma in siblings and offspring of glaucoma patients was 9.2 times higher than in controls. The Baltimore Eye Survey revealed an age-race adjusted odds ratio of 2.85 for an association between POAG and a history of glaucoma amongst first degree relatives<sup>3</sup>.

**Central Corneal Thickness (CCT):** Goldmann applanation tonometry is affected by the CCT. An increase in the CCT is associated with an artificially raised IOP, while a decrease in the CCT causes the IOP to be less than the actual IOP.

**Diabetes Mellitus:** A statistical association between diabetes and POAG has been reported in several case control studies. This may be because diabetics often undergo a detailed eye examination to rule out retinal involvement. The Baltimore Eye Survey did not find any statistical correlation between diabetes mellitus and POAG. However individuals where POAG was diagnosed prior to the study, a positive correlation did exist. The Beaver Dam and Blue Mountain studies found that the odds of a diabetic having POAG were two times greater than those of a non-diabetic. Diabetes mellitus may or may not be a risk factor for POAG. However diabetics tend to have higher IOP than non diabetics.

**Systemic Hypertension:** The Barbados and Baltimore study did not find a statistical correlation with systemic hypertension. However individuals with diastolic perfusion pressures less than 30 mmHg were six times more likely to have POAG than those with a perfusion pressure of 50 mmHg or more.

**Myopia:** Myopes have more problems with vision, need glasses and are more frequently subjected to ocular examination, thus having greater opportunity to be diagnosed as POAG. Wilson et al in a case control study have reported that patients with POAG were twice more likely to have myopia than controls. The Blue Mountain Study showed

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a statistical association between POAG and myopia of 1.5 dioptres and more.

**Migrane:** Migraine headaches or a vasospastic tendency are risk factors for POAG. However this association remains controversial. Vasospasm can theoretically encourage optic nerve head damage by decreasing blood flow to the optic nerve head.

**DIAGNOSIS**

**Symptomatology:** POAG patients have few symptoms in the early stages. Rarely a high IOP may cause a browache. Transient corneal edema from a raised IOP may cause coloured haloes. Patients with advanced damage often have altered vision.

**Evaluation:** Careful determination of history and physical findings often helps in timely diagnosis. These are centred around ocular and systemic risk factors. A review of past records helps in detailing refractive error, ocular and/or systemic disease, medication used (with a special emphasis on steroid usage), intolerance to medication and previous ocular surgery. Involvement of glaucoma amongst family members and impact on quality of life, should also be inquired.

**Examination:** Stereo biomicroscopic examinaion of the anterior segment in POAG is usually normal. However slit lamp examination helps exclude secondary glaucoma with open angles. Measurement of IOP, assessing structural damage to the optic nerve, documenting functional loss with automated perimetry and evaluating the status of the angle outflow structures on gonioscopy are essential pre-requisites to diagnosis of POAG.

**1) IOP**

The diagnosis of POAG generally includes an IOP measurement >21mmHg. Goldman applanation tonometry (GAT) is the proven gold standard for variable force tonometry in patients with normal corneas and normal or abnormal scleral rigidity. It is based on the Imbert-Fick Law. Corneal thickness above or below the normal standard 0.52mm may also impact erroneous IOP measurements, approximately 0.5mmHg/10mm difference from the standard<sup>4</sup>.

**2) Examination of the nerve head**

Glaucomatous optic neuropathy is described by morphological changes in the intra papillary and para papillary region of the optic nerve head and retinal nerve fiber layer.

**A ) Intra papillary changes**

- ◆ Disc size            ◆ Disc shape            ◆ Rim size & cup size
- ◆ Rim shape (Vessel signs)

**B) Parapapillary characteristics**

- ◆ RNFL                    ◆ Hemorrhages            ◆ Vessel diameter
- ◆ Parapapillary atrophy (alpha and beta)

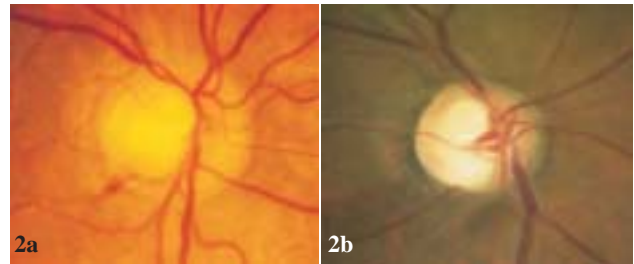
The emphasis should be on stereoscopic evaluation of the optic nerve head with changes in the neuroretinal rim and not just estimation of the cup disc ratio. This will aid in early diagnosis of glaucoma alone coupled with drawings provides for valid documentation<sup>5</sup>. (Table 2)



**Figure 1 :** A large but normal optic disc with a large cup disc ratio. Note the normal shape of the neuroretinal rim - broadest inferiorly, followed by the superior disc region. The rim is smallest in the temporal disc region. "ISNT" rule

**Table 2 :** Checklist to assess changes in the optic nerve head

1. Determine disc size (Elschnig's canal )
2. Check for unusual disc shape
3. Determine cup / rim size in relation to disc size
4. Evaluate rim shape (smallest rim width?)
5. Check RNFL (red-free illumination)
6. Look for disc hemorrhages: Rule out glaucoma
7. High myopia: Rule out glaucoma



**Figure 2 a.:** Splinter or flame shaped haemorrhages , in early glaucoma are usually located at the inferotemporal or superotemporal margin of the disc. Though not pathognomic for glaucoma they are only suggestive of a progressive disc damage in glaucoma .

**Figure 2b :** Evident inferior notch

**OPTIC NERVE IMAGING TECHNIQUES IN GLAUCOMA**

The evaluation of the ONH and nerve fiber layer, essential and critical in glaucoma, until recently have been subjective with a high inter observer and intra observer variability. The parameters of IOP and automated perimetry can miss the diagnosis of glaucoma, especially in the early stages. In fact upto 40% of the ganglion cells must be lost for a detectable loss on automated perimetry because optic nerve damage is irreversible. Early detection is crucial. The objective of imaging of the optic nerve head and retinal nerve fibre layer is to precisely quantify (with maximum reproducibility) these and also help in the early detection of glaucoma.

Stereoscopic photography allows the physician to document longitudinal changes in the optic nerve head. Colour photography with a 15 degree field gives optimal magnification. Interpretation may be subjective. Two National Eye Institute sponsored clinical trials and also the Memantine Study have used qualitative evaluation of stereoscopic optic disc photographs as an outcome measure indicating an acceptance of stereoscopic optic disc photography as a valid tool for detection and monitoring of glaucoma.

**Newer imaging modalities** like the GDX Vcc, OCT and the HRT are evolving technologies which as of now have no proven role in the diagnosis of glaucoma. The use of the HRT has been validated in the followup of glaucoma patients to document progression.

**3) Visual field examination**

is a clinical component of glaucoma management. In the early stages perimetry is important as a diagnostic tool. When performed as a diagnostic tool in glaucoma the question is "Is the field normal or abnormal". And in case it is abnormal "Are the defects glaucomatous"<sup>6</sup>. The sensitivity of the visual field is by determining the threshold value at each point by the bracketing technique (4-2 on the Humphrey and 4-2-1 on the Octopus perimeter). After presenting a light stimulus the machine waits for a yes/no response. If the stimulus is not seen, the intensity of the light seen is increased in steps of 4dB, till it is seen (machine records this as supra threshold level). Subsequently, light stimuli are decreased in steps of 2dB till the

stimulus is not seen (infra-threshold). Octopus perimeters make one more movement in steps of 1dB. The actual threshold is between the supra-threshold and infra threshold.

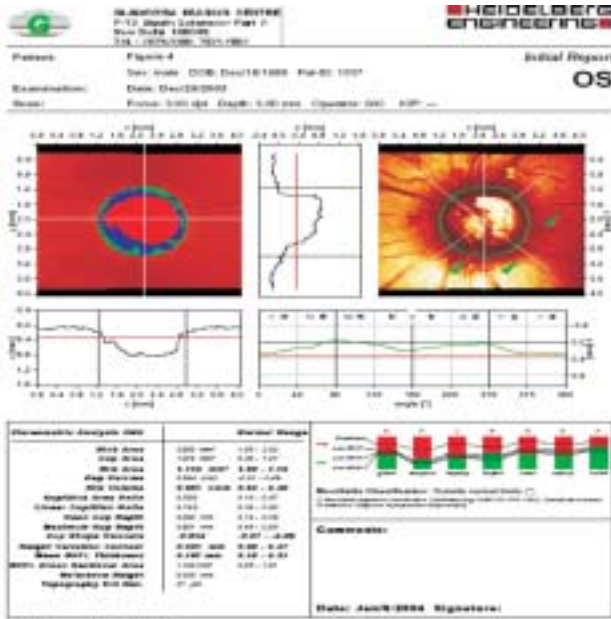


Figure 3 : HRT initial report for a glaucoma suspect

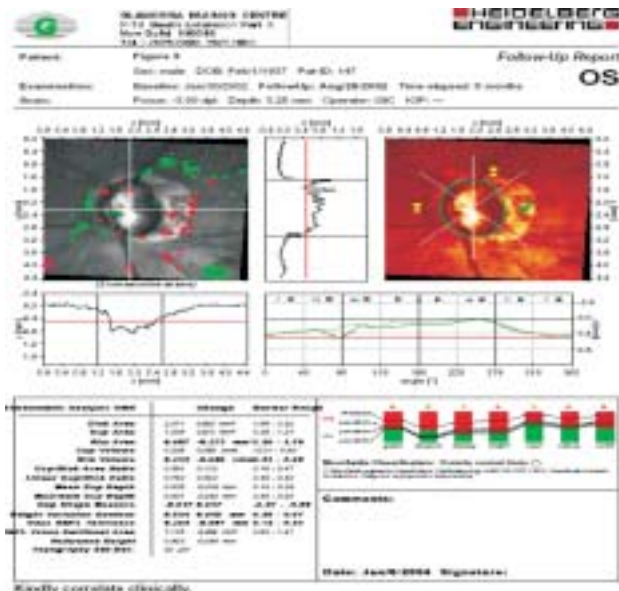


Figure 4 : HRT followup report. Areas with increased cupping are represented in red in the black and white image. Change in parameters are listed in the stereometric parameters.

Threshold determination at each point of the visual field is tedious and time consuming. Because by definition threshold is tested by the staircase algorithm, where every patient can see only 50% of the stimuli presented, newer techniques aim to make the procedure as short as possible, to ensure that the patient maintains concentration and thus provides better reliability. Swedish Interactive Thresholding Algorithm (SITA) on the Humphrey perimeter and Tendency Oriented

Perimetry (TOP) on the Octopus perimeter is based on the fact that a response at one location has implications at the point tested and also its neighbouring points. Just as one tested point is normal, other points on the visual field are likely to be normal too.

**Progression:** Though individual fields can be compared, progression is best assessed using Eye suite perimetry software on the Octopus perimeters and the GPA on Humphrey perimeters.

**4) Aqueous outflow structures**

are typically open on gonioscopy. Its important to rule out intermittent closure in an angle which is open with a tendency to close. Likewise when dealing with an asymmetrical rise in IOP, traumatic angle recession also needs to be excluded.

**5) Ocular blood flow**

Glaucomatous optic neuropathy can occur from pressure dependant and pressure independent factors. Pressure independent factors may be related to optic nerve head blood supply. This is indicated by the presence of disc haemorrhages, retinal vein occlusion, association of normal tension glaucoma (NTG) with migraine, vasospasm and Raynaud’s phenomenon, systemic hypotension, nocturnal dips in diastolic blood pressure, myocardial and cerebral infarcts, blood loss and altered coagulability.

Vascular risk factors should be taken into consideration in the management of intermittent glaucoma when the intraocular pressure is never more than 21 mmHg (diurnal variation) with a normal central corneal thickness and when visual fields show severe and progressive alterations. Methods to assess ocular blood pressure include fluorescein angiography, scanning laser ophthalmoscopy, videography, laser Doppler velocimetry, laser speckle phenomenon, blue field entoptic phenomenon, pulsatile ocular blood flow, colour doppler imaging and oculodynamography.

At the present time role of blood flow measurement influencing clinical decisions in relation to glaucoma management and also changes noted with drugs are unclear. These techniques remain more of research tools.

Table 3 : Differential Diagnosis of POAG

Diagnosis	Differentiating Features
Normal-tension glaucoma	IOP < 21 mm Hg on diurnal testing
Creeping angle closure glaucoma	Closed angle on gonioscopy
Ocular hypertension	Lack of optic nerve damage
Pseudoexfoliative glaucoma	Exfoliative material seen on lens capsule with dilatation, irregular trabecular pigment
Steroid-induced glaucoma	History of steroid use
Pigmentary glaucoma	Iris transillumination defects, concave iris contour, marked trabecular pigment
Undiagnosed traumatic glaucoma	Subtle angle recession, pigment deposition in angle; history of trauma
Juvenile onset glaucoma	Anterior iris insertion
Mild inflammatory glaucoma	Subtle anterior chamber cells and flare
Elevated episcleral venous pressure	Dilated episcleral veins

**DIFFERENTIAL DIAGNOSIS (TABLE 3) MANAGEMENT**

**Ocular hypertension:** Traditionally OHT has been defined by an IOP >21mmHg in the absence of glaucomatous optic nerve damage and visual field loss with open angles on gonioscopy. Since there is a strong association between IOP and glaucoma, these patients are at risk of developing such changes with time and warrant regular measurement of IOP and examination of optic nerve damage. However not all patients are at risk of developing POAG. There is also no way of predicting with certainty who will progress on to POAG.

Elevated IOP, abnormalities of the optic nerve head, black race, advancing age, myopia, family history of glaucoma, and

cardiovascular disorders are significant risk factors for development of the disease. However it is important to know that no single risk factor or group of factors has yet been able to predict the development of glaucomatous damage with reliability.

Most treating physicians would prefer to initiate treatment at a certain level of IOP even if the optic nerve and fields are normal based on the belief that beyond that pressure, there is a greater likelihood to develop glaucomatous damage, thus justifying treatment. Goldmann preferred starting treatment at an IOP level of 25 mmHg<sup>7</sup>. Others have suggested 30mmHg as a guideline for initiating treatment in the absence of any apparent damage. Situations where initiation of treatment at low IOP can be considered include, in addition to risk factors described earlier, venous occlusion, one eyed, unlikely to come for followup and where disc and field assessment is not possible. In the Ocular Hypertension Study (OHTS) 1637 patients with an IOP >21 mmHg, no disc or visual field damage were subjected to a 20% reduction in IOP versus observation for visual field loss and nerve damage.<sup>8</sup> At the end of 5 years a 20% reduction in IOP reduced the risk of developing field loss from 9.5% to 4.4%. All patients with an IOP more than 21mmHg do not need treatment. It would perhaps be reasonable to say that all IOP's more than 25 mmHg need be treated. In the presence of risk factors described, treatment may be begun at lower IOP.

**POAG:** Though there is enough evidence that the damage in glaucoma can be pressure dependent or pressure independent, IOP is the only factor which can be modulated to date. The aim of treatment today is to lower the IOP to a level where the rate of loss of ganglion cells does not exceed the loss of ganglion cells from the normal age related decay, without affecting the patients quality of life. This level of IOP is called **target pressure**.

### **Choosing a target pressure**

Although it is difficult to specify exact guidelines for target IOP levels, the following levels may be used as a reasonable guide IOP level prior to treatment: Any IOP greater than 30mmHg should be reduced to at least the low 20s<sup>9</sup>.

### **Optic nerve related damage**

Eyes with cup-to-disc ratios greater than 0.5, slight asymmetry of the cup-to-disc ratio or IOP, high myopia, a strong family history of glaucoma, or African ancestry should have IOPs below 18mmHg. Patients with early glaucomatous optic disc damage and visual field loss above or below central fixation should have IOPs below 18 mmHg. Patients with moderate to advanced glaucomatous optic disc damage (cup-to-disc ratios greater than 0.8) and superior and inferior arcuate scotomatous visual field loss should have IOPs consistently below 15 mmHg (many would choose a target of 12mmHg). Patients with advanced glaucomatous optic disc damage (cup-to-disc ratios greater than 0.9) and extensive visual field loss within the central 10 degrees of fixation require an IOP below 12mmHg.

Rate of progression of glaucoma, age of patient, life expectancy of patient, presence of other risk factors necessitates lower IOP. The target pressure varies amongst patients and may need to be modified during the course of the disease, if damage to the ONH progresses despite IOP's within the desired target range.

## **TREATMENT**

A ) Intraocular pressure can be reduced either by decreasing the amount of aqueous humor produced by the ciliary body or by increasing its outflow through the trabecular meshwork, through the uveoscleral pathway, or through a surgically created pathway. Treatment is usually begun with a topical drug. If

necessary, other topical or systemic drugs are added. When drugs fail to control the intraocular pressure, laser energy applied to the trabecular meshwork (laser trabeculoplasty) may be used to increase aqueous outflow. When drugs and laser trabeculoplasty fail to control the intraocular pressure, a new route for aqueous egress can be created surgically.

**MEDICAL TREATMENT** is both, an art and a science. The goal of treatment is to preserve visual function. Lowering the IOP is only a secondary goal. It is necessary to tailor the treatment to the needs of the patient and when doing so, the following need to be kept in mind<sup>10</sup>

- A) The target tissues of topically applied ocular hypotensive medication are within the eye. Ocular conditions which can limit bio availability such as tear film deficiency, corneal scarring, chronic non-specific blepharoconjunctivitis and intra ocular inflammation may co-exist.
- B) Patient's compliance with instructions for instilling eye drops can be improved by educating patient about nature of the disease, emphasizing need for life long treatment, assessing patient's ability to instill eye drops correctly and in accordance to dosage schedule, educating patient about possible side effects, avoiding eye drops with specific side effects, using drops which affect patients daily routine minimally, can the treatment regimen maintain the desired target IOP for 24 hours in a day, is the patient amenable to follow up to assess the response to treatment, simpler the treatment regimen better the compliance, fewer side effects mean better patient compliance, topical preparations contain preservatives which may cause conjunctival inflammation and cytotoxic effects on the ocular surface. Preservative free preparations would be ideal, particularly when multiple drugs are being used. However no such drugs are available in India.

Most drugs for glaucoma are applied topically. Because of the brief contact time and the strong protective barrier of the eye, the drug solutions need to be concentrated. Excess drug drains through the nasolacrimal duct into the nose, where it may be absorbed into the systemic circulation. For example, Timolol administered to one eye enters the bloodstream in a concentration sufficient to cause a measurable decrease in intraocular pressure in the opposite eye<sup>11,12</sup>. Patients who use topical drugs should be taught to occlude the nasolacrimal duct with either digital pressure or simple eyelid closure for about five minutes, this maneuver increases intraocular drug concentrations and decreases systemic concentrations<sup>13</sup>.

There is no single accepted drug of choice in glaucoma therapy. The initial drug of choice could vary depending on the likely compliance with treatment, socioeconomic and health status of the patient, efficacy of the drug and the geographical location of the treating physician. The drug given initially to patients with most types of glaucoma is a non selective, topical beta adrenergic-antagonist drug, such as Timolol maleate (in the absence of any contraindication), because of the excellent pressure lowering efficacy, long duration of action, and few ocular side effects of this class of drugs. A second drug, if needed, might be a prostaglandin analogue (such as Latanoprost/ Bimatoprost) or an alpha 2 adrenergic agonist (Brimonidine). However the choice of the initiating drug could also be prostaglandin analogue or selective alpha 2 adrenergic agonists.

Topical carbonic anhydrase inhibitors (such as Dorzolamide) constitute the third choice. Cholinergics like Pilocarpine, have often been relegated to the last because of their ocular and visual side effects. However in the Indian context they provide effective IOP

Table 4 : Side Effects of Glaucoma Medications

Medication Class	Mechanism of Action	Efficacy	Ocular Side Effects	Systemic Side Effects	Relative Contraindications
<b>Parasympathomimetics</b> Pilocarpine HCL 1-4% Pilocarpine Nitrate 1,2, 4 %	Increased outflow through the trabecular meshwork	++(+)	Miosis, dim vision accommodative spasm, induced myopia, posterior synechiae, cataracts*, iris cysts* pseudopemphigoid*, retinal detachments	Headaches brow ache	Uveitis, neovascular glaucoma, retinal breaks, succinylcholine induced general anesthesia.
<b>Non-Selective Adrenergic Agonists</b> Dipivefrin HCl 0.1%	Increased outflow	++(+)	Hyperemia, blepharoconjunctivitis, adrenochrome deposition, mydriasis, pseudopemphigoid, cystoid macular edema, stains, soft contacts lenses	Headache, anxiety, palpitations, elevated blood pressure incidence (fewer side effects with Dipivefrin)	Aphakia, pseudophakia, narrow angles, patients using reserpine, MAO inhibitors or tricyclic, antidepressant, labile hypertension. Cardiac arrhythmias thyrotoxicosis
<b>α Adrenergic Agonists</b> Apraclonidine 0.5 , 1% Brimonidine 0.15 , 0.2%	Decreased aqueous production Increased unweoscleral outflow	++(+) ++	Toxic dermatitis, blepharoconjunctivitis, lid retraction+, conjunctival blanching+, hypotension and apnea in babies and children	Dry mouth, lethargy	Babies and young children patients using MAO inhibitors or sedatives, significant cardiac, renal hepatic, or cerebrovascular disease, Raynaud's disease, thromboangitis obliterans
<b>β Adrenergic Antagonists Selective</b> Betaxolol HCL 0.25, 0.5%  <b>Non selective</b> Timolol Maleate 0.25, 0.5% Levobunolol 0.5% Carteolol 1% Metipranolol 0.3%	Decreased aqueous production	+++ ++betaxolol	Corneal anesthesia, blepharoconjunctivitis, delayed choroidal detachments	Bronchoconstriction, bradycardia, exacerbates heart block and congestive heart failure, fatigue, malaise, depression, dizziness, impotency, memory loss (fewer side effects with betaxolol)	Asthma, chronic obstructive pulmonary disease, bradycardia second or third degree heart block, congestive heart failure brittle diabetes, thyrotoxicosis, myasthenia gravis. Use with caution in patients taking reserpine , guarmethidine quindine (Contraindications of greater concern with non-selective β-blockers)
<b>Prostaglandins</b> Latanoprost 0.005 Bimatoprost 0.03% Travoprost 0.004% Unoprostone	Increases Unweoscleral outflow	++++	Iris color change (hazel and mixed green/brown irides), conjunctival hyperemia, uveitis, cystoid, macular edema, hypertrichosis	Myalgias	
<b>CAIs</b>  <b>Oral</b> Acetazolamide 125, 250mg	Decreases aqueous production	+++	Transient myopia, delayed choroidal detachments	Metallic taste to food, malaise, depression, weight loss, anorexia, chronic diarrhea, kidney stones, stevens-Johnson syndrome, aplastic anemia, metabolic acidosis, hypokalemia, acidosis with chronic aspirin use	Sulfa allergy, Kidney stones, diabetic ketoacidosis, chronic respiratory acidosis, hypokalemia, patients using thiazide diuretics or phenytoin sodium, sickle cell anemia, hepatic disease
Topical Dorzolamide 2% Brinzolamide 1%		++(+)	Burning on instillation (dorzolamide)	Metallic taste, theoretical potential for same side effects as oral CAIs but no definitive evidence to date	Significant sulfa allergy

lowering which is cost effective. It is important to select the right candidates-aphakes and pseudophakes who are not high myopes. When therapy with a topical drug is instituted, it is to be applied to one eye, with the opposite, untreated eye used as a control. This method makes it possible to determine whether any change in intraocular pressure is due to the drug or to the normal variation of intraocular pressure. However this is usually not possible in the Indian scenario.

If there is no response, the drug should be discontinued in order to avoid unnecessary cost and side effects. If there is a substantial decrease in intraocular pressure but the pressure remains high, another drug should be added. Different classes of drug have additive effects on intraocular pressure<sup>14-17</sup>. Exceptions are nonselective beta adrenergic-antagonist drugs and nonselective adrenergic agonist drugs, which have little additive effect when given together. Cholinergic drugs and Prostaglandins with adequate spacing can be used together. It is also good to remember that multiple drops are less likely to be instilled correctly as compared to single preparations and that combination drops are more likely to be instilled correctly than drops from multiple bottles. Fixed drug combinations offer the advantage of less toxicity by preservatives and lower costs, than fixed preparations. Combination therapy with identical mechanism of action should be avoided.

Although there are numerous medications available with different modes of action, about 2/3 of patients require combination treatment. With monotherapy a 25 % reduction can be expected in the relative IOP. From combination therapy 35% and from maximal medical therapy 40% of IOP reduction from baseline.

**Maximal Medical Therapy (MMT):** When patient is on representative medication from each of the of available groups of antiglaucoma medication.

**Maximal Tolerable Medical Therapy (MTMT) :** MMT where drugs to which the patient is intolerant, have been excluded, in an effort to achieve medical control of IOP. Systemic carbonic anhydrase inhibitors may be added if the IOP remains uncontrolled with MMT or in situations where the IOP is extremely elevated. The patient's tolerance may dictate whether these medications are used for a short or long time. Because of their potential for side effects they are not used on a long term basis.

## TREATMENT OF PREGNANT AND LACTATING WOMEN

With careers gaining precedence over families, more and more people are consciously delaying having children early. As a result one is more likely to see younger women with glaucoma in the child bearing age group. Caution is suggested in while treating glaucoma in them. Literature on toxic effects of anti glaucoma medication in pregnant and lactating women is scarce and one must use his or her own judgement. A higher IOP maybe tolerated during pregnancy and lactation, rather than risk the possible adverse effects of the medication. Treatment if needed should be minimal and naso lacrimal duct obstruction should be encouraged to reduce systemic absorption. Minimising/adjusting the use of medication in lactating mothers can also be done. Drops may be used immediately after a feed to minimize the drug concentration in the milk.

## LASER TREATMENT

Most patients with POAG can be controlled by antiglaucoma medications. Alternatively, argon laser trabeculoplasty (ALT)/selective laser trabeculoplasty (SLT) provides a clinically significant reduction of IOP in approximately 75% of initial treatments<sup>18</sup>. The advantages of trabeculoplasty over medical treatment include lack of systemic adverse effects, minimal patient compliance, and decreased incidence of ocular problems that could possibly compromise subsequent surgical therapy<sup>19</sup>. Because it lacks the complications of filtering surgery, trabeculoplasty should also be considered for patients inadequately controlled on maximum medical therapy. However, it seldom reduces the number of required glaucoma medications. The AGIS noted that, in African American patients uncontrolled by medical therapy, initial treatment with ALT provided better preservation of visual function than trabeculectomy.

**Indications for ALT are:** patients who are poor candidates for conventional medical management, patients in whom a target IOP level is unlikely to be achieved with topical medications, visual field loss such that any further progression would affect the patient's quality of life, patients who have a known rate of progression, such that quality of life would suffer unless rapid IOP stabilization occurs at a target pressure level.

## SURGICAL TREATMENT

Glaucoma surgery is needed in patients who have a progressive visual field loss or optic nerve damage on MTMT. Indications for primary filtering surgery include patients who are poor candidates for conventional medical treatment, in whom the target IOP is unlikely to be achieved with topical medications alone, visual field loss is such that further progression is likely to affect the patient's quality of life, patients with rapidly progressive glaucomatous optic neuropathy where quality of life would suffer unless rapid IOP lowering occurs to the desired target level<sup>20</sup>. Filtering surgery reduces the IOP and often eliminates the need for medical treatment. Although effective in 85 to 95% of previously unoperated eyes, the potential success of the operation must be measured against the potential effect of complications on the patient's quality of life. Although long-term control is often achieved with filtering surgery, many patients will require repeat surgery or supplemental medical management, or both. Glaucoma surgery combined with cataract extraction, may be indicated in patients who require visual rehabilitation with cataract extraction, in addition to IOP lowering.

Aqueous drainage devices are generally reserved as a last resort for patients with glaucoma that is refractory to standard filtering surgery. This includes patients with extensive conjunctival scarring, chronic inflammation, and ocular trauma. IOP lowering with glaucoma drainage devices is generally not as effective as with filtering surgery. Cyclophotocoagulation is another alternative for patients with glaucoma that is refractory to other interventions and where the visual potential is poor.

B) The end result in glaucoma is irreversible damage to the optic nerve head. Since the end result is damage to the retinal ganglion cells and because factors other than IOP can be responsible extensive research in vitro and in vivo is ongoing to detect **Pharmacological interventions aimed at preventing retinal ganglion cell death (neuroprotection)**. Some of these include include :

- Prevention of initiation of apoptosis programme by brain derived neurotrophin delivery to RGC, Forskolin 6 increases level of cyclic AMP and signal transduction inducers.
- Protection of undamaged but at risk axons and ganglion cells from noxious stimuli released by proximate damage to issue or

retrograde axonal degeneration-NMDA glutamate receptor antagonists (block excitotoxicity), Calcium channel blockers (block program by which apoptosis is signaled) and active or passive immunization against myelin basic protein (MBP)

- Rescue of marginally damaged axons and RGC-antioxidants (decrease levels of oxygen radicals), Nitric Oxide synthase inhibitors and Lazaroids (which block lipid peroxidation)

Various **strategies for regeneration** of RGC axons include:

- Utilizing the ability of axons to extend into *peripheral* nerve grafts-autologous sciatic nerve or other nerve grafts, donor grafts with HLA matching, use of purified or engineered molecules from peripheral nerve to induce extension and genetically induce peripheral nerve molecules in optic nerve.
- Regulating the immune response* within the optic nerve-autologous activated macrophages to phagocytose myelin debris and active or passive immunization against myelin basic proteins.

In conclusion primary open angle glaucoma is characterized by a typically progressive glaucomatous optic neuropathy with correlating visual field loss. IOP is one of the risk factors responsible for this damage to the optic nerve. However even though factors other than IOP are involved in the pathogenesis of glaucoma, IOP is the only factor that can be modulated to date. The decision to treat is individualized depending on the whether the level of IOP will lead to progressive nerve damage. Available treatment algorithms rely on medical management to achieve the target IOP, failing which filtering surgery can be resorted to. In the Indian context, early filtering surgery to achieve the desired target pressure is a viable alternative. Laser trabeculoplasty is an intermediate step. The role of neuroprotection is not yet established clinically.

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