



Recent advances in glaucoma management

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Dear Friends
Season's Greeting !!

Glaucoma is acquired chronic progressive optic neuropathy characterized by optic nerve head changes and visual field changes which may or may not be associated with increase in intraocular pressure. Advances in glaucoma treatment are needed as available options do not appear to halt the progression of the disease. Hence, recent advances in glaucoma diagnosis and management do promise to develop therapies which are not solely dependent on lowering of intraocular pressure.

Rho kinase inhibitors is a group of guanosine triphosphatases (GTPases) enzyme which lower intra ocular pressure by reducing resistance to aqueous outflow with the help of relaxation of cells in trabecular outflow by decreasing myosin light-chain phosphorylation.^{1,2} Some of the Rho kinase inhibitors in clinical trials are: AR-12286 (Aerie pharmaceuticals), K 115 (Kowa pharmaceuticals),³ Y-39983 (also known as SNJ-1656). They can be used as an alternative to prostaglandin analogues and other drugs.

Surgical devices reduce intraocular pressure in a predictable way along with greater safety profile. The main hurdle is the cost of these implants like: *Ex-press mini shunt* is a stainless steel implant which is used under flap of sclera for controlled flow of aqueous humor post-operatively. This causes less hypotony induced surgically.^{4,6} Erosion of implant within a year of surgery is reported.⁷

Ologen™ implant is a biodegradable lyophilized implant made of porcine collagen matrix used at the end of surgery in order to provide a scaffold for growth of fibroblast. This reduces scarring of sub-conjunctival tissue. Ologen is equally as efficient as mitomycin C.⁸ Devices that aim to increase the aqueous flow from inside the eye into Schlemm's canal:

Glaukos istent is a 1 × 0.3 mm implant made of titanium for insertion into Schlemm's canal through trabecular pathway. Results are promising in cases of open angle glaucoma.⁹ *Trabectome* is an electrocautery device which is used for stripping of trabecular meshwork, thereby creating direct connection between anterior chamber and canal of Schlemm's. There is around 40 percent reduction of average intraocular pressure after surgery.¹⁰ The significant postoperative complication seen is intraoperatively blood in anterior chamber which is invariably seen in all cases.

Patients with diagnosis of secondary open-angle glaucoma respond better with this device.¹¹ Other devices facilitating flow into Schlemm's canal include. *Hydrus implant* (a nickel titanium implant designed for insertion into Schlemm's canal) and Stegmann canal expander (a tube with fenestrations is used for insertion into Schlemm's canal). Both of the above implants are still under clinical trials. One more device like *CyPass micro-shunt* (a 6 mm tubular shunt) is inserted into the suprachoroidal space. Hence it enhances uveoscleral outflow. It is also undergoing a clinical trial.¹²

Production of aqueous humor can also be suppressed transcleral cyclophotocoagulation.¹³ Newer modalities have been devised which include: *EyeOPI*: This device delivers external ultrasound energy in order to destroy a part of ciliary body which is prime source for production of intraocular aqueous humor. As ciliary body is destroyed production of aqueous comes to a halt.¹⁴

Neuroprotection, Neuromodulation and Neuro-recovery: Glaucoma is a neurodegenerative condition comprised of Retinal Ganglion Cell apoptosis. Different strategies are in pipeline in order to prevent RGC apoptosis i.e. neuroprotection, or to retard RGC apoptosis i.e. neuro-modulation or reverse the process of apoptosis i.e. neuro-recovery There are numerous pathways that aid in apoptosis of retinal ganglion cells.^{15,16} The pathways though complex do provide an opportunity for pharmacotherapeutic development. Brimonidine has been shown to exert neuro-protective benefit apart from its IOP lowering capabilities.¹⁷ Another new drug in neuro-protection group is memantine. This compound is an N-methyl-D-aspartate (NMDA) receptor antagonist and has proven its efficacy in animal models.^{18,19}

Apoptosis of retinal ganglion cells can also be achieved by drugs that interfere with the glutamate excitotoxic cascade including calcium channel blockers and inhibitors of glutamate release.¹⁸ Brimonidine also belongs to this group. Other medicines include those interfere with interaction of growth factors with Retinal ganglion cells like TNF-alpha blockers, nicotinamide that supplies and increase energy supply to retinal ganglion cells and those with neurotrophic properties like BDNF, NGF.¹⁸ Very little is known about their efficacy and safety profile.

There has been a lot of research in therapies of glaucoma and many new researches and ideas are in

pipeline. More advances is awaited regarding early detection, efficacious treatments and neuroprotection.

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How to cite this article: Maurya RP. Recent advances in glaucoma management. *Indian J Clin Exp Ophthalmol* 2019;5(2):140-1.