International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 10 (1): January-February- 2020

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences **Review Article……!!!**

Received: 05-12-2019; Revised: 25-12-2019; Accepted: 01-01-2020

GLAUCOMA AND ITS TREATMENT: A REVIEW ARTICLE

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Keywords:

Intraocular pressure, Open angle glaucoma, Ttrabeculectomy, Blindness.

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ABSTRACT

Glaucoma is the second highest cause of blindness worldwide with an estimated half of the glaucoma populations unaware of their disease. Glaucoma is a neurodegenerative disorder of the eye. It is a condition characterized by increased intraocular pressure more than 21 mm Hg resulting in optic nerve damage. When damage to the optic nerve fibers occurs, blind spots usually go undetected until optic nerve is significantly damaged. Leading cause of blindness especially in older people. Increased intraocular pressure (IOP) and subsequent retinal ganglion cell (RGC) death leading to loss of visual field characterizes the pathology of primary open angle glaucoma which is the most common form. Current treatment options for glaucoma are Laser surgery, Trabeculectomy. Glaucoma is a group of eye diseases which result in damage to the optic and vision loss. The most common type is open-angle glaucoma with less common types including closed-angle glaucoma and normal-tension glaucoma. Open-angle glaucoma develops slowly over time and there is no pain. Side vision may begin to decrease followed by central vision resulting in blindness if not treated. Closed-angle glaucoma can present gradually or suddenly. The sudden presentation may involve severe eye pain, blurred vision, mid-dilated pupil, redness of the eye, and nausea. Vision loss from glaucoma, once it has occurred, is permanent. Risk factors for glaucoma include increased pressure in the eye, a family history of the condition, migraines, high blood pressure, and obesity.

INTRODUCTION

Types of glaucoma:

Glaucoma has been classified into specific types:

1. Primary glaucoma and its variants

1. Primary open-angle glaucoma, also known as chronic open-angle glaucoma, chronic simple glaucoma, glaucoma simplex

High-tension glaucoma

Low-tension glaucoma

Primary angle closure glaucoma, also known as primary closed-angle glaucoma, narrow-angle glaucoma, pupil-block glaucoma, acute congestive glaucoma

Acute angle closure glaucoma (*aka* AACG)

Intermittent angle closure glaucoma

Superimposed on chronic open-angle closure glaucoma ("combined mechanism" – uncommon)

Variants of primary glaucoma

Pigmentary glaucoma

Exfoliation glaucoma, also known as pseudoexfoliative glaucoma or glaucoma capsular

Primary juvenile glaucoma

Primary angle closure glaucoma is caused by contact between the iris and trabecular meshwork, which in turn obstructs outflow of the aqueous humor from the eye. This contact between iris and trabecular meshwork (TM) may gradually damage the function of the meshwork until it fails to keep pace with aqueous production, and the pressure rises. In over half of all cases, prolonged contact between iris and TM causes the formation of synechiae (effectively "scars").

These cause permanent obstruction of aqueous outflow. In some cases, pressure may rapidly build up in the eye, causing pain and redness (symptomatic or so-called "acute" angle closure). In this situation, the vision may become blurred, and halos may be seen around bright lights. Accompanying symptoms may include a headache and vomiting.

Diagnosis is made from physical signs and symptoms: pupils mid-dilated and unresponsive to light, cornea edematous (cloudy), reduced vision, redness, and pain. However, the majority of cases are asymptomatic. Prior to the very severe loss of vision, these cases can only be identified by examination, generally by an eye care professional.

Once any symptoms have been controlled, the first line (and often definitive) treatment is laser iridotomy. This may be performed using either Nd: YAG or argon lasers, or in some cases by conventional incisional surgery. The goal of treatment is to reverse and prevent, contact between the iris and trabecular meshwork. In early to moderately advanced cases, iridotomy is successful in opening the angle in around 75% of cases. In the other 25%, laser iridoplasty, medication (pilocarpine) or incisional surgery may be required.

Primary open-angle glaucoma is when optic nerve damage results in a progressive loss of the visual field. This is associated with increased pressure in the eye. Not all people with primary open-angle glaucoma have eye pressure that is elevated beyond normal, but decreasing the eye pressure further has been shown to stop progression even in these cases.

The increased pressure is caused by trabecular blockage. Because the microscopic passageways are blocked, the pressure builds up in the eye and causes imperceptible very gradual vision loss. Peripheral vision is affected first, but eventually the entire vision will be lost if not treated.

Diagnosis is made by looking for cupping of the optic nerve. Prostaglandin agonists work by opening uveoscleral passageways. Beta-blockers, such as timolol, work by decreasing aqueous formation. Carbonic anhydrase inhibitors decrease bicarbonate formation from ciliary processes in the eye, thus decreasing the formation of Aqueous humor. Parasympathetic analogs are drugs that work on the trabecular outflow by opening up the passageway and constricting the pupil. Alpha 2 agonists (brimonidine, apraclonidine) both decrease fluid production (via. Inhibition of AC) and increase drainage.

2.Developmental glaucoma

Primary congenital glaucoma

Infantile glaucoma

Glaucoma associated with hereditary or familial diseases

3. Secondary glaucoma

Inflammatory glaucoma

Uveitis of all types

Fuchs heterochromic iridocyclitis

Phacogenic glaucoma

Angle-closure glaucoma with mature cataract

Phacoanaphylactic glaucoma secondary to rupture of lens capsule

Phacolytic glaucoma due to phacotoxic meshwork blockage

Subluxation of lens

Glaucoma secondary to intraocular hemorrhage

Hyphema

Hemolytic glaucoma, also known as erythroclastic glaucoma

Traumatic glaucoma

Angle recession glaucoma: Traumatic recession on anterior chamber angle

Postsurgical glaucoma

Aphetic pupillary block

Ciliary block glaucoma

Neovascular glaucoma

Drug-induced glaucoma

Corticosteroid induced glaucoma

Alpha-chymotrypsin glaucoma. Postoperative ocular hypertension from use of alpha chymotrypsin.

Glaucoma of miscellaneous origin

Associated with intraocular tumors

Associated with retinal detachments

Secondary to severe chemical burns of the eye

Associated with essential iris atrophy

Toxic glaucoma

4. Neovascular glaucoma, an uncommon type of glaucoma, is difficult or nearly impossible to treat, and is often caused by proliferative diabetic retinopathy (PDR) or central retinal vein occlusion (CRVO). It may also be triggered by other conditions that result in ischemia of the retina or ciliary body. Individuals with poor blood flow to the eye are highly at risk for this condition.

Neovascular glaucoma results when new, abnormal vessels begin developing in the angle of the eye that begins blocking the drainage. Patients with such condition begin to rapidly lose their eyesight. So medications known as anti-VEGF agents. These injectable medications can lead to a dramatic decrease in new vessel formation and, if injected early enough in the disease process, may lead to normalization of intraocular pressure. Currently, there are no

high-quality controlled trials demonstrating a beneficial effect of anti-VEGF treatments in lowering IOP in people with neovascular glaucoma.

5. Toxic glaucoma is open angle glaucoma with an unexplained significant rise of intraocular pressure following unknown pathogenesis. Intraocular pressure can sometimes reach 80 mmhg (11 kpa). It characteristically manifests as body inflammation and massive trabecular oedema that sometimes extends to Schlemm's canal. This condition is differentiated from malignant glaucoma by the presence of a deep and clear anterior chamber and a lack of aqueous misdirection. Also, the corneal appearance is not as hazy. A reduction in visual acuity can occurred followed neuroretinal breakdown.

Associated factors include inflammation, drugs, trauma and intraocular surgery, including cataract surgery and vitrectomy procedures. Gede Pardianto (2005) reported on four patients who had toxic glaucoma. One of them underwent phacoemulsification with small particle nucleus drops. Some cases can be resolved with some medication, vitrectomy procedures or trabeculectomy. Valving procedures can give some relief, but further research is required.

6. Absolute glaucoma

Absolute glaucoma is the end stage of all types of glaucoma. The eye has no vision, absence of pupillary light reflexand pupillary response, and has a stony appearance. Severe pain is present in the eye. The treatment of absolute glaucoma is a destructive procedure like cyclocryo application, cyclophoto coagulation, or injection of 99% alcohol.

Types of glaucoma

Open angle glaucoma or Wide angle glaucoma or chronic simple glaucoma:

In this type, there is narrowing of anterior chamber angle that causes decrease in the rate of aqueous outflow and increase in intraocular pressure.It can be considered as a degenerative disease that causes loss of trabecular meshwork. It results in gradual loss of pheripheral vision.

Closed angle glaucoma or Narrow angle glaucoma or Acute Congestive glaucoma:

In this type, there is increase in pressure exerted by posterior chamber that moves iris forward thereby closing the ocular angle and preventing the drainage of aqueous humor.it is an emergency situation characterized by sudden rise in intraocular tension to very high values (40-60mmhg).

Symptoms and Signs:

1. Photophobia

2. Lacrimation
3. Blepharospasm
4. Enlarged eyeball
5. Minimal blurring of vision
6. Mild headache, ocular pain
7. Corneal edema, corneal enlargement more than13 mm diameters
8. Sclera become thin and appears blue

Pathophysiology

The underlying cause of open-angle glaucoma remains unclear. Several theories exist on its exact etiology. However, the major risk factor for most glaucomas and the focus of treatment is increased intraocular pressure. Intraocular pressure is a function of production of liquid aqueous humor by the ciliary processes of the eye, and its drainage through the trabecular meshwork. Aqueous humor flows from the ciliary processes into the posterior chamber, bounded posteriorly by the lens and the zonules of Zinn, and anteriorly by the iris. It then flows through the pupil of the iris into the anterior chamber, bounded posteriorly by the iris and anteriorly by the cornea. From here, the trabecular meshwork drains aqueous humor via the scleral venous sinus (Schlemm's canal) into scleral plexuses and general blood circulation. In open/wide-angle glaucoma, flow is reduced through the trabecular meshwork, due to the degeneration and obstruction of the trabecular meshwork, whose original function is to absorb the aqueous humor. Loss of aqueous humor absorption leads to increased resistance and thus a chronic, painless buildup of pressure in the eye.In close/narrow-angle, the iridocorneal angle is completely closed because of forward displacement of the final roll and root of the iris against the cornea, resulting in the inability of the aqueous fluid to flow from the posterior to the anterior chamber and then out of the trabecular network. This accumulation of aqueous humor causes an acute increase in pressure and pain.

The inconsistent relationship of glaucomatous optic neuropathy with increased intraocular pressure has provoked hypotheses and studies on an atomic structure, eye development, nerve compression trauma, optic nerve blood flow, excitatory neurotransmitter, tropic factor, retinal ganglion cell/axon degeneration, and glial support cell, immune system, aging mechanisms of neuron loss, and severing of the nerve fibers at the sclera edge. Although the pathogenesis of glaucoma is not fully understood, the level of intraocular pressure is related to retinal ganglion cell death. The balance between secretion of aqueous humor by the ciliary

body and its drainage through 2 independent pathways determines the intraocular pressure. In patients with open angle glaucoma, there is increased outflow through the trabecular meshwork. In contrast, the access to the drainage pathways is obstructed typically by there is in patients with angle closure glaucoma. Intraocular pressures can mechanical stress and strain on the posterior structures of the eye, notably the lamina cribrosa and adjacent tissues. Glaucomatous optic neuropathy can occur in individuals with intraocular pressures within the normal range. Impaired microcirculation, altered immunity, exciyotoxicity, and oxidative stress may also cause glaucoma. Primary neural pathological processes may cause secondary neurodegeneration of other retinal neurons and cells in the central visual pathway by altering their environment and increasing susceptibility to damage.

The increased pressure causes compression of the retina and the optic nerve and causes progressive, permanent loss of eyesight if left untreated.

Diagnosis:

1. Tonometry: Tonometry is often used as a diagnostic tool.
2. The tonometer is gently pressed against the eyeball and the resistance (internal pressure) is measured. This requires that the eye be numbed prior to the test.
3. Gonioscopy: it can be used to determine if the angle where the iris meets the cornea is open or closed.
4. Perimetry: it is an essential method used to determine if there is any loss of visual field.
5. Slit Lamp Examination: it is another method of diagnosis of patients with suspected glaucoma.
6. Stereo Disc Photography: of the optic disc is performed to determine if there is abnormal cupping in the nerve head.

Latest Treatment of Glaucoma:

Measurement of Treatment

The modern goals of glaucoma management are to avoid glaucomatous damage and nerve damage, and preserve visual field and total quality of life for patients, with minimal side effects. This requires appropriate diagnostic techniques and follow-up examinations, and judicious selection of treatments for the individual patient. Although intraocular pressure is only one of the major risk factors for glaucoma, lowering it via various pharmaceuticals and/or surgical techniques is currently the mainstay of glaucoma treatment.

Vascular flow and neurodegenerative theories of glaucomatous optic neuropathy have prompted studies on various neuroprotective therapeutic strategies, including nutritional compounds, some of which may be regarded by clinicians as safe for use now, while others are on trial.

Medication

Latanoprost

Intraocular pressure can be lowered with medication, usually eye drops. Several classes of medications are used to treat glaucoma, with several medications in each class.

Each of these medicines may have local and systemic side effects. Adherence to medication protocol can be confusing and expensive; if side effects occur, the patient must be willing either to tolerate them or to communicate with the treating physician to improve the drug regimen. Initially, glaucoma drops may reasonably be started in either one or in both eyes.Poor compliance with medications and follow-up visits is a major reason for vision loss in glaucoma patients. A 2003 study of patients in an HMO found half failed to fill their prescriptions the first time, and one-fourth failed to refill their prescriptions a second time. Patient education and communication must be ongoing to sustain successful treatment plans for this lifelong disease with no early symptoms.

The possible neuroprotective effects of various topical and systemic medications are also being investigated.

Prostaglandin analogs, such as latanoprost, bimatoprost and travoprost, increase uveoscleral outflow of aqueous humor. Bimatoprost also increases trabecular outflow.

Topical beta-adrenergic receptor antagonists, such as timolol, levobunolol, and betaxolol, decrease aqueous humor production by the epithelium of the ciliary body.

Alpha2-adrenergic agonists, such as brimonidine and apraclonidine, work by a dual mechanism, decreasing aqueous humor production and increasing uveoscleral outflow.

Less-selective alpha agonists, such as epinephrine, decrease aqueous humor production through vasoconstriction of ciliary body blood vessels, useful only in open-angle glaucoma. Epinephrine's mydriatic effect, however, renders it unsuitable for closed-angle glaucoma due to further narrowing of the uveoscleral outflow (i.e. Further closure of trabecular meshwork, which is responsible for absorption of aqueous humor).

Miotic agents (parasympathomimetics), such as pilocarpine, work by contraction of the ciliary muscle, opening thetrabecular meshwork and allowing increased outflow of the

aqueous humor. Echothiophate, an acetyl cholinesterase inhibitor, is used in chronic glaucoma.

Carbonic anhydrase inhibitors, such as dorzolamide, brinzolamide, and acetazolamide, lower secretion of aqueous humor by inhibiting carbonic anhydrase in the ciliary body.

Laser

Argon laser trabeculoplasty (ALT) may be used to treat open-angle glaucoma, but this is a temporary solution, not a cure. A 50-µm argon laser spot is aimed at the trabecular meshwork to stimulate the opening of the mesh to allow more outflow of aqueous fluid. Usually, half of the angle is treated at a time. Traditional laser trabeculoplasty uses a thermal argon laser in an argon laser trabeculoplasty procedure.

A newer type of laser trabeculoplasty uses a "cold" (nonthermal) laser to stimulate drainage in the trabecular meshwork. This newer procedure, selective laser trabeculoplasty (SLT), uses a 532-nm, frequency-doubled, Q-switched Nd: YAG laser, which selectively targets melanin pigment in the trabecular meshwork cells. Studies show SLT is as effective as ALT at lowering eye pressure. In addition, SLT may be repeated three to four times, whereas ALT can usually be repeated only once.

Nd:YAG laser peripheral iridotomy (LPI) may be used in patients susceptible to or affected by angle closure glaucoma or pigment. During laser iridotomy, laser energy is used to make a small, full-thickness opening in the iris to equalize the pressure between the front and back of the iris, thus correcting any abnormal bulging of the iris. In people with narrow angles, this can uncover the trabecular meshwork. In some cases of intermittent or short-term angle closure, this may lower the eye pressure. Laser iridotomy reduces the risk of developing an attack of acute angle closure. In most cases, it also reduces the risk of developing chronic angle closure or of adhesions of the iris to the trabecular meshwork.

Surgery: Diode laser cycloablation lowers IOP by reducing aqueous secretion by destroying secretory ciliary epithelium.

Conventional surgery to treat glaucoma makes a new opening in the trabecular meshwork, which helps fluid to leave the eye and lowers intraocular pressure.

Glaucoma surgery

Both laser and conventional surgeries are performed to treat glaucoma. Surgery is the primary therapy for those with congenital glaucoma. Generally, these operations are a temporary solution, as there is not yet a cure for glaucoma.

Canaloplasty

Canaloplasty is a nonpenetrating procedure using micro catheter technology. To perform a canaloplasty, an incision is made into the eye to gain access to the Schlemm's canal in a similar fashion to a viscocanalostomy. A micro catheter will circumnavigate the canal around the iris, enlarging the main drainage channel and its smaller collector channels through the injection of a sterile, gel-like material called viscoelastic. The catheter is then removed and a suture is placed within the canal and tightened.

By opening the canal, the pressure inside the eye may be relieved, although the reason is unclear, since the canal (of Schlemm's) does not have any significant fluid resistance in glaucoma or healthy eyes. Long-term results are not available.

Trabeculectomy

The most common conventional surgery performed for glaucoma is the trabeculectomy. Here, a partial thickness flap is made in the scleral wall of the eye, and a window opening is made under the flap to remove a portion of the trabecular meshwork. The scleral flap is then sutured loosely back in place to allow fluid to flow out of the eye through this opening, resulting in lowered intraocular pressure and the formation of a bleb or fluid bubble on the surface of the eye.

Scarring can occur around or over the flap opening, causing it to become less effective or lose effectiveness altogether. Traditionally, chemotherapeutic adjutants, such as mitomycin C (MMC) or 5-fluorouracil (5-FU), are applied with soaked sponges on the wound bed to prevent filtering blebs from scarring by inhibiting fibroblast proliferation. Contemporary alternatives to prevent the scarring of the meshwork opening include the sole or combinative implementation of no chemotherapeutic adjuvant such as the ologen collagen matrix, which has been clinically shown to increase the success rates of surgical treatment.

Collagen matrix prevents scarring by randomizing and modulating fibroblast proliferation in addition to mechanically preventing wound contraction and adhesion.

Glaucoma drainage implants

Professor Anthony Molteno developed the first glaucoma drainage implant, in Cape Town in 1966. Since then, several types of implants have followed on from the original, the Baerveldt tube shunt, or the valved implants, such as the Ahmed glaucoma valve implant or the express Mini Shunt and the later generation pressure ridge Molteno implants. These are indicated for glaucoma patients not responding to maximal medical therapy, with previous failed guarded

filtering surgery (trabeculectomy). The flow tube is inserted into the anterior chamber of the eye, and the plate is implanted underneath the conjunctiva to allow a flow of aqueous fluid out of the eye into a chamber called a bleb.

The first-generation Molteno and other non valved implants sometimes require the ligation of the tube until the bleb formed is mildly fibrosed and water-tight. This is done to reduce postoperative hypotony—sudden drops in postoperative intraocular pressure.

Valved implants, such as the Ahmed glaucoma valve, attempt to control postoperative hypotony by using a mechanical valve.

Ab interno implants, such as the Xen Gel Stent, are transscleral implants by an ab interno procedure to channel aqueous humor into the non-dissected Tenon's space, creating a subconjunctival drainage area similar to a bleb. The implants are transscleral and different from more other ab interno implants that do not create a transscleral drainage, such as, cypass, or Hydrus.

The ongoing scarring over the conjunctival dissipation segment of the shunt may become too thick for the aqueous humor to filter through. This may require preventive measures using antifibrotic medications, such as 5-fluorouracil or mitomycin-C(during the procedure), or other nonantifibrotic medication methods, such as collagen matrix implant, or biodegradable spacer, or later on create a necessity for revision surgery with the sole or combinative use of donor patch grafts or collagen matrix implant. And for glaucomatous painful blind eye and some cases of glaucoma, cyclocryotherapy for ciliary body ablation could be considered to be performed.

Laser-assisted non penetrating deep sclerectomy

The most common surgical approach currently used for the treatment of glaucoma is trabeculectomy, in which the sclera is punctured to alleviate intraocular pressure.

Non penetrating deep sclerectomy (NPDS) surgery is a similar, but modified, procedure, in which instead of puncturing the scleral bed and trabecular meshwork under a scleral flap, a second deep scleral flap is created, excised, with further procedures of deroofing the Schlemm's canal, upon which, percolation of liquid from the inner eye is achieved and thus alleviating intraocular pressure, without penetrating the eye. NPDS is demonstrated to cause significantly fewer side effects than trabeculectomy. However, NPDS is performed manually and requires higher level of skills that may be assisted with instruments. In order to prevent wound adhesion after deep scleral excision and to maintain good filtering results,

NPDS as with other non-penetrating procedures is sometimes performed with a variety of biocompatible spacer or devices, such as the Aqua flow collagen wick, ologen Collagen Matrix, or Xenoplast glaucoma implant.

Laser-assisted NPDS is performed with the use of a CO_2 laser system. The laser-based system is self-terminating once the required scleral thickness and adequate drainage of the intraocular fluid have been achieved. This self-regulation effect is achieved as the CO_2 laser essentially stops ablating as soon as it comes in contact with the intraocular percolated liquid, which occurs as soon as the laser reaches the optimal residual intact layer thickness.

Both internationally and in the United States glaucoma is the second-leading cause of blindness. Globally cataracts are a more common cause. Glaucoma is also the leading cause of blindness in African Americans, who have higher rates of primary open angle glaucoma. Bilateral vision loss can negatively affect mobility and interfere with driving.

A meta-analysis published in 2009 found that people with primary open angle glaucoma do *not* have increased mortality rates, or increased risk of cardiovascular death.

Retinal nerve fiber layer thickness with the stratus OCT is the most recent advancement in technology that aids in diagnosis of glaucoma.

2. Laser Trabeculoplasty: It is a form of laser intraocular pressure in glaucoma. It is used when eye drop medications are not lowering the eye pressure enough or are causing significant side effects. It may sometimes be used as initial treatment in glaucoma.

3. Trabeculectomy (filtration surgery): in this surgery a piece of tissue in the drainage angle of the eye is removed creating an opening. The opening is partially covered with a flap of tissue from the sclera, the white part of the eye, and the conjunctiva, the clear thin covering over the sclera. This new opening allows fluid, aqueous humor to drain out of the eye by passing the clogged drainage channels of the trabecular meshwork. As the fluid flows through the new drainage opening, the tissue over the opening rises to form a little blister or bubble called a bleb. The bleb is located where the sclera, or white of the eye. During office visits after surgery, the doctor looks at the bleb to make sure that fluid is still draining out of the new opening. Not all blebs have to be easily seen to work.

4.Diaton Tonometer: The newest advancement, in tonometry is Diaton tonometer.It measures intraocular pressure through the eyelid.Diaton requires no contact with cornea no anesthetic drops,no risk of infecting.Diaton tonometer is intended for use by inpatient and outpatient clinics such as Hospitals, Emergency rooms, Nursing and elderly homes.

5. Beta- blockers: used in a variety of glaucoma eye drops, beta-blockers were at one time the drugs of first choice in treating glaucoma. These drugs work by decreasing fluid production in the adjunct to or in combination with prostaglandins. Beta blockers used in glaucoma treatment are Tim optic XE (Merck), Istalol (ISTA) and Betoptic S (Alcon).

Timolol maleate (0.25, 0.5%)

Levobunolol(0.25, 0.5%)

CONCLUSION: Glaucoma is a common neurodegenerative disorder characterized by loss of RGC, ultimately leading to reduction of the visual field and potential blindness. All current research is geared towards treatment options, the possibility of RGC regeneration should be explored to search for glaucoma.

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