

A Detailed Study of Glaucoma in Adults, Its Pathogenesis, Diagnosis and Management

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ABSTRACT

As the second most prevalent cause of blindness in the world, after cataracts, glaucoma diagnosis and treatment are crucial topics for general physicians to know. Glaucomas can often be categorised based on three key factors: the extent to which the anterior chamber angle is open or closed, the intensity of the onset (acute or chronic), and the underlying cause (primary or secondary). Most cases of glaucoma are primary, indicating the absence of any comorbidities. Nevertheless, secondary glaucomas may arise from a range of visual illnesses as their root cause. Individuals who are susceptible to developing chronic glaucoma should undergo regular eye examinations in order to detect the condition at an early stage and prevent the progressive deterioration of vision that may occur prior to diagnosis. Glaucoma leads to impairments in both central and peripheral vision fields due to damage to the optic nerve and the retinal nerve fibre layer. All current treatments, including drugs, lasers, and procedures, aim to reduce intraocular pressure (IOP) because it is the only factor that can be changed and is crucial in the progression of the condition. Pharmacotherapy is the usual first-line treatment, although its effectiveness is constrained by noncompliance, adverse effects, and cost. While laser and surgical methods offer the ability to effectively lower intraocular pressure (IOP) for extended periods and at a lower cost compared to medicine, they come with increased risks during the process and a higher likelihood of treatment not being successful. Various modern minimally invasive glaucoma operations have replaced conventional incisional therapies because they offer improved safety and reduced efficacy decreases. While the long-term success of minimally invasive glaucoma surgeries still needs to be determined by large-scale randomised trials, these methods have greatly transformed the surgical treatment of glaucoma.

Keywords- Glaucoma, Pathogenesis, Diagnosis, Management.

I. INTRODUCTION

Glaucoma is a progressive visual neuropathy that causes the cupping of the optic disc and the loss of

retinal ganglion cells[1]. This is one definition of glaucoma. There are currently 3.5% of persons between the ages of 40 and 80 who are affected by the condition, making it the leading cause of permanent blindness

across the entire world. Glaucoma is on the rise in countries with low incomes, where resources are scarce, and it is anticipated that it will affect 112 million people by the year 2040[2]. Although early discovery can slow down the progression of the condition, a timely diagnosis is sometimes delayed due to the fact that visual field loss is frequently asymptomatic until the later stages of the disease. This is despite the fact that early detection can slow down the advancement of the condition. Glaucoma is typically brought on by a number of factors, including elevated intraocular pressure (IOP), being of a non-Caucasian ethnicity, being of an advanced age, and having a positive family history[3]. Glaucoma is a chronic disorder that affects the majority of individuals, and treatment for it helps those who have it[4].

Aqueous humour is expelled from the eye through the semiporous trabecular meshwork (TM) located in the iridocorneal angle of the anterior chamber. This occurs after the aqueous humour has travelled through the pupil, the posterior chamber, the lens, and the remaining components of the eye anatomy[5]. Following the passage of aqueous humour into the Schlemm canal, which is a circumferential vascular collection duct, distal collector channels are discharged into the episcleral venous system. The aqueous humour does not drain sufficiently when the angle is blocked or when there is more resistance through the meshwork. This results in an increased intraocular pressure (IOP), which ultimately leads to glaucoma[6]. There is a correlation between elevated intraocular pressure (IOP) and the loss of retinal ganglion cells, which is a characteristic feature of a progressive and irreversible ocular neuropathy. Patients are regarded to have ocular hypertension if they do not exhibit any additional symptoms of glaucoma and have a normal intraocular pressure (IOP). On the other hand, patients who have an expanded optic disc but have a normal IOP are considered to be suspects of glaucoma. Even though there is a large body of research that describes the risk factors and the aetiology of glaucoma, there is still a lack of comprehensive understanding of the biological foundation of the disease[7]. The vascular and biomechanical hypotheses of glaucoma state that ganglion cells are subject to death when the intraocular pressure (IOP) is excessively high, which in turn causes damage to the optic nerve head (ONH)[8] According to the vascular hypothesis, hypoxia and ischemic damage to the oncogene on the head (ONH) are caused by decreased perfusion pressure. On the other hand, the biomechanical theory proposes that abnormally small scleral fenestrations at the ONH are the cause of these harmful effects. The intraocular pressure (IOP) is considered to be normal in one-third of instances of normal tension glaucoma, despite the fact that it plays a part in both versions of the glaucoma theory[9].

Since neurodegeneration has been connected to Alzheimer's disease and cognitive decline, it is possible

that it plays a role in the pathophysiology of glaucoma. High intraocular pressure (IOP) is the sole risk factor that can be controlled and consistently contributes to the advancement of the illness. This is true regardless of the numerous pathogenetic theories[10].

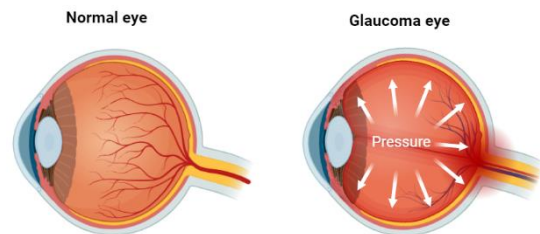


Fig 1: Normal eye vs Glaucoma eye

The goal of treatment for glaucoma is to lower intraocular pressure (IOP) by employing various methods, including laser techniques, medications, and/or surgical procedures. Typically, pharmacotherapy is the initial line of defence, and laser and surgical procedures are added for eyes that have inadequate first reactions in order to further reduce intraocular pressure (IOP). Incisional procedures that reroute the flow of aqueous humour beyond the damaged angle and into the subconjunctival area, so forming a filtration bleb, include filtration techniques such as trabeculectomy and tube shunt implantation[11]. These are examples of incisional surgeries.

Traditional incisional techniques are associated with a considerable risk of complications including as endophthalmitis, scar tissue proliferation, and conjunctival haemorrhage. Despite the fact that these operations are beneficial in lowering intraocular pressure (IOP), they are also associated with those consequences[12]. Because of the fading impact of the intraocular pressure-lowering surgery, the reoperation rates after five years are significant (15.1% for trabeculectomy, 14.0% for tube shunt implantation, and 18.3% for EX-PRESS shunt). As a result of the high reoperation rates, it is required to perform procedures that strengthen the typical aqueous outflow while protecting the conjunctiva from being manipulated during surgical procedures[13].

As a consequence of this, a number of MIGSs, which are minimally invasive glaucoma operations, have been developed for the treatment of POAG. These surgeries prevent damage to the conjunctiva[14]. In spite of the fact that minimally invasive glaucoma procedures are not as efficient as standard filtration treatments in terms of lowering intraocular pressure (IOP), they are quite safe[15].

II. PATHOPHYSIOLOGY

Signals are transmitted from the photoreceptors to the neurons of the central nervous system. The neurons then process the signals and transmit them to

other parts of the brain through the optic nerve through the process of transmission. Ganglion cell nuclei in the retina are responsible for sending their axons to the optic disc[16]. These axons then travel through the optic disc in a manner similar to that of a sieve alongside the retinal arteries. A structure made of collagen is known as the lamina cribrosa. The axons of the optic nerve are wrapped in myelin, and the optic nerve continues behind the lamina cribrosa[17]. The impairment of axonal transport in optic nerve fibres, as well as structural changes and remodelling of the lamina cribrosa, are all consequences of papillary hypoperfusion. Papillary hypoperfusion is caused by an increase in the gradient across the lamina cribrosa, which is caused by low perfusion pressure, low cerebrospinal fluid pressure, and/or elevated intraocular pressure. To be more specific, open-angle glaucoma is distinguished by the presence of larger holes in the anterior lamina cribrosa region[18].

Vision gradually deteriorates as more and more retinal ganglion cells are lost, beginning in the center-periphery and spreading outward until only a tiny portion of the field is unimpaired. This process begins in the center-periphery and continues until only a small portion of the field is unimpaired. Additional functional deficits include difficulties in reading, as well as issues in perceiving colours and contrasts. Exactly how retinal ganglion cells are eliminated from the retina is still a mystery to us[19]. The classification of the various types of glaucoma is determined by the structural changes that occur in the anterior area of the eye. There is some drainage through the ciliary body and uveoscleral outflow (the root of the iris), but the predominant location of drainage for aqueous humour is the chamber angle[20].

There is a connection between the iris and the posterior surface of the cornea, as well as the canal of Schlemm, which is located at the end of the chamber angle, which is situated beneath the trabecular meshwork. An abrupt obstruction of the outflow of aqueous humour through the trabecular meshwork and the canal of Schlemm results in a significant increase in intraocular pressure[21]. This is in contrast to open-angle glaucoma, which occurs when the chamber angle is macroscopically open. Acute angle closure is the disease that describes this situation. Alterations in the chamber angle, which may be observed with a gonioscope, have the potential to result in an escalated intraocular pressure in patients with secondary open-angle glaucoma[22]. Within the context of pigmentary glaucoma, these alterations may take the form of pigment deposition, while in pseudoexfoliation glaucoma, they may be protein deposition. There is currently a lack of understanding regarding the factors that lead to patients with primary open-angle glaucoma having high intraocular pressure[23].

In healthy persons, the normal intraocular pressure demonstrates significant variation between

chronobiology and individuals, with an average value of 15.7 mm Hg. This is the case even in healthy individuals. It is controlled by ensuring that there is a continuous flow of aqueous humour moving out of the ciliary body[24]. Therefore, an increase in the outflow resistance could potentially result in an increase in the intraocular pressure. This could take place as a consequence of gonioscopically discernible changes in the chamber angle, as is the case with secondary open-angle glaucoma; alternatively, it could not take place at all, as is the case with open-angle glaucoma that was there from the beginning. In spite of the fact that the intraocular pressure is typically within normal levels, normal-pressure glaucoma can nonetheless develop and lead to glaucomatous changes in the optic nerve[25]. It is true that the prevalence of glaucoma varies from region to region; nonetheless, the intraocular pressure is normal in thirty percent of people who are of European descent. It would suggest that the underlying cause of this problem is an intraocular pressure that is within the normal range but is nevertheless higher than the pressure sensitivity of the optic disc[26]. The significance of the optic disc's sensitivity to pressure is further shown by the fact that a reduction in pressure of twenty-five percent lowers the risk of glaucoma progression by fifty percent[27]. It appears that vascular changes are involved in the aetiology of open-angle glaucoma, and more specifically, normal-pressure glaucoma. For instance, a person who has normal blood pressure may experience an abnormally significant drop in blood pressure throughout the night[28].

III. DIAGNOSIS

Symptoms of Glaucoma

Ocular pain that spreads, impaired vision, reddening of the conjunctiva, and occasionally vomiting and nausea accompanied by a hard, inflexible globe are all symptoms that are associated with acute angle closure[29]. An emergency that requires immediate medical intervention in order to prevent irreversible vision loss is referred to as a "ophthalmological" emergency. The majority of persons who have advanced open angle disease are unaware that they have the condition because the disease usually does not present any symptoms at that stage[30].

It is estimated that approximately one third of individuals who are diagnosed with this syndrome already have it in one eye at a late or advanced stage when they are diagnosed. It was discovered by Gramer and colleagues that ten to twenty percent of patients already possessed binocular visual field deficits, which precluded them from obtaining a car at the clinic when they presented themselves[31].

Early detection of Glaucoma

Until the disease has reached that stage, it does not become sympathomimetic until it has completed its progression. According to the German Ophthalmological

Association, patients should begin receiving screenings on a regular basis around the age of 40 in order to discover eye disorders at an earlier stage[32]. As a result of the low prevalence of the disorder as well as the low sensitivity and specificity (e_1 and e_2) of the test, there is a significant percentage of false positives (more than 65 percent, and significantly greater in younger individuals), and more testing needs to be carried out following any positive discovery. Regular checkups are especially crucial for people who are at risk for developing diseases since they allow for the early detection and treatment of these conditions[33]. With regard to this subject, there have been no random, controlled trials carried out up until this point. Glaucoma screening examinations are not covered by any of the statutory health insurance companies in Germany or any of the other European countries, and there is no obligation that these examinations be performed universally across the population.

IV. MANAGEMENT OF GLAUCOMA

Medical therapy

According to the American Academy of Ophthalmology Preferred Practice Pattern (2020), a reduction in intraocular pressure (IOP) of twenty percent to thirty percent at an early stage is an appropriate goal to restrict the development of illness[34]. Even for eyes that have normal tension glaucoma, this recommendation is still valid. It is important to give careful consideration to the intraocular pressure (IOP) at each and every follow-up session. If the patient's condition continues to deteriorate, the target intraocular pressure level ought to be decreased even lower.

In the treatment of glaucoma, the medication that reduces intraocular pressure has been the standard treatment for a significant amount of time[35]. There has been a significant shift in the pharmacotherapy of glaucoma as a result of the introduction of beta blockers, prostaglandin analogues, alpha agonists, and topical carbonic anhydrase inhibitors (CAIs) during the course of the past few decades[36]. When compared to their predecessors, the topical pilocarpine and the systemic oral CAIs, these medications are superior in terms of their efficacy and safety. In accordance with the generally accepted principles of pharmacotherapy, the objective of achieving the proper intraocular pressure (IOP) range ought to be performed with the least amount of medication and the fewest possible adverse effects[37]. Corticosteroids, both ocular and systemic, have a propensity to cause glaucoma; hence, persons who are at risk for developing glaucoma should be administered with caution. Prostaglandin analogues, also known as PGAs, are by far the most popular choice of therapy when it comes to the treatment of ocular arterial hypertension, also known as OAH[38]. The enhanced uveoscleral outflow that occurs as a consequence of the presence of prostaglandin analogues makes it possible

for aqueous humour to travel through the ciliary muscle and into the supraciliary and suprachoroidal areas, thereby compensating for the decreased intraocular fluid outflow[39]. The administration of prostaglandin analogues on a once-daily basis is not only safe but also has a low risk of systemic side effects and is well tolerated. The most significant adverse effects on the eyes are the formation of eyelashes, the colouring of the iris, and uveitis infections. The usefulness of PGAs over the long run has been called into question due to the fact that the majority of them are unable to target the principal outflow channel (TM)[40]. When it comes to lowering intraocular pressure (IOP), the newly approved latanoprostene bunod 0.024% may be administered via the transocular channel rather than the uveoscleral route. It is more effective than timolol 0.5% and has a safety profile that is comparable throughout the three-month follow-up period.

Cholinergic agonists, such as pilocarpine, are responsible for miosis and their ability to increase conventional outflow by reducing outflow resistance. Prostaglandin analogues represent a significant improvement over these prescription medications. One of the reasons why beta blockers and PGAs finally took its place was that pilocarpine, which was an excellent drug for glaucoma in the 1970s and 1980s, had a dose plan that required it to be administered four times per day[41]. Both beta blockers and CAIs are aimed at the creation of aqueous humour by the ciliary body, which ultimately results in a reduction of the intraocular pressure being experienced. When applied topically, CAIs have the ability to reduce the production of bicarbonate ions once they have penetrated the eye. Their target is the ciliary body epithelium. Despite the fact that the dorzolamide 2% and brinzolamide 1% CAIs are taken twice or three times a day, they are not considered to be first-line therapy because they are not as effective as PGAs and beta blockers. Systemic CAIs, such as methazolamide and acetazolamide, have a large rate of adverse effects, which restricts their use. This is despite the fact that they are useful in treating ACG[42]. After only one month of treatment, intolerance is experienced by fifty percent of the patients. The sympathetic nerve terminals in the ciliary body epithelium are blocked by beta blockers, which are antagonists of beta adrenergic receptors. This results in a decrease in the amount of water that is produced by the body[43].

Cardioselective beta blockers, which are distinct from nonselective beta blockers, are frequently well tolerated by patients who suffer from asthma and chronic obstructive pulmonary disease (COPD). The use of beta blockers comes with a number of advantages, including the fact that they are inexpensive and only need to be taken once each day. When applied topically, beta blockers are able to enter the bloodstream; however, they are unable to be metabolised by the liver in its first-pass process. This puts the patient at risk for bronchial

constriction as well as arrhythmias. Reducing the amount of systemic absorption that occurs after topical application can be accomplished by either gently occluding the puncture site or closing the eyes for two minutes. Both brimonidine and iopidine are examples of alpha-adrenergic agonists that are applied topically and have the ability to reduce intraocular pressure (IOP) by increasing outflow and decreasing the production of aqueous humour[44]. Because they are considered second-line treatments, they are often administered in conjunction with other medications and taken twice or three times each day. Since a retrospective study found that combination treatment (CAI+PGA) was more common in everyday practice than alpha-2 agonists plus PGA, it is possible that the use of alpha-2 agonists is associated with a greater number of adverse effects. Rho kinase inhibitors are a relatively new class of drugs that function by reducing the pressure in the episcleral veins and increasing the level of outflow that occurs through the conventional channels. The efficiency of the rho kinase inhibitor netarsudil 0.02%, which was approved by the FDA in 2017, in decreasing blood pressure is comparable to that of timolol 0.5%; however, the incidence of side effects is more prevalent with netarsudil[45]. In the short term, pharmacotherapy is helpful; however, when it is used over a longer period of time, it is not only expensive but also causes adverse effects and is ineffectual, which prevents it from attaining the intraocular pressure (IOP) that is needed. The fact that less than half of glaucoma patients continue to take antiglaucoma medications as prescribed after a year is another important cause for concern. This is because nonadherence to the administration schedule is even more concerning[46].

Laser therapy

It may be time to investigate supplemental laser therapy in the event that local treatment does not result in a reduction in intraocular pressure (IOP) or leads to only a slight reduction in IOP. When it comes to pressure laser treatments, laser trabeculoplasty and cyclophotocoagulation are two examples of procedures that can either increase or decrease the amount of aqueous humour in the environment[47]. It is estimated that the latter lowers intraocular pressure (IOP) by at least twenty percent in forty-seven percent of the eyes that are treated, and this is before we even consider the major adverse effects[48]. Both can be employed through the micropulse laser technology, despite the fact that their efficacy has not been completely examined; yet, both are possible[49]. In situations where local treatment is unable to bring about a reduction in intraocular pressure (IOP) or only brings about a slight reduction, it may be time to investigate the possibility of complementary laser therapy[50]. When it comes to pressure laser treatments, laser trabeculoplasty and cyclophotocoagulation are two examples of procedures that can either increase or decrease the amount of aqueous humour in the environment[51].

The second method lowers intraocular pressure (IOP) by at least 20 in 47 percent of the eyes that are targeted, and this is true even after taking into consideration the possibility of undesirable effects and consequences. Both can be employed through the micropulse laser technology, despite the fact that their efficacy has not been completely examined; yet, both are possible[52][53].

V. CONCLUSION

The development of glaucoma is influenced by a wide variety of factors that are not fully understood, and researchers are always attempting to improve their ability to diagnose the illness and create treatments that are successful. All aspects of treatment, including recovery times, safety records, and treatment outcomes, have seen significant improvements with the introduction of MIGSs. It is recommended that future research concentrate on developing MIGS devices that are more effective than traditional incisional treatments in terms of their ability to lower intraocular pressure (IOP). Glaucoma, which is a progressive form of optic neuropathy, can result in a loss of vision in either the central or peripheral regions that can last a lifetime. The intraocular pressure (IOP) is one of the risk factors that can be controlled. The presence of glaucoma in one's family, the fact that one is older, and the fact that one is not white are all additional major risk factors. Glaucoma is the most common cause of blindness that would be permanent on a global scale. When intraocular pressure (IOP) lowers by thirty to fifty percent, the process typically comes to a standstill. For example, having an African heritage and being fairly old are both risk factors that can be considered. The fact that it is so common and has such a high mortality rate makes it a significant public health concern. The number of people aged 40 and older accounts for 3.5% of the overall population. Glaucoma has the potential to kill as much as forty percent of the nerve fibres that are found in the retina. The optic cup goes through gradual and unequal alterations as a consequence of this, and the visual field narrows as a direct consequence of this. The reduction in size of the neural rim is a consequence of the destruction of ganglion cells and the axons that connect them. When the neural rim is thinning or shrinking, certain regions may experience neuronal loss and atrophy depending on the circumstances. Intraocular pressure (IOP) has the potential to cause mechanical stress and strain on the posterior structure of the eyes, particularly the lamina cribrose. Depending on the percentage of cells that are positively disposed, the number of intraocular pressure (IOP) cells that die is determined. The aqueous outflow from trabecular meshwork is found to be more challenging for people who have OAG. Because to obstructions in the pupil, the majority of Asian people who experience angle closure do so because of this condition. An elevated intraocular pressure (IOP), which is also referred to as a translaminal pressure gradient,

has been identified as the only modifiable factor for diabetic retinopathy (OAG) that has been discovered so far. It is important to note that being older (between the ages of 21 and 23), being female, and being of advanced age are all risk factors for angle closure. In addition, the American Academy of Optometry contemplated the utilisation of ophthalmology GSS; however, in the end, they chose not to do so because of its restricted applicability to three stages: no field loss, moderate field loss, and severe field loss.

As a capacity, the Esterman rating system was acknowledged by the American Medical Association in the year 1984. It was discovered during the pilot testing that this GSS did not take into consideration all of the phases that occur during the evolution of glaucoma itself. The approach that is based on HVF testing allows for stage assignments, which is one of the similarities between the CIGTS and AGIS systems. This makes it simple to adjust the test to a variety of centres. When it comes to utilising the HVF characteristics, the Bascom Palmer GSS employs a method that is quite simplified. As a result of the complexity of the computations that were necessary, it was believed that the CIGTS and AGIS scoring systems had a greater potential for scoring errors.

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