Abstract

Glaucoma is a treatable yet incurable disease that affects all demographic and age groups, and is diagnosed in all parts of the world. It is a general descriptive term for a myriad of diseases that have different degrees of severity. The disease may remain undiagnosed for years due to lack of overt symptoms, but left untreated, the final outcome is blindness. The primary modes of treatment are surgery and topical drug therapy, with new drugs constantly being developed. Some of these have side effects but are considered by the medical community to be generally safe to use. The surgical option is used for acute cases where there is a spike in intraocular pressure that may occur within hours or minutes leading to overt symptoms such as pain, with an immediate risk of a reduced visual field. The best form of disease treatment remains early detection, which is occurring in the developed world with increasing effectiveness, but lags in the developing world due in large part to the lack of trained medical personnel.

Introduction

Glaucoma is a disease of the eye found primarily in adult aging populations around the world, including the United States [1-3]. In all its forms, glaucoma has been estimated to affect approximately 70 million people worldwide [4]. The true prevalence may be underestimated, as this disease (among others) is underreported in the developing world [5]. Glaucoma accounts for about 8% to 14% of all cases of blindness [6-8] with reported rates depending on the criteria used to diagnose these conditions [9].

There are two major forms of the disease: open- and closed-angle glaucoma. The term angle refers to the space or area between the cornea and the iris. If the area that contains the trabecular meshwork becomes blocked, then intraocular pressure in the eye increases, with a resulting reduction or loss in vision. Elevated intraocular pressure damages the ganglion cell and axons that make up part of the retinal nerve layer, resulting in changes to the optic cup and leading to narrowing of the field of vision. Normally, excess intraocular fluid is dispersed from the center of the eye via the trabecular meshwork, thus maintaining a normal level of pressure (<20 mm Hg) inside the eyeball. Should this meshwork be blocked or compromised so that drainage cannot occur, pressure builds inside the eye, leading to ocular damage.

Reported glaucoma rates have increased in many developing countries because improvements in education and methods of diagnosis have led to better detection. Ultimately, a better educated populace and better diagnosis -i.e., increased awareness leads to a decrease in the rate of sight loss due to glaucoma, as is the case in developed countries. However, in regions such as Africa and India, glaucoma remains underdiagnosed. In many countries, there is a shortage of trained medical personnel to treat patients, as well as a lack of available medications to treat patients who are diagnosed [5]. It is important to remember that glaucoma, like high blood pressure, is a disease that can be treated but never really cured.

The various classes of glaucoma drugs function as therapeutic agents by different mechanisms, but the two most common are reduction of aqueous humor though the trabecular meshwork [10]. Adrenergic agonists such as brimonidine are an example. Cholinergic agents such as pilocarpine influence the papillary block. Prostaglandins modulate glaucoma by increasing the uveoscleral outflow [11]. Patients often become refractory to their medications over time. Initially patients are usually advised to use topical drops once a day. Over time, this may increase to twice a day, often with 2 or more drug combinations.

Open-angle glaucoma

Open-angle glaucoma (OAG) is the most common of the syndromes of this disease. It can occur either unilaterally or bilaterally. Recent estimates place the incidence at about 2% [1]. The incidence was highest in blacks and lowest in whites [1]. It is chronic in nature, usually progressing at a slow rate and increasingly affecting vision over a period of years or decades. Often there are no overt signs or symptoms of the disease up to the point of vision loss.

The risk factors for this disease include age, race, smoking and family history (genetics). Statistical analysis has shown a link between OAG and diabetes mellitus [12]. OAG results from obstruction of outflow of excessive aqueous humor from the interior of the eyeball via the trabecular meshwork. In normal individuals, the trabecular meshwork is open and freely exposed to the excess aqueous humor as it relates to the iris. In individuals who have OAG, the angle is at least partially blocked in such a way that the free flow of aqueous humor to the trabecular meshwork is impeded, eventually leading to a “cupping” or depression of the optic nerve. OAG may result from either a pupillary block or a plateau iris. The pupillary block condition is enhanced by a shallow anterior chamber, increased lens thickness, and a smaller axial length. As the lens thickens, often because of advancing age, the pupil...
may be dilated midway, resulting in a ballooning forward of the iris. As fluid begins to build up, the meshwork is partially obstructed and the angle narrows.

**Treatment for open-angle glaucoma**

The treatment for this OAG is usually drug therapy in the form of drops that are administered on a daily basis [10]. Surgery may be used in some cases, but this is not the preferred treatment option.

**Closed-angle glaucoma**

Closed-angle glaucoma (CAG) is more serious than OAG. This form of the disease may develop quickly, often with associated pain. Immediate medical attention may be required to prevent vision loss. The condition is similar to a clogged bathroom drain where something covers the drain opening, completely preventing fluid from leaving the drain. In the case of CAG, the iris of the eye may not be as open as it should be. There is often a genetic component to this, with the condition being more prevalent in Asian populations [6]. Should the pupil open too quickly or become too large, then the iris will completely cover the trabecular meshwork, causing a complete cutoff of the meshwork from the aqueous humor. Intraocular pressure increases, often rapidly, perhaps within minutes. This is considered a medical emergency, because irreversible damage to the optic nerve may occur. Symptoms include severe pain, halting, photophobia, blurred vision, and headaches. CAG may be acute, subacute, or chronic [13]. These conditions may not be mutually exclusive in the same person. Acute CAG occurs suddenly with an almost immediate spike in intraocular pressure. Subacute CAG develops when the trabecular meshwork is closed by the iris and then opens without intervention/treatment. Chronic CAG occurs when the angle between the iris and the trabecular meshwork closes slowly over time. Scarring of the iris may result.

**Treatment for closed-angle glaucoma**

Treatment may involve surgery to remove a portion of the iris so fluid can drain into the trabecular meshwork, thus relieving symptoms of the disease. This is often a permanent resolution to the problem, although it is recommended that this condition be treated as an ongoing medical issue, because chronic CAG may still occur.

**Other types of glaucoma**

**Normal tension glaucoma**

Normal-tension glaucoma (NTG) is a syndrome that is characterized by damage to the optic nerve with no increase in intraocular pressure above the normal range of 12-22 mm Hg. The cause of this syndrome is not clear, but there appear to be three major risk factors, including age, sex, and race. Most NTG patients are over age 60, women appear to be more susceptible than men, and the prevalence of NTG is higher in Asian than in European populations [14]. NTG may be diagnosed by observing the optic nerve for damage. It is currently treated taking measures to lower the intraocular pressure. Alternative methods include use of calcium channel blockers to increase perfusion in the optic nerve head.

**Congenital (childhood) glaucoma**

This type of glaucoma occurs in about 1 of every 10,000 to 20,000 live births in the western world and is the second leading cause of blindness worldwide [15]. It appears in the first year of life and may be more prevalent in certain ethnic groups [16]. It is caused by a structural defect in the trabecular meshwork of the eye which is due to genetic factors. The syndrome is an autosomal recessive developmental disorder [17]. It is corrected by microsurgery or by eye-drop therapy using beta-blockers or prostaglandins [18].

**Iridocorneal endothelial syndrome**

Iridocorneal endothelial syndrome is characterized by an overabundance of corneal endothelial cells which spread to and block the trabecular meshwork, leading to increased intraocular pressure. Damage may occur to this drainage system due to the presence of these cells, which bind the iris to the cornea. Symptoms may include hazy vision or halting. Treatment is often surgical, with recent work done using endothelial keratoplasty [19].

**Neovascular glaucoma**

Neovascular glaucoma (NG) may be considered in the category of secondary glaucoma because it often results from another syndrome, such as diabetic retinopathy. It is characterized by the presence of new blood vessels associated with the iris and angle which block the flow of excess fluid out of the eye. Thus, reduction of intraocular pressure is key in treatment. This may be done by either drug therapy or by surgery [20].

**Other glaucoma conditions**

Pigmentary glaucoma and pseudoexfoliative glaucoma are two conditions that may be technically classified as a form of secondary glaucoma in which another syndrome is responsible for increased intraocular pressure. Pigmentary glaucoma occurs when granules at the rear of the iris break off and clog the trabecular meshwork.

Pseudoexfoliative glaucoma occurs when small sections of the outer lens of the eye collect between the cornea and the iris, clogging the trabecular meshwork. Treatment for both these conditions involves either surgery or topical medication.

Traumatic glaucoma occurs subsequent to injury. It can be caused by blunt force trauma. Treatment may either be surgical or by topical medications.

**Conclusion**

The various forms of glaucoma will continue to present major medical problems in all parts of the world for some time to come, affecting all ages, demographic, and ethnic categories. Whereas drug treatment options continue to change and often improve, the basic mechanism of action for both the older and the more recently developed compounds remains the same, namely lowering the intraocular pressure of the eye to prevent the optic nerve damage which inevitably occurs over time without treatment. Development of new anti-glaucoma drugs is essential because patient become refractory to medication over time. Surgery remains a secondary option, except in rare or extreme cases. Early diagnosis and monitoring remain the best ways of treatment and prevention of blindness due to glaucoma.

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