Glaucoma Update – What Physicians and the Public Need to Know

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Glaucoma is one of the leading causes of blindness in the world. It is the second leading cause of blindness in China⁽¹⁾ and the United States⁽²⁾. The World Health Organisation⁽¹⁾ estimates that East Asia may contribute to 50% of the 5.1 million glaucoma blind in the world and glaucoma accounts for 22.7% of blindness in China. The probability of bilateral blindness from glaucoma is estimated at 10%^(3,4) even with treatment⁽³⁾. Despite these facts, 50%⁽⁵⁾ to 90%⁽⁶⁻⁸⁾ of glaucomas in the developed world remain undetected.

Population studies show that glaucoma prevalence increases dramatically with age⁽⁵⁻⁷⁾. The elderly population is therefore at increased risk of developing glaucoma. As the elderly population grows in Singapore, we need to anticipate an increase in glaucoma that will exact a toll on the elderly, their families and the health care system.

What is glaucoma?

The definition and understanding of glaucoma has changed significantly in recent years. Glaucoma is still often associated with pain, raised eye pressure and blurred vision. In reality, the large majority of glaucomas are asymptomatic, with normal eye pressure and visual acuity. Sight is lost gradually, unnoticed, until there is severe loss in the advanced stages when central acuity is affected. Glaucoma is therefore known as the "sneak thief of sight". Increased awareness of this reality is important for earlier detection and treatment of glaucoma, as blindness from glaucoma is irreversible and most cases present late.

The term "glaucoma" encompasses a whole spectrum of disease conditions. Glaucoma can be defined as an eye condition that leads to progressive optic nerve damage and visual field loss. The cause of glaucoma may be primary, the most common form; or secondary, due to other ocular pathology. In the past, glaucoma was equated with raised eye pressure. Many population prevalence studies have since shown that this pressure concept of glaucoma is inaccurate. Amongst the Chinese elderly in Singapore, 60%⁽⁸⁾ of glaucomas have normal pressures and would potentially be missed if intraocular pressure measurement was the primary means of detection. Although raised intraocular pressure is definitely associated with a higher risk⁽⁵⁾ of glaucoma, it is not diagnostic, but one of many risk factors for glaucoma.

Types of glaucoma and prevalence patterns

The two major types of glaucoma are primary open

angle glaucoma (POAG) and primary angle closure glaucoma (PACG). POAG is the most common type of glaucoma and presents silently. Normal tension glaucoma (NTG) is a subtype of POAG in which the intraocular pressure (IOP) is below 21 mmHg. It is in fact the NTG component of POAG that is the most prevalent type of glaucoma in many populations (5,6,8,17). PACG was previously considered the predominant form of glaucoma in Singapore from clinic-based studies (9,10). Clinic-based prevalence figures will however be skewed because the more symptomatic and advanced glaucomas will present at the clinic. Clinic-based studies also favour the detection of glaucomas with raised eye pressure because IOP measurement is the predominant method for initial glaucoma screening. Population prevalence figures from the Chinese elderly in Singapore however show that POAG, together with NTG, outnumber PACG in a ratio of 2.8:1. It is the NTG that is the most common glaucoma amongst the Singapore elderly, comprising 60% of all glaucomas(8). IOP measurement alone is therefore inadequate in detecting glaucoma.

Primary angle closure glaucoma is the next most common type of glaucoma in Singapore. The prevalence of PACG amongst Asians (8,12,14) is significantly higher than amongst Caucasian populations^(7,11). The Chinese elderly are particularly prone to developing PACG. PACG can present in three ways, as an acute angle closure attack, intermittent angle closure or chronic angle closure. PACG has traditionally been regarded as a symptomatic glaucoma with pain, redness and blurred vision. It is however, the chronic, silent presentation of PACG that is predominant as demonstrated in many population prevalence studies(6-8,11-14). A six-year follow-up of individuals at risk of developing angle closure revealed that the majority (68%) who progressed onto frank angle closure glaucoma were asymptomatic(15). Intraocular pressures are usually normal in the early stages of PACG as much of the drainage angle of the eye can be closed before the pressure becomes abnormal. Intermittent angle closure glaucoma is characterised by repeated short episodes of raised intraocular pressure, but with normal pressures most of the time. IOP measurement is therefore also limited in the early detection of PACG.

The overall glaucoma prevalence in our elderly

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Visiting Glaucoma Specialist Singapore National Eye Centre Chinese population is $4.8\%^{(8)}$. This is comparable with those in many other populations. In Japan⁽⁶⁾ and Mongolia⁽¹²⁾ the glaucoma prevalence amongst the elderly is 6.1% and 6.3% respectively. The Beaver Dam study⁽⁷⁾ in the United States reported a prevalence of 3.5% in a predominantly Caucasian population aged 65 years and older. The Baltimore study⁽¹¹⁾ reported a prevalence of 6.5% in the Black population aged 60 years and older.

Clinical presentation of Glaucoma

Glaucoma has traditionally been divided into the acute and chronic glaucomas. In acute glaucoma, the patient presents with acute pain, redness and blurred vision. Chronic glaucoma, however, is silent and leads to progressive loss of vision that usually goes unnoticed by the patient until it is severe. POAG and most PACG cases present this way. The presentation of acute glaucoma is dramatic and the severity of the symptoms often forces the patient to seek treatment. It is not surprising therefore that many associate glaucoma with the symptoms of an acute glaucoma attack. Chronic glaucomas, on the other hand, are asymptomatic and typically diagnosed incidentally and late, when visual loss is advanced⁽³⁾.

Chronic glaucomas comprise the very large majority of glaucomas and acute glaucomas constitute the tip of the iceberg. Major glaucoma prevalence studies in the United States (7,11) and Japan⁽⁶⁾ reported no cases of acute glaucoma. In Mongolia⁽¹²⁾, 2 out of 22 glaucoma cases had acute glaucoma. In the study in Singapore, amongst the Chinese elderly⁽⁸⁾, one case of acute neovascular glaucoma was identified, compared with 23 chronic silent glaucomas. The prevalence of undiagnosed glaucoma in a population is a reflection of patient health care patterns, patient awareness, accessibility to health care and health care practices and policies. In the United States, 50% to 90% of the glaucomas are undiagnosed. In Japan, 80%(6) of glaucomas are undiagnosed. In Singapore, amongst the Chinese elderly, 76% to 96% of glaucomas are undiagnosed⁽⁸⁾. Physician awareness and public education are vital in preventing blindness from glaucoma.

Why glaucoma patients present late

In chronic glaucoma, there are no symptoms to alert the patient to the condition in the earlier stages. The slow progression to blindness often goes unnoticed or is ignored until it is too late. There are various reasons for this:

- 1) Peripheral vision is naturally less distinct. The blindness from glaucoma starts in the peripheral visual field and progresses centrally. It is only when central vision is affected, typically in the advanced stages, that Snellen acuity is affected.
- 2) The loss of visual field in one eye can be subtle, even when there is significant loss. This is because the scotomas or blind spots from glaucoma are negative scotomas and are not

apparent. They are not seen as dark spots in the field of vision. They are similar to the physiological blind spot that is not seen because of higher cortical "filling in" of the defect. Some patients notice these scotomas only when objects to the side are not seen; or people seem to suddenly appear in front of them as they miss seeing them coming from the side. Patients with significant field loss are understandably more prone to accidents.

- 3) Glaucoma is a bilateral condition but often affects both eyes asymmetrically. Visual field loss in one eye can therefore be compensated for by the field of the fellow eye which "fills up" the defect when both eyes are used simultaneously. Some patients only notice the extent of loss of vision when one eye is covered⁽³⁾.
- 4) In chronic glaucomas associated with raised eye pressure, the elevation in pressure is gradual and typically does not give rise to any obvious signs or symptoms.
- 5) Deteriorating vision is often too readily accepted as a fact of life when one ages. Some elderly ignore their symptoms or delay seeking treatment. Others attribute their poor vision to some other reversible condition such as cataract or the need for spectacles. As a result, detection and treatment is often delayed.

Most chronic glaucomas are still diagnosed late with many presenting with established blindness in one eye⁽³⁾. Increased awareness of the silent nature of glaucoma and the nature of vision loss is important in promoting earlier detection and preventing galucoma blindness. The way in which vision is lost in glaucoma is not easily understood by many. Most people firmly equate their quality of vision with central acuity. Even some glaucoma patients with advanced peripheral visual field loss do not understand the gravity of their condition because they still have a reasonable amount of residual vision and acuity. As a result, glaucoma treatment compliance is poor and eventually the central vision is also permanently lost to glaucoma.

Importance of early detection

Blindness from glaucoma is irreversible. The severity of glaucoma damage at the time of diagnosis is important because the more advanced the disease, the faster the rate of subsequent damage and the more difficult it is to prevent further damage. Treatment needs to be more aggressive with attendant greater potential for side effects and complications. The threat of blindness is always more imminent in such cases and this also has a great impact on the psychological well-being of the patient. The aim of treatment is to preserve useful vision for the rest of the patient's lifetime. Glaucoma treatment does not always prevent further deterioration but generally slows down the rate of progression. Early detection of glaucoma is therefore important in preventing blindness.

Diagnosis of glaucoma

Glaucoma diagnosis is based on a combination of risk factors from the history and clinical findings. Risk factors include a raised eye pressure⁽⁵⁾, age^(6,7,11), a family history⁽¹⁷⁾ of glaucoma and high myopia⁽¹⁸⁾. The basic clinical examination for glaucoma includes:

- 1) Slit lamp examination
- 2) Intraocular pressure measurement
- 3) Detailed optic nerve examination
- 4) Visual field examination
- 5) Gonioscopy, to examine the drainage angles

Advances in the understanding of glaucoma have led to changes in the way glaucoma is diagnosed. The diagnosis of glaucoma has become more complex as the simple measurement of IOP is no longer adequate. Other components of the clinical examination such as optic nerve and visual field examination are now more important in the diagnosis of glaucoma. Gonioscopy is important in the detection of early PACG as the IOP, optic nerve and visual fields are likely to be normal. The diagnosis of glaucoma is also complicated by the fact that some individuals have clinical findings that are suggestive, but insufficient to confirm the diagnosis of glaucoma. This is particularly true in early glaucoma when clinical signs are not overt. Such individuals are known as "glaucoma suspects" and on follow-up, some will progress on to frank glaucoma.

Screening for Glaucoma

Screening for glaucoma is a controversial issue because no screening method has shown a satisfactory balance of sensitivity, specificity and positive predictive value. Intraocular pressure alone is inadequate for glaucoma screening for both POAG and PACG. Gonioscopy is the gold standard for PACG detection and visual field examination seems to be the best method for POAG screening. Both have limitations in being applied widely in mass screening.

High-risk groups should, however, be screened. Major risk factors include a raised intraocular pressure, age and a positive family history for glaucoma. A raised eye pressure(16) is an important risk factor with the probability of glaucoma rising exponentially with higher pressures. Age is a major risk factor⁽³⁻⁵⁾ with the risk of glaucoma increasing up to 9 times(3) with advancing age. The American academy of ophthalmology recommends that all individuals above the age of 40 years should have regular eye examinations. A positive family history is important(17) and increases the risk of glaucoma up to 5 times⁽¹⁸⁾ that of the general population. Individuals with symptoms suggestive of intermittent angle closure should also be screened. The typical symptoms are unilateral browache or headache, sometimes associated with haloes and typically occurring in the evening. These symptoms are often mistaken for a headache because they are transient and are often relieved after sleep. Other minor risk factors include high myopia¹⁹ and hypertension²⁰ in the elderly. Migraine,²¹ nocturnal hypotension²² (sometimes related to treatment for systemic hypertension) and diabetes mellitus²³ are also associated with glaucoma. Individuals with these risk factors should be screened.

Treatment of Glaucoma

The large majority of glaucomas cannot be cured. The aim of treatment is to prevent further loss of vision. Treatment for glaucoma generally does not halt progressive damage but slows it down⁽¹⁶⁾. Glaucoma is a chronic condition and entails lifelong treatment and follow-up. An exception to this is early PACG before significant permanent angle closure and damage has occurred. In such a situation, a laser peripheral iridotomy is curative. Such cases are usually seen in intermittent angle closure, or the fellow eye of a patient with unilateral acute angle closure glaucoma.

The treatment of glaucoma has changed significantly. The mainstay of current glaucoma treatment is to lower the IOP. There is now a multitude of new glaucoma eyedrops available with different modes of action and side effects. Multiple drug therapy, compliance and cost are important issues, as glaucoma requires life-long treatment. The effectiveness of laser trabeculoplasty in POAG has been verified in recent collaborative studies (24,25). It is not invasive, has fewer complications than surgery and is not associated with the side effects and compliance issues of eye drops. Laser trabeculoplasty has an efficacy between medication and surgery(24). Lasers have a particularly important role in the treatment of early PACG. Early laser treatment in such cases may prevent the onset of significant chronic angle closure and optic nerve damage and thus obviate the need for lifelong medication or surgery.

New surgical advances, principally in the use of anti-scarring agents such as Mitomycin C and 5-fluorouracil⁽²⁶⁾ have resulted in greater intraocular pressure lowering and better success rates but not without increased risk of complications. Greater intraocular pressure lowering is however sometimes necessary with advanced disease. Despite these advances, it is often not possible to completely halt glaucoma deterioration, be it with medication, lasers or surgery.

Apart from pressure lowering treatment, neuroprotection and neural regeneration are being researched and may be treatment options in the future.

SUMMARY

With the aging population in Singapore, glaucoma will be more prevalent. The majority of glaucomas are silent and typically present late with advanced damage. A large proportion of glaucomas remain undetected. Screening for glaucoma is the only way to detect glaucoma early and high-risk groups should be screened. Early detection is important in preventing blindness as treatment is more difficult and less effective in the advanced stages of glaucoma. Greater awareness amongst physicians and the public is vital in the prevention of glaucoma blindness.

REFERENCES

- Thylefors B, Negrel AD, Parajasegaram R, Dadzie KY. Global data on blindness. Bull World Health Organisation 1995; 73:115-21.
- 2. Leske MC. The epidemiology of open-angle glaucoma: a review. Am J Epidemiol 1983; 118:166-91.
- 3. Hattenhauer MG, Johnson DH, Ing HH, Kerman DC, Hodge DO, Yawn BP, et al. The probability of blindness from open-angle glaucoma. Ophthalmology 1998; 105(11):2099-104.
- 4. Quigley HA. Number of people with glaucoma worldwide. Br J Ophthalmol 1996; 80(5):389-93.
- Sommer A, Tielsch JM, Katz J, Quigley HA, Gottsch JD, Javitt J, Singh K. Relationship between intraocular pressure and primary open angle glaucoma among white and black Americans: the Baltimore Eye Survey. Arch Ophthalmol 1991; 109:1090-5.
- Shios Y, Kitazawa Y, Tsukahara S, Akamatsu T, Mizokami K, Futa R, et al. Epidemiology of glaucoma in Japan - a nationwide glaucoma survey. Jpn J Ophthalmol 1991; 35:133-55.
- Klein BEK, Klein R, Sponsel WE, Franke T, Cantor LB, Martone J, et al. Prevalence of glaucoma: the Beaver Dam Eye Study. Ophthalmology 1992; 99 (Pt10):1499-504.
- 8. Sim DHJ, Goh LG, Ho T. Glaucoma pattern amongst the Chinese elderly in Singapore. Ann Acad Med Singapore 1998; 27:819-23.
- Loh RCK. The problems of glaucoma in Singapore. Singapore Med J 1968; 9:76-80.
- 10. Lim ASM. Primary angle-closure glaucoma in Singapore. Aust J Ophthalmol 1979; 7:23-30.
- 11. Tielsch JM, Sommer A, Katz J, Royall RM, Quigley HA, Javitt J. Racial variations in the prevalence of primary open-angle glaucoma. JAMA 1991; 266:369-74.
- Foster PJ, Baasanhu J, Alsbirk PH, Munkhbayar D, Uranchimeg D, Johnson GJ. Glaucoma in Mongolia: a population-based survey in Hovsgol province, northern Mongolia. Arch Ophthalmol 1996; 114:1235-41.
- 13. Congdon NG, Quigley HA, Hung PT, Wang TH, Ho TC. Screening techniques for angle-closure glaucoma in rural Taiwan. Acta Ophthalmol 1996; 74:113-9.
- 14. Jacob A, Thomas R, Koshi SP, Braganza A, Muliyil J. Prevalence of primary glaucoma in an urban south Indian

- population. Indian J Ophthalmol 1998; 46:81-6.
- 15. Wilensky JT, Kaufman PL, Frohlichstein D, Gieser DK, Kass MA, Ritch R, et al. Follow-up of angle-closure glaucoma suspects. Am J Ophthalmol 1993; 115:338-46.
- 16. Armaly MF, Krueger DE, Maunder L, Becker B, Hetherington J, Kolker AE, et al. Biostatistical analysis of the collaborative glaucoma study. Arch Ophthalmol 1980; 98:2163-71.
- 17. Tielsch JM, Katz J, Sommer A, Quigley HA, Javitt J. Family history and risk of primary open-angle glaucoma: the Baltimore Eye Survey. Arch Ophthlamol 1994; 112:69-73.
- 18. Miller SJ. Genetics of glaucoma and family studies. Trans Ophthalmol Soc UK 1978; 98:290-2.
- Perkins ES, Phelps C. Open-angle glaucoma, ocular hypertension, low tension glaucoma, and refraction. Arch Ophthalmol 1982; 100:1464-7.
- Tielsch JM, Katz J, Sommer A, Quigley HA, Javitt J. Hypertension, perfusion pressure, and primary openangle glaucoma; a population-based assessment. Arch Ophthalmol 1995; 113:216-21.
- 21. Wang JJ, Mitchell P, Smith W. Is there an association between migraine headache and open-angle glaucoma? Findings from the Blue Mountains Eye Study. Ophthalmology 1997; 104:1714-9.
- Hayreh SS, Zimmerman MB, Podhajsky P, Alward WL. Nocturnal arterial hypotension and its role in optic nerve head and ocular ischemic disorders. Am J Ophthalmol 1994; 117:603-24.
- 23. Wilson MR, Hertzmark E, Walker AM. A case-control study of risk factors in open-angle glaucoma. Arch Ophthalmol 1987; 105:1066-71.
- 24. Glaucoma Laser Trial Research Group: The Glaucoma laser trial (GLT) and Glaucoma Laser Trial Follow-up Study: 7. Results. *Am J Ophthalmol* 1995; 120:718-31.
- 25. The Advanced Glaucoma Intervention Study (AGIS):4. Comparison of treatment outcomes within race. Seven-year results. Ophthalmology 1998; 105(7):1146-64.
- 26. The Fluorouracil Filtering Surgery Study Group: Fiveyear follow-up of the Fluorouracil Filtering Surgery Study. *Am J Ophthalmol* 1996;121:349-366.