Current Understanding of the Treatment and Outcome of Acute Primary Angle-Closure Glaucoma: An Asian Perspective
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Abstract

Introduction: Primary angle-closure glaucoma (PACG) is a major cause of blindness among Asians. A better understanding of the disease will improve the treatment and outcome of this condition. Methods: A literature review of all recent publications on PACG was carried out. Articles were retrieved using a key word search of MEDLINE, PubMed and Science Citation Index databases. Results: Following laser peripheral iridotomy for acute angle-closure, Asians were found to have a higher tendency to develop a subsequent rise in intraocular pressure compared to Caucasians. Furthermore, the extent and severity of visual field damage was more severe in Asians than Caucasians, particularly in eyes that presented insidiously with chronic PACG. Prophylactic laser iridotomy in the contralateral eye was found to be highly effective in preventing acute angle-closure attacks. Conclusion: PACG is more difficult to manage and is associated with more severe long-term visual morbidity in Asians than Caucasians. Regular follow-up of patients with PACG is important for the early detection of progression of the disease and visual field deterioration.

Key words: Iridotomy, Visual field

Introduction and Epidemiology

Primary angle-closure glaucoma (PACG) is a major cause of irreversible blindness in Asia and many parts of the world. It is a particularly serious problem in East Asia, where it represents the major form of glaucoma. This is in stark contrast to the situation in Europe and North America, where Caucasians are rarely affected by PACG, and primary open-angle glaucoma (POAG) is the dominant form. Singapore is reported to have the highest incidence of acute primary angle closure (APAC) of any country studied to date, with an island-wide incidence of 12.2 per 100,000 per year in those aged 30 years and older. The proportion of registered blindness attributable to glaucoma ranged from 21% to 26%, with PACG outnumbering POAG as the cause by a ratio of 4.5:1.

The prevalence of PACG is highly race-dependent, with the lowest rates found in European whites and highest in the Inuit, with that of East Asians lying in between. Females are affected 3 to 4 times as often as men, which may be related to the fact that they have gonioscopically narrower angles compared to men. Increasing age is also a major risk factor for developing PACG, with the relative risk of acute angle-closure glaucoma in patients above the age of 60 being 9 times higher compared to younger patients.

PACG – Clinical Types and Definition

This disease is traditionally classified as acute, subacute, intermittent, or chronic, based on the various modes of presentation. As we know it, the acute form involves a sudden increase in intraocular pressure (IOP) that results in dramatic symptoms, causing patients to promptly seek medical attention. The chronic form (also termed creeping angle-closure glaucoma) presents insidiously, with patients often seeking medical attention late in the course of the disease. Patients with intermittent angle-closure glaucoma have a history of mild intermittent attacks, with the eyes returning to normal in between attacks.

While patients with acute angle closure present with dramatic symptoms, this occurs in a minority of those with PACG diagnosed in population-based surveys in African and Asian countries. The majority of patients present with the chronic, asymptomatic form of the disease. However, there is often significant overlap in the clinical
presentation, as patients with underlying chronic disease may also present acutely during the course of the disease, and patients with acute angle closure can subsequently go on to develop chronic angle-closure glaucoma.

At present, there is a degree of discrepancy involving nomenclature and classification of PACG. Having an established system for classification is important for improving our understanding of the disease and the interpretation of findings in the literature. Foster et al\textsuperscript{16} and Friedman\textsuperscript{17} have proposed a new method of classifying PACG. Patients with primary angle closure include both asymptomatic people with occludable angles who have not had an acute attack, and those who have had an attack that was treated promptly and suffered no detectable nerve damage. In this classification, the term “glaucoma” is reserved for people who have glaucomatous optic neuropathy combined with visual field deficit. This is in keeping with previous evidence that most patients (60% to 70%) suffering an acute, symptomatic episode of angle closure recover without optic disc or visual field damage, at least in the short term.\textsuperscript{18,19}

By placing such emphasis on end-organ damage as the defining characteristic of glaucoma, Foster et al\textsuperscript{16} thus categorised individuals as:

1. **Primary angle closure suspects** (in which appositional contact between the peripheral iris and posterior trabecular meshwork is possible),
2. **Primary angle closure** (where the patient is symptomatic and there are signs of disturbed structure or function, but no visually significant optic nerve damage), and
3. **PACG** (where glaucomatous optic nerve damage is present, along with visual field defects).

In this scheme of things, persons suffering an acute, symptomatic rise in IOP would not be considered to have glaucoma, unless they showed evidence of optic nerve damage.

**Management and Long-term Outcome**

Chinese eyes have thick dark-brown irides.\textsuperscript{20,21} It is noted that using exclusively argon or neodymium-doped yttrium aluminium garnet (Nd:YAG) lasers alone for peripheral iridotomies in these dark irides is associated with a higher complication and failure rate compared to Caucasians,\textsuperscript{22} studies have shown that the use of sequential argon laser and Nd:YAG laser results in a reduction of the total laser energy required, thereby reducing collateral damage to the iris.\textsuperscript{20,21} In patients with high IOP refractory to medical therapy, argon laser peripheral iridoplasty is advocated to break the cycle of IOP escalation, allowing definitive laser PI to be performed once the corneal oedema has cleared. In addition, cataract extraction has been found to lower the IOP in PAC, by helping to open up and widen the narrow angle, deepen the anterior chamber, and to attenuate the anterior positioning of the ciliary processes in eyes with PAC,\textsuperscript{23} thereby relieving any pupil block element.

APAC is an ocular emergency that requires urgent treatment to prevent irreversible glaucomatous optic nerve damage. A study conducted in India showed that the 5-year incidence of progression from primary angle closure suspects to primary angle closure was 22%.\textsuperscript{24} Aung et al\textsuperscript{25} found that in Asian eyes with acute angle closure, the majority (58.2%) were unsuccessfully treated with laser PI alone and required the addition of anti-glaucoma medication or filtering surgery. In contrast, in Caucasian populations, IOP was controlled with peripheral iridectomy (surgical or laser) alone in 65% to 76% of eyes, and in up to 84% to 99% of eyes if additional medication was used.\textsuperscript{26-29} Only 1% to 13% of eyes were found to eventually require trabeculectomy for IOP control.\textsuperscript{30,31}

The literature suggests the presence of an iridotomy does not in itself provide protection against the later development of a rise in IOP. In Asians who did go on to develop an increase in IOP, most did so within the first 6 months following the acute attack (76.6%) and the majority were asymptomatic,\textsuperscript{25} while most Asians (93.7%) who developed chronic glaucoma did so within the first 5 months after the acute attack, underscoring the importance of closely monitoring these patients post-iridotomy.\textsuperscript{32}

This condition was also associated with significant long-term visual morbidity in Asians,\textsuperscript{33} with a third of the patients having severely cupped discs (cup:disc ratio of >0.9) and half of all subjects having some degree of glaucomatous optic neuropathy. In contrast, previous studies on Caucasians showed that only 12.5% of patients had a cup:disc ratio of >0.6 three years after initial presentation, and most of the subjects did not have significant glaucoma or visual field loss.\textsuperscript{26} Aung et al\textsuperscript{25} also showed significant progression of disease in Asian patients with APAC, where almost half (47.8%) were diagnosed with glaucoma at a mean follow-up period of 6 years and one-fifth were found to be blind in the attack eye (glaucoma being the cause in about half of the cases).

Several postulations have been put forward, attempting to explain this phenomenon of higher visual morbidity in Asians as compared to Caucasians. One possible reason is that patients are generally seen later,\textsuperscript{25} often up to several days after the onset of the acute symptoms. Also, the acute attack may be unresponsive, with many patients not responding well to simple first-line medical management. During the acute attack, high IOPs may also directly damage the optic nerve and cause glaucomatous changes.\textsuperscript{34} Lastly, as Chinese eyes have thick brown irides, higher laser energy is required to penetrate these irides during laser PI.\textsuperscript{20,21} This results in a greater degree of pigment
release and inflammation, which may in turn cause greater trabecular damage and subsequent elevation in IOP.

**Clinical Outcome of Fellow Eyes**

Fellow eyes of patients presenting with acute angle-closure glaucoma are at risk of developing a similar attack because of the similar anatomical structure in both eyes. Previous studies have documented that without treatment, a high proportion of contralateral eyes of patients with acute angle-closure glaucoma go on to sustain acute attacks or develop some form of angle-closure glaucoma.\(^{35,38}\) Lowe\(^{39}\) showed that without treatment, 51.3% (58 out of 113) of patients developed an acute attack in the contralateral eye, with up to a third of those occurring in the first year. Thirty-three per cent to 72% of contralateral eyes of patients presenting with acute angle-closure glaucoma were found to have some form of PACG.\(^{35,36}\) Furthermore, no medical regime has been shown to be entirely protective against acute angle closure, as patients maintained on pilocarpine still continued to develop an acute attack.\(^{39}\) As such, peripheral iridotomy to the fellow eye has been advocated as prophylaxis against the development of acute angle closure in the long-term. Not surprisingly, more recent studies which have made a distinction with APAC have shown that more than 80% retained good vision in the contralateral eye.\(^{39}\) Optic disc parameters in the fellow eye after an episode of APAC were also not significantly changed.\(^{40}\)

Studies in Caucasians have shown that prophylactic laser PI or surgical peripheral iridectomy in fellow eyes were equally effective in preventing acute angle-closure.\(^{20,35,37}\) In Asian patients with APAC, laser PI to fellow eyes showed similar efficacy as prophylaxis against the development of acute angle-closure, with none of the patients developing an acute attack during the mean follow-up period of 50.8 months.\(^{41}\) Prophylactic laser PI was also effective in preventing a subsequent rise in IOP in 88.8% (71/80) of fellow eyes, and may also help to treat any glaucoma present in these eyes by relieving any pupil block element. However, a chronic rise in IOP was still seen in 8.8% of fellow eyes and like that seen in the afflicted eye, this rise was seen early, within the first 4 months after presentation in 83.3% of patients.\(^{41}\) This yet again underscores the need for close monitoring – this time in the fellow eye, and it is recommended that prophylactic laser PI to fellow eyes be performed early.

**Visual Field Loss in PACG**

Because PACG is uncommon in the Caucasian population, most of the previous studies on visual field loss have been on open-angle glaucoma.\(^{42-49}\) Literature on visual field loss in PACG is lacking.\(^{50-54}\) In a study by Rhee et al,\(^{50}\) PACG patients were found to have more generalised field loss than POAG patients. Gazzard et al\(^{55}\) compared the characteristics of visual field defects in PACG and POAG in 234 subjects, and found that the mean deviations (POAG group, -13.3 dB; PACG group, -18.0 dB) indicated more severe visual loss in subjects with PACG. In subjects with POAG, the superior hemifield was more severely affected than the inferior. This was less pronounced in subjects with PACG. These findings suggest that PACG may be more visually destructive than POAG.

Few studies have looked at the extent of visual field loss in acute angle closure.\(^{18,54-56}\) In order to have an accurate assessment of visual field loss from the acute angle-closure event alone, one needs to differentiate between patients with pre-existing chronic angle-closure glaucoma and those without pre-existing disease. The limitation of many of the previous studies on acute angle-closure glaucoma is that patients with pre-existing disease are often not clearly identified and are included in the analyses. As a result, the field loss reported in many patients may have been due to pre-existing chronic glaucoma rather than the acute event.

Previous studies have demonstrated that despite significantly elevated IOP during acute angle closure, prompt treatment resulted in little long-term sequelae in terms of visual field defects.\(^{18,19,54}\) Aung et al\(^{54}\) showed that the majority of Asian eyes (62%) had no detectable visual field loss 6 months following an acute angle closure attack, but those that did develop abnormal visual fields tended to develop hemifield defects, consistent with that of nerve fibre bundle pattern loss. In addition, visual acuity shortly after an acute primary angle closure episode was generally good,\(^{57}\) suggesting that early and adequate control of the IOP during the acute episode can help to preserve much of the visual function of these eyes. This was the case in Caucasian populations as well, with the majority (60% to 75%) of patients who suffered an acute, symptomatic episode of angle-closure having no long-term visual field defects.\(^{18,19}\)

Interestingly, there has been evidence to show that visual field loss in patients with PACG that had a previous acute angle closure attack tended to be milder as compared to patients with asymptomatic and more insidious disease.\(^{52,58}\) Ang et al\(^{52}\) found that only 17.5% of patients with a previous acute event had end-stage visual field loss compared to 52.8% of patients with asymptomatic disease. Several reasons may account for this – because of the absence of dramatic symptoms, subjects with asymptomatic disease may remain undiagnosed and present later in the course of the disease. This results in longer periods of exposure to raised IOP and an increased likelihood of more severe glaucomatous optic nerve damage. This is similar to POAG, where the level of IOP has been shown to be a risk factor for visual field progression and is even more so in
PACG patients. Conversely, symptomatic patients present earlier, receiving earlier treatment and IOP control. The visual morbidity of PACG may therefore be related to the finding that the asymptomatic form of the disease is so visually destructive.

Conclusion

PACG is an important cause of visual morbidity in Asia and many parts of the world. Differences in the natural history and long-term outcome of the disease between Asians and Caucasians may reflect ethnic differences in the clinical course of PACG in these patients. There is a genetic and anatomic predisposition for Asian eyes to develop angle-closure glaucoma and Asian eyes have a greater tendency for peripheral anterior synchiae formation than other races, leading to a higher incidence of chronic or creeping angle closure despite a patent peripheral iridotomy. Other contributory factors in the pathogenesis of PACG include the greater degree of angle crowding caused by progressive lens thickening or a plateau iris configuration.

Asian eyes are known to be more prone to developing severe attacks of acute angle closure compared to Caucasians. This results in greater angle and trabecular damage, resulting in diminished aqueous outflow, and ultimately, raised IOP occurring weeks to months later. In addition, Asian patients with PACG were found to be less responsive to medical and laser therapy, and may require earlier intervention and closer monitoring. The conventional approach of treating PACG with laser peripheral iridotomy first followed by medication, then surgery in a step-wise manner may be effective in situations where patients can attend regular follow-up sessions. However, in situations where this is not possible, as may be the case in many developing Asian countries, early surgical intervention may be required to prevent further progression of the disease and blindness.

Ophthalmologists should be alert to the potential risk of significant visual loss in patients with PACG, particularly those with asymptomatic disease. Furthermore, in view of its insidious nature, greater efforts will need to be targeted at screening and early detection of this condition. With careful follow-up at these early stages, and timely intervention, disease progression can be halted. There is a pressing need for further research on this visually destructive disease.

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