Fundamental Concepts of Chronic Angle-closure Glaucoma

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INTRODUCTION
Chronic angle-closure glaucoma (CACG) is often asymptomatic. Many patients are diagnosed as chronic open-angle glaucoma (COAG) until accurate gonioscopy is performed. CACG is the most common form of angle-closure glaucoma (ACG) seen in the clinic, as well as in population-based surveys. This article describes diagnostic and therapeutic concepts of CACG.

CLINICAL CHARACTERISTICS AND SUBTYPES OF CHRONIC ANGLE-CLOSURE GLAUCOMA

Clinical Characteristics
CACG is composed of two clinical entities: angle-closure and glaucomatous optic neuropathy (GON) with functional and structural changes. Angle-closure, which is a mechanical blockade of the trabecular meshwork, precedes the development of glaucomatous optic neuropathy.

The onset of CACG is generally gradual but could be a consequence of an acute episode of angle-closure (AAC). In another word, CACG could develop after one or several AAC attacks, or gradually develop from appositional closure or creeping angle. The clinical presentation includes signs and symptoms of optic neuropathy and angle-closure.

Subtypes of CACG
Based on symptoms, CACG can be categorized into two main subtypes, asymptomatic and symptomatic CACG.

Asymptomatic CACG
Asymptomatic CACG is a more common subtype. The sign and symptom are similar to open-angle glaucoma except findings associated with angle-closure. The patient has no symptom of pain nor headache or history of acute attack. The eye gradually develops angle-closure from appositional closure to synechial closure, so called ‘creeping’ angle-closure. However, iridotrabecular contact slowly increases in circumference and height leading to compromised outflow and raised IOP. Prolonged contact leads to PAS as well as acquisition of pigment at the angle. Even in area without PAS, there was evidence of loss of endothelial cells and reactive repair processes. Based on a clinic-based study, patients with asymptomatic CACG were older than patients in the symptomatic group, were more often men, more likely to have either diabetes mellitus or hypertension.

Symptomatic CACG
Symptomatic CACG develops after AAC or intermittent angle-closure attack. Patient has variable degree of pain and headache, from very mild and vague aching pain to classic signs and symptoms of AAC. The visual symptoms like halo and blurred vision can be quite variable as well. On slit lamp examination, the ocular sign of ischemic sequel of AAC is usually seen in the anterior segment including distortion of iris tissue (iris whirling), necrosis of subcapsular lens epithelium (glaukomflecken), and pupillary distortion and dilatation. There is also a significant decrease in the corneal endothelial cell density in CACG eyes that have had AAC attack, which is more pronounced than those with intermittent attack. Delay in presentation (>24 hours) and unresponsiveness to medical treatment in termination of the acute attack in an acute angle-closure glaucoma patient had been identified as a significant risk in developing CACG. Symptomatic CACG eyes were more hypermetropic and had more iridocorneal synechiae and large areas where the pupillary ruff was absent.

PATHOGENESIS AND NATURAL HISTORY OF CACG

Risk Factors of Angle-closure
Eyes with relatively smaller anterior segment are prone to develop angle-closure. Eyes with chronic angle-closure glaucoma have different anterior segment anatomical relationships when compared to normals. The eye at risk tends to be hypermetropic with a shallow anterior chamber, a relatively anteriorly positioned lens and a short axial length. East or Southeast Asian ethnic background is an important risk factor for the development of chronic angle-closure glaucoma. Other demographical risk factors include older age, female gender and a familial tendency. Both increasing age and female
gender are known to have shallower anterior chamber which predispose angle-closure. Such association is observed in all races.\textsuperscript{17} Shallow anterior chambers are a significant risk factor for angle-closure in East Asians, although the nature of the association is specific to the individual population.\textsuperscript{18} There is still a controversy why East Asians have more prevalence of ACG as some known biometric risk factors are not different to other ethnic groups.\textsuperscript{19} A clinic-based study comparing the angle width of Asians, Afro-Americans, and Caucasians, demonstrated no statistically significant difference between the three groups. But the iris joins the scleral wall more anteriorly in Asians, slightly more posteriorly in Afro-Americans, and most posteriorly in Caucasians. Thicker lens, anteriorly positioned of the lens\textsuperscript{20} and smaller corneal diameter are also identified as risk factors.\textsuperscript{21-23} The role of the ciliary body anatomy and ciliary processes in the pathogenesis of this condition requires further investigation. Uptodates, there is no exact gene identified specifically for ACG.\textsuperscript{24}

**Mechanisms of Angle-closure**

There are several angle-closure mechanisms that play part in causing anatomical angle-closure. These include pupillary block, plateau iris, thick peripheral lens, lens-related causes, and ciliary block. Classification of mechanism into four level of blockage identifies obstructions to aqueous flow at different levels is widely accepted and practical.\textsuperscript{25} Pupillary block is the most common mechanism and presents in almost every case, other mechanism must also be identified. This leads to the common clinical observation and the use of terminology like ‘residual’ glaucoma, or so called ‘post-iridectomy’ glaucoma, was commonly used in the past for ACG after successful iridectomy.\textsuperscript{26} The terminology signifies that other mechanisms, in addition to pupillary block, probably co-exist in the angle-closure eye. A rather comprehensive study using biometry, UBM and gonioscopy, demonstrated that approximately half of the CACG eyes may have multiple mechanisms contributing to the closure of drainage angle.\textsuperscript{27}

**Angle-closure Glaucoma Cascade**

Angle-closure glaucoma can be viewed as a cascade of events (Fig. 1). The initial stage or the beginning of the cascade are the eyes that have relative anatomical abnormalities predisposing to the development of angle-closure and proceeding on to the final and common stage of glaucomatous neuropathy. Based on International Society of Geographical Epidemiological Organization (ISGEO) classification, the term ‘angle-closure suspect (ACS)’ is suggested for the initial stage. This is similar to ‘occludable’ angle that is commonly used in the clinic. ‘Occludable’ describes eye that the angle is closeable or the trabecular meshwork become non-visible but with normal IOP, disk and field. Clinicians sometimes use the term of ‘narrow’ angle interchangeably with ‘occludable’, though these two terms are not similar. The term “narrow” also reflects what clinician actually sees with slit lamp biomicroscopy and gonioscopy. Lots of debates have been going on to determine which terminology best reflects the condition. Recently, the Association of International Glaucoma Society (AIGS) suggested that ‘anatomical narrow angle (ANA)’ may be more appropriate as it represents the actual findings. The term ‘ANA’ emphasizes that the angle inlet is narrow as identified on gonioscopy and is likely to close under certain condition. If these eyes are treated early enough, angle-closure will not occur, thus preventing the cascade of angle-closure events. In another word, if angle-closure mechanism(s) can be corrected in time, most eyes return to normal.

If ACS is not treated early enough, it may develop into the next stage of angle-closure. The drainage angle is then closed with or without PAS. The mechanism of angle-closure could be single or multiple. As a result, IOP raises either acutely or chronically leading to the next stage coined ‘angle-closure (AC)’. At this stage, even if the angle-closure mechanism is corrected, IOP is still high. The magnitude of IOP rise depends on outflow reserve and degree of trabecular damage. The underlying angle-closure mechanism must be identified and corrected.

If treatment fails to prevent further and long-standing IOP rise, the eye progress to the final stage of the cascade. This is when glaucomatous optic neuropathy is evidenced, usually with detectable functional defect. The stage is ‘angle-closure glaucoma (ACG)’ when both angle-closure and glaucomatous optic neuropathy are present together. Clinically, the eye is diagnosed as CACG.
Clinical Significance of Different Disease Stage

Differentiating angle-closure into different stages does have clinical significance. Each stage indicates the presence or absence of the different end organ damage, which implies severity and chronicity of the condition, leads to better understandings of the treatment outcome. For example, the efficacy of LPI in prevention of IOP rise depends on the stage of angle-closure. In primary angle-closure suspect (PACS), a prophylactic LPI prevent further IOP rise in 97 percent based on a population-based study in an East Asian population. Another study showed that LPI successfully prevented further IOP rise in 89 percent of fellow eyes (in patients with acute attack) without the need for additional glaucoma treatment in the long-term. These fellow eyes could be viewed as good representatives of the high risk angle-closure suspect (ACS) eyes. Another retrospective study demonstrated that once the eye already had acute angle-closure attack, only 41.8 percent were successfully treated with LPI alone while the rest developed IOP rise that requiring further treatment at a mean follow-up of 50.3 months. However, in eyes with established glaucomatous optic neuropathy at diagnosis (ACG eyes), despite the presence of a patent LPI, most eyes require further treatment to control IOP. In a retrospective review of 83 ACG eyes, only five eyes (6%) did not require any treatment after LPI in the long-term.

So LPI is very effective in preventing angle-closure if it is performed early enough at the ACS stage. But if ACS already turns into AC stage, LPI alone become less effective and not optimal. However, when glaucomatous optic neuropathy is evidenced, LPI is not effective in treating or preventing further IOP rise. Majority of such eyes fail to have IOP control without medication or filtering surgery. Whether there are other mechanisms of angle-closure that cannot corrected with LPI or extensive damage has already occurred at the drain are to be investigated in each individual. The essence is that staging of angle-closure is important to the treatment approach and outcome determination.

TREATMENT CONCEPTS

Basic Principles

There are three basic principles of treatment in CACG. First, remove angle-closure by modification and correction of the angle-closure mechanism(s). Second, control the IOP and other associated risk factors. And third, monitor and maintain the structural and functional integrity of the optic disk and the retinal nerve fiber layer similar to treating other type of glaucomatous optic neuropathy.

Management Steps of CACG

There are five steps in the management of CACG (Table 1). The first step is to document the angle-closure and glaucoma by examination of the angle structures, including the trabecular meshwork, and the extent of the angle-closure by slit-lamp examination or gonioscopy. Indentation gonioscopy will help to determine the presence of PAS. UBM provides a high resolution image of the anterior segment structures and their relationships. UBM is currently the best imaging technique to view the posterior chamber and ciliary body, surpassing gonioscopy for dynamic study of the angle and revealing more information such as occludable angles.

The second step is to identify and correct the angle-closure mechanism. Pupillary block is the most common mechanism and is easily corrected by laser peripheral iridotomy (LPI) to open the angle. However, other mechanisms also need to be identified. As discussed earlier in this chapter, LPI is very effective for preventing increased IOP in eyes with occludable angles and ACS but is less effective for eyes with AAC and those with GON.

The third step is performing LPI and use of medication to control IOP. Medical therapy has recently become more important for CACG as the IOP may remain high even after successful iridotomy and iridoplasty. The efficacy of prostaglandin in CACG therapy was proven in a large-scale randomized multi-center study. The IOP reduction was 30 to 33 percent for eyes receiving latanoprost, compared with 20 percent for eyes receiving timolol.

This is followed by the next step of reassessment and further treatment. Even after successful LPI, most patients with CACG require further treatment, either because of multiple mechanisms of angle-closure or because the angle structure has been damaged to some extent. Patients therefore need to be reassessed after LPI for further treatment in the form of iridoplasty, medication, or surgery. Iridoplasty is effective for AAC, but has no proven efficacy for CACG. However, there is evidence to suggest that it is highly effective for pure plateau iris syndrome in Caucasians.

The final step in the management of CACG is to monitor IOP, optic disk, and visual fields, and to perform periodic gonioscopy. Glaucoma surgery by trabeculectomy remains the next step for IOP control. However, the success is highly
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dependent on postoperative care and management, and the outcome is variable.

SUMMARY

Fundamental concepts of CACG are important and must be understood well by clinician to successfully diagnosis, treating and assessing the outcome of CACG. The angle-closure glaucoma cascade, mechanism of angle-closure, and risk factors are described. Appropriate approach must be made by identifying angle-closure mechanisms and stage of the disease. The treatment concept is also outlined. LPI remains an important step in treatment, but most eyes with CACG need further treatment to control IOP, which relies largely on medication.

REFERENCES


