EXPERT RECOMMENDATIONS FOR GLAUCOMA MANAGEMENT IN ASIA

Practical clinical guide for ophthalmologists to implement the quality of intraocular pressure (QoIOP) control concept in Asian patients with glaucoma

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The information disclosed is based on the best available scientific data as interpreted by an expert faculty of ophthalmologists from across Asia with a special interest in glaucoma and a desire to implement the quality of intraocular pressure (QoIOP) control concept in clinical practice across the region. The development of this document followed an iterative process, with regular feedback and input from all members of the expert faculty.

This document includes a comprehensive overview of the considerations for ophthalmologists to implement the QoIOP control concept in Asian patients with glaucoma. Availability of assessment tools, diagnostics, and treatments may differ between countries across Asia, as well as within regions and clinics. The information presented is not intended to promote or recommend any indication, dosage, or other claim not supported by licensed product information. Santen only supports the promotion of products in a manner consistent with approved labeling. References to specific drugs, instruments, and other products are made for illustrative purposes only and are not intended to constitute an endorsement of such.

The information presented provides guidance for the pattern of practice, not for the care of any individual. While all efforts have been made to provide solid clinical evidence for all information contained within this paper, this is not always available; some information therefore is based on the opinion and clinical experience of the expert faculty. The information is intended to meet the general needs of most ophthalmologists and patients, it cannot possibly meet the needs of all. Any treatment decisions should be made on an individual patient basis after evaluation of the benefits and risks of available therapies. Important points to consider in making decisions in clinical practice include: (1) clinical circumstances (personal and material settings, clinical practice guidelines, etc.); (2) appropriateness of the direct application of the information to the patient's symptoms and signs; (3) the availability and/or limitations in tools, treatments, and time of the attending physician; (4) the resource constraints imposed by the medical facility; and (5) health insurance system limitations.

Asian glaucoma expert faculty members:

Dr Seng Kheong Fang (International Specialist Eye Centre, Malaysia)

Dr Ronnie George (Sankara Nethralaya, Chennai, India)

Prof. Kessara Pathanapitoon (Faculty of Medicine, Chiang Mai University, Thailand)

Assoc. Prof. Shamira Perera (Singapore National Eye Centre, Singapore)

Prof. Chungkwon Yoo (Department of Ophthalmology, Korea University Hospital, Korea University College of Medicine, Korea)

List of abbreviations

AGIS	Advanced Glaucoma Intervention Study
APGS	Asia Pacific Glaucoma Society
BAK	Benzalkonium chloride
CAI	Carbonic anhydrase inhibitors
CCT	Central corneal thickness
CLS	Contact lens sensors
EGS	European Glaucoma Society
GAT	Goldmann applanation tonometry
HFA	Humphrey Field analyzer
LASIK	Laser assisted in situ keratomileusis
LiGHT	Laser in Glaucoma and Ocular Hypertension
MIGS	Minimally invasive (or micro-incisional) glaucoma surgery
NTG	Normal-tension glaucoma
OCT	Optical coherence tomography
OH	Ocular hypertension
OPP	Ocular perfusion pressure
OSD	Ocular surface disease
OSDI	Ocular Surface Disease Index
PACG	Primary angle-closure glaucoma
PAPS	Prostaglandin-associated periorbitopathy syndrome
PF	Preservative-free
PGA	Prostaglandin analogs
POAG	Primary open-angle glaucoma
QoIOP	Quality of intraocular pressure
SITA	Swedish Interactive Thresholding Algorithm
SLT	Selective laser trabeculoplasty
UKGTS	United Kingdom Glaucoma Treatment Study
VF	Visual field
WDT	Water drinking test

Table of contents

Abstract

Glaucoma is the leading cause of irreversible blindness around the world, affecting a disproportionately high number of patients in Asia (~60%). Providing effective glaucoma treatment in Asia can be challenging because of numerous factors: a general lack of awareness of the importance of glaucoma screening, an insufficient ability to correctly evaluate, diagnose and monitor patients, restricted access to appropriate medications, and poor treatment adherence. Currently, glaucoma management is mainly focused on the quantity-based numerical reduction of intraocular pressure (IOP) rather than holistic, quality-based approaches to glaucoma and IOP management. In addition to IOP reduction, key considerations should include: rate of response to treatment, long-term control of IOP as well as visual field (VF) stability, the role and impact of 24-hour fluctuations in IOP, and the importance of ensuring patients adhere to their prescribed treatments. Together, these considerations constitute the quality of IOP (QoIOP) control concept.

Introduction

Overview of glaucoma in Asia

By 2040, it is estimated that ~111.8 million patients aged 40–80 years will be living with glaucoma globally.[1] This is a significant rise from the 2020 global estimate of ~76 million,[1] and is largely attributable to the increase in glaucoma cases predicted in Asia (from ~59.5 million cases in 2020 to ~80.9 million, in 2040).[2]

Furthermore, by 2040, South-Central Asia is expected to have the highest number of patients with primary open-angle glaucoma (POAG; ~23.3 million) and secondary glaucoma (~4.3 million), surpassing East Asia which is currently ranked first for these subtypes. East Asia is still expected to have the highest number of patients with primary angle-closure glaucoma (PACG; ~9.1 million).[2]

Given the large and increasing number of patients currently living with glaucoma across Asia, particularly in South-Central and East Asia, it is vital that patients are identified and managed appropriately using quality-based approaches to reduce the burden on patients and healthcare systems.

Challenges to effective glaucoma management in Asia

Screening

While patient education and population-based screening initiatives are key, such programs can be difficult to implement and are largely dictated by the national health insurance system or policies. In resource-poor countries, this can be further complicated by a lack of access to adequate resources and acceptable screening techniques.[2] Thus, it is important to focus on improving partnerships between ophthalmologists, optometrists, and allied healthcare professionals to increase awareness of early detection as well as better implementation of the QoIOP control concept in clinical practice following diagnosis.

"To date, a Malaysian initiative to encourage partnerships between ophthalmologists and optometrists has shown promising results in urban areas, while rural involvement has been more challenging. Additionally, nurses in Thailand are being trained to evaluate patients, and social media initiatives during World Glaucoma Week have been used to raise awareness and educate patients on glaucoma."

– Commentary by faculty members

Diagnosis and beyond

Another challenge faced by ophthalmologists relates to diagnosing different types of glaucoma, which brings into question the best method for screening patients to ensure a correct diagnosis.

"It is important to consider glaucoma beyond quantity-based IOP measurements and incorporate ancillary testing of visual field (VF) and/or gonioscopy to evaluate the optic nerve or anterior chamber angle as part of a quality-based approach."

– Commentary by faculty members

Such measurements are particularly important for the diagnosis and management of normal-tension glaucoma (NTG), as patients with this glaucoma subtype present with IOP that is within the normal range.[3]

"Despite the importance of looking beyond quantity-based IOP measurements, there is currently little emphasis on performing ancillary testing."

– Commentary by faculty members

Relying on quantity-based IOP measurements alone, and consequently overemphasizing IOP reduction, may lead to other clinically relevant aspects of glaucoma being overlooked.

Where access to VF and/or gonioscopy is limited, it may be tempting to rely on optical coherence tomography (OCT) to support diagnosis. However, this non-standard technique often results in false-positives ('red disease') that lead to misdiagnosis and unnecessary treatment.[4] OCT is less sufficient for the detection of disease progression in patients with advanced glaucoma, even with macular or retina nerve fiber layer scans, and thus should not be used as a replacement for VF testing.[5]

Further complications may arise when attempting to diagnose glaucoma in patients with other ocular conditions. For example, high myopia (refractive error of ≥-6.00 diopters) not only increases a patient's risk for developing glaucoma,[6] but may lead to optic nerve changes that are indistinguishable from those seen in patients with glaucoma.[4] Given the prevalence of high myopia is increasing, particularly in patients from East Asia,[6] it is important to consider its impact on glaucoma diagnosis. Additionally, although a large cup-to-disc ratio has historically been used to diagnose glaucoma and predict the likelihood of disease progression, there are large differences in the size and shape of optic discs which make cup-to-disc ratio assessment unreliable.

Follow-up assessment to determine response/VF preservation and the rate of VF progression is important when monitoring glaucoma, to enable the provision of long-term, quality-based assessment and informed treatment choices. While IOP measurements determined during office hours may be considered normal or within the target IOP range, these measurements do not reflect IOP fluctuations throughout the day, which are known to increase the risk of accelerated disease progression.[7,8] In fact, the Advanced Glaucoma Intervention Study (AGIS) reported that for every 1 mmHg increase in IOP fluctuation, the odds of VF progression increases by ~30%.[9] As

such, by relying on singular IOP measurements alone to assess treatment adequacy, a large number of patients may receive inadequate management, leading to further visual impairment or even blindness.[10] This highlights the importance of VF assessments as part of a quality-based approach to glaucoma management. However, the challenges of performing VF testing noted above will need to be overcome to allow ophthalmologists to provide targeted care for patients. Increasing awareness and placing an emphasis on the need for more frequent VF testing as part of a quality-based approach may help secure better resources to enable sufficient VF analysis.

Guideline-recommended glaucoma therapies

While the Asia Pacific Glaucoma Society (APGS) and European Glaucoma Society (EGS) guidelines outline ideal treatment practices in the absence of more specific local guidelines, such guidelines may not be relevant across Asia due to lack of access to appropriate treatments in some countries. The cost of prostaglandin analogs (PGAs) is generally not an issue across the Asia Pacific region, but other barriers are faced such as limited market access. Additionally, the quality of ophthalmic generics is a global issue, largely occurring because clinical studies are not usually required for the approval of generics in ophthalmology.[5]

Poor patient adherence to glaucoma treatment

Patient adherence is a complex issue with multiple and varied contributing factors.[11] Non-adherence rates of up to 80% have been reported for medical treatments in general,[12] and critically, a lack of adherence has been associated with VF progression and blindness in patients with glaucoma.[12,13]

Side effects of glaucoma medications can have a major impact on adherence to treatment. Corneal and conjunctival toxicity commonly result from a reaction to preservatives, particularly benzalkonium chloride (BAK), in glaucoma medications.[14]

"In the short-term, adverse effects may include hyperemia, while evidence of ocular surface disease (OSD) may be seen in the long-term."

– Commentary by faculty members

Prostaglandin-associated periorbitopathy syndrome (PAPS) is also now recognized as a clinical and cosmetic side effect of long-term treatment with topical PGA, particularly in patients over 60 years.[15] The occurrence of PAPS may not only have an impact on treatment adherence,[15] it can also affect IOP measurements, potentially confounding follow-up assessment to determine treatment response and monitor disease progression.

Poor treatment adherence has been associated with VF progression and blindness.[12,13] Therefore, better communication with patients to educate them on the side effects and expected benefits from treatment may lead to improved treatment adherence, and should form part a

quality-based approach to glaucoma management. Furthermore, initiating PF formulations for the treatment of dry eye disease (or switching to such medications as needed) may help to mitigate the negative effects experienced by patients.[16]

Moving away from quantity-based IOP measurements and toward QoIOP control in clinical practice

A shift in mindset from 'quantity-based IOP measurements' to 'quality-based IOP control' is needed for better management and treatment of patients with glaucoma. Given the large and increasing number of patients currently living with glaucoma across Asia, particularly in South-Central and East Asia,[1,2] it is vital that clear and consistent, practical clinical guidelines are available to assist ophthalmologists with the implementation the QoIOP control concept in clinical practice.

The QoIOP concept incorporates five key areas to provide a holistic approach to glaucoma and IOP management:

1. IOP reduction
2. IOP response rate
3. Long-term IOP control and VF stability
4. Twenty-four (24)-hour fluctuations
5. Treatment adherence and persistence in patients

This paper outlines and provides a detailed discussion of these key aspects, to provide ophthalmologists with a better understanding of the QoIOP control concept with the hope of facilitating wider implementation of QoIOP throughout Asia.

Methods

Three meetings were held between August 2020 and October 2022 to solicit insights and feedback from glaucoma experts from the Asia Pacific region. The aims of these meetings were to address the importance of the QoIOP control concept, the challenges associated with its practical implementation, and to develop a practical clinical guide for ophthalmologists.

The aim of this paper is to provide recommendations from glaucoma experts to inform ophthalmologists about the QoIOP control concept, to facilitate wider implementation of QoIOP throughout Asia.

Results: Considerations for ophthalmologists to implement the QoIOP control concept in Asian patients with glaucoma

IOP reduction

Suggested target IOP (range)

The ultimate aim when treating patients with glaucoma is to reduce IOP to slow the deterioration of VF and maintain or improve the patient's quality of life.[5] Target IOP is defined by the APGS as 'the pressure range estimated to slow or halt disease progression' while the EGS guidelines define target IOP as 'the upper limit of IOP judged to be compatible with [the] treatment goal'.[5,17] There are various methods for calculating the target IOP; however, all provide similar target ranges according to the stage of glaucoma. As such, no specific algorithm is recommended. Initial target ranges are outlined in Figure 1.

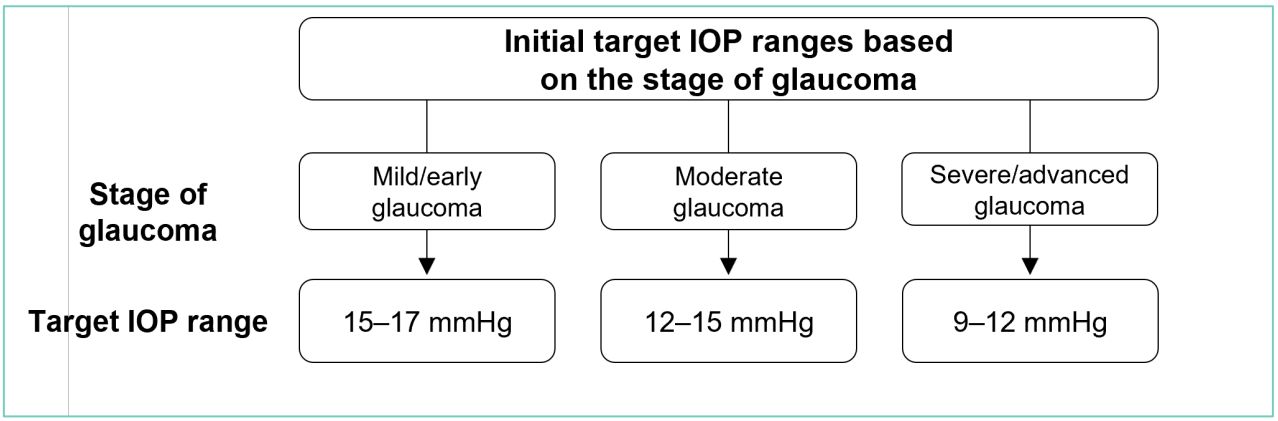

Figure 1: Initial target IOP ranges based on the stage of glaucoma.[5,17]
IOP: intraocular pressure.

"Although the guideline above outlines target IOP ranges based on numerical values, target IOP may need to be set on a case-by-case basis. For example, when initially prescribing treatment for patients with severe/advanced glaucoma, setting a numerical IOP target or target range can be useful as these patients require a more significant initial reduction in IOP. However, for patients with mild/early or moderate glaucoma, it may be useful to set the target IOP based on a percentage reduction from baseline instead. This can be used throughout the patient life cycle and adjusted as needed or updated to numerical values during follow-up visits. This may help to make the goal more 'realistic'. An important factor to keep in mind is that it may be difficult to achieve a 20% IOP reduction in patients whose initial baseline IOP that is very low (e.g. early teens). In this case, numerical targets may be more appropriate."

– Commentary by faculty members

The stage of glaucoma (e.g. mild/early, moderate, or severe/advanced) is determined based on the severity of mean VF defect (rather than IOP measurement), where the mean VF defect ranges are defined as follows:[5]

- Mild/early glaucomatous loss: mean VF defect of ≤6 decibels
- Moderate glaucomatous loss: mean VF defect of >6 decibels and ≤12 decibels
- Severe/advanced glaucomatous loss: mean VF defect of >12 decibels

Several additional factors should be considered when setting the target IOP for individual patients, including the patient's life expectancy, baseline IOP, additional risk factors (e.g. pseudoexfoliation syndrome/glaucoma), and the estimated rate of progression (a patient expected to have a fast rate of progression will require a lower target IOP).[5,17] Other factors to consider include family history, planned interventions and any expected adverse outcomes, patient preference, socio-economic factors, as well as the non-glaucomatous eye (if applicable).[5]

Furthermore, it is important to also consider the possibility of confounding factors when performing IOP measurements. Decreased central corneal thickness (CCT) is a known independent risk factor for glaucoma progression. In addition, in patients with thin corneas, IOP measurements may be underestimated. Additionally, an awareness of a patient's ocular history may facilitate better understanding of results and a tailored treatment and monitoring approach. For example, the laser assisted in situ keratomileusis (LASIK) procedure is known to cause corneal thinning; patients who have previously undergone this procedure may need more careful monitoring to compensate for their artifactually lower IOP measurements.[18] It is also important to note that average baseline CCT ranges may differ between patient populations (for example, a mean CCT of ~505 µm [SD ~30 µm] has been observed in patients from rural India and in Mongolians compared with a mean CCT of ~540 µm [SD ~35 µm] in patients from Europe or in Chinese Singaporeans).[17] As such, a thorough understanding of the patient's CCT will enhance interpretation of IOP.[17]

The EGS also recommends that a patients' target IOP is re-evaluated regularly, and adjusted where there is evidence of disease progression (per quality-based assessments) or where a patient has developed ocular or systemic comorbidities (Figure 2).[5]

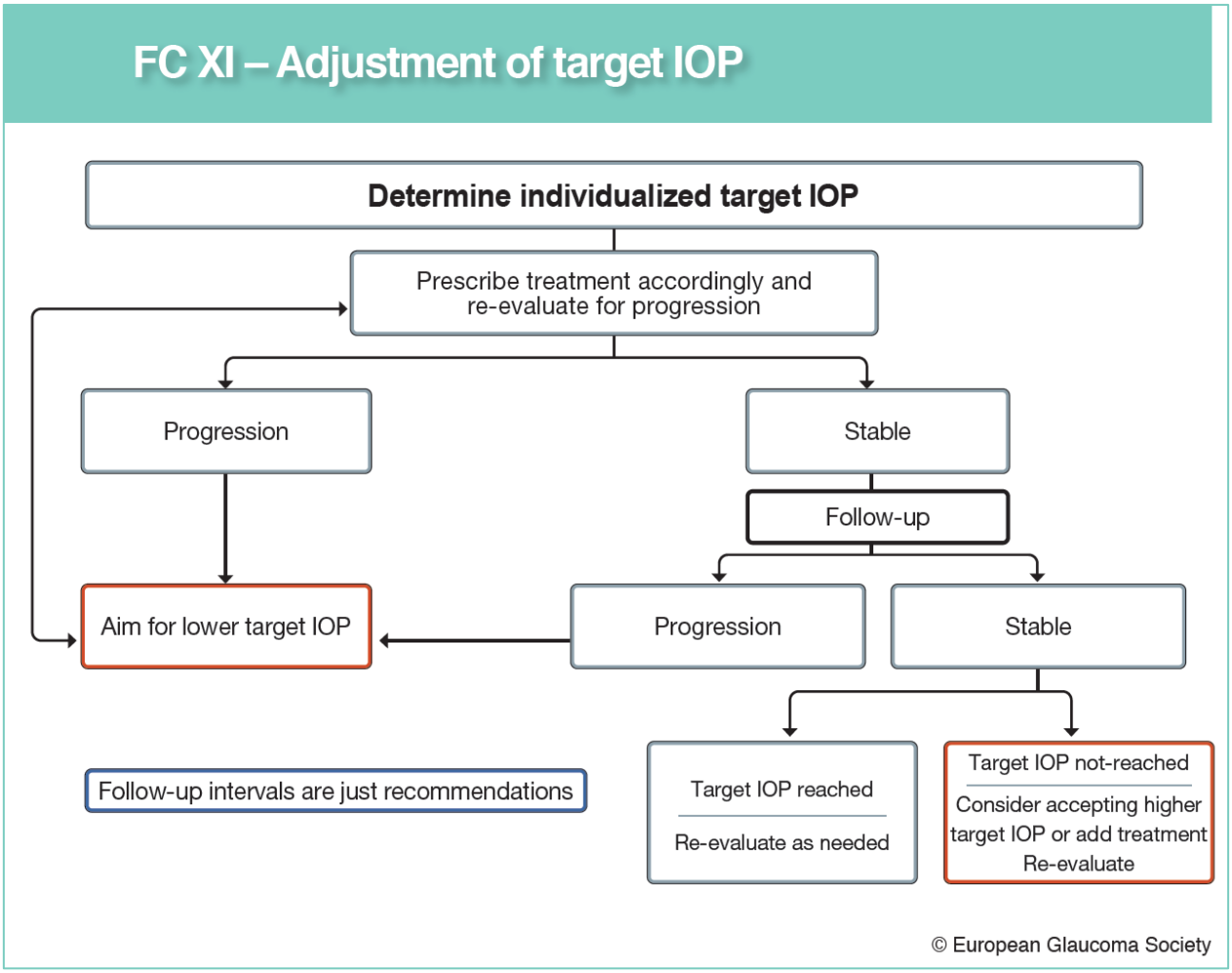

Figure 2: Adjustment of target IOP.
Source: European Glaucoma Society (EGS) Terminology and Guidelines for Glaucoma. 5th ed.[5]
IOP: intraocular pressure; NR: not reached.

IOP reduction methods

For newly diagnosed patients, both the APGS and EGS guidelines recommend initiating treatment with monotherapy.[5,17] Overall, medications within the PGA drug class have the greatest efficacy for reducing IOP with a good safety profile, and are thus recommended for first-line treatment. Other types of anti-glaucoma medications include β-receptor antagonists (β-blockers; selective and non-selective), α_2-adrenergic agonists (selective), carbonic anhydrase inhibitors (CAI), Rho kinase inhibitors, cholinergic drugs, and hyperosmotic agents (Table 1).[5,17]

Four PGAs (bimatoprost, latanoprost, travoprost, and tafluprost), have been shown to selectively target the F-prostanoid receptor and exhibit similar mean IOP-lowering capabilities in patients with POAG and NTG.[19-21] If IOP control is insufficient following initial monotherapy, it is recommended to switch patients to a different monotherapy rather than adding another medication.[5,17] There is evidence to suggest that some patients who did not respond to initial treatment with one PGA may respond to a different PGA upon switching.[21] This may therefore be

considered, in addition to switching to a drug of a different class.[5] It should be noted that patients with very high IOP and severe disease at baseline may be initiated with fixed-dose combinations or combination therapy with medications from different drug classes.[5,17]

If IOP control is insufficient following monotherapy, the addition of a second medication (with a different pharmacological action) may be considered. However, as part of a quality-based approach to patient care, it is important to keep in mind that addition of a second medication may reduce patient adherence to treatment as well as increase preservative exposure, increasing the risk of adverse reactions to treatment. Fixed-dose combinations are therefore preferred.[5,17]

"Fixed-dose combinations of PGA-β-blockers are preferred over other combinations."

– Commentary by faculty members

The fixed-dose combination of tafluprost-timolol is generally well accepted for IOP control. Evidence suggests that in patients with POAG and ocular hypertension (OH) who have ceased PGA or β-blocker monotherapy due to insufficient IOP control or intolerance may benefit from switching to tafluprost-timolol fixed-dose combination.[22] Patients can administer the drug in the morning or evening,[22,23] and Konstas and colleagues demonstrated significantly reduced 24-hour IOP with either morning or evening administration of tafluprost-timolol fixed-dose combination compared with latanoprost. Evening dosing with tafluprost-timolol was associated with significantly improve daytime and 24-hour IOP control when compared with morning dosing.[23]

Table 1. Dosage and efficacy of various anti-glaucoma drug classes.[5,17,24-27]

Drug class	Mechanism of action	Daily dosage	Efficacy (IOP reduction)
PGAs	Increases aqueous outflow via uveoscleral pathway	1x	25–35%
β-blockers*	Decreases aqueous humor production	1x to 2x	20–25%
α_1-blockers	Increases aqueous outflow via uveoscleral pathway	2x	15–20%
α_2-agonists†	Decreases aqueous humor production and increases aqueous outflow via uveoscleral pathway	2x to 3x	18–25%
α_1β-blockers	Increases aqueous outflow via uveoscleral pathway	2x	20%
CAIs Topical Systemic	Decreases aqueous humor production	 2x to 3x 2x to 4x	 20% 30–40%
Rho-kinase inhibitors	Increases aqueous outflow via trabecular meshwork	1x to 2x	20%
Cholinergic drugs	Increases aqueous outflow via trabecular meshwork	3x to 4x	20–25%
Hyperosmotic agents	Dehydrates and reduces vitreous volume	Stat dose(s)	15–30%
EP2 receptor agonists	Increase aqueous outflow via trabecular meshwork and uveoscleral pathway	1x	15–35%
Nitric oxide donating-PGA	Increase aqueous outflow via trabecular meshwork and uveoscleral pathway	1x	26–34%

Proprietary fixed-dose combinations	As described for each monotherapy		
β-blocker + CAI		2x	25–30%
β-blocker + PGA		1x	25–35%
β-blocker + pilocarpine		2x	25–30%
β-blocker + α_2-agonist		2x	25–35%
CAI + α_2-agonist		2x to 3x	25–35%
Rho-kinase inhibitor + PGA		1x	30–36%

*If a patient is taking systemic β-blockers, the decrease in IOP with topical β-blockers is likely to be reduced, and the potential for systemic side effects increased: consider other drug classes first; †α_2-Agonists are absolutely contraindicated for patients taking MAOIs and for children <2 years.

CAI: carbonic anhydrase inhibitors; EP2: E-prostanoid subtype 2; PGA: prostaglandin analog.

Newer anti-glaucoma medications have emerged in recent years, and include non-prostaglandin, selective E-prostanoid subtype 2 (EP2) receptor agonists, Rho kinase inhibitors, and nitric oxide donating-PGAs. Omidenepag isopropyl is a promising PGE2 receptor agonist with similar IOP-lowering capabilities to traditional PGAs. Furthermore, as omidenepag is a non-prostaglandin agonist, it exerts its IOP-lowering mechanism without causing PAPS, a common side effect of traditional PGAs.[28]

The MERCURY-1 and MERCURY-2 studies reported that Rho kinase inhibitors (i.e. netarsudil or ripasudil) can reduce IOP in patients with POAG or OH.[29,30] However, this class of drug appears to be inferior compared with timolol or latanoprost monotherapies.

"The expert faculty concluded that combination of Rho kinase inhibitors with latanoprost or timolol may lead to an additional reduction in IOP compared with monotherapy using any of these three medications."

– Commentary by faculty members

It was noted that none of the trials included in the review reported data related to disease progression (e.g. VF defects, evaluation of optic discs) or patient reported outcomes, thus, more research is needed to confirm the role of Rho kinase inhibitors for the treatment of glaucoma.[31]

Latanoprostene bunod is an example of a nitric oxide donating-PGA that can lower IOP in patients with POAG and OH.[32] It provides a dual mechanism of action for IOP reduction (via conversion of the active ingredient to latanoprost acid and nitric oxide, both of which are capable of independently lowering IOP), and may be superior to monotherapy with latanoprost or timolol. Furthermore, latanoprostene bunod is generally well tolerated, with a safety profile similar to that of latanoprost.[32]

Safety and tolerability considerations (topical medications)

Preservatives are responsible for many of the adverse effects observed in patients administering topical glaucoma medications, causing discomfort and poor treatment adherence. The presence of preservatives, particularly BAK which is found in ~70% of ophthalmic medications, has been associated with corneal and conjunctival toxicity.[14] More specifically, BAK is commonly found in glaucoma medications, with concentrations ranging from 0.004% to 0.02% per mL (Table 2).[24-26,33-43] Wolfram and colleagues have demonstrated that patients using preservative-containing medications are more than twice as likely to report non-adherence compared with those on PF formulations.[44] Furthermore, real-world data have shown that switching to PF-fixed-dose combinations improves patient tolerability without compromising IOP reduction.[22] Given the increased likelihood of VF progression and blindness in patients who are non-adherent to their anti-glaucoma medications,[12,13] initiating or switching to PF-fixed-dose combinations should be considered as part of QoIOP control practice. Furthermore, given the risk of developing OSD with the use of preservative-containing medications, PF medications should be preferentially prescribed for pre-operative patients and those with pre-existing OSD.

Long-term and/or unilateral use of traditional PGAs is also commonly associated with development of periocular changes and PAPS, reported in >40% of patients treated for at least three months, and >60% of patients after six months of treatment.[45,46] Furthermore, patients aged >60 years are up to three times more likely to develop signs of PAPS.[15,46] PAPS is characterized as a constellation of adverse events occurring around the eye, including hyperpigmentation of the iris and skin around the eye, excessive eyelash growth, deepening of the upper eyelid sulcus, flattening of the lower eyelid bags, mild enophthalmos, orbital fat atrophy, tight orbit and eyelids, inferior scleral show, and involution of dermatochalasis.[47-49] Furthermore, PAPS is markedly more frequent and severe in patients treated with bimatoprost compared with latanoprost and travoprost.[50]

"Nonetheless, PAPS should be considered as a part of a quality-based management approach, as it can impact on adherence to PGAs, the patient's QoL, and may lead to erroneous IOP measurements."

– Commentary by faculty members

Clear communication to inform patients of the possible side effects of treatment and that PAPS is generally reversible upon halting treatment is vital for managing patient expectations and improving treatment adherence, and should be incorporated as part of the QoIOP control concept.

Table 2. Concentrations of BAK used in common glaucoma medications

Glaucoma medication	Trade name	BAK concentrations (% per mL)
Latanoprost	Xalatan	0.02%
Latanoprostene bunod	Vyzulta	0.02%
Apraclonidine	Iopidine	0.01%
Brinzolamide	Azopt	0.01%
Pilocarpine	Isopto Carpine	0.01%
Travoprost	Travatan Travatan Z	0.015% 0%
Netarsudil	Rhopressa	0.015%
Timolol	Tiopex/Timoptol	0.012%
Dorzolamide	Trusopt	0.0075%
Brimonidine	Alphagan Alphagan P	0.005% 0%
Bimatoprost	Lumigan	0.005%
Omidenepag isopropyl	Eybelis (Asia) Omlonti (US)	0.005%
Ripasudil	Glanatec	0.004%
Tafluprost	Taflotan Taflotan-S (Asia) Zioptan (US)	0.001% 0% 0%

Other options for lowering IOP

Selective laser trabeculoplasty

Selective laser trabeculoplasty (SLT) is a painless laser procedure conducted in the outpatient setting to reduce IOP by increasing the trabecular meshwork aqueous outflow.

It may be useful in a select group of patients, i.e. those who are 1) young, 2) have high IOP, 3) have difficulty using eye drops correctly, and/or 4) have early-to-moderate disease."

– Commentary by faculty members

The Laser in Glaucoma and Ocular Hypertension (LiGHT) trial examined the effects of SLT compared with eye drops alone, as first-line treatment in patients with POAG or ocular hypertension. The trial demonstrated that patients in the SLT group achieved their target IOP at more study visits (93.0%) compared with patients receiving eye drops alone (91.3%), and 74.2% did not require eye drops at 36 months post-SLT. Additionally, first-line SLT was more cost-effective (based on UK standards) compared with the use of eye drops in the first-line.[57] It should be noted that the majority of patients in the trial were Caucasian, with Asian patients accounting for less than 10% of patients in either treatment arm.[57]

"As such, results from this trial should be interpreted carefully when considering SLT as an option for Asian patients while results from similar ongoing studies in Asian populations are awaited."

– Commentary by faculty members

Nonetheless, it is important for patients to be aware that any benefit obtained from SLT will not be permanent (although the procedure can be repeated), and follow-up appointments to monitor their glaucoma are advised.[57]

"Anecdotally, second- or third-line SLT can result in an IOP reduction of ~15–20% in approximately 60% of patients after two months, while SLT in the first-line is successful in two thirds of patients."

– Commentary by faculty members

Surgery

Patients who have failed medical and/or laser treatment may require surgery to control IOP and minimize glaucoma progression;[17] however, challenges associated with availability of and accessibility to these procedures across the Asia Pacific region may be significant barriers to use of these techniques.

"The only minimally invasive (or micro-incisional) glaucoma surgery (MIGS) procedure available in Thailand is Xen®, which is only partially reimbursed in a small proportion of patients (~20%), while in India, accessibility to SLT has improved in recent years but access is largely limited to major cities."

– Commentary by faculty members

Tips and tricks: IOP reduction

1. Target IOP range must be set prior to initiating treatment, based on ocular and patient-specific factors
2. Confounding factors such as CCT must be considered when measuring IOP
3. Record the initial IOP, documenting the time and the type of IOP measurement. Share this information with specialists upon referral
4. Monotherapy is recommended as first-line treatment, except in cases with very high IOP and severe disease. If more than one treatment is required, consider fixed-dose combinations. The highest reduction of IOP is obtained with PGAs
5. Alternative treatment options including SLT and surgery are available as first line therapy in some cases and for patients who have failed treatment with topical anti-glaucoma therapies

IOP response rate

Why is it important to consider IOP response rate?

"Response rate data should be key when selecting anti-glaucoma medication, and it is important to consider response rates with different types of medications. The percentage reduction in IOP compared with baseline must be considered to determine when and if a patient has responded to treatment. As such, accurate recording of a patient's initial IOP measurement is critical for assessment of patient response to treatment as part of the QoIOP concept. Baseline IOP should be provided to glaucoma specialists upon referral; without this, it becomes difficult to assess the mean IOP reduction and response rate of the medications in patients who have already commenced treatment. Additional information to be documented includes the time of IOP measurements (since IOP is known to fluctuate during the day), as well as the type of tonometer used (i.e. air-puff tonometer or Schiotz analog tonometer [which are less reliable but sometimes used in rural hospitals in Thailand] vs Goldmann applanation tonometry [GAT])."

– Commentary by faculty members

There is evidence that patients who do not respond to a PGA may respond better when switched to another PGA. A prospective, randomized, multicenter cross-over study by Mizuguchi et al. showed that some patients only responded to one type of PGA administered (i.e. tafluprost vs travoprost), where a small number of patients did not respond to either medication.[21]

"Additionally. switching to omidenepag isopropyl may be an option for patients who do not respond to a PGA."

– Commentary by faculty members

Furthermore, the EGS guidelines note that for patients who previously had poor response to monotherapy, combination therapy consisting of two agents with different modes of action can improve response rates.[5]

When to conduct IOP measurements to determine response rate to medication

"To determine the response to treatment accurately, an appropriate amount of time should be allowed for the medication to elicit a response. Typically, in patients who are treated with PGAs, response to medication should be assessed after four weeks of treatment, but it is important to keep in mind that some patients may be defined as delayed (or late) responders to treatment."

– Commentary by faculty members

A Japanese study reported that 10–15% of patients exhibited a better response after an additional four weeks of treatment.[58]

"Similarly, a review of 100 patients showed that for patients with early glaucoma and a poor initial response to treatment, an additional 3–4 weeks of treatment may be required to accurately measure treatment response rates (unpublished data, Prof. Chungkwon Yoo). For other anti-glaucoma medications, assessment of treatment response after two weeks of treatment should be sufficient, though high incidence of hyperemia is seen with Rho kinase inhibitors meaning true assessment of response to treatment may occur after three months.

Hyperemia may be driving the delayed responses seen in some patients, however this side effect typically improves over time. As such, it may be prudent to follow patients prior to their initial assessment of efficacy after four weeks of treatment to assess the presence of any side effects and thus likelihood of a delayed response."

– Commentary by faculty members

The Monocular Trial, which demonstrated utility in assessing a patient's response to medication based on the response in one eye, may also be useful for estimating a patient's likely response to treatment.[59]

How to define 'non-response' to treatment

While the expected response rates to glaucoma medications are known (Table 1), the definition of 'non-response' to treatment is poorly defined and varies across studies. Mizoguchi and colleagues,[21] along with others,[60,61] have used 10% as the cut-off value to define non-response. Others define non-responders as those whose IOP was not reduced by 20% compared with baseline,[62] or based on either 15% or 20% reduction in IOP compared with baseline.[63] Alternatively, an open-label study of bimatoprost in patients with POAG or OH refractory to latanoprost defined non-responders based on an absolute reduction in IOP of <3 mmHg compared with baseline.[64]

"Taking the expected variability observed with IOP measurements into consideration, the 10% threshold for non-response to monotherapy appears reasonable, with clinical judgment to be used on a case-by-case basis. For example, for patients with severe disease, the non-response cut-off may need to be 15% when compared with baseline. It is important to note that these definitions related to patients receiving an initial monotherapy. In patients receiving a secondary glaucoma medication, a less substantial decrease in IOP can be expected."

– Commentary by faculty members

Tips and tricks: IOP response rate and timing of IOP measurements

1. Unless immediate IOP reduction is necessary, obtain 2 or more untreated IOP readings at different times for the baseline IOP (especially in eyes with IOP within normal range). It is important to document the initial *untreated* IOP and inform glaucoma specialists when referring patients
2. Monocular trial is helpful to assess the medication efficacy in eyes with low-teen untreated IOP
3. Regarding delayed responders: some eyes may show delayed responses to PGA. Re-assess the medication efficacy in another 2–4 weeks if the initial response seems insufficient in eyes with early glaucomatous damage
4. In patients who are poor responders, consider the following:
   a. Check patient adherence to medication and/or side effects
   b. Switch to another PGA or other medications such as OMDI
   c. Switching to a fixed combination (PGA/BB, CAI/BB, AA/BB, CAI/AA)
5. For assessment of the medication efficacy, it is desirable to measure IOP at a similar time of the day to minimize the effect of diurnal IOP variations

Long-term IOP control and VF stability

Why is it important to consider long-term IOP control?

Maintaining long-term IOP control reduces the risk of disease progression. The AGIS demonstrated that for every 1 mmHg increase in IOP fluctuations, the odds of VF progression increased by approximately 30%.[9] As such, assessment of long-term IOP control, as well as the method(s) employed to achieve it, should be a key consideration when implementing the QoIOP control concept in clinical practice.

Several studies have highlighted the long-term IOP-lowering effects of PGAs. Of note, the LOTUS study retrospectively examined the long-term safety and efficacy of three PGAs (tafluprost, travoprost, and latanoprost) in Korean patients with POAG or NTG who had received one of the three PGAs as initial monotherapy prior to study initiation. The study showed no significant difference in VF progression between patients who received tafluprost, travoprost, or latanoprost monotherapies, demonstrating the role of PGA monotherapy in minimizing VF progression in patients with early-stage glaucoma.[20] Additionally, the United Kingdom Glaucoma Treatment Study (UKGTS) study which evaluated latanoprost in patients with POAG across ten sites in the UK was the first randomized placebo-controlled trial to show that the use of IOP-lowering medication preserved VF in this patient population.[65] Two caveats to note are that the majority (~90%) of study participants were White, and the study excluded patients with advanced glaucoma (defined as mean VF deviation >–10 decibels in the better eye or >–16 decibels in the worse eye).

When to assess VF: Recommended frequency of VF evaluation

Rates of VF progression are known to vary from patient to patient.[66] Evaluation of VF progression over time (in conjunction with assessments to determine long-term IOP control) is essential to identify patients with disease progression, and allows ophthalmologists to better understand the quality of IOP control achieved by the prescribed IOP reduction methods. It is clear that VF testing should be carried out more than once per year, with the EGS recommending six tests (three tests/year) in the first 2 years following diagnosis to assess VF progression.[5] Chauhan and colleagues suggest that at least three examinations are required each year to detect moderate progression (~0.5 decibels/year) after 4.3 years, or fast progression (~2 decibels/year) after 1.7 years (at 80% power); the time taken to detect disease progression is extended if fewer examinations are performed.[10] However, a UK-based study has shown that the number of VF tests performed in practice falls below the recommended number, largely because of a lack of resources/impracticality, and difficulties faced by patients when undertaking the test.[66]

"Even for glaucoma specialists, achieving the recommended number of tests is difficult. As such, some aim to complete 5 VF tests during the first 2 years, while others perform 2

VF tests in the first 6 months followed by another within the next 6–12 months (depending on the stage of the glaucomatous damage).”

– Commentary by faculty members

Of course, the frequency of VF testing should be modified based on the stage of disease. For example, more frequent testing is required for patients who have a high risk of VF loss or those with advanced disease in whom it is more difficult to detect progression.[10,67]

“It is also worth noting that in patients with pre-perimetric/early stage glaucoma, structural changes usually precede functional VF changes. Some patients develop VF progression in the non-linear rate. Therefore, a focus should also be placed on monitoring and evaluation of structural changes when determining glaucoma progression in an attempt to avoid a delay in the identification of VF changes in these patients.”

– Commentary by faculty members

VF analysis and interpretation

Analysis of VF progression can be based on ‘events’ (i.e. analysis comparing a patient’s VF status at a follow-up examination to baseline), or ‘trends’ (i.e. the rate of change based on a regression analysis).[5,10]

Automated perimetry is most commonly performed using the Humphrey® Field Analyzer (HFA and HFA2; Zeiss, Jena, Germany), which operates Swedish Interactive Thresholding Algorithm (SITA) Standard 24-2 and SITA Fast 24-2. As the name suggests, the Fast program can be performed in a shorter period of time compared with the Standard program, which should make VF assessment easier for patients. However, at lower VF sensitivities, the SITA Standard method is more precise than SITA Fast,[68] and therefore is the ideal method for testing if the patient can tolerate it. A newer version (HFA3) can perform SITA Faster 24-2 and SITA Faster 24-2c, which takes even less time than to perform. Yet ophthalmologists should use caution if using the faster program as although it has shown a similar perimetric test results when compared with SITA Standard 24-2 and SITA Fast 24-2, its ability to detect early disease is limited.[69] As such, SITA Faster 24-2c may have some utility in a selected patient population (e.g. very old patients who find the VF assessment very difficult), or its use may be prioritized at follow-up visits rather than for initial testing (though switching test methods is not recommended as

It is acknowledged that resource availability varies throughout the Asia Pacific region, which puts an added strain on the existing challenges associated with the management of glaucoma patients. It is acknowledged that while it may be feasible to perform optimal VF examinations in a particular country or region, in others, it may not. The discussion related to equipment/resources is based on best practices, which should be afforded to everyone.

mentioned earlier).[5,10] In this case, if an abnormal result is seen using the SITA faster 24-2c, a more thorough and standard VF test such as the SITA Standard 24-2 should be performed.

The Octopus perimeter (Haag-Streit, Köniz, Switzerland) is an alternative option for VF assessment, which provides results that are analogous to those produced using the HFA.[67] For this perimeter, the algorithms commonly used are the Dynamic Strategy, and tendency-oriented perimetry, the latter providing a fast option for testing.[5]

Furthermore, the 24-2 test pattern is considered the gold standard for assessment of VF in patients with, or suspected to have, glaucoma, while the 10-2 test pattern may be useful in patients with advanced VF loss.[5,17]

"Additionally, the 10-2 test pattern may be utilized in patients with suspected central involvement based on clinical assessment or imaging (e.g. OCT demonstrated involvement of the macular ganglion cell layer)."

– Commentary by faculty members

How to achieve an adequate number of VF tests to monitor disease progression

Lack of resources/testing impracticality remains a barrier to performing an adequate number of VF tests. While it is noted that it may not be possible in all jurisdictions, expansion of testing times and locations to allow VF testing to occur outside of scheduled hospital visits (e.g. two weeks prior) may help to achieve an adequate number of tests. For example, this may be facilitated through engagement and development of networks with optometrists. However, logistics related to the safe and confidential transfer of data from external/satellite sites must be considered."

– Commentary by faculty members

Crabb and colleagues also highlighted several barriers to VF testing that may discourage patients from performing the test. Their research showed that patients dislike VF testing because they find the test procedure too long and tiring, and find it difficult to concentrate.[66] Additionally, patients expressed concern about the communication/instructions received on how to perform the test, what to expect from it, and how to interpret the results.[66] This highlights the importance of providing clear communication to patients, to explain what to expect from the test (with respect to dim lighting and stimuli), even of providing a demonstration (especially for perimetric novices).[5] Such measures are needed to overcome barriers for patients and help to achieve the required number of VF tests in order to monitor disease progression, which is essential for determining the quality of the IOP control achieved with treatment.

"One suggestion may be to have a technician present (by the patient's side) while performing the test, to talk the patient through what is required and answer any questions

as they arise. Furthermore, it is important to explain the VF testing process and need for frequent tests during the patient's first visit, so they are aware of the testing requirements from treatment commencement. Highlighting the impact on important patient-centric aspects, such as the impact on their ability to performance activities of daily life is essential, and patient reported outcome measurements need to be taken into consideration."

– Commentary by faculty members

Tips and tricks: Long-term IOP control and VF stability

1. Evaluation of VF progression over time (in conjunction with assessments to determine long-term IOP control) is essential to identify patients with disease progression
2. Achieving the recommended number of VF tests is difficult, even for glaucoma specialists. The frequency of VF testing should be modified based on the stage of disease
3. The structural change can occur before functional change. Some patients develop visual field progression in the non-linear rate therefore we should monitor both structure and function in detecting glaucoma progression
4. Use caution if using the SITA-faster program: it has shown similar perimetric test results when compared with SITA Standard 24-2 and SITA Fast 24-2, but its ability to detect early disease may be limited. Consider 10-2 tests in patients with advanced VF loss and/or suspected central involvement
5. Providing a demonstration/explanation and support on how to perform the VF test may help overcome barriers for patients and help to achieve the required number of VF tests

24-hour IOP fluctuations and monitoring

Why is it important to consider IOP fluctuations?

Multiple studies show that large and irregular 24-hour fluctuations, which may not be accurately detected by single office-hour IOP measurements, are associated with, and considered a risk for, VF deterioration in glaucoma.[7,8,70-72] Furthermore, IOP can fluctuate over a 24-hour period by more than 10 mmHg in patients with glaucoma, compared with 2–6 mmHg in healthy subjects. This has prompted the investigation of extended-hour IOP monitoring, particularly in patients who are at high risk for disease progression or those with unexplained progression (i.e. patients with VF deterioration despite normal office IOP measurements).[7,8,73]

As such, it is important to think beyond singular IOP measurements as a means of assessing treatment adequacy and consider monitoring of 24-hour IOP fluctuations, to gain a better understanding of the quality of IOP control achieved with therapy.

However, extended-hour IOP monitoring is time-consuming and impractical for both patient and clinician. Thus, assessment of fluctuations commonly relies on repeated IOP measurements with the GAT or air-puff tonometer over an extended period of time during office hours.[74]

IOP terminology

Peak IOP: highest IOP measurement in a series

Trough IOP: lowest IOP measurement in a series

IOP fluctuation: changes in IOP throughout the day and/or over several days

Types of IOP fluctuations:

- Ultra-short term: occur within minutes
- Short term: occur over hours to days
- Long term: occur over months or years

Extended-hour IOP: mean IOP measurement during an extended period

Office IOP: IOP measured during office hours

Circadian IOP: IOP variation during a single 24-hour period

Diurnal IOP: IOP measured during the day

Nocturnal IOP: IOP measured during the night

Additionally, home tonometry may be employed. When using equipment such as the iCare HOME (Icare Finland Oy, Vantaa, Finland) patient compliance as well as the patient's ability to correctly use the equipment must be considered. The iCare HOME may be useful for patients who continue to progress despite office IOP appearing to be controlled. However, it is known to be difficult for patients to use which may lead to the reporting of incorrect IOP measurements or underestimate of IOP compared with GAT.[75]

"Difficulty is commonly seen in patients who are older/frail or those who have PAPS/tight eye lids. Additionally, access to the iCare HOME equipment may be limited in some countries, and even if it is available, it is not affordable to majority of patients, making extended-hour IOP monitoring increasingly difficult. Given cost is a major prohibitive factor, implementation of rental programs whereby patients are able to lease the equipment for a reduced cost may prove to be helpful."

– Commentary by faculty members

Continuous 24-hr IOP monitoring has been evaluated using the SENSIMED Triggerfish® (SENSIMED AG, Etagnières, Switzerland) contact lens sensors (CLS), however, there are several caveats to consider. Cost is a major prohibitive factor, with the estimated cost of the SENSIMED Triggerfish® CLS (based on the UK's National Institute for Health and Care Excellence website estimates) is ~£500 per single-use contact lens.[76]

"Furthermore, the SENSIMED Triggerfish® CLS is not readily accessible in certain countries (such as Thailand, Malaysia, and India) and is only available for research purposes in others (i.e. Korea). Interpretation of results can be challenging and the ability of patients to use the device correctly despite proper training may also pose a barrier to clinical utilization of the device."

– Commentary by faculty members

When and how to measure IOP to determine IOP fluctuations

"Given the difficulties associated with extended-hour IOP monitoring, it is recommended that it is prioritized in patients who are high risk for disease progression and/or those with unexplained progression when implementing the QoIOP concept. Where continuous extended-hour IOP monitoring using a device such as the SENSIMED Triggerfish® CLS is unavailable, consider measuring IOP at different times (e.g. morning, afternoon, and evening on different visits). An alternative monitoring time-course of IOP measurements is to measure every 2–4 hours from 8 am to 5 pm using a GAT. Despite the potential difficulties with the iCare HOME, its use may also still prove valuable for gaining additional information otherwise missed during office visits."

– Commentary by faculty members

Air-puff tonometry may be more convenient and preferred by patients as a non-contact method of measurement. However, IOP values determined using air-puff tonometry, particularly in patients with an IOP of >24 mmHg, may be higher than IOP determined using a GAT.[77] This suggests that air-puff tonometry is not the most reliable method of IOP assessment, although its utility in mass screenings of IOP may still be valid.

The Ocular Response Analyzer® (Reichert Technologies, Munich, Germany) is another non-contact device which analyses the corneal hysteresis to calculate the corrected (cornea compensated) IOP measurement.[5] Thus, it may be useful in patients with a history of refractive surgery. To date, the Ocular Response Analyzer® has generally been used for research purposes only and is costly, so its use in mainstream clinical practice is yet to be seen. Furthermore, given the success and acceptance of pacemakers and glucose-monitoring implants, implantable intraocular devices may eventually be used for continuous and long-term IOP monitoring, and would eliminate any confounding corneal factors present when using a CLS or traditional tonometers.[78]

Ocular perfusion pressure

The 'vascular theory' of glaucoma indicates that if perfusion pressure decreases (spontaneously or due to antihypertensive medications), blood flow to the optic nerve may become insufficient and could lead to glaucomatous optic neuropathy. Ocular perfusion pressure (OPP) relates to the difference in arterial and venous blood pressure in the eye, where venous pressure is marginally higher than IOP under normal circumstances.[79,80] As a result, the mean OPP can be calculated by substituting venous pressure such that mean OPP is equal to the difference between the mean arterial pressure and IOP:[80]

Mean OPP = 2/3 (diastolic BP + 1/3 [systolic BP – diastolic BP]) – IOP

where mean arterial pressure is equal to diastolic BP + (1/3 [systolic BP – diastolic BP]).

Although studies have demonstrated that low OPP is associated with an increased risk for development and progression of glaucoma,[81,82] the relationship between blood pressure, IOP, and OPP is complex.[79,83] It is also important to consider that measurement of OPP using the calculation above provides an estimate only.[79] As such, OPP has limited use in routine clinical practice as it is difficult to accurately assess and can be more challenging to evaluate than 24-hour IOP.

Water drinking test

Originally designed as a diagnostic tool for glaucoma, the water drinking test (WDT) is currently under investigation for the prediction of IOP fluctuations and estimation of peak IOP (as solicited during the test).[84] The mechanism of IOP elevation during the WDT remains unclear, but it is thought to provide an indirect measure of the outflow facility of the eye, where it is expected that patients with an intact and active outflow facility would experience a rapid IOP recovery. Patients with a compromised outflow facility are more likely to experience a sustained elevation of IOP.[84]

Susanna and colleagues have retrospectively assessed the WDT in a group of patients with treated POAG, to determine the association between the magnitude and timing of IOP peaks elicited during the WDT and glaucoma-related VF loss.[85] Generally, following baseline IOP

assessment, the test involves the patient ingesting 800 mL of water within a five-minute period. The patient's IOP is then measured approximately three additional times at 15-minute increments and the highest IOP recorded is regarded as the peak IOP during the WDT.[84,85] Patients are required to stop ingesting liquid two hours before the test.[85] However, it is currently unclear where the WDT test fits into glaucoma management and more research in this field is needed.

Tips and tricks: 24-hour IOP fluctuations and monitoring

1. Extended hours IOP monitoring should be prioritized in patients who are high risk for disease progression and/or those with unexplained progression
2. Where continuous extended hours IOP monitoring using a device such as the SENSIMED Triggerfish® CLS is unavailable, consider measuring IOP at different times and/or home monitoring
3. Consider measure IOP at different times, such as morning, afternoon and evening on different visits
4. Despite high costs and difficulties with patient utilisation, the iCare HOME may be valuable for gaining additional information otherwise missed during office visits
5. Air-puff tonometry is not the most reliable method of IOP assessment, although its utility in mass screenings of IOP may still be valid

Treatment adherence and persistence in patients

Why is it important to consider treatment adherence?

Patient adherence to treatment is a complex issue, with several contributing factors. These include patient-related factors such as the incorrect administration of prescribed medication, safety and tolerability issues, and other factors such as access to transport or forgetfulness;[11,86] and clinician-related factors such as time constraints, making it difficult to identify patients who are non-adherent/accurately assessing adherence and appropriately communicate with patients about the importance of adherence, how to correctly administer medications, and the expected side effects.[5] Additionally, restrictive reimbursement policies which make patient access to certain medications unobtainable.

How to identify and improve patient adherence

Non-adherence can be extremely difficult to identify.[5] However, it remains critical to identify patients who are non-adherent to avoid misinterpretation as poor treatment response and subsequent prescription of additional, unnecessary therapies.[87] Monitoring of refill adherence (where the expiry of the medication and expected prescription refill is known) is an adequate measure of treatment adherence that may be useful to assist clinicians identify non-adherent patients.[87] Gently questioning patients about their glaucoma and treatment strategy may help to elicit self-reporting of non-adherence, for example, asking how often they collect their prescription or if they have forgotten to use their eye drops in the last week.[5,87] Additionally, asking patients to demonstrate instillation of their eyedrops may help to identify incorrect technique,[5] which should be followed up with training if needed.

"Assessment of side effects may also help identify patients who might not be administering the correct dose (based on limited evidence side effects)."

– Commentary by faculty members

In general, patient adherence may be enhanced using some simple strategies, including simplifying the treatment regimen (i.e. prescribe medications with lower toxicity and complexity such as once-daily or single-dose PF glaucoma medications), providing adequate patient education and improving communication, encouraging the use of reminders/alarms to avoid missing doses.

Simplifying the treatment regimen

Barriers to adherence, such as side effects of treatment and of preservatives, may be overcome by initiating or switching to PF formulations.[16]

"Using fixed-dose combinations or single-dose units when possible may help to reduce the burden of treatment on patients, where the use of single-dose units also allows for easier identification of non-adherence based on the unused medication.

In patients experiencing ocular side effects, it is important to consider the role of, and adequately assess patients for, OSD. It is important to note however, that symptoms may not necessarily match the signs when using the Ocular Surface Disease Index (OSDI)[88], and that frequent administration of the OSDI may not be feasible in clinical practice. Overall, it is agreed that PF medications are preferred in pre-operative patients, as well as patients with pre-existing OSD."

– Commentary by faculty members

For patients who develop OSD as a result of anti-glaucoma medication, treatment of the OSD symptoms may also greatly improve patient adherence and tolerability.[16]

"If available, switching to a long-term drug delivery system may be useful for improving patient adherence to treatment."

– Commentary by faculty members

Patient education and communication

A potential strategy to educate patients on the benefits of treatment adherence is to utilize VF results to explain the disease to patients, including why it is important to continue using the medication prescribed to stabilize the disease. In cases where early imaging data (e.g. from OCT) are available, images captured over time may be used to show and explain to the patient how their glaucoma has progressed, reinforcing the need to use their medications as prescribed.

"It is also important to educate patients about any expected side effects before initiating treatment. For example, when prescribing treatment with PGAs, patients should be informed about the potential for developing conjunctival hyperemia, highlighting that it is not sight-threatening and reversible, and that most patients are able to tolerate mild (Grade 1–2) conjunctival hyperemia."

– Commentary by faculty members

Given the time restraints faced by doctors, reimbursement models around the world would likely need to change to facilitate and incentivize ophthalmologists to take the time to educate and counsel patients. Educational pamphlets, videos, and links to online patient educational resources to help explain the disease to patients may also be helpful. Employing nurse counselors to connect with and educate patients is a popular and effective alternative. It should be noted however, that the impact of educational interventions on patient adherence does vary between studies, with some finding it to have little impact.[89]

Reminders/alarms

There is evidence to suggest that the use of tele-reminders may help to improve patient adherence.[86,90,91] Encouraging patients to set an alarm or reminder using their smart phone (if available) may help improve treatment adherence.[5] Utilization of adherence-specific resources such as the Aiming for Continuous Treatment program, may also result in better treatment adherence among patients with glaucoma. The Aiming for Continuous Treatment program distributed in Asia in conjunction with Glaucoma society from 2022 onwards, and provides patients with hard copy materials and/or access to a phone application designed to deliver reminders and educate patients on the importance of adhering to, and persisting with, their glaucoma medication.

Furthermore, asking patients to check the unused units of the medications prescribed may make them more aware of their lack of adherence, prompting more diligent administration of their medications.

Tips and tricks: Treatment adherence and persistence

1. Patients who are non-adherent need to be identified to avoid misinterpretation of lack of a response as a poor treatment response
2. Treatment adherence may be improved by prescribing medications with lower toxicity and complexity such as once-daily or single-dose preservative free glaucoma medications
3. Improved communication with the patient and their immediate family members (care-givers) is needed to educate patients, manage patient's expectations, and improve adherence
4. Patients should be encouraged to set reminders/alarms to improve treatment adherence
5. Educational pamphlets, videos and links to online resources on the importance of treatment, regular monitoring and follow up, and treatment adherence should be provided to patients and immediate family members

Conclusion

A large and increasing number of patients is currently living with glaucoma across Asia, particularly in South-Central and East Asia. It is more important than ever that glaucoma is identified early to ensure patients can receive adequate treatment to reduce the burden of disease. However, glaucoma detection rates remain low, due to a lack of early diagnosis strategies. Asia has several challenges to providing effective glaucoma management, including the approach of focusing on quantity-based IOP measurements and IOP reduction alone. This approach, however, must change so that patients are provided with a holistic approach to glaucoma and IOP management.

The QoIOP control concept highlights the need to evaluate key factors, including the rate of response to treatment, the long-term control of the patient's IOP, as well as VF stability, the role and impact of 24-hour fluctuations, and the importance of ensuring patients adhere to their prescribed treatments.

This paper provides ophthalmologists with a better understanding of the QoIOP control concept, with the aim of facilitating wider implementation of QoIOP throughout Asia, to move away from quantity-based IOP measurements and quality-based IOP control in clinical practice.

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