Editorial

Perspective on early lens extraction for primary angle-closure glaucoma

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Primary angle-closure glaucoma (PACG) is a subtype of glaucoma that affects 16 million people worldwide, of whom 4 million are bilaterally blind. This prevalence of PACG is expected to increase to 21 million cases by 2020, and it is expected that 5.3 million people will become bilaterally blind by the disease. The majority of those affected by PACG are Asians, which currently account for 87% of all cases (1).

PACG is characterized by optic nerve damage, increased intraocular pressure (IOP) or peripheral anterior synechia, and iridotrabecular contact of at least 180° viewed through gonioscopy (2,3). It differs from primary angle closure (PAC) in that the PACG case presents with evidence of increased IOP or peripheral anterior synechia, but without glaucomatous optic neuropathy (3).

Initial therapy for PACG consists of performing laser peripheral iridotomy (LPI), which creates a channel through the peripheral iris in order to relieve the pupillary block component (2), however a significant number of patients also require further medical therapy and/or surgery to control their elevated IOP (4).

During recent years, numerous studies have investigated lens extraction surgery as a treatment for PACG (5-11). For example, phacoemulsification surgery in patients with PACG has repeatedly led to a significant and sustained reduction in IOP, thereby controlling PACG progression. Notably, Barbosa *et al*. showed that clear lens extraction was more effective than topical medications in controlling IOP after LPI surgery in five consecutive cases of PACG. In particular, the investigators reported four of the five patients achieving IOP <22 mmHg without requiring any topical medications after phacoemulsification (5). Similarly, Lam *et al*. (7) studied a cohort of 62 patients with PACG of Chinese ethnicity and showed phacoemulsification to be superior to LPI in lowering IOP 18 months after an acute PAC episode. They also showed that patients who had been treated with phacoemulsification required significantly less medications (mean: 0.03±0.18) to control their IOP 18 months post-operatively compared to the LPI group (mean: 0.90±1.14). Tham *et al*. further showed that phacoemulsification and trabeculectomy were comparable at reducing IOP in medically uncontrolled PACG patients, with trabeculectomy causing more adverse events compared to phacoemulsification (8).

Although the exact mechanism by which lens extraction surgery lowers IOP is not fully understood, hypotheses include: (I) anterior chamber (AC) deepening and increased trabecular outflow due to lens removal with backward rotation of the ciliary body, relieving compression on the trabecular meshwork and canal of Schlemm; (II) post-operative release of prostaglandin F-2 contributing to increased uveoscleral outflow; (III) post-operative fibrosis and contraction of the posterior lens capsule causing traction on the ciliary body, resulting in hyposecretion of

aqueous humor; (IV) an increased AC volume resulting from removing a 5-mm thick crystalline lens and replacing it by a 1-mm thick artificial lens increases the volume of AC required to be filled by aqueous humor (11).

Although many studies, including the above, reported the role of lens extraction in PACG, they have been met with skepticism. While LPI is first line standard of care, a very safe and tested procedure with minimal adverse effects, lens extraction is an invasive surgery with potential, but rare, post-operative complications such as retinal detachment, endophthalmitis, and cystoid macular edema. Furthermore, intraocular lens (IOL) insertion leads to decreased accommodation, which might be uncomfortable, especially for younger patients. In addition to these concerns, systematic literature reviews conducted by independent researchers have questioned the efficacy of clear lens extraction in PACG. In a 2006 Cochrane database systematic review, Friedman and Vedula concluded that there was little evidence from high quality randomized trials or non-randomized studies to support lens extraction as treatment of chronic PACG (12). Another comprehensive literature review by Tarongoy similarly expressed uncertainty at the role of lensectomy for treating PACG (13).

The recent results of the effectiveness of early lens extraction for the treatment of PAC glaucoma (EAGLE) study, offer fresh, systematic and much more convincing evidence of the use of lens extraction in PACG patients (3). Consisting of 419 participants with early stage disease from 30 hospitals in five countries (Australia, mainland China, Hong Kong, Malaysia, United Kingdom), the EAGLE study followed patients for 36 months and performed a head to head comparison of clear lens extraction with LPI to determine comparative efficacy for each treatment (3). Assessing IOP, quality of life (QoL) scores and incremental cost effectiveness ratios, the study showed increased efficacy and decreased serious adverse events amongst patients who received lens extraction surgery compared to LPI. The study concluded that patients receiving clear lens extraction had a 0.052 higher mean health status score on the European Quality of Life-5 Dimensions (EQ-5D) questionnaire (95% CI, 0.015–0.088, P=0.005) compared to patients treated with LPI. Furthermore, mean IOP was also 1.18 mmHg lower (95% CI, –1.99 to –0.38, P=0.004) in the clear lens extraction group compared to the LPI group. The study also measured the economic consequences of performing lens extraction surgery: 179 of the patients recruited in the United Kingdom had their associated costs of performing LPI or lens extraction recorded. Amongst study participants, lens extraction cost £981 (95% CI, £612–£1,317) more on average compared to LPI. However, patients treated with lens extraction also had a mean Quality Adjusted Life Year (QALY) gain of 0.069 (95% CI, –0.017 to 0.159), demonstrating measurable benefits in patients' life quality with the increased treatment cost. No patients in either group had any serious adverse events, however irreversible loss of vision occurred in only one patient who received clear lens extraction compared to three patients who received standard of care.

Though far from conclusive, this study offers the most significant evidence to date of the effectiveness of clear lens extraction as an effective treatment for PACG. Through its large sample size and international multi-center study design, the EAGLE study offers the largest and most diverse patient cohort out of any study examining the therapeutic role of phacoemulsification in PACG. Not only does this study demonstrate significant therapeutic advantages, but also addresses adverse effects issues, showing clear lens extraction to be a relatively safe alternative to the current standard of care.

It is important to note however, that this study excluded patients younger than 50 years to avoid patients losing accommodation post-operatively. As a result, the study's QoL score did not take into account the potential discomfort that would be experienced by younger patients who were treated with phacoemulsification. Secondly, the study also excluded certain patient groups, limiting its generalizability. Specifically, patients with advanced glaucoma or concurrent cataracts, as well as those who had PAC with IOP less than 30 mmHg were excluded. Thirdly, all clear lens extraction surgeries in this study were performed by highly experienced surgeons, which may explain the low complication rates. Fourthly, visual field outcomes for both LPI and lens extraction groups did not differ significantly after 36 months, therefore, longer follow-up may be needed to show potential functional differences between the groups. Finally, the mean age of enrolled patients in this study was 67, at which age most patients develop some degree of cataracts. Hence, the term "clear lens extraction" should be used with caution when studying this patient segment.

In conclusion, the EAGLE study has validated the role of clear lens extraction in treating PACG, showing convincing evidence of the therapeutic benefits over LPI. However, further studies are needed before lens extraction can replace

LPI as the gold standard in treating PACG.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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