Role of Lens Extraction in Primary Angle Closure Disease

Anubha Rathi, Reetika Sharma, Bhaskar Jha, Shibal Bhartiya, Anita Panda
Glaucoma Services, Dr RP Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

Correspondence: Anita Panda, Glaucoma Services, Dr RP Centre for Ophthalmic Sciences, All India Institute of Medical Sciences
New Delhi, India, e-mail: anitap49@yahoo.com.

ABSTRACT
An eye with angle closure glaucoma is anatomically characterized by a short axial length, a shallow anterior chamber, a thickened lens that is situated relatively anteriorly and a small corneal diameter. These conditions may lead to the development of relative pupillary block. Pupillary block is classically managed with a peripheral iridectomy which provides a route for the aqueous to drain. But in cases of an anteriorly placed thickened lens, appositional closure may persist even after a peripheral iridectomy has been done. In such cases lens extraction has been proved to have a significant role. This review aims to explore the available evidence about lens extraction in primary angle closure patients.

Keywords: Primary angle closure glaucoma, Lens extraction, Cataract surgery, Phacoemulsification, Papillary block.

INTRODUCTION
Glaucoma is a major cause of blindness worldwide. Primary glaucoma affects 67 million people worldwide with Asians accounting for almost half of this number.\(^1\,^2\) It is a leading cause of irreversible blindness all over world as well as in India. Quigley et al in 2006,\(^22\) conducted a study that predicted that there will be 60.5 million people with open angle glaucoma (OAG) and angle closure glaucoma (ACG) in 2010, increasing to 79.6 million by 2020, and of these, 74% will have OAG. Women will comprise 55% of OAG, 70% of ACG and 59% of all glaucoma in 2010. Asians will represent 47% of those with glaucoma and 87% of those with ACG. Bilateral blindness will be present in 4.5 million people with OAG and 3.9 million people with ACG in 2010, rising to 5.9 and 5.3 million people in 2020, respectively. Glaucoma is of two types: Open angle and angle closure. Although open angle glaucomas are more common, angle closure glaucomas are more severe and more likely to result in irreversible blindness.\(^3\) But if treated at an early stage, a significant number of these cases are preventable.\(^4,^5\)

Primary angle closure disease (PACD) includes primary angle closure suspect (PACS), primary angle closure (PAC), primary angle closure glaucoma (PACG) and acute primary angle closure (APAC). As per the latest ISGEO (International Society of Geographical and Epidemiologic Ophthalmology),\(^6\) PACD is classified into:

- Normal intraocular pressure (IOP)
- No peripheral anterior synechiae (PAS)
- No disk/field changes
- Nonvisibility of posterior trabecular meshwork in >3 quadrants
- PAC: PACS with:
  - Elevated IOP (appositional) and/or PAS (synechial) and/or iris atrophy, distortion of iris pattern, excessive pigment deposition on trabecular surface
  - No disk/fundal changes
- PACG:
  PAC with evidence of disk and field damage.

MECHANISM OF PAC
Three main factors are known to contribute to PAC; namely pupillary block, lens induced and plateau iris configuration.

Pupillary block is the most commonly associated factor.\(^13,\,14\) Of interest here is the lens-induced PAC which usually does not respond to PI. The most significant clinical hallmarks of an eye with angle closure are the shallow anterior chamber (AC) and narrow angle. The best explanation for the shallower AC is the age-related increase in lens thickness and more anterior position of the lens frequently in a smaller eye.\(^7-\,10\)

Authors conducted studies in the subtypes of PACG and documented that eyes with PACG have significant anatomical differences from normal eyes.\(^15\) They were found to have a thinner iris and shorter trabecular ciliary process distance in addition to a narrow angle.\(^11\) Acute primary angle closure eyes were confirmed to have the narrowest angle recess. In eyes with PAC, older age and a shallower ACD appear to be the important cause of increased forward bowing of the iris resulting in the pupillary block.\(^12,\,16\)
LENS-INDUCED MECHANISM OF PAC

Various studies conducted all over the world point toward a considerable role of lens in PACD. Tarongoy et al\textsuperscript{22} in a review article evaluated the role of lens in the pathogenesis of PACD. They reviewed various studies done earlier which showed anatomical differences in the eyes with PACD as compared to normal eyes. An eye with angle closure glaucoma is anatomically characterized by a short axial length, a shallow anterior chamber, a thickened lens that is situated relatively anteriorly and a small corneal diameter.\textsuperscript{17-21} These conditions are conducive to the development of relative pupillary block. Pupillary block is classically managed with a peripheral iridectomy which provides a route for the aqueous to drain. But in cases of an anteriorly placed thickened lens, appositional closure may persist even after a peripheral iridectomy has been done. In such cases lens extraction has been proved to have a significant role.

With the glaucoma burden of the world in mind and the expanding numbers of ophthalmologists being trained in cataract surgery, it is a welcome thought to believe that lens extraction could have a role in PAC patients.

RECENT ADVANCES: ROLE OF CLEAR LENS EXTRACTION IN PACG

Several studies have described the role of phacoemulsification in cases of PACG. Few studies which advocate the role of early or clear lens extraction in such cases, are in the line. There are very few available reports which studied the effect of clear lens extraction in PACG. Other than these, a randomized control trial (RCT; EAGLE) is underway.\textsuperscript{3} These reports were extrapolated from various studies conducted in cases of PACG with cataract where cataract extraction was done. They believed that lens bulk does not increase with lens opacity \textit{per se},\textsuperscript{22} hence, clear lens extraction should benefit in the same way as cataract extraction. It is likely that many patients with PACG develop cataracts at a later stage of life due to ageing and due to the effect of conventional glaucoma treatment,\textsuperscript{23} which may cause cataract progression but by this stage irreversible glaucoma damage and sight loss may have occurred. It is proposed that early lens extraction will improve glaucoma control by opening the drainage angle.

In the absence of any proven and published randomized control trial for the role of clear lens extraction in case of PACG, this extrapolation is, hence, acceptable. A RCT addressing CLE specifically is warranted. Ravi Thomas et al\textsuperscript{24} cited similar concern in a review article recently.

THE ROLE OF LENS EXTRACTION IN PACG

Dada T et al\textsuperscript{25} in their published work in Sep 2011, studied 46 eyes with PACG for changes in angle parameters after phacoemulsification using ultrasound biomicroscopy. They reported that mean preoperative IOP (25.0 ± 5.4 mm Hg) was reduced to 15.8 ± 3.8 mm Hg (p = 0.0001) at 3 months postoperatively. Other ocular parameters studied were angle chamber depth (ACD), trabecular iris angle (TIA), angle opening distance (AOD) at 250 and 500 µm from scleral spur using ultrasound biomicroscopy (UBM). Significant angle widening noted postoperatively. They concluded that phacoemulsification in eyes with PACG results in significant widening of the anterior chamber angle. This results in better IOP control after surgery and decreases the need for glaucoma medications. These findings are of clinical significance in obviating the need for simultaneous filtering surgery in eyes with PACG undergoing phacoemulsification cataract surgery.

Ming Zhi et al\textsuperscript{26} in an interventional case series conducted in China in 2003, studied 18 eyes with PACG who underwent phacoemulsification and intraocular lens (IOL) implantation. There was a 9 mm Hg drop in mean preoperative and first day postoperative IOP (22.8 vs 13.8 mm Hg, p = 0.012) and a 10.2 mm Hg drop in mean preoperative and seventh day postoperative IOP (22.8 vs 13.2 mm Hg, p < 0.002). They concluded that phacoemulsification and posterior chamber IOL implantation may be useful in the treatment of PACG in Chinese patients.

Tarongoy et al\textsuperscript{27} in a review article, stated the role of lens in the pathogenesis of ACG. They also stated that lensectomy eliminates pupillary block, widens the angle to lessen angle crowding, thus reducing the iridotrabecular proximity, and is the only treatment alternative that reduces, if not corrects the responsible anatomic predisposition to angle closure. Medical management and LPI remain the most common modes of treatment of an acute attack but newer approaches including early lens removal are gaining popularity because of their potential long-term success in IOP control.

Ken Hayashi et al\textsuperscript{28} in 2000 conducted a comparative interventional study in Japan. They studied the changes in anterior chamber angle width and depth after IOL implantation in eyes with PACG. Seventy-seven eyes with PACG were studied and they found that AC angle width increased from 18.9 ± 4.0 preoperative to 36.7 ± 4.0 degrees postoperative at 12 months (p < 0.0001). ACD also increased significantly from 1.89 ± 0.33 mm preoperative to 3.94 ± 0.26 mm postoperatively at 12 months (p < 0.0001).
Hayashi et al in 2001\textsuperscript{29} studied the effect of cataract surgery on IOP control in glaucoma patients. They studied 74 eyes with ACG and 68 eyes with OAG. In the ACG group, the mean IOP dropped from 21.4 + 3.9 mm Hg preoperative to 14.5 + 2.6 mm Hg at 24 months follow-up (p < 0.0001). They concluded that cataract surgery substantially reduced IOP and the number of medications required for IOP control in glaucomatous eyes. Specifically, cataract extraction normalized the IOP in most eyes with ACG.

Pereiera et al\textsuperscript{30} conducted a study in 2003 to report quantitative changes in the anterior segment configuration after phacoemulsification and foldable IOL implantation by means of UBM. Twenty-one eyes were studied. Main outcome measures included central ACD, iris-lens contact distance, iris-lens angle (ILA), angle opening distance at points 250 (AOD250) and 500 µm (AOD500) from the scleral spur, TIA, iris thickness 500 µm from the scleral spur (IT), trabecular-ciliary process distance (TCPD), iridociliary process distance (ICPD), iris-zonule distance (IZD), iris-scleral angle (ISA), and ciliary process-scleral angle (CPSA). After surgery, central ACD was also measured from the cornea to the IOL (ACD) and from the cornea to the pupillary plane (ACD2). The variables IT, TCPD, ICPD, IZD and CPSA did not significantly change after surgery (p < 0.01). Central ACD increased to approximately 30% after surgery (approximately 850 µm; p < 0.001). Anterior chamber angle significantly increased, by approximately 50% of the initial value, by the three measurement methods used: AOD250 (p < 0.002), AOD500 (p < 0.001) and TIA (p < 0.003). The ISA increased by approximately 10° (30%) after surgery (p < 0.001). They concluded that after phacoemulsification and foldable IOL implantation, UBM revealed that the iris diaphragm shifted backward, deepening the anterior chamber by approximately 850 µm and widening its angle by approximately 10°. These findings may be of clinical significance in eyes with angle closure glaucoma or with occludable angles.

Nonaka et al\textsuperscript{31} conducted a study in 2005 in Japan to investigate the frequency of residual angle closure after resolution of pupillary block by laser peripheral iridotomy and the effects of subsequent cataract surgery to resolve angle closure completely. Residual angle closure after iridotomy was seen in 27 (38.6%) of 70 eyes. Eyes with IOP of >20 mm Hg or with a glaucomatous visual field defect before iridotomy had a significantly higher incidence of residual angle closure after iridotomy than eyes without these findings (p < 0.05). In all the eyes with residual angle closure after iridotomy, the response to the prone position test became negative after cataract surgery, with significant lowering of IOP (p < 0.01). They concluded that residual angle closure after iridotomy was common, especially in eyes with primary angle closure and poorly controlled IOP or glaucomatous optic neuropathy. Cataract surgery was effective in resolving completely the residual angle closure after iridotomy and lower IOP.

**ROLE OF LENS EXTRACTION IN PAC**

There is limited literature available evaluating the effect of lens extraction in cases of PAC. Recent reports have discussed the effectiveness of this procedure in patients with PAC and nipping the bud in its prime itself as 28.5% of PAC cases are expected to progress to PACG in 5 years and can later lead to irreversible blindness.

Nonaka, Kikuchi et al\textsuperscript{32} conducted a retrospective interventional case series in Japan in 2004. They studied one randomly selected eye from each of 31 consecutive Japanese patients (9 eyes of 9 men and 22 eyes of 22 women) with PAC, treated with lens extraction and examined by UBM within 1 month before and again at 3 months after surgery. Of these, 10 eyes of 10 patients had undergone a laser peripheral iridotomy, and 1 eye a laser peripheral iridoplasty. They found that surgery significantly deepened the AC (p < 0.01); the average increase in ACD was 1.36 mm (2.03 + 0.30 before surgery and 3.39 + 0.21 after surgery), a 68% increase from the preoperative value. Similarly, AOD500 increased significantly after surgery (p < 0.01); this increase averaged 0.16 mm (0.09 + 0.07 before surgery and 0.25 + 0.09 after surgery), which represented 182% of the preoperative value. The position of the ciliary processes shifted significantly to a more posterior position after surgery (p < 0.01); the increase of TCPD averaged 0.18 mm (0.51 + 0.09 before surgery and 0.69 + 0.12 after surgery), a 34% increase from the preoperative value. IOP drop noted from 18.2 + 4.1 as the mean preoperative value to 14.3 ± 2.7 mm Hg as the mean postoperative value. They concluded that cataract surgery attenuated anterior positioning of the ciliary processes in eyes with primary angle closure, concomitant with significant widening of the angle. Cataract surgery resulted in not only complete dissolution of lens volume and pupillary block, but also attenuation of the anterior positioning of the ciliary processes, all of which contributed to postoperative widening of the angle in eyes with PAC.

**ROLE OF LENS EXTRACTION IN ACUTE ATTACK OF ANGLE CLOSURE GLAUCOMA**

Lam DS et al\textsuperscript{33} in 2008 conducted a randomized trial to compare the efficacy of early phacoemulsification vs laser peripheral iridotomy (LPI) in the prevention of IOP rise in patients after APAC. They studied 62 eyes with APAC.
Subjects were randomized to receive either early phacoemulsification or LPI after aborting APAC by medications. Patients were followed up on day 1; week 1 and months 1, 3, 6, 12 and 18. Predictors for IOP rise were studied. They found out that the prevalences of IOP rise for the LPI group were 16.1, 32.3, 41.9 and 46.7% for the follow-ups at 3, 6, 12 and 18 months respectively. There was only one eye (3.2%) in the phacoemulsification group that had IOP rise at all follow-up time points (p < 0.0001). Treatment by LPI was associated with significantly increased hazard of IOP rise [hazard ratio (HR), 14.9; 95% confidence interval (CI), 1.9 to 114.2; p = 0.009]. In addition, a maximum IOP at presentation > 55 mm Hg was associated with IOP rise (HR, 4.1; 95% CI, 1.3-13.0; p = 0.017). At 18 months, the mean number of medications required to maintain IOP ≤ 21 mm Hg was significantly higher in the LPI group (0.90 ± 1.14) than in the phacoemulsification group (0.03 ± 0.18, p < 0.0001). Mean IOP for phacoemulsification group (12.6 ± 1.9 mm Hg) was consistently lower than that of the LPI group (15.0 ± 3.4 mm Hg, p = 0.009). Mean shaffer grading for the phacoemulsification group (2.10 ± 0.76) was consistently greater than that of the LPI group (0.73 ± 0.64, p < 0.0001). Hence, they concluded that early phacoemulsification appeared to be more effective in preventing IOP rise than LPI in patients after abortion of APAC. High presenting IOP of >55 mm Hg is an added risk factor for subsequent IOP rise. For patients with coexisting cataract and presenting IOP of >55 mm Hg, early phacoemulsification can be considered as a definitive treatment to prevent IOP rise. Jacobi et al34 in 2002 evaluated the safety and efficacy of primary phacoemulsification and intraocular lens implantation (PPI) for acute ACG. Forty-three eyes of 43 patients with acute ACG and uncontrolled IOP were treated by PPI. Thirty-two eyes of 32 patients treated by conventional surgical iridectomy (CSI) constituted the control group. They found that glaucoma control was achieved in 31 eyes (72%) in the PPI group and in 11 (35%) in the CSI group (p = 0.01). Mean preoperative IOP was 40.5 ± 7.6 mm Hg (standard deviation) and 39.7 ± 7.8 mm Hg respectively (p = 0.46). Mean postoperative IOP was 17.8 ± 3.4 mm Hg (PPI group) and 20.1 ± 4.2 mm Hg (CSI group) after a mean follow-up of 10.2 ± 3.4 months (p = 0.03). Postoperatively, the mean number of ocular

Table 1: Role of lens extraction in PACG

<table>
<thead>
<tr>
<th>Authors</th>
<th>Years</th>
<th>Region</th>
<th>No. of cases</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dada et al</td>
<td>2011</td>
<td>Delhi</td>
<td>46 eyes</td>
<td>Preoperative mean IOP was 25.0 ± 5.4 mm Hg which was reduced to 15.8 ± 3.8 mm Hg (p = 0.0001) at 3 months. Other ocular parameters studied were ACD, TIA, AOD at 250 and 500 μm from scleral spur using UBM. Significant angle widening was noted postoperatively.</td>
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<tr>
<td>Ming Zhi Z et al</td>
<td>2003</td>
<td>China</td>
<td>18 eyes</td>
<td>Mean 9 mm drop in preoperative and first-day postoperative IOP</td>
</tr>
<tr>
<td>Tarongoy P, Ho CL, Walton DS (a review)</td>
<td>2009</td>
<td>Japan</td>
<td>74 eyes with ACG 68 eyes with OAG</td>
<td>Lensectomy dramatically widens the angle and eliminates pupillary block.</td>
</tr>
<tr>
<td>Ken Hayashi et al</td>
<td>2001</td>
<td>Japan</td>
<td>77 eyes with PACG</td>
<td>Mean IOP and number of medications postsurgery were dramatically found to be reduced specifically in PACG.</td>
</tr>
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<td>Hayashi et al</td>
<td>2000</td>
<td>Japan</td>
<td>77 eyes with PACG</td>
<td>AC angle width increased from 18.9 ± 4.0 preoperative to 36.7 ± 4.0° postoperative at 12 months (p &lt; 0.0001). ACD also increased significantly from 1.89 ± 0.33 mm preoperative to 3.84 ± 0.26 mm postoperatively at 12 months (p &lt; 0.0001).</td>
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<td>Frederico Pereiera et al</td>
<td>2003</td>
<td>Germany</td>
<td>21 eyes</td>
<td>UBM was used to measure preoperative and postoperative angle parameters. AC angle widened by 50% postoperative.</td>
</tr>
<tr>
<td>Nonaka et al</td>
<td>2005</td>
<td>Japan</td>
<td>70 eyes</td>
<td>Residual angle closure after iridotomy seen in 27 of 70 eyes, especially in eyes with primary angle closure and poorly controlled IOP or glaucomatous optic neuropathy. Cataract surgery was effective to resolve it completely and lower IOP.</td>
</tr>
</tbody>
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hypotensive medications was 0.18 ± 0.45 (PPI group) and 0.45±0.62 (CSI group) (p = 0.0001). Relative increase in postoperative best-corrected visual acuity (logarithm of the minimum angle of resolution) was 0.52 ± 0.29 (PPI group) and 0.19 ± 0.21 (CSI group) respectively (p = 0.0001). Additional surgery was necessary in 5 eyes (11.5%) in the PPI group and in 20 eyes (63%) in the CSI group (p = 0.01). Intraoperative and postoperative complications were few and manageable. They concluded CSI in patients with acute ACG and it was effective in reducing IOP initially but was associated with multiple surgical reinterventions. Conversely, primary phacoemulsification turned out to be safe and effective in reducing IOP and improving visual acuity. These results affirm that lens extraction may be considered the better procedure in uncontrolled ACG.

CONCLUSION

Once the pupillary block mechanism for primary angle closure disease has been dealt with by performing a laser iridotomy, a thickened-anteriorly displaced lens (clear/cataractous) seems to be the major factor for progressive angle closure disease. An early lens extraction may therefore be curative, if done before complete synechial closure of the angle has set in. Though till date there is a paucity of studies on early or clear lens extraction in cases of primary angle closure disease, there is an increasing interest on this front owing to a favorable risk-benefit ratio with advancements in microincision cataract surgery. Most of the studies and trials that have been done advocate a clear role of lens extraction in PACG, however majority of studies have been performed in patients with some degree of lenticular opacification. Lens extraction also holds a promising role in case of PAC and in acute attack of angle closure, once acute attack has been aborted successfully with medical therapy with/without adjuvant laser therapy. In eyes with PACS, a regular follow-up may be done and surgery may not be advocated in these cases as majority of cases do not progress to PAC/PACG.

In eyes with advanced PACG with near total cupping or visual field defects involving the central 10°- phaco-trabeculectomy or a two-stage surgery (phaco followed later by trabeculectomy) may be done. We await the results of ongoing clinical trials on early lens extraction in PAC/PACG which will help us to further refine our treatment approach.

REFERENCES

3. EAGLE Study Protocol. Available at: https://viis.abdn.ac.uk/HSRU/eagle/.
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