Cataract Surgery and Intraocular Pressure

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Key Words

Cataract surgery · Glaucoma · Intraocular pressure · Phacoemulsification · Trabeculectomy · Combined surgery

Abstract

Cataract surgery is one of the most performed surgeries in the developed world. In addition to its significant impact on visual acuity, phacoemulsification has been hailed as a potential intraocular pressure (IOP)-lowering procedure. While current evidence suggests an overall significant and sustained decrease in IOP to exist after cataract surgery, the specific ocular characteristics that could help predict which patients are likely to benefit from this IOP-lowering effect remain unclear. This definition is important in glaucoma patients if this surgery is to be used in the treatment for this disease. Our review aims to summarize the literature on the subject, depicting possible mechanisms behind this IOP decrease, which type of patients are more likely to benefit from this surgery for IOP-lowering purposes and ultimately help optimizing disease management for the increasing number of patients with concomitant glaucoma and cataract.

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Introduction

Cataract and glaucoma are ranked as the leading causes of blindness worldwide (51 and 8%, respectively) [1]. In developed countries, glaucoma is the second leading

cause of irreversible blindness (after diabetic retinopathy) and this burden tends to increase as the population ages [2]. A similar trend is seen with cataract, whose prevalence is also age-related – the global prevalence of 15.5% rises to 45.9% in those over 75 years and is expected to duplicate by 2020 [3]. Unsurprisingly, both diseases frequently coexist in the elderly population in a proportion that is likely to increase.

Given this data, cataract surgery rises as one of the most common surgical procedures performed worldwide and it has been suggested to be of clinical benefit for both diseases. Besides removing the opacified lens, cataract surgery has been suggested to reduce intraocular pressure (IOP) in eyes either with or without glaucoma, although with variable magnitude and influenced by several factors, including anterior chamber anatomy and angle configuration (open-angle vs. angle-closure) [4]. Also, it has the ability to increase the accuracy of functional and structural analyses currently used for diagnosing and evaluating glaucoma and its progression, since a visually significant cataract may act as a confounder. Therefore, it seems reasonable to assume that a conjoint treatment could be established, with cataract surgery being part of glaucoma treating algorithms. However, questions remain on how it would best fit in the clinical management of these patients.

This review focuses on how cataract surgery might influence IOP control in both healthy individuals and glaucoma patients with cataract. In this particular setting, intrinsic glaucoma anatomical and physiological factors

Table 1. Clinical studies reflecting the effect of lens extraction on IOP in patients without glaucoma, ocular hypertension, OAG, CACG and acute ACG

Authors	n	Follow-up	IOP pre → post, mm Hg	ΔIOP	p value
Without glaucoma					
Pohjalainen [6], 2001	137	25 months	16.3 → 12.7	-3.4	0.001
Shingleton [7], 2006	59	60 months	15.9 → 13.4	-1.5	<0.0001
Ocular hypertension					
Mansberger [5], 2012	63	38 months	23.9 → 19.8	-4.1	<0.001
POAG					
Kim [14], 1999	31	16 months	18.1 → 15.2	-2.9	<0.001
Shingleton [15], 1999	61	12 months	17.0 → 15.9	-1.1	n.s.
Pohjalainen [16], 2001	38	26 months	18.4 → 15.1	-3.3	0.001
Hayashi [10], 2001	68	24 months	20.7 → 15.2	-5.3	<0.0001
Lai [11], 2004	34	20 months	20.4 → 15.7	-4.7	<0.05
Mathalone [17], 2005	24	24 months	17.0 → 15.1	-1.9	n.s.
Shingleton [7], 2006	55	60 months	18.4 → 16.6	-1.8	0.005
Poley [18], 2009	124	10 years	17.8 → 15.1	-2.7	<0.001
CACG					
Hayashi [10], 2001	68	24 months	21.0 → 15.0	-6.0	<0.001
Lai [11], 2004	31	20 months	27.4 → 14.8	-12.7	<0.05
Liu [12], 2006	29	3 months	ND (>20.0) → 14.3	ND	ND
Lai [13], 2006	21	21 months	19.7 → 15.5	-4.2	0.02
Acute ACG					
Jacobi [8], 2002	43	24 months	40.5 → 17.80	-22.70	ND
Su [9], 2011	16	3 months	48.81 → 10.70	-38.09	<0.001

n.s. = Not significant; ND = no data.

that influence IOP and that may be potentially predictive of the effect that lensectomy might have on IOP control will be focused on. For open-angle glaucoma (OAG) and angle-closure glaucoma (ACG), current surgical options will be compared to each other, discussing the clinical aspects that influence the choice of surgical treatment.

Ocular Biometric Parameters

Predicting Post-Operative IOP

In the 1970s, Bigger and Becker reported a lower IOP after cataract extraction in glaucoma patients [5]. Since then, and particularly in the last decade, many studies have consistently shown a variable IOP decrease after cataract surgery (table 1) [5–18].

Pre-operative angle configuration is pointed out as one of the main factors contributing to this variability, as higher IOP reductions are observed with partially or completely closed angles. Besides angle anatomy, many other factors were independently related to IOP reduc-

tion of cataract surgery including aqueous humour dynamics, ocular comorbidities and, most importantly, pre-operative IOP.

After lens removal, even eyes without glaucoma experience anatomical changes in the anterior chamber, and many biometrical factors are modified. For instance, an increase in anterior chamber depth (ACD), angle opening distance and anterior chamber area are to be expected [19–21]. These anatomical factors are particularly relevant in ACG, typically characterized by a narrow angle and a shallow anterior chamber that progressively decrease as the lens becomes thicker and more anteriorly positioned. When submitted to phacoemulsification, ACG patients undergo a significant increase in ACD and angle width when comparing with OAG patients or even with control patients [21]. These biometrical changes correlate with IOP in all groups, with a more pronounced IOP reduction ($p = 0.02$) in ACG patients than in OAG patients or the control group [10].

Given these anatomical and biometric parameters, some predictive indexes of post-operative IOP were cre-

Table 2. Rate of conversion of ocular hypertension to glaucoma or normal IOP [21]

Study	n	Follow-up years	Treatment	Δ IOP, mm Hg	Conversion to glaucoma		Conversion to normal IOP	
					factor	%	factor, mm Hg	%
OHTS [5]	817	5.0	observational	21–32	↓ visual field	9.5	IOP <21	0.0
OHTS [5]	817	5.0	medication	21–32	↓ visual field	4.4	IOP <21	0.0
Poley [18, 27]	81	4.1	Phaco + IOL	20–31	start of medical treatment	1.1	IOP <20	74.7

OHTS = Ocular Hypertensive Treatment Study; Phaco = phacoemulsification; IOL = intraocular lens. Adapted from Poley et al. [18].

ated. In 2005, Issa et al. [22] developed a predictive index for IOP reduction in patients without glaucoma based on two anatomical factors – IOP and ACD – and concluded that it correlated better with IOP variation than each of the parameters individually considered. Also, Liu et al. [23] suggested another formula for eyes with ACG based on IOP and ACD that would allow to predict the IOP variation after cataract surgery [$IOP = 6.354 + 0.186 (IOP \times ACD)$; $R^2 = 49\%$]. One year after the surgery, the product of IOP and ACD predicted that eyes with a ratio of <35 have a better probability of achieving an IOP ≤ 12 mm Hg post-operatively. Although these indexes are neither validated nor globally implemented, they might be helpful when making decisions regarding which surgical procedure to perform, whether a simple lens extraction would suffice to control the IOP or a more invasive (yet more effective) procedure would be necessary. Finally, many other biometric factors have been proposed as independent predictors of post-operative IOP – anterior chamber area, anterior chamber width, lens thickness – but their usefulness warrants further investigation [20, 24, 25].

IOP Reduction in Anterior Chambers with an Open Angle

IOP decrease may not only depend on anatomical factors relating to narrow angles. Poley et al. [18] suggest that lens removal allows the posterior capsule to move posteriorly, dislodging the zonula over the ciliary body with a consequent widening of Schlemm's canal and aqueous humour drainage improvement. Another proposed mechanism states that the ultrasounds used in the phacoemulsification procedure are responsible for an abrupt rise in the anterior chamber pressure, producing inflammatory cytokines (mostly IL-1) that stimulate metalloproteinase production and trabecular meshwork remodelling, facilitating humour drainage [26]. As such, and also as stated by Poley et al. [27], pre-operative IOP

is the best predictor of post-operative IOP, as the IOP variation in OAG patients appears to be proportional to the magnitude of the pre-operative IOP [28].

Ocular Hypertension

Ocular hypertension is defined as an IOP higher than normal (21 mm Hg) in the absence of visual field loss or optic nerve damage. It is, by itself, the main risk factor for progression to glaucoma. According to the Ocular Hypertensive Treatment Study [5], phacoemulsification with intraocular lens implantation decreases IOP in this subset of patients proportionally to their pre-operative IOP. Poley et al. [18, 27] evaluated the impact of phacoemulsification on the progression of ocular hypertension for 10 years and concluded that cataract surgery, by providing a bigger IOP reduction, might be responsible for a lower progression to glaucoma (table 2). However, evidence is still missing on the role cataract surgery might have as a preventive measure of ocular hypertension progression to glaucoma.

Angle-Closure Glaucoma

Primary angle closure is defined as the presence of irido-trabecular contact impairing aqueous humour outflow through a diffuse obstruction of the trabecular meshwork and it usually results from a shallow anterior chamber and angle-crowding of the anterior segment. The occurrence of a closed angle is more likely as the distance between iris and trabecular meshwork decreases, and the risk of irido-trabecular contact rises exponentially from an angle opening of 20° [29]. Owing to the intrinsic role of the lens in the anterior chamber anatomy in patients with primary angle closure, its surgical extraction might be useful in the treatment and management of acute and chronic ACG.

Table 3. Comparison of LPI and phacoemulsification with intraocular lens implantation

	LPI	Phaco	p value	Study
Long-term IOP control				
>21 mm Hg	46.7%	3.3%	<0.0001	Lam [30], 2008
<22 mm Hg	61.1%	89.5%	0.034	Husain [31], 2012
Angle-opening (Shaffer)	0.73	2.10	<0.0001	Lam [30], 2008
Medication necessary to control IOP	0.90	0.03	<0.0001	Lam [30], 2008
IOP at 18 months, mm Hg	15.0	12.6	0.009	Lam [30], 2008
PAS, degrees	228.6	101.3	<0.0001	Lam [30], 2008

Phaco = Phacoemulsification with intraocular lens implantation.

With an unresolved acute angle closure crisis, lens extraction results in a steep reduction in IOP (table 1). As a thick lens boosts pupillary block and consequent angle closure, its removal allows for expansion of anterior chamber dimensions and angle width, promoting aqueous humour outflow and IOP reduction. Also, even when compared with laser peripheral iridotomy (LPI), this treatment modality presents with further advantages (table 3): better long-term IOP control after resolution of an acute crisis, lesser need for long-term medication in order to maintain an optimal IOP, wider angle and fewer peripheral anterior synechiae (PAS) formation, with a smaller risk of a second angle closure crisis or progression to chronic angle closure, which is approximately 58.1% after LPI [30, 31]. It is, however, a riskier procedure due to the shallow anterior chamber, the vulnerability of the corneal endothelia and an atonic iris [32].

In the absence of a cataract or in eyes with good visual acuity, the clinical benefit of cataract surgery is still under debate and LPI appears to have the best risk-to-benefit ratio. Nonetheless, when a cataract is present, lens extraction is suggested as the best choice once the acute crisis is duly aborted [32]. Also, when IOP at presentation is higher than 55 mm Hg (which is an independent factor of long-term uncontrolled IOP), patients are less likely to require IOP-lowering therapy if treated with early cataract extraction, when comparing with LPI [30].

In the presence of PAS, the anterior chamber angle becomes chronically closed with permanent obstruction of aqueous humour drainage. IOP is now almost entirely dependent on the extent of trabecular meshwork damage, which can be directly inflicted by the PAS themselves or derive indirectly from the elevated IOP – whether hypertensive spikes or continuously high pressure. IOP becomes continuously elevated when more than 180° of angle are occluded by PAS and when it surpasses 270°, med-

ical therapy is usually ineffective and filtering surgery is required [33].

Traditionally, the approach to the patient with primary ACG is a stepped combination of medical and laser therapy; glaucoma surgery is indicated as a second-line option when these treatments fail. However, cataract extraction is being increasingly considered for primary ACG management owing to its capacity to restore the anatomy of the anterior chamber with the lens extraction, often without the need for further medication.

In primary ACG patients with a clear lens, both phacoemulsification and trabeculectomy are effective in reducing IOP (reduction of 8.4 mm Hg or 34% for phacoemulsification vs. 8.9 mm Hg or 36% for trabeculectomy; $p > 0.05$). Trabeculectomy-treated patients seemed to have a smaller need for additional drugs than phacoemulsification-treated patients (although not statically significant, $p = 0.16$); likewise, trabeculectomy was also associated with significantly more surgical complications than phacotrabeculectomy (46 vs. 4%, $p = 0.001$) [34]. The most frequent long-term complication is cataract formation (33%), adding the need for another surgical procedure to restore the visual acuity [34]. Also, it is estimated that half the patients with chronic angle-closure glaucoma (CACG) undergoing trabeculectomy will need lens extraction within 5 years [35].

Based on these clinical trials, it has been a subject of debate whether early clear lens extraction would be of any clinical benefit in controlling moderate CACG or even in CACG prevention. In a 2006 meta-analysis, Friedman and Vedula [36] concluded that there was no solid evidence supporting this clear lens extraction for glaucoma treatment. Nowadays, however, recent clinical trials contradict this view and defend phacoemulsification as a valuable option based on it being a safer, faster and more economical procedure than every other surgical proce-

cedure for CACG. By contrast, there is currently no role for clear lens extraction for CACG prevention in patients with angle-closure suspect or chronic angle closure [37]. In an attempt to answer this question, the EAGLE trial (The Effectiveness of Early Lens Extraction with Intraocular Lens Implantation for the Treatment of Primary Angle-Closure Glaucoma) is currently under way. Beginning in 2011, it is a multicentric prospective randomized clinical trial comparing clear-lens extraction and LPI in patients with newly diagnosed chronic angle-closure or CACG [38]. The primary outcomes include IOP, patient's quality of life and cost-effectiveness, with a follow-up of 3 years, after which we might be able to confirm phacoemulsification as a valuable option for the current practice of CACG treatment.

Besides phacoemulsification and trabeculectomy, there is a third surgical option combining both procedures: phacotrabeculectomy or combined surgery. When compared with phacoemulsification, combined surgery seems to be slightly more effective for IOP control ($p > 0.05$) with fewer medications. Likewise, the rate of surgical complications is significantly higher in the combined surgery group, as well as the optic neuropathy progression rate [39, 40]. Notwithstanding the need for a smaller amount of medication after trabeculectomy and the greater decrease in IOP following combined surgery, the higher rate of surgical complications outweighs this small benefit. In situations where drug reduction is a priority, trabeculectomy remains the more appropriate option [41]. Several authors defend that in the presence of an advanced glaucoma combined surgery is the best option, since it offers a better IOP control than phacoemulsification and, when compared to trabeculectomy, has comparable efficacy in controlling IOP and reducing the requirement for glaucoma drugs with a smaller re-intervention rate [42].

Open-Angle Glaucoma

IOP increase in OAG is not related to angle crowding factors but rather due to aqueous humour drainage impairment at the trabecular meshwork level. Medical therapy is the first line of treatment in the majority of cases, with filtering surgery playing a role in patients where target IOP is either not achieved or is not likely to be sustained in cases of young patients or poorly tolerated medical therapy. However, filtering surgery is not the only surgery glaucoma patients are likely to have. In fact, 30% of all the patients who underwent cataract surgery in the

US under Medicare were reported to have concomitant glaucoma [43]. This significant epidemiological factor makes it even more important to incorporate this surgery in the practice patterns of glaucoma management. Similarly to CACG, there are three surgical options to consider: phacoemulsification, trabeculectomy or combined surgery (phacotrabeculectomy). Depending on glaucoma severity, patient approach should be individually tailored:

Mild Glaucoma. For a patient with a troublesome cataract but a mild, well-controlled glaucoma requiring few medications and minor optic nerve damage, phacoemulsification alone is a reliable option. Lens removal improves visual acuity and may allow for better disease evaluation and follow-up. Furthermore, there is a possibility of a phacoemulsification-related small IOP-lowering effect, aiding in IOP control – average reduction of 1.5–3.0 mm Hg (table 1). However, there is still a risk of complications associated with this surgery, notably hypertensive spikes.

Moderate Glaucoma. In this group of patients, clinical decisions are particularly dependent on individual characteristics. Phacoemulsification remains a valuable surgical option in patients with an otherwise controlled IOP, although requiring a higher degree of attention because of the more frequent hypertensive spikes. However, in a patient whose IOP is above target, the pros and cons of a combined surgery should be discussed with the patient. On the one hand, combining cataract surgery and trabeculectomy would allow to correct two problems with a single operative procedure (since cataract surgery after filtering surgery is almost inevitable) and would avoid the hypertensive spikes after phacoemulsification. On the other hand, combined surgery is associated with more post-operative complications and a not so significant IOP decrease (if compared with trabeculectomy alone) [44, 45]. It should be noted, however, that patients with moderate glaucoma tend to have a higher IOP target, which would make them good candidates for a one-time combined procedure. In the presence of an incipient cataract and moderate glaucoma or when IOP is not within the ideal range, glaucoma control is the priority. First-line surgical approach is trabeculectomy, but other less cataractogenic procedures might be considered, particularly non-penetrating procedures such as deep sclerectomy and viscocanalostomy, despite its smaller success rate when compared to trabeculectomy [46].

Advanced Glaucoma. When there is severe glaucoma, there is a high risk of visual acuity loss due to IOP spikes or IOP fluctuations and the priority is a more aggressive IOP-lowering strategy. The best surgical option is trab-

eculectomy with posterior cataract removal – sequential approach. Lens extraction should be performed in a second surgical procedure delayed for at least 6 months and ideally for 2 years, but with the penalty of significantly decreasing trabeculectomy filtering efficacy [47]. It should be kept in mind that in special cases – owing to increasing age, comorbidities or operative/anaesthetic contraindications – patients who are not candidates for two separate visits to an operation theatre can be considered for combined surgery. In this line of thought, there are those who support that, given the overall effect that phacoemulsification has on a previous filtration bleb, the final outcome of both surgical approaches (combined vs. sequential) will be very similar. The only clinical trial comparing both surgical approaches shows a similar IOP value. However, pre-operative IOP values are not mentioned and it is, therefore, impossible to come to any conclusion about the extent of IOP reduction seen with both procedures [48].

Novel Surgical Approaches

A range of novel surgical alternatives has emerged in recent years. These new techniques are minimally invasive, mostly intended to be combined with cataract surgery so as to provide an additional IOP reduction and a further decrease in the burden of glaucoma medication. These include endoscopic cyclophotocoagulation, trabecular micro-bypass stent (iStent), trabeculotomy ab interno (Trabectome), canaloplasty and two more recent ab interno procedures, the Hydrus and CyPass devices.

Endoscopic cyclophotocoagulation consists of laser coagulation of ciliary processes and, when combined with phacoemulsification, allows for an IOP reduction ranging from 17.6 to 46.9% [49]. However, the majority of data comes from retrospective, uncontrolled case reports, with only one randomized controlled study reporting a significant IOP and glaucoma medication decrease in the treatment group (17.6 vs. 4.2% decrease in IOP and 57.5 vs. 0% decrease in medication) during a 3-year follow-up [50]. Also, there is concern about the high rate of post-operative complications comparing to drainage devices.

The iStent (Glaukos Corp., Laguna Hills, Calif., USA) is a device that is internally inserted into Schlemm's canal, allowing the aqueous humour to bypass the trabecular meshwork from the anterior chamber directly into Schlemm's canal. The largest controlled, randomized clinical trial reported a high proportion of patients achieving an IOP <21 mm Hg (61 vs. 50%, $p = 0.036$) at 2 years' follow-

up [51]. Also, a decrease in IOP-lowering medication was detected in 81.3%.

The ab interno trabeculotomy, or Trabectome (NeoMedix Inc., Tustin, Calif., USA), uses an electrocautery to remove a section of trabecular meshwork. Several retrospective, uncontrolled trials have reported an IOP decrease ranging from 4 to 7 mm Hg with the combination of the Trabectome with phacoemulsification, as well as an important drop in the number of glaucoma medications [49]. However, evidence concerning the IOP-lowering effect of the Trabectome alone remains inconclusive.

Finally, canaloplasty (iScience Interventional Corp., Menlo Park, Calif., USA) consists of the cannulation of Schlemm's canal with consequent stretch of the trabecular meshwork and seems to be a novel approach with a higher IOP reduction (40% or 10 mm Hg) when combined with phacoemulsification; however, associated drawbacks are the development of conjunctival scarring that could limit the efficacy of a subsequent trabeculectomy and the higher rate of surgical complications [52].

Hydrus (Ivantis Inc., Irvine, Calif., USA) is a new Schlemm's canal scaffold that increases aqueous humour outflow. Preliminary results from a 6-month follow-up clinical trial show promising results (average 4.7 mm Hg IOP reduction) due to its double mechanism of action – perforation of the trabecular meshwork and dilation of Schlemm's canal [53]. The CyPass (Transcend Medical, Menlo Park, Calif., USA) is a polyamide implant inserted into the suprachoroidal space through the angle region to promote the uveoscleral outflow. Outcomes reported show an IOP reduction of 37% in medically uncontrolled eyes and a 50% decrease in glaucoma medications during a 6-month follow-up, with very few side effects [54].

These new methods are most suitable combined with phacoemulsification in mild to moderate primary open-angle glaucoma (POAG) when lower magnitude IOP reductions are sufficient; however, solid randomized controlled clinical trials comparing these combined approaches to phacoemulsification alone are still lacking for the majority of these new techniques and, to date, it is impossible to discern their true potential for disease management.

Conclusion

There is evidence that cataract surgery results in a modest long-lasting decrease in IOP in both POAG and CACG patients. Due to the inherent anatomical charac-

teristics of each type of glaucoma, this hypotensive effect is more prominent in eyes with CACG, in which lens extraction widens the anterior chamber. Phacoemulsification is becoming progressively more important for CACG control due to its ability to remodel anterior chamber anatomy and there is a current debate on whether clear lens extraction has a good risk-to-benefit ratio for CACG prevention and/or treatment.

On the other hand, for POAG-related ocular hypertension, primarily caused by trabecular meshwork dysfunction, cataract surgery results in a more limited IOP decrement, and its mechanism remains poorly understood. In these patients, this procedure has a minor impact on IOP control, but this modest and variable IOP decrease can still be clinically significant and help patients reach their target IOP. However, for the management of

advanced glaucoma with uncontrolled IOP, priority should be given to a more aggressive IOP lowering strategy – such as filtering surgery – and cataract surgery should be delayed. Combined surgery – phacotrabeculectomy – is a surgical procedure without a formal indication, but might be useful for some situations. Future studies with well-designed, large, prospective randomized trials are still lacking, but current data suggests this widespread surgery will find its proper place in the practice pattern of glaucoma management.

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