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Review Article

Is the Long-Term Use of Topical Carbonic Anhydrase Inhibitors and Beta-Blockers Necessary after Intraocular Lens Replacement Surgery?

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Abstract

Intraocular pressure (IOP) tends to increase during and after intraocular lens (IOL) replacement surgery, a common procedure for cataracts. There are varied risk factors in IOP-rise following IOL replacement surgery, including preoperative condition, devices, procedures, physician/surgeon-experience, anatomical variables, and pre-, peri-, and post-surgical drug applications. The most notable and effective prevention, management, and treatment method of post-surgical IOP-rise (and non-surgically-related glaucoma) is applying carbonic anhydrase inhibitors and beta-blockers. However, many physicians customarily continue to prescribe these medicines beyond their effective and necessary use. This prolonged prescribing might well protect the physician, guarding against the possibility of increased IOP post-surgically, but might cause the patient (or insurance company) unwarranted expense and adverse effects from the long-term prescription use in the absence of harmful IOP. These IOP-reducing drugs are efficacious; nevertheless, evidence-based research regarding any benefits of their prolonged application following IOL replacement surgical is limited.

Keywords: *Cataract; Glaucoma; Intraocular Pressure; Intraocular Lens; Replacement Surgery*

Abbreviations

BB: Beta-Blocker; CAI: Carbonic Anhydrase Inhibitor; IOL: Intraocular Lens; IOP: Intraocular Pressure; OVD: Ophthalmic Viscosurgical Device

Introduction

Postoperative elevation of intraocular pressure (IOP) is a frequent side effect after intraocular lens (IOL) replacement surgery (commonly performed due to cataracts). In most patients, the IOP-increase is transient and ideally not associated with any long-term sequelae (such as diminution of vision) [1]. However, a spike in IOP can be disastrous in patients with pre-existing glaucoma, ischemia due to atherosclerosis, or optic nerve damage [2].

In studies regarding high-risk patients, the incidence of IOP-rise (>28 mmHg) during the postoperative period was 46.4% [1,3]. In most patients, the spike in IOP typically occurred within 3–7h after the surgery and lasted for 24h; however, the most crucial period, especially in high-risk glaucoma patients, was the initial 3–4h when IOP could rise to 30 mmHg [4,5]. Ideally, the IOP-spike immediately after

the surgery was determined to be approximately 30 mmHg; however, it might rise to 40 mmHg [5,6]. According to experts, an increase of 50% or 10 mmHg compared to the preoperative values can be considered significant [6,7]. When IOP in patients with single-digit preoperative IOP value increases to 25–30 mmHg during the postoperative period, they require immediate medical intervention [1,5,8,9].

The most constant underlying cause for a rise in IOP immediately after IOL-replacement surgery is inflammatory changes in the anterior chamber due to surgical trauma and the subsequent release of prostaglandins [4,5]. A consensus among researchers and surgeons is that managing the IOP-spike in the immediate postoperative period following IOL-replacement surgery limits or prevents cystoid macular edema [4,5,10]. It is also believed that prophylactic management of raised IOP in the postoperative period is essential. Without IOP-lowering drugs, there is a high probability that a sudden rise in IOP might lead to the patient experiencing debilitating eye pain, nausea, and vomiting—causes for an emergency room visit.

Discussion

Risk factors for elevated IOP

Common risk factors attributed to the postoperative rise in IOP following IOL-replacement surgery include the following:

- Residual viscoelastic material: Ophthalmic viscosurgical devices (OVDs) are used for space maintenance in the eye while implanting the intraocular lenses. Further, with the development of advanced OVDs, the indications also diversified, including protecting the corneal endothelium, stabilizing pupil size, and floppy iris syndrome [11]. There is a high probability that persistent OVDs in the lens capsule might obstruct the trabecular meshwork, resulting in a postoperative rise in IOP, especially if it persists until the end of the surgery. Compared to the cohesive variety of OVDs, the dispersive type of OVDs remain in the eye chambers for more extended periods as they tend to adhere to intraocular structures, such as the cornea, IOL, and iris. Using a substance with high viscosity requires prolonged rinsing of the eye chamber, which is not safe during the surgery's final stages [11].

- Procedure: There are several documented variations of phacoemulsification that impact IOP [1,12].

- The surgeon's experience: Documented reports suggest there is a higher risk of postoperative IOP-rise after IOL-replacement surgery when performed by less-experienced surgeons or ophthalmologists [1,6,8].

- Preoperative IOP: According to a study by O'Brien., *et al*. (2007), the risk of a rise in postoperative IOP increases within the initial 2–3h and after 24h of the surgery. The higher the baseline IOP, the greater the risk for postoperative IOP-spike [13]. However, a direct correlation between glaucoma and the risk of IOP-spike was not established.

- Axial length: Although Cho., *et al*. (2008) suggested that axial length was not related to IOPs measured preoperatively and during the postoperative period, IOP tended to rise in eyes with axial length longer than 25 mm, compared to a decrease in IOP in eyes with axial length shorter than 25 mm [14]. Researchers documented these findings on the 1st day, 3rd day, and after the 5th week of surgery. The underlying cause was most likely an increase in the depth of the anterior chambers of the eyes with shorter axial length compared to those with longer axial lengths.

- Postoperative corticosteroid use: Postoperative rise in IOP can be attributed to corticosteroid therapy, such as topical administration of prednisolone acetate (1.5%) more than three times daily [15].

- Tamsulosin intake: Reports suggest that IOP in the postoperative period might significantly increase in patients taking tamsulosin [16].

Management of IOP

Various strategies are used to address elevated IOP following surgery, such as removing the OVD, choosing sutureless surgical techniques, and prophylactic and postoperative drugs administration. Typically prescribed drugs include carbonic anhydrase inhibitors (CAIs), such as acetazolamide, brinzolamide, and dorzolamide, topical beta-blockers (BBs), such as timolol, and a combination of CAIs and BBs [1,4,5].

The safety and efficacy of acetazolamide in the prevention and management of postoperative IOP-rise have been documented in clinical trials [17] compared to alpha agonists, such as apraclonidine.

In a clinical trial conducted by Dayanir., *et al*. (2005), oral acetazolamide's efficacy was compared to topical brinzolamide (1%). The study concluded that brinzolamide's efficacy in maintaining or preventing IOP-rise in the postoperative period was identical to that of acetazolamide during the initial 4–6h (phacoemulsification). However, the researchers in this particular trial found that brinzolamide's efficacy was better compared to acetazolamide between 18–24h after surgery. Ocular discomfort reported with the use of brinzolamide was less compared to acetazolamide [18].

Rainer., *et al*. (1999) performed a clinical trial comparing the efficacy of dorzolamide 2% (a CAI) and latanoprost 0.005% (a prostaglandin analog) on IOP following small-incision cataract surgery. The study found that 6h after the procedure, both dorzolamide and latanoprost significantly reduced elevated IOP; however, IOP-reduction could only be maintained by dorzolamide 24h after surgery [19]. Similar findings were noted in other clinical trials comparing the efficacy of various CAIs and prostaglandin analogs [20].

In a clinical trial conducted by Lai., *et al*. (2000), the efficacy of latanoprost was compared to that of timolol gel in preventing ocular hypertension after phacoemulsification and IOL implantation [21]. Through a randomized, double-blind study, it was determined that—compared to a single-dose of latanoprost administered in the immediate postoperative period—a single-dose of timolol gel administered simultaneously in another group of patients produced a significant decrease in the IOP measured 2h (4.77 mmHg) and 24h (2.99 mmHg) after surgery [21].

Rainer., *et al*. (2003) investigated the efficacy of a fixed-dose combination of dorzolamide and timolol on IOP following cataract surgery, performed using sodium chondroitin sulfate 4%-sodium hyaluronate 3% (Viscoat). The fixed-dose combination did not prevent the IOP-spike owing to the use of Viscoat [22].

In a comparative randomized case study, Georgakopoulos., *et al*. (2013) explored the efficacy of a fixed-dose combination of brinzolamide-timolol in reducing transient IOP-rise following phacoemulsification during the first 24h [23]. The treatment group (52 eyes) in the study received a fixed-combination dose of brinzolamide and timolol, while the control group (40 eyes) did not receive any drugs. The IOP measured in the postoperative period at an interval of 6h, 12h, and 24h was significantly lower in the treatment group than the control group. None of the patients were found to have more than 10 mmHg rise in IOP in the treatment group; however, the control group patients had elevated IOP more than 10 mmHg in 10% and 20% of the eyes measured at 6h and 12h, respectively [23].

Several studies have supported the efficacy of a combined dose of timolol and dorzolamide/brinzolamide in lowering the postoperative elevation of IOP following IOL-replacement surgery.

Konstas., *et al*. (2013) compared the efficacy of brinzolamide+timolol or brimonidine+timolol fixed-combination with travoprost therapy in open-angle glaucoma [24]. They found that both drug combinations resulted in a significant decrease in IOP compared to travoprost (prostaglandin analog) monotherapy; the brinzolamide+timolol combination demonstrated superior efficacy than the brimonidine+timolol combination in lowering IOP, especially during the afternoon and nighttime [24].

Ornek., *et al*. (2013) analyzed the efficacy of a fixed-dose combination of 1% brinzolamide and 0.5% timolol on IOP following phacoemulsification and IOL-replacement surgery [25]. The researchers found that IOP measured postoperatively at 2h and 24h was significantly lower in the treatment group than the control group [25].

Numerous reports have specified the need to maintain IOP following phacoemulsification and IOL-replacement surgery, which can have disastrous effects otherwise, especially in patients with pre-existing glaucoma and various eye conditions. A fixed-dose combination of BBs, like timolol, and CAIs, like brinzolamide+dorzolamide, was prescribed for managing such issues. The dosage schedule of the therapy, based on literature, was single-dose administration immediately during the postoperative period. In most cases, the IOP-rise normalized within the initial 24h of surgery [1,4,5,25].

Over-utilization of IOP-reducing drugs?

It has been noted that physicians continue to prescribe the drug combination beyond the immediate postoperative period (for weeks or sometimes several months) [26]. According to various published reports, prolonged therapy with these two drugs is not rational [27]; instead, it increases the finanicial burden to the patient (or insurance company) with a heightened risk of adverse drug reaction.

The clinical trials analyzing the efficacy and safety or compared different drugs for lowering IOP in the postoperative period after IOL-replacement surgery were designed for the initial 24h. No patients in the study received these drugs beyond 24h post-surgery, except those taking these drugs for pre-existing glaucoma. Moreover, the latest follow-up IOP measurement did not extend beyond 24h.

Conclusion

Ophthalmologists are aware of the risk of elevated IOP following IOL-replacement surgeries and take adequate measures to prevent such events through appropriate drug therapies, specifically a CAI and BB combination. (General and Family Medicine practitioners should likewise be aware of such, as patients may question the continual taking of these medicines.) However, all medical practitioners should be advised not to prescribe these drugs for a prolonged period, unless required. Scientific data confirming the benefits of the long-term administration of these drug combinations are limited.

Conflict of Interest Statement

The authors declare that this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

References

1. Grzybowski A and Kanclerz P. "Early postoperative intraocular pressure elevation following cataract surgery". *Current Opinion in Ophthalmology* 30.1 (2019): 56-62. https://pubmed.ncbi.nlm.nih.gov/30489361/

2. Levkovitch-Verbin H., *et al.* "Intraocular pressure elevation within the first 24 hours after cataract surgery in patients with glaucoma or exfoliation syndrome". *Ophthalmology* 115.1 (2008): 104-108. https://www.aaojournal.org/article/S0161-6420(07)00339-9/abstract

3. Ahmed II., *et al.* "Revisiting early postoperative follow-up after phacoemulsification". *Journal of Cataract and Refractive Surgery* 28.1 (2002): 100-108. https://www.sciencedirect.com/science/article/abs/pii/S0886335001009944

4. Levkovitch-Verbin H., *et al.* "Intraocular pressure elevation within the first 24 hours after cataract surgery in patients with glaucoma or exfoliation syndrome". *Ophthalmology* 115.1 (2008): 104-108. https://www.aaojournal.org/article/S0161-6420(07)00339-9/abstract

5. Tranos P., *et al.* "Postoperative intraocular pressure spikes: the need to treat". *Eye* 18.7 (2004): 673-679. https://www.nature.com/articles/6701319

6. Bömer TG., *et al.* "Intraocular pressure rise after phacoemulsification with posterior chamber lens implantation: effect of prophylactic medication, wound closure, and surgeon's experience". *British Journal of Ophthalmology* 79.9 (1995): 809-813. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC505265/

7. Kim WJ., *et al.* "Effect of Preoperative Factor on Intraocular Pressure after Phacoemulsification in Primary Open-angle Glaucoma and Primary Angle-closure Glaucoma". *Korean Journal of Ophthalmology* 33.4 (2019): 303-314. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6685830/

8. Slabaugh MA., *et al.* "Risk factors for acute postoperative intraocular pressure elevation after phacoemulsification in glaucoma patients". *Journal of Cataract and Refractive Surgery* 40.4 (2014): 538-544. https://pubmed.ncbi.nlm.nih.gov/24440104/

9. Elfersy AJ., *et al.* "IOP Elevation After Cataract Surgery: Results for Residents and Senior Staff at Henry Ford Health System". *Journal of Glaucoma* 25.10 (2016): 802-806. https://pubmed.ncbi.nlm.nih.gov/27027228/

10. Jarstad JS., *et al.* "Immediate Postoperative Intraocular Pressure Adjustment Reduces Risk of Cystoid Macular Edema after Uncomplicated Micro Incision Coaxial Phacoemulsification Cataract Surgery". *Korean Journal of Ophthalmology* 31.1 (2017): 39-43. https://pubmed.ncbi.nlm.nih.gov/28243022/

11. Bissen-Miyajima H. "Ophthalmic viscosurgical devices". *Current Opinion in Ophthalmology* 19.1 (2008): 50-54. https://pubmed.ncbi.nlm.nih.gov/18090898/

12. Kohnen T., *et al.* "Evaluation of intraocular pressure with Healon and Healon GV in sutureless cataract surgery with foldable lens implantation". *Journal of Cataract and Refractive Surgery* 22.2 (1996): 227-237. https://pubmed.ncbi.nlm.nih.gov/8656390/

13. O'Brien PD., *et al.* "Risk factors for a postoperative intraocular pressure spike after phacoemulsification". *The Canadian Journal of Ophthalmology* 42.1 (2007): 51-55. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3665039/

14. Cho YK. "Early intraocular pressure and anterior chamber depth changes after phacoemulsification and intraocular lens implantation in nonglaucomatous eyes. Comparison of groups stratified by axial length". *Journal of Cataract and Refractive Surgery* 34.7 (2008): 1104-1109. https://pubmed.ncbi.nlm.nih.gov/18571076/

15. Kersey JP and Broadway DC. "Corticosteroid-induced glaucoma: a review of the literature". *Eye* 20.4 (2006): 407-416. https://pubmed.ncbi.nlm.nih.gov/15877093/

16. Bonnell LN., *et al.* "One-day postoperative intraocular pressure spikes after phacoemulsification cataract surgery in patients taking tamsulosin". *Journal of Cataract and Refractive Surgery* 42.12 (2016): 1753-1758. https://pubmed.ncbi.nlm.nih.gov/28007106/

17. Kasetti SR., *et al.* "Preventing intraocular pressure increase after phacoemulsification and the role of perioperative apraclonidine". *Journal of Cataract and Refractive Surgery* 28.12 (2002): 2177-2180. https://pubmed.ncbi.nlm.nih.gov/12498856/

18. Dayanir V., *et al.* "Medical control of intraocular pressure after phacoemulsification". *Journal of Cataract and Refractive Surgery* 31.3 (2005): 484-488. https://pubmed.ncbi.nlm.nih.gov/15811735/

19. Rainer G., *et al.* "Effect of dorzolamide and latanoprost on intraocular pressure after small incision cataract surgery". *Journal of Cataract and Refractive Surgery* 12 (1999): 1624-1629. https://www.semanticscholar.org/paper/Effect-of-dorzolamide-and-latanoprost-on-pressure-Rainer-Menapace/22d4e8e57562eaa3b50b9b726184b810f3503782

20. Ermis SS., *et al.* "Comparing the effects of travoprost and brinzolamide on intraocular pressure after phacoemulsification". *Eye* 19.3 (2005): 303-307. https://pubmed.ncbi.nlm.nih.gov/15258611/

21. Lai JS., *et al.* "Latanoprost versus timolol gel to prevent ocular hypertension after phacoemulsification and intraocular lens implantation". *Journal of Cataract and Refractive Surgery* 26.3 (2000): 386-391. https://pubmed.ncbi.nlm.nih.gov/10713234/

22. Rainer G., *et al.* "Effect of a fixed dorzolamide-timolol combination on intraocular pressure after small-incision cataract surgery with Viscoat". *Journal of Cataract and Refractive Surgery* 29.9 (2003): 1748-1752. https://pubmed.ncbi.nlm.nih.gov/14522295/

23. Georgakopoulos CD., *et al.* "Brinzolamide-timolol fixed combination for the prevention of intraocular pressure elevation after phacoemulsification". *Clinical and Experimental Ophthalmology* 41.7 (2013): 662-667. https://pubmed.ncbi.nlm.nih.gov/23432730/

24. Konstas AG., *et al.* "Comparison of 24-hour intraocular pressure reduction obtained with brinzolamide/timolol or brimonidine/timolol fixed-combination adjunctive to travoprost therapy". *Journal of Ocular Pharmacology and Therapeutics* 29.7 (2013): 652-657. https://www.liebertpub.com/doi/10.1089/jop.2012.0195

25. Ornek K., *et al.* "Effect of 1% brinzolamide and 0.5% timolol fixed combination on intraocular pressure after cataract surgery with phacoemulsification". *International Journal of Ophthalmology* 6.6 (2013): 851-854. https://pubmed.ncbi.nlm.nih.gov/24392336/

26. Lee SY., *et al.* "Effect of chronic anti-glaucoma medications and trabeculectomy on tear osmolarity". *Eye* 27.10 (2013): 1142-1150. https://europepmc.org/article/med/23846375

27. Zhang X., *et al.* "Ocular Surface Disease and Glaucoma Medications: A Clinical Approach". *Eye Contact Lens* 45.1 (2019): 11-18. https://pubmed.ncbi.nlm.nih.gov/30199425/

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