Intraocular pressure rise after phacoemulsification with posterior chamber lens implantation: effect of prophylactic medication, wound closure, and surgeon's experience

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Abstract

***Aims*—A prospective clinical trial was carried out to evaluate the effect of prophylactic medication, the technique of wound closure, and the surgeon's experience on the intraocular pressure rise after cataract extraction.**

***Methods*—In 100 eyes, the intraocular pressure was measured before as well as 2–4, 5–7, and 22–24 hours after phacoemulsification and posterior chamber lens implantation. Each of 25 patients received either 1% topical apraclonidine, 0·5% topical levobunolol, 500 mg oral acetazolamide, or placebo. Forty four eyes were operated with sclerocorneal sutureless tunnel and 56 eyes with corneoscleral incision and suture. Sixty three operations were performed by experienced surgeons (more than 300 intraocular operations) and 37 by inexperienced surgeons (less than 200 intraocular operations).**

***Results*—The pressure increase from baseline to the maximum 5–7 hours after surgery did not differ significantly (p=0·8499) for apraclonidine (9·5 mm Hg), levobunolol (7·2 mm Hg), acetazolamide (7·8 mm Hg), and placebo (8·6 mm Hg). The increase was significantly (p=0·0095) lower in eyes with corneoscleral tunnel (5·5 mm Hg) than in eyes with corneoscleral suture (10·5 mm Hg) and significantly (p=0·0156) lower for experienced (6·6 mm Hg) than for inexperienced surgeons (11·2 mm Hg).**

***Conclusions*—The intraocular pressure rise after phacoemulsification and posterior chamber lens implantation depends strongly on the technique of wound closure and the surgeon's experience. Compared with these two factors, the effect of prophylactic medication can be neglected.**

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Intraocular pressure increase frequently occurs in the early period after cataract extraction.[1–5] Pressure rises to high levels are often painful and have been associated with complications such as anterior ischaemic optic neuropathy, corneal oedema, and deterioration of visual field in glaucomatous eyes.[6–9] The increase in intraocular pressure is more pronounced with the use of viscoelastic substances, especially when left in the anterior chamber.[10–14] Maximum pressure rises usually occur between 6 and 8 hours after surgery.[6]

Various antiglaucomatous agents have been used to prevent the intraocular pressure rise after cataract extraction. Oral acetazolamide[15 16] and topical timolol[16–19] lowered the pressure rise in the early period after intracapsular and extracapsular cataract extraction. Levobunolol proved to be superior to timolol 4–7 hours after extracapsular cataract extraction.[20] Apraclonidine lowered the intraocular pressure rise after uncomplicated phacoemulsification[21] and extracapsular cataract extraction[22 23] when given 30 minutes to 1 hour before surgery, whereas immediate postoperative treatment with apraclonidine was ineffective.[22 24] Miotics are frequently used to promote miosis and prevent intraocular pressure rise. Intracameral[25–28] and topical[24] carbachol reduced the pressure rise for at least 24 hours. Intracameral acetylcholine[28–30] and topical viscous pilocarpine[24 28 31] lowered the intraocular pressure rise for at least 6 hours after extracapsular cataract extraction, whereas pilocarpine solution was ineffective.[24 31]

Although phacoemulsification with posterior chamber lens implantation is being performed increasingly, only few reports on the prevention of intraocular pressure rise in the early postoperative period are available for this technique.[21 30] We conducted a randomised, double masked, and placebo controlled study to compare the effect of topical levobunolol, topical apraclonidine, and oral acetazolamide in preventing intraocular pressure rise in the early period after phacoemulsification and posterior chamber lens implantation. Furthermore, we compared the effect of prophylactic medication on the intraocular pressure rise with the effect of the surgeon's experience and the operation technique.

Patients and methods

A total of 100 patients scheduled for cataract extraction with phacoemulsification and posterior chamber lens implantation were randomly assigned to one of the following groups: (1) two drops 1% apraclonidine hydrochloride 1 hour before and one capsule placebo immediately after surgery, (2) two drops 0·5% levobunolol 1 hour before and one capsule placebo immediately after surgery, (3) two drops placebo (artificial tears) 1 hour before and one sustained release capsule of 500 mg acetazolamide immediately after surgery, or

(4) two drops of artificial tears 1 hour before and one capsule placebo immediately after surgery. A sample size of 22 eyes in each treatment group was calculated to be necessary to detect a real difference in mean intraocular pressure rise of 5 mm Hg between two treatment groups with a statistical power of 90%, assuming a standard deviation of 5 mm Hg for the mean increase in intraocular pressure and accepting a type I error $\alpha \leq 0{\cdot}05$ to be significant in a two tailed t text. A sample size of 25 was chosen for each treatment group.

There were 72 women and 28 men in the study. The average age was 73·0 (SD 11·0) years. Exclusion criteria were history of glaucoma, uveitis, previous intraocular surgery, corneal disorders complicating applanation tonometry, and contraindications against the medication used in the study. The study was approved by the independent human study committee of the University Eye Hospital, Freiburg. Informed consent was obtained from all patients.

All patients underwent uncomplicated phacoemulsification with implantation of a three piece (diameter of optics 6·5 mm) posterior chamber lens. Operations were performed by seven different surgeons. Five 'experienced' surgeons had performed intraocular surgery for 2 to 8 years and had done 300 to 2000 intraocular operations. Two 'beginners' had performed intraocular surgery for 2 and 4 months and had done fewer than 200 intraocular operations at the beginning of the study. A total of 63 eyes were operated by experienced and 37 eyes by inexperienced surgeons. On the preoperative day, one drop of gentamicin 0·5%, one drop of indomethacin 10%, and one drop of scopolamine 0·25% were instilled in three sets at 60 minute intervals. On the operation day, one drop of gentamicin 0·5%, one drop of indomethacin 10%, one drop of scopolamine 0·25%, and one drop of phenylephrine hydrochloride 10% were instilled in four sets at 30 minute intervals, beginning 2 hours before surgery. Each patient received a retrobulbar block (4·0 (SD 1·0) ml) with 2% mepivacaine hydrochloride. Constant pressure of 40 mm Hg was applied for 10 minutes, using a Geuder balloon. A 7 mm wide corneoscleral lamellar incision (56 eyes) or a 7 mm wide and 3·5 mm long sclerocorneal tunnel (44 eyes) were prepared without perforating into the anterior chamber. The anterior chamber was opened by a 3·2 mm incision. After phacoemulsification, the remaining cortex was removed with an irrigation aspiration device, using balanced salt solution. For implantation of the posterior chamber lens, the wound was enlarged to 7 mm. Intracameral acetylcholine and methylcellulose were given before the implantation and aspirated afterwards. In eyes with corneoscleral incision, wound closure was performed with a continuous 10–0 nylon suture consisting of four to six stitches. In eyes with sclerocorneal tunnel, no suture was necessary. Subconjunctival gentamicin sulphate (1 ml) and betamethasone acetate (1 ml) were injected. A patch with 1% pilocarpine ointment was given at the end of the procedure to promote miosis.

Intraocular pressure was measured by two investigators (TB and WL), who knew the patient's randomisation number but were not informed about the medication and the surgeon. All measurements were performed by applanation tonometry, using the same Goldmann applanation tonometer for a particular patient at each time interval. To correct for astigmatism, the mean of the measurements taken with tonometer prism aligned horizontally and vertically was calculated. Measurements were taken in miosis and mydriasis the day before surgery, as well as 2–4, 5–7, and 22–24 hours after surgery. The mean of the preoperative measurements in miosis and mydriasis was taken for baseline value. After each measurement, possible wound fistulation was checked using fluorescein. Four patients with visible fistulae were excluded. A further 18 patients were excluded owing to violation of the study protocol (12 patients) or posterior capsule rupture with vitreous prolapse (six patients). One patient treated with apraclonidine received 500 mg intravenous acetacolamide because of a painful pressure elevation of up to 48 mm Hg at the 5–7 hour measurement point and was also excluded. Overall, 123 patients were recruited, of whom 23 were excluded. In case of exclusion, one of us (JF) was informed about the patient's randomisation number to extend the randomisation list by the medication for which the excluded patient had been scheduled.

Mean intraocular pressures were analysed by the paired Wilcoxon signed rank test, a non-parametric version of the paired Student's t test. Mean intraocular pressure rises were compared by Scheffé's analysis of variance, which is very robust to violation of the assumption of equal variances. Differences of the frequency in pressure rises were analysed by Fisher's exact test for 2×2 contingency tables.

Results

The four treatment groups did not differ significantly with regard to the patient's age and sex, the baseline IOP, the time needed for phacoemulsification, the surgeon's experience, and the proportion of wound closure with tunnel or suture. There were also no significant differences between the experienced surgeons and the beginners and between the tunnel operated and suture operated eyes for these characteristics.

A significant increase in mean intraocular pressure from baseline to the 2–4 hour postoperative period (p always $\geq 0{\cdot}0075$) and the 5–7 hour postoperative period (p always $\geq 0{\cdot}0008$) was noted in all treatment groups (Table 1). The pressure rise was less pronounced 22 to 24 hours after surgery but, compared with baseline, still significant (p always $\geq 0{\cdot}0324$) except for the levobunolol group ($p = 0{\cdot}6069$). All groups had a maximum intraocular pressure at 5–7 hours after surgery. The maximum pressure rise from baseline to

Table 1 Mean (SD) intraocular pressure (mm Hg)

		No of eyes	Baseline*	Postoperative period (hours) 2–4	5–7	22–24
Treatment	Apraclonidine	25	16·6 (3·0)	22·6 (9·5)	26·1 (9·9)	22·4 (6·8)
	Levobunolol	25	16·0 (3·8)	21·6 (9·4)	23·2 (8·7)	16·4 (4·4)
	Acetazolamide	25	16·3 (3·6)	24·0 (9·9)	24·1 (9·6)	20·1 (6·7)
	Control	25	16·0 (3·2)	23·7 (9·4)	24·6 (9·9)	20·6 (8·7)
Technique of wound closure	Tunnel	44	15·9 (3·6)	19·8 (7·0)	21·5 (8·7)	19·2 (7·1)
	Suture	56	16·4 (3·2)	25·5 (10·4)	26·9 (9·5)	20·4 (7·1)
Experience (number of intraocular operations)	more than 300	63	15·9 (3·4)	20·7 (7·7)	22·5 (8·3)	19·3 (6·5)
	less than 200	37	16·7 (3·3)	26·9 (10·8)	27·9 (10·5)	20·8 (7·9)

*Mean of the preoperative measurements in miosis and mydriasis.

the 5–7 hour postoperative period did not differ significantly among all treatment groups (p=0·8499, Fig 1).

Compared with controls none of the agents significantly (p always ≥0·273) influenced the number of eyes with an intraocular pressure of a least 30 mm Hg or at least 40 mm Hg at one or more postoperative measurements (Table 2).

To reduce the possibility of bias and to lower standard deviations, an analysis of variance was performed which included the technique of wound closure and the surgeon's experience as independent variables (Figs 2 and 3). However, the differences in mean intraocular pressure rise between the four treatment groups were still insignificant (p=0·4481). A significantly lower mean pressure rise was found for the tunnel group (5·5 (8·8) mm Hg) compared with the suture group (10·5 (9·6) mm Hg, p=0·0095) and for experienced surgeons (6·6 (8·3) mm Hg) compared with inexperienced surgeons (11·2 (10·8) mm Hg, p=0·0156). Furthermore, pressure levels of at least 30 mm Hg were significantly (p=0·0045) more often found in the suture group than in the tunnel group and pressure rises of at least 40 mm Hg were significantly (p=0·0019) more often found for inexperienced than for experienced surgeons (Table 2).

Among the experienced surgeons, the difference in intraocular pressure rise between the tunnel group (4·4 (7·0) mm Hg) and the suture group (9·2 (8·9) mm Hg) was more pronounced than among the inexperienced surgeons (tunnel group: 9·9 (13·2) mm Hg; suture group: 11·7 (10·2) mm Hg). The interaction was not statistically significant (p=0·22).

Discussion

Most of the clinical studies on the pharmacological prevention of intraocular pressure rise after cataract extraction have been performed with intracapsular[6 16–18] and extracapsular[19 20 22–29 31] technique, whereas reports on the prevention of intraocular pressure rise after phacoemulsification are rare.[21 30] Extracapsular cataract extraction with nucleus expression was associated with higher postoperative pressure rises than cataract extraction by phacoemulsification.[4] Hence, the effect of prophylactic, intraocular pressure lowering medication could be more pronounced in extracapsular operated eyes. For phaceoemulsification and posterior chamber lens implantation, Araie and coworkers[21] found a preventive effect with the use of apraclonidine. Eyes pretreated with apraclonidine had a small and insignificant intraocular pressure rise, whereas placebo treated eyes had a significant pressure rise of about 5·0 mm Hg. Although our surgical technique in the suture group (use of a viscoelastic substance before lens implantation, intraocular lens diameter of 6·5 mm, wound closure by a running suture) was very similar to their procedure, we only found slight (smaller than 2 mm Hg) and insignificant differences in the intraocular pressure rise between the control group and the treatment group. An estimation of the statistical power was performed by calculating the confidence intervals of the difference between each treatment group and the control group.[32] This revealed that, with a probability of ≥90%, the pressure lowering effect of the tested medications is ≤5 mm Hg.

One might argue that the intraocular pressure lowering effect of the medication was masked by the pilocarpine ointment, given at the end of the procedure. However, the mean intraocular pressure rise of 8·6 mm Hg in our control group with pilocarpine ointment was greater than in comparable, previous

Table 2 Eyes with increased intraocular pressure

		Intraocular pressure ≥40 mm Hg No	%	Intraocular pressure ≥30 mm Hg No	%
Treatment	Apraclonidine	13	52	2	8
	Levobunolol	6	24	2	8
	Acetazolamide	13	52	3	12
	Control	9	36	4	16
Technique of wound closure	Tunnel	11	25	2	5
	Suture	30	54	9	16
Experience (number of intraocular operations)	More than 300	21	33	2	3
	Less than 200	20	54	9	24

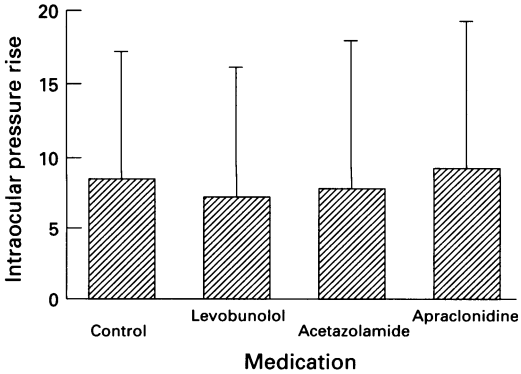

Figure 1 Comparison of the mean intraocular pressure rise from baseline to the 5–7 hour postoperative period for each treatment group. Error bars represent 1 SD.

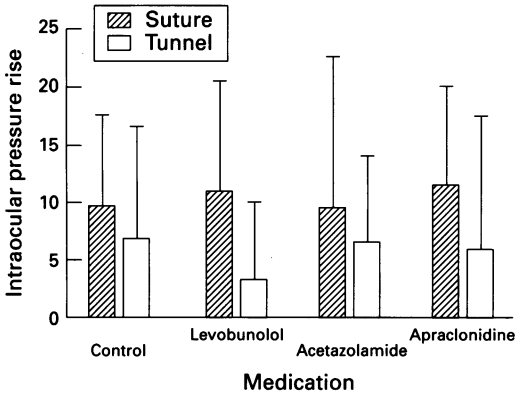

Figure 2 Comparison of the mean intraocular pressure rise from baseline to the 5–7 hour postoperative period for each treatment group, split by the technique of wound closure. Error bars represent 1 SD.

studies.[4 21 30] These studies reported a mean intraocular pressure rise of about 5 mm Hg after phacoemulsification and posterior chamber lens implantation without intraocular pressure lowering medication. Furthermore, a reduction of postoperative intraocular pressure rise was only found for viscous pilocarpine, whereas pilocarpine solution was ineffective.[24 28 31] The effect of pilocarpine ointment has, as far as we know, not been studied up to now. Moreover, pilocarpine has been shown to have an additive effect on β blockers[33–36] and acetazolamide[37] in chronic open angle glaucoma and on apraclonidine after laser iridotomy.[38] For these reasons, a masking effect by the patch with pilocarpine ointment at the end of the operation appears unlikely.

The preoperative use of a non-steroidal anti-inflammatory agent might by another reason for the failure of medical prevention of intraocular pressure rise, as flurbiprofen blocked the ocular hypotensive effect of apraclonidine in normotensive and glaucomatous monkey eyes.[39] However, pretreatment with flurbiprofen did not interfere with the intraocular pressure lowering effect of apraclonidine and timolol[40] and also did not block apraclonidine's effect on aqueous flow in normal human volunteers.[41]

Various factors have been discussed as reducing outflow of the trabecular meshwork and leading to intraocular pressure rise after cataract extraction: trabecular damage following limbal incision and suture,[42] absorption or entrapment of exudated serum components into the trabecular meshwork[43] and remaining viscoelastic material.[44] Watertight wound closure is usually considered as a prerequisite for intraocular pressure rise.[18 21] Our results show that wound closure by a corneoscleral suture leads to a pressure increase about twice higher than wound closure by a corneoscleral tunnel. The mean intraocular pressure rise from baseline to the 5–7 hour period was significantly lower in tunnel operated (5·5 (8·8) mm Hg) eyes than in suture operated eyes (10·5 (9·6) mm Hg). We feel that microleakage of the tunnel, not visible in fluorescein test, is the most probable mechanism for the less pronounced pressure rise in tunnel operated eyes. This hypothesis is supported by a study from Calissendorf and coworkers.[45] To some extent, they found a positive correlation between the intraocular pressure rise after extracapsular cataract extraction and the tightness of suturing as estimated by keratometry. Calissendorf and coworkers suspected a leakage in the eyes with lower astigmatism. Another plausible reason for the less pronounced pressure rise in tunnel operated eyes is the absence of a limbal incision and suture, traumatising the trabecular meshwork.

Furthermore, our results reveal that the surgeon's experience is an important factor for the postoperative intraocular pressure rise. The mean pressure rise in eyes operated by experienced surgeons (6·6 (8·3) mm Hg) was about half the pressure rise in eyes operated by beginners (11·2 (10·8) mm Hg). This finding is not surprising, as beginners often perform intraocular surgery in a more traumatising manner than experienced surgeons. A stronger trauma leads to a more pronounced release of serum proteins and iris pigment into the anterior chamber and also to a greater direct damage to the trabecular meshwork.

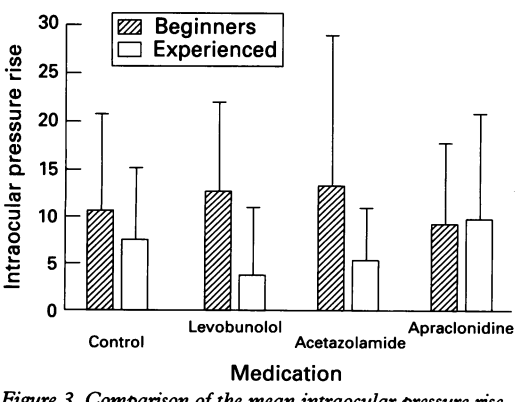

Figure 3 Comparison of the mean intraocular pressure rise from baseline to the 5–7 hour postoperative period for each treatment group, split by the surgeon's experience. Error bars represent 1 SD.

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