Randomised fellow eye comparison of the effectiveness of dorzolamide and apraclonidine on intraocular pressure following phacoemulsification cataract surgery

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Abstract

Purpose To compare the effectiveness of 2% dorzolamide and 0.5% apraclonidine on intraocular pressure (IOP) following phacoemulsification cataract surgery.

Methods This prospective, randomised study comprised 54 eyes of 27 consecutive patients with age-related cataract scheduled for cataract surgery in both eyes. In each patient the eye with the higher degree of cataract was randomly assigned to receive one drop of either dorzolamide or apraclonidine immediately after surgery. The fellow eye was operated on later and received the other treatment. Cataract surgery was performed with a superior 6.0 mm sutureless frown incision, phacoemulsification and implantation of a three-piece PMMA intraocular lens. The IOP was measured pre-operatively as well as 6 h and 20–24 h and 1 week post-operatively.

Results The mean pre-operative IOP was not significantly different between the groups (dorzolamide group, 14.9 ± 2.3 mmHg; apraclonidine group, 14.6 ± 2.5 mmHg; $p = 0.450$). At 6 h post-operatively, the mean IOP was significantly lower in the dorzolamide than in the apraclonidine group (15.6 ± 3.9 mmHg vs 18.0 ± 4.0 mmHg; $p < 0.001$). An IOP increase of more than 5 mmHg at 6 h post-operatively occurred in 3 (12%) eyes in the dorzolamide group and in 9 (36%) eyes in the apraclonidine group ($p = 0.034$). At 20–24 h post-operatively and at 1 week post-operatively no difference was found between the groups.

Conclusions 2% Dorzolamide is more effective than 0.5% apraclonidine in preventing the early post-operative IOP increase following phacoemulsification cataract surgery.

Key words Apraclonidine, Cataract surgery, Dorzolamide, Intraocular pressure, Phacoemulsification

An increase in post-operative intraocular pressure (IOP) in the first 24 h following cataract surgery is well documented.^{1–4} The main reason for this increase is the remaining presence of viscoelastic substances in the eye.^{5,6} To avoid post-operative IOP spikes thorough removal of viscoelastic substances is vital. Surgical techniques for the removal of viscoelastic substances, especially from behind the intraocular lens, have been described,^{7,8} but complete prevention of a post-operative IOP increase has not been achieved with any technique.

Various antiglaucomatous agents have been applied to control post-operative IOP but reports are difficult to compare and often contradictory, since post-operative IOP varies from patient to patient and depends on surgical technique.

Dorzolamide hydrochloride is a highly water-soluble carbonic anhydrase inhibitor; apraclonidine hydrochloride a relatively selective α_2 agonist. Both reduce IOP by inhibiting aqueous humour production in normal and glaucomatous eyes.^{9–11} They have also been reported to help control post-operative IOP following cataract surgery.^{12–18}

The purpose of this study was to compare the effectiveness of 2% dorzolamide and 0.5% apraclonidine in controlling the post-operative IOP increase following phacoemulsification cataract surgery.

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Table 1. Pre-operative and post-operative intraocular pressure (mmHg)

Time	Treatment group		<i>p</i> value
	Dorzolamide	Apraclonidine	
Pre-operative	14.9 ± 2.3 (10–18)	14.6 ± 2.5 (10–18)	0.4498
6 h post-operative	15.6 ± 3.9 (10–23)	18.0 ± 4.0 (10–26)	0.0004
20–24 h post-operative	13.9 ± 3.4 (9–21)	14.8 ± 4.9 (8–27)	0.2413
1 week post-operative	13.6 ± 2.1 (8–18)	13.7 ± 2.3 (10–19)	0.9043

Values are the mean ± SD (range).

Patients and methods

In this prospective, randomised study 54 eyes of 27 consecutive patients with bilateral age-related cataract scheduled for cataract surgery in both eyes and implantation of an intraocular lens (IOL) were included. Exclusion criteria were previous ocular surgery, ocular hypertension (IOP higher than 22 mmHg), pseudoexfoliation syndrome, pigment dispersion syndrome, primary or secondary glaucoma, or hypersensitivity to sulfonamides. Two patients had to be excluded from the study: one had a post-operative hypotony due to a leaking incision in one eye, and the other patient did not return for surgery of her second eye. Consequently, data on 50 eyes of 25 patients were taken for statistical analyses in this study. Fifteen patients were women, 10 were men. The mean patient age was 75.7 ± 10.5 (range 54–92) years. In each patient the eye with the higher degree of cataract was operated on first and randomly assigned to receive either 2% dorzolamide (Trusopt, MSD) or 0.5% apraclonidine (Iopidine, Alcon) after cataract surgery. The fellow eye was operated on after a maximum interval of 4 weeks and received the other treatment after cataract surgery. In the dorzolamide group there were 11 right and 14 left eyes and in the apraclonidine group 14 right and 11 left eyes. One drop of the assigned treatment was instilled immediately after surgery, before patching the eye with a betamethasone–neomycin ointment (Betnesol-N, Glaxo Wellcome).

All patients were operated on in a standardised fashion by the same surgeon (R.M.) who was masked to treatment assignment. Approximately 1–2 h before surgery diclofenac (Voltaren Ophtha, CIBA Vision), phenylephrine 2.5%, tropicamide 1% (Mydraticum Agepha, Vienna) and cyclopentolate 1% (Cyclopentolat 1% Thilo, Alcon) eye drops were instilled. After peribulbar anaesthesia, a superior 6.0 mm frown incision was performed. Phacoemulsification of the nucleus was followed by aspiration of the cortical remnants and

cleaning of the capsular bag. The capsular bag was expanded with sodium hyaluronate 1% (Ophthalin, CIBA Vision), and a three-piece PMMA-IOL (MC 220, Dr Schmidt) was implanted into the capsular bag. The sodium hyaluronate was then aspirated thoroughly from the retrolental space and the anterior chamber. No miotic agent was used intracamerally. The incision was left sutureless. Capsular rupture did not occur in any patient.

After surgery and instillation of the assigned treatment and again at the 6 h visit the eye was patched with betamethasone–neomycin ointment (Betnesol-N). Treatment at the 20–24 h visit consisted of diclofenac (Voltaren Ophtha) and prednisolone (Ultracortenol, CIBA Vision) eye drops.

The baseline IOP was measured by Goldmann applanation tonometry 1 day before surgery. The IOP was measured again with the same Goldmann applanation tonometer 6 and 20–24 h after surgery. The tightness of the wound was checked with the Seidel test. The ophthalmologist who measured the IOP was masked to the treatment group assignment. A routine follow-up including IOP measurement was performed 1 week after surgery.

The sample size was calculated so that a true group difference in changes of pressure values of 2 mmHg could be detected with a probability of 90%. As the standard deviation of the pressure change was not known at the beginning of the study, it was estimated to be 3.5 after recruitment of 21 patients (Cox's half sampling method¹⁹) in order to arrive at a total of 25 available patients. Group comparisons of the pre- and post-operative IOP values and the changes in pressure in the two groups from pre-operatively to 6 h, 20–24 h and 1 week post-operatively were compared using paired *t*-tests. Additionally, pre-operative values were compared with those after 6 h, 20–24 h and 1 week separately for each group using paired *t*-tests. The proportion of patients with an IOP increase of more than

Table 2. Intraocular pressure change (mmHg) from pre-operatively to 6 h, 20–24 h and 1 week post-operatively

Time	Treatment group				<i>p</i> value ^b
	Dorzolamide	<i>p</i> value ^a	Apraclonidine	<i>p</i> value ^a	
6 h post-operative	0.8 ± 3.5 (–7 to 6)	0.2904	3.3 ± 3.8 (–2 to 9)	0.0002	0.0004
20–24 h post-operative	–1.0 ± 3.5 (–7 to 6)	0.1778	0.2 ± 5.4 (–7 to 9)	0.8213	0.1078
1 week post-operative	–1.2 ± 1.8 (–5 to 2)	0.0018	–1.0 ± 1.9 (–5 to 2)	0.0175	0.2832

Values are the mean ± SD (range).

^aDifference compared with pre-operatively.

^bGroup comparison.

Table 3. Number and percentage of eyes with an intraocular pressure increase of more than 5 mmHg

Time	No. of eyes (%)		p value
	Dorzolamide	Apraclonidine	
6 h post-operative	3 (12%)	9 (36%)	0.0339
20–24 h post-operative	1 (4%)	4 (16%)	0.0833

5 mmHg was compared using McNemar’s test for paired proportions. A p value < 0.05 was considered statistically significant.

Results

Table 1 shows the mean pre-operative and post-operative IOP values. The pre-operative IOP was not significantly different between the two groups. At 6 h post-operatively, the mean IOP was significantly lower in the dorzolamide group. At 20–24 h and at 1 week post-operatively, there was no significant difference between the two groups.

Mean IOP changes from pre-operatively to 6 h, 20–24 h and 1 week post-operatively are listed in Table 2. Whereas the mean IOP did not significantly increase at 6 h post-operatively in the dorzolamide group, it did in the apraclonidine group. At 20–24 h post-operatively mean IOP did not change significantly in either group. At 1 week post-operatively, there was a significant mean IOP decrease in both groups compared with the pre-operative mean IOP. Group comparisons showed a statistically significant difference in mean IOP change at 6 h post-operatively. No difference between the groups was found at 20–24 h and at 1 week post-operatively.

Table 3 shows the number and percentage of eyes with an IOP increase of more than 5 mmHg. At 6 h post-operatively there were significantly fewer eyes with an IOP increase of more than 5 mmHg in the dorzolamide group than in the apraclonidine group using McNemar’s test. The maximum IOP increase was 6 mmHg in the dorzolamide group and 9 mmHg in the apraclonidine group, respectively.

Discussion

Our findings indicate that a single post-operative administration of 2% dorzolamide is more effective in preventing the early post-operative IOP increase following phacoemulsification cataract surgery than that of 0.5% apraclonidine. At 6 h post-operatively, the mean IOP was significantly lower in the dorzolamide than in the apraclonidine group. In the dorzolamide group the mean IOP increased only slightly by about 1 mmHg, whereas in the apraclonidine group the mean IOP increased significantly by about 3.5 mmHg. At 20–24 h and at 1 week post-operatively the mean IOP was not different between the groups.

Since the post-operative IOP increase varies with the individual we chose a within-patient study design allowing an intra-individual comparison of the two antiglaucomatous agents studied. However, a control

group is not practicable in this study design. In a previous study¹³ in which cataract surgery was performed by the same surgeon (R.M.) with the same removal technique of the viscoelastic substance (1% sodium hyaluronate), the untreated control group showed an IOP increase of about 5 mmHg at 6 h post-operatively.

Our results are similar to those of Zohdy *et al.*,¹² who also found that dorzolamide in a single administration is effective in reducing the IOP increase following phacoemulsification cataract surgery. In their study the mean post-operative IOP increase was slightly higher than in our study, which might be related to differences in the surgical technique. In the literature, no further study reporting on post-operative IOP increase under dorzolamide was found.

Several studies have shown that apraclonidine administered as a single post-operative dose is effective in preventing the IOP increase following anterior segment laser surgery.^{20–22} Whereas for anterior segment laser surgery the surgical technique is relatively uniform, for cataract surgery various different surgical techniques are used. Therefore it is difficult to compare the results of studies on prevention of the post-operative IOP increase. For manual extracapsular cataract extraction (ECCE) several studies have shown that apraclonidine is effective in reducing the post-operative IOP.^{14–18} Other studies, however, found that apraclonidine has no effect in reducing the post-operative IOP increase.^{23–25} For phacoemulsification cataract surgery a literature search showed only three articles reporting on the post-operative IOP increase under apraclonidine. Araie and Ishi¹⁷ found that apraclonidine is effective in preventing the post-operative IOP increase when administered before and after surgery. Conversely, Byrd and Singh²⁴ and Bömer *et al.*²⁶ reported that apraclonidine has no effect in preventing the post-operative IOP increase. In those studies, however, apraclonidine was administered pre-operatively.

In conclusion, the post-operative IOP increase varies from patient to patient and depends on the surgical technique used. Therefore, studies using a within-patient comparison of post-operative IOP following cataract surgery performed by a single surgeon in a standardised fashion are preferable. The findings of our study indicate that the single post-operative administration of 2% dorzolamide is more effective in preventing the early post-operative IOP increase following phacoemulsification cataract surgery than that of 0.5% apraclonidine.

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