Effect of oxybuprocaine 0.4% in preventing surgically induced miosis

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SUMMARY In a group of 68 patients a double-blind study was performed to assess the effect of preoperative oxybuprocaine 0.4% (Dorsacaine, Novesin) eye drops in comparison with a placebo in preventing surgically induced miosis during extracapsular cataract extraction. One drop of oxybuprocaine 0.4% or placebo was instilled 10 and 5 minutes preoperatively. The pupil diameter was recorded at different stages of the operation. It was found that oxybuprocaine reduced the amount of pupil constriction during the operation significantly as compared with the placebo group, facilitating the removal of lens material and the implantation of an intraocular lens. The effect of oxybuprocaine is considered to be due to anaesthetic action on sensory nerves in the eye, which may inhibit the release of a miotic substance.

Miosis induced by surgical trauma is a frequent problem during extracapsular cataract surgery. In spite of vigorous preoperative dilatation with both anticholinergic and sympathicomimetic agents the pupil diameter constricts during the operation. The removal of lens material and the implantation of an intraocular lens in the posterior capsule bag are hampered by this pupil constriction. Epinephrine can be used in the irrigating solution¹ or injected in small quantities into the anterior chamber.^{2,3} These solutions are toxic for the endothelium and cause a loss of corneal endothelial cells.⁴

Mechanical and chemical stimulation of the iris⁵⁻⁹ and intracranial stimulation of the trigeminal nerve^{6,10-13} produce miosis, increased vascular permeability, and elevation of the intraocular pressure. The reaction seems to be mediated by prostaglandins and by an atropine-resistant neurogenic pathway. The relative contribution of these 2 depends upon the type of stimulus applied.⁸ Prostaglandin-synthesis inhibitors reduce the amount of miosis during mechanical irritation of the iris significantly both in animals^{6,9,14-17} and in humans.^{18,19} Topical anaesthetics also reduce the amount of miosis during irritation of the iris in animals.^{8,14,17,20}

A double-blind study was performed to define

clinically the effect of preoperative treatment with oxybuprocaine 0.4% eye drops in comparison with a placebo in preventing surgically induced miosis during extracapsular cataract surgery in humans.

Patients and methods

SUBJECTS

Between June 1982 and January 1983 a total of 68 patients underwent an extracapsular lens extraction of one eye because of senile cataract. The patients were randomly assigned to the oxybuprocaine or the control group. Their ages ranged from 38 to 91 years, with a mean of 72 years. There was no statistically significant difference between the 2 groups in sex and age distribution. No patient had a history of ocular disease other than cataract. Two patients were excluded from the study; one had a rupture of the posterior capsule and in the other the mydriasis was insufficient to express the nucleus. Finally, the study comprised 66 patients, 33 in the oxybuprocaine and 33 in the control group.

SURGICAL PROCEDURE

The surgery was carried out under general anaesthesia by 3 of the authors, using the same surgical technique. After a corneoscleral incision the eye was entered at the 12 o'clock position and the anterior capsule was opened. The wound was enlarged with corneoscleral scissors, and the lens nucleus was expressed. The lens

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Fig. 1 Surgically induced miosis in the oxybuprocaine group (mean 0.6 mm) and in the placebo group (mean 1.1 mm) after expression of the lens nucleolus. n = Percentage of total number of patients.

■ = Oxybuprocaine. □ = Placebo.

cortical remnants were removed by irrigation and aspiration.

MEDICATIONS

Indomethacin eye drops¹⁹ were instilled at 7.00 pm and 9.00 pm on the night preceding surgery and 3 times on the day of surgery: 2 hours, 1 hour, and 20 minutes preoperatively. Mydriasis was achieved by instillation of eye drops containing tropicamide 0.5% with phenylephrine 5% at 55, 45, 35, and 15 minutes before the scheduled operation time. Either oxybuprocaine 0.4% eye drops or placebo eye drops were instilled 10 and 5 minutes preoperatively.

OBSERVATIONS

The diameter of the pupil was measured to 0.25 mm under the operating microscope with callipers. Recordings were made at the beginning of the opera-

tion, after capsulotomy, after expression of the lens nucleus, and at the end of the irrigation and aspiration period. The colour of the iris and duration of the operation were also recorded.

Results

There was no statistical difference in pupil diameter between the 2 groups at the beginning of the operation: the mean pupil diameter was 8.1 mm in both groups. The relevant results are given in Figs. 1 and 2. The pupillary constriction from the beginning of the operation till after expression of the lens nucleus was less in the oxybuprocaine pretreated group than in the control group (Table 1). The statistical evaluation of these results was performed by Student's *t* test. It was found that this difference was highly significant ($p < 0.001$).

Fig. 2 Surgically induced miosis in the oxybuprocaine group (mean 2.0 mm) and in the placebo group (mean 2.4 mm) up to the end of the irrigation and aspiration.

n = Percentage of total number of patients. ■ = Oxybuprocaine.

□ = Placebo.

Table 1 Mean pupillary constriction (mm) in the oxybuprocaine and in the placebo group at the different stages of the operation

	Oxybuprocaine	Placebo
After capsulotomy	0.5	0.7
After expression of lens nucleus	0.6	1.1
After irrigation/aspiration	2.0	2.4

The pupillary constriction during the operation—from the beginning of the operation up to the end of the irrigation and aspiration—was also less in the oxybuprocaine pretreated group than in the control group (Table 1). This difference was also statistically significant ($p < 0.05$, Student's *t* test).

In this clinical study there were factors that could possibly have influenced the results. Sometimes it was impossible to start the operation exactly at the scheduled time because of delay in the operation schedule. These factors could be excluded, as no significant difference was found (Wilcoxon test) between the oxybuprocaine and the control group. Nor was there any difference in pupil constriction in relation to different iris colours.

Discussion

We found that oxybuprocaine had a significant inhibitory effect on surgically induced miosis. Extracapsular cataract surgery causes considerable trauma to the eye, particularly to the iris and the cornea. Experimental injuries, such as topical application of 1% nitrogen mustard on the rabbit eye, were found to cause 2 distinct episodes of increase in intraocular pressure (IOP)—an immediate rise in IOP reaching a peak within 40 minutes, and a second rise in IOP reaching a maximum between 5 and 8 hours.⁹ At the same time miosis and an increase in vascular permeability occurred. The early hypertensive phase was completely blocked by retrobulbar ethanol, but the second rise in IOP was not.⁹ Indomethacin treatment did not affect the initial IOP rise, but it completely blocked the second hypertensive phase.⁹

The miotic response after laser stimulation of the iris and after nitrogen mustard is largely dependent upon the presence of intact and functional sensory nerves.^{21,22} It is well known that local anaesthetics may block the nervous impulse.²³ Since the rate of absorption across mucous membranes is exceedingly rapid²⁴ and the concentration of oxybuprocaine in the iris and cornea is high after a subconjunctival injection,²⁵ we may assume that, apart from the cornea, oxybuprocaine can also block nervous impulses in the iris. It has been found that electrical stimulation of sensory nerves causes a release of sub-

stance P in the peripheral nerve endings¹³ and intracamerally injection of substance P causes a strong miosis. Retrobulbar treatment with capsaicin, an agent that depletes sensory nerve endings of substance P, prevents the early IOP increase and miosis induced by nitrogen mustard²⁶ and by mechanical irritation of the iris.¹⁷ Since substance P is present in nerve fibres in the ciliary body, iris, and cornea of animals^{27,28} and in human corneas and irides,²⁹ it is most likely that substance P plays a major role in pupillary miosis in the rabbit and probably also in humans. Therefore, oxybuprocaine might partially prevent pupillary miosis by blocking the nerve impulses.

This process of blocking the nerve impulses may inhibit the release of substance P. In earlier experiments, it was found that indomethacin eye drops reduced the amount of pupil constriction during extracapsular cataract extraction significantly.¹⁹ In this study it was found that the addition of oxybuprocaine eye drops further inhibited the pupillary miosis during extracapsular cataract extraction. However, the pupillary constriction was only partially blocked. Perhaps further investigations will lead to drugs that can prevent the pupillary constriction more completely during surgical manipulation.

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