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The influence of oxybuprocaine (Novesine) on the intraocular pressure

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Abstract. Patients with raised intraocular pressure often have lower tension during hospital admissions than on out-patient measurement, even though the therapy is the same. A prospective study on 18 volunteers and 10 glaucoma patients was set up to find out whether oxybuprocaine eyedrops or repeated applanation tonometry could have anything to do with this.

The tension was measured at least 3 times a day with the non-contact tonometer (NCT). In the case of the volunteers oxybuprocaine was instilled into the eye 3 times a day for one week. In the case of the patients the tension in one eye was measured with the Goldmann tonometer on several days after the application of oxybuprocaine drops. No reduction in intraocular pressure was found during the observation period, nor was there an obvious difference between the test eyes and the control eyes. In hospital, patients had at 11 o'clock in the morning intraocular pressure which was on the average 2.2 ± 1.5 mmHg lower than that measured at out-patient checks, in spite of receiving the same therapy.

Introduction

During hospitalization of glaucoma patients the intraocular pressure measured is often lower than that found at out-patient checks although the same treatment is being given. Hyams et al. (1982) performed a study on 13 patients and found significantly lower tension during hospitalization at 8 o'clock in the morning. They ascribed this to reduction in stress. There is a structural resemblance between oxybuprocaine and the B-blocker metipranolol, which is known to have a slight local anaesthetic effect apart from its B-blocking action (Draeger et al., 1983). The aim of this study was to determine whether the use of oxybuprocaine by volunteers and the frequent practice of applanation tonometry on hospitalized glaucoma patients caused a reduction in ocular tension. As an anaesthetic is not needed when the non-contact tonomer is used, and hardly any massage effect or damage to the corneal epithelium is produced, this seemed to be the instrument of choice for the study of the effect of an anaesthetic (Forbes et al., 1974).

Material and methods

This study consisted of 2 parts: one experiment with 18 volunteers and one investigation with 10 glaucoma patients.

In the group of 18 volunteers (10 men, 8 women, average age 31 ± 8 years), in the first 3 days the daily variations in pressure were determined, using the American Optical Non-Contact Tonometer (NCT). Measurements were made 3 times a day according to the method ascribed by Shields (1980). In order to reduce the influence of the ocular pulse, which is synchronous with the heartbeat, the measurements in each eye were repeated until 3 measurements were obtained with a maximum variation of 3 mmHg. The right eye was always measured first.

In the next seven days the pressure in both eyes was measured again at the same times, after which one drop of oxybuprocaine was instilled into one eye, chosen at random. Five minutes later the measurements were repeated in order to detect any immediate effect of the anaesthetic. After this oxybuprocaine week the pressure was measured again 3 times a day for 3 days without oxybuprocaine, and this measurement was repeated after 5 min in order to see if a massage effect was produced. The measurements were averaged and analysed per person. For the graphic representation the observation time was divided into four periods: first, a basis curve with the average values obtained during the first three days from all the volunteers together, then a second period with the results of the first four days in which Novesine was used and a third period covering the last three days in which oxybuprocaine was given. The last part of the curve shows the measurements from the three wash-out days.

The average age of 10 patients (5 men, 5 women) was 64 years (38–80 years). They all had bilateral glaucoma which had caused damage to the optic nerve and visual field defects. In 7 patients glaucoma simplex was diagnosed, the 3 other patients had a low tension glaucoma. The indication for hospitalization was glaucoma observation, laser trabeculoplasty or a filtering operation. Two patients were having no medical therapy, the others were being treated with Timolol, pilocarpine or both. One patient received in addition 375 mg acetazolamide per day. The therapy was not altered during the study. The medication was always given after the measurements had been made. For two days the intraocular pressure was measured at least 4 times a day in order to register the daily variations in the tension with therapy. One eye was selected for applanation tonometry, depending on the treatment for which the patient had been admitted. A few minutes after the NCT measurements one applanation measurement was carried out with the Goldmann tonometer of the Haag Streitt slitlamp, first a drop of oxybuprocaine and a wet Ayerst fluostrip were used. The experiment was ended when the therapy was changed. The results were analysed individually and subdivided into 3 periods: a first basis period, a second period with one or more days of applanation tonometry and a third period with the results of the last day.

Results

The average NCT measurements of the 18 volunteers are shown in Figure 1. The individual patterns of the pressure measurements of the third day curve versus the last day of Novesine are shown for each volunteer in Figure 2. Both figures show the same picture: there is no tendency to reduction in tension in the test eyes during the observation period, nor is there a change in intraocular pressure when these eyes are compared with the contralateral control

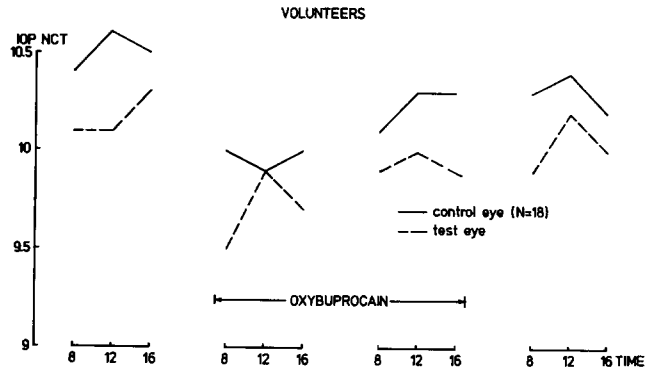

Figure 1. Control eye versus test eye in 18 volunteers. The left-hand set of curves represents the average basic pressure during the first three days, the second set of curves the same during the next four days and the third set the same during the last 3 days. The interrupted line represents the eye which was treated with oxybuprocaine during the second and third periods. The right-hand curves show the average in the wash-out period of 3 days.

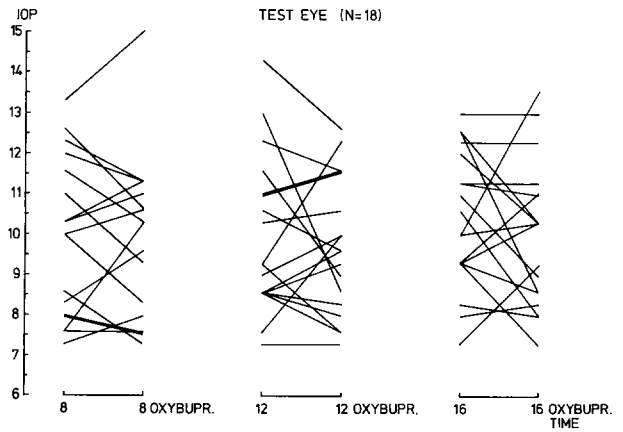

Figure 2. Pattern of the individual intraocular pressures of the eyes of the 18 volunteers which were treated with oxybuprocaine at 8.00, 12.00 and 16.00 hours respectively. On the left is the pressure without, and on the right with, oxybuprocaine.

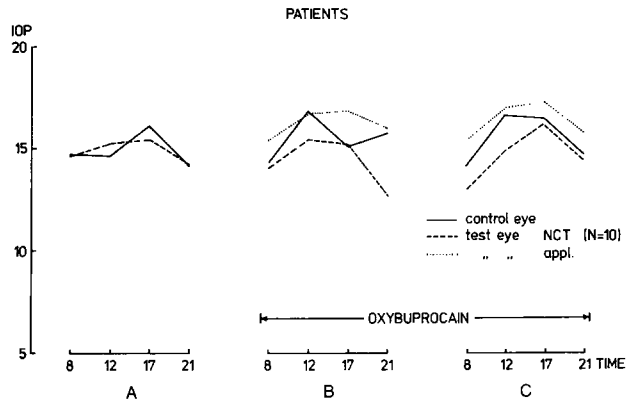

Figure 3. Average daily pressure curves of 10 patients with the non-contact tonometer. A: with therapy; B: the same on one or more days of combined NCT and Goldmann applanation tonometry of the test eye; C: the last day of the experiment as described under B. Continuous line = NCT measurement of control eye; interrupted line = NCT of test eye; dotted line = Goldmann applanation reading of test eye.

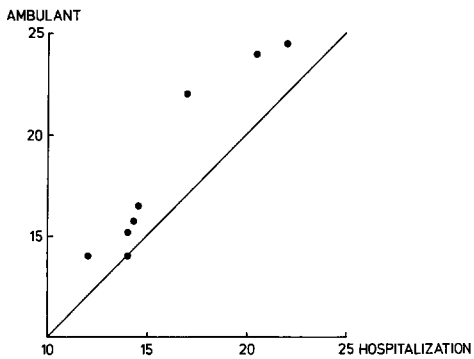

Figure 4. Scattergram of the Goldmann tonometer readings during hospital admission (abscissa) and at out-patient check-up (ordinate), both taken at 11 o'clock. $P < 0.01$, Pearson's correlation coefficient $r = 0.95$.

eyes. The student's t-test for the paired measurements in Figure 2 showed no significant difference between the two series. Inspection of the measurements shows a slight immediate tension-reducing effect after oxybuprocaine. The first measurement was on the average 9.9 ± 1.7 mmHg; five minutes after the instillation of Novesine the average pressure was 9.4 ± 1.6 mmHg. This 0.5 mmHg difference was however not significant when compared with the control eyes: first measurement 10.2 ± 1.8 mmHg and five minutes later 10.0 ± 1.8 mmHg. A second measurement of the intraocular pressure after five minutes without the administration of oxybuprocaine showed no change

in pressure (n = 54). The average values were, for the right eye: 10.2 ± 1.6 mmHg on the first reading and 10.0 ± 1.6 mmHg on the second reading, and for the left eye: 10.2 ± 1.9 and 10.3 ± 1.9 mmHg respectively. The tension pattern of the patients is shown in Figure 3.

Here again no noticeable change in intraocular pressure was found after Goldmann applanation. The variations in intraocular pressure in the control eyes were remarkably similar, the curves obtained from the first eye ran almost parallel to those from the second eye. The fluctuations measured with the Goldmann tonometer also correlated well with these readings, but the tension measured with the Goldmann tonometer was on the average 1.9 mmHg higher ($p < 0.01$).

The NCT readings five minutes after applanation tonometry did not differ significantly from the first measurements. During hospital admission the average pressure at 11 o'clock in the morning was lower than the out-patient measurements before hospitalization, the treatment being the same. In Figure 4 the results of Goldmann applanation on 8 eyes of 8 patients before and during hospital admission are compared; the 2 remaining patients had not used medication in the morning before the out-patient examination. The average decrease in intraocular pressure was 2.2 ± 1.5 mmHg, which is a significant change ($p < 0.01$).

Discussion

The Goldmann tonometer is one of the most frequently used instruments for measuring the intraocular pressure (Phelps and Phelps, 1979). Goldmann himself (Goldmann and Schmidt, 1957) reported that repeated applanation tonometry caused the intraocular pressure to fall and Stocker (1958) stated further that even a simulated measurement, with the tonometer held for a moment above the eye, had a tension reducing effect. This tension reduction after frequent measurement is exponential and, after about 20 min of measurement every other minute, reaches a basic value which is about 5 mmHg lower than the original tension (Bechrakis, 1966; Krakau and Wilke, 1971). Moses (1961) showed that this reduction in pressure was greater if extra ophtaine was instilled into the eye, and that the effect was greatest in the eye which was longest in contact with the anaesthetic. Applanation tonometry causes damage to the corneal epithelium, so that medication can penetrate better into the eye (Worthen et al., 1974). The short-term effect of topical anaesthesia has been studied by others. Jenkins found a fall in tension of 1.4 mmHg in an NCT study on 7 patients (Jenkins and Shakespeare, 1973). Draeger (Draeger et al., 1975) noted that the use of a topical anaesthetic increased the correlation between NCT measurements and the Draeger applanation tonometer and Moses (Moses et al., 1962) described better correlation between the Goldmann tonometer and the Mackay Marg tonometer if topical anaesthesia was also used before the latter examination.

The influence of the sensory innervation via the trigeminal nerve on the intraocular pressure has been recognized for a long time. Perkins (1957) found ipsilateral rise in intraocular pressure on stimulation of the intact trigeminal nerve in rabbits and dogs. Experiments performed by Alper (1975) on monkeys showed that section of the ophthalmic branch of the trigeminal nerve resulted in a 0.5 mmHg lower intraocular pressure on the side of the section.

The rise in intraocular pressure following chemical damage to the cornea (Butler et al., 1979), which is ascribed to the release of inflammatory mediators including substance P, does not occur after destruction of the ipsilateral sensory innervation. In addition, this rise in intraocular pressure can be prevented by previous treatment with 0.4% oxybuprocaine benoxinate (Butler et al., 1979; van Rij et al., 1984). It is also now a well-known fact that local anaesthesia blocks the nerve impulse.

We also found a slight reduction in intraocular pressure five minutes after the administration of oxybuprocaine. This can be due either to the direct influence of the oxybuprocaine on the intraocular tension or to the reduced sensitivity to the examination. After anaesthesia there is less reflex lacrimation and we know that the non-contact tonometer gives higher results if the eye is very wet (Wittenberg and Green, 1976).

With our study method we did not find a long-term influence of Novesine or frequent applanation on the intraocular pressure. This study therefore can give no answer to the question why patients have lower intraocular pressure during a hospital admission. Perhaps it is the combined influence of more vigilance with respect to the therapy, more regular meals and a restricted quantity of food and drink, and a different psychological climate in the hospital, which is at the bottom of the difference. Probably the patient's inexact application of the therapy at home is the most important factor (Rocheblave, 1983; Granström, 1982). Experiments with a non-compliance monitor have confirmed this (Kass et al., 1984). Better motivation of the patient, which is stimulated by information and explanation, can often result in a great improvement (Zimmerman and Ziegler, 1984).

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