

(−)-tropicamide is a more potent muscarinic blocker by a factor of 50 to 75.

Relative to the effects observed in the nonpigmented iris, tropicamide isomers are two to three times less active in the pigmented irises. These results are very similar to the blocking effects of atropine in the two types of irides. Detailed studies with atropine indicate that the drug is absorbed by the pigment cell melanin in the dark iris. The loss of atropine to the melanin granules could decrease the free concentration of the drug in the vicinity of the muscarinic receptor. Thus the apparently diminished concentration will produce lesser mydriatic effects. This factor obviously does not exist in the nonpigmented eye. The reverse is expected during the wash-off studies. Relative to that observed in the nonpigmented iris, the blocking effects of (−)-tropicamide were very slowly reversed. During the wash-off, the blocker which is accumulated by the melanin granule could be slowly released to produce relatively prolonged local muscarinic block.

During this study, on several occasions, the optical rotation of the isomers was checked through the courtesy of Dr. D. D. Miller of the Division of Medicinal Chemistry of our College.

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REFERENCES


Intraocular pressure after optic nerve transection. DONALD M. SERAFANO AND RICHARD F. BRUBAKER.

Intraocular pressure response to systemically administered osmotic agents was studied in albino rabbits with one optic nerve transected and the fellow optic nerve left intact. There was a significant increase in intraocular pressure of both eyes following water ingestion but no significant difference in the pressure rise of the two eyes. There was a significant decrease in intraocular pressure of both eyes following glycerol ingestion but no significant difference in the pressure fall of two eyes. These results do not support the hypothesis that the optic nerve carries fibers which are part of the control system for intraocular pressure.

In 1969, Riise and Simonsen1 studied a series of patients who had suffered unilateral optic nerve lesions from trauma. Eyes with traumatized optic nerves had less intraocular pressure rise following water ingestion. They postulated that the optic nerve served as a communicating pathway between the eye and an osmoreceptor in the hypothalamus.

In 1970 Krupin et al.2 reported an animal model for investigating the relationship between optic nerve lesions and intraocular pressure. They demonstrated that optic nerve transection reduced the intraocular pressure response to systemically administered osmotic agents. After a series of experiments3–8 they concluded that a sensitive osmoreceptor exists in the hypothalamus, which may regulate or modify the response of the eye to osmotic agents via an optic nerve pathway. Cox et al.9 have cited preliminary evidence that, in the rabbit, this receptor may be associated with the supraoptic nucleus.

The purpose of this study was to attempt to confirm the observation that cutting the optic nerve decreases the eye's response to osmotic agents and to determine whether such a change could be explained by local effects rather than neural feedback effects.

Methods. Intraocular pressure was measured with a floating-tip gas tonometer, the Pneumotonometer. This instrument was recalibrated for the living rabbit eye. By means of the closed-stopcock method of calibration, the gas flow of the
Fig. 1. Control tests—baseline preoperative and postoperative intraocular pressures. There is no significant difference in intraocular pressure when comparing the eyes pre- and postoperatively.

Control test plus oral-gastric (OG) tube. Passage of the tube without injection of osmotic agent had no significant effect on intraocular pressure.

Pneumatonograph was reduced to the point where application of the sensor to the eye in the horizontal position produced less than a 6 mm Hg rise in intraocular pressure at 20 mm Hg. A reliable and linear calibration curve was then constructed for conversion of instrument reading to P<sub>e</sub> over the range 10 to 30 mm Hg.

Nine albino rabbits weighing 1.7 to 3.1 kg were selected. Baseline intraocular pressure differences between fellow eyes were less than 2 mm Hg. One optic nerve, chosen by random assignment, was transected, and a sham operation was performed on the fellow eye in the same manner as that reported by Krupin et al.<sup>2</sup>

Four weeks postoperatively each animal was examined. Eyelid blink reaction to confrontation, pupil reaction to light, optic nerve color, and the central retinal artery patency were tested. During the fifth postoperative week, osmotic studies were begun. Each animal was fasted overnight and tested in the morning. At least 5 days' rest elapsed between repeat testings in a given animal.

A control study was done to evaluate the effect of the testing circumstances on intraocular pressure. Baseline intraocular pressure was recorded and compared to the preoperative values. An oral gastric tube was passed into the stomach and removed but no osmotic agent was given. Intraocular pressure was measured at 15 min intervals thereafter.

In subsequent studies, the same procedure was followed, but in addition water or glycerin, in varying dosages, was infused through the oral gastric tube at time zero. Intraocular pressure was measured at 15 min intervals. Blood pressure was determined with a modified Grant-Rothschild pressure capsule over the central auricular<sup>10</sup> artery.

Statistical evaluation was performed on all data with the t test for paired samples.

Results. The mean intraocular pressure of the nine eyes assigned to have optic nerve transection was not significantly different, prior to surgery, than the mean intraocular pressure of the nine fellow eyes assigned to have the sham procedure. Five weeks postoperatively, there was still no significant difference between the mean intraocular pressures in these two groups of eyes (Fig. 1).

Passage of the oral gastric tube without instillation of osmotic agents had no significant effect on baseline intraocular pressure in either group of eyes (Fig. 1).
Fig. 3. Intraocular pressure response to hyperosmotic agent—glycerol in two doses. Intraocular pressure was significantly lowered by 30 min with 0.5 cc/kg dose and by 15 min with 1.5 cc/kg. When the cut and uncut eyes are compared, the lowering in intraocular pressure showed no significant difference.

Instillation of 75, 100, or 200 ml of water into the stomach produced a significant rise of intraocular pressure in both groups of eyes at 30 min. The larger the dose of water, the greater was the pressure rise. No significant difference in the pressure response of the cut and sham side was found at any of the three doses tested (paired t test, p >0.05) (Fig. 2).

Instillation of 0.5 and 1.5 ml/kg of a 75% solution of glycerol into the stomach produced a significant lowering of intraocular pressure in both groups of eyes at 30, 45, and 60 min. The higher dose produced a more rapid effect and an effect of greater amplitude and duration. No significant difference in the pressure response of the cut and sham side was found at any time at either dosage (paired t test, p >0.05) (Fig. 3).

In five animals, blood pressure was measured at time 0, 10, 20, and 30 min following instillation of 200 ml of water. No significant change in systolic or diastolic blood pressure was found at 10, 20, or 30 min following dosing.

Discussion. In this group of animals, we were unable to demonstrate any difference in resting intraocular pressure or differences in the responsiveness to osmotic agents between eyes with cut optic nerves and eyes with intact optic nerves. Considering our own results and those of the other workers cited, we have concluded that cutting the optic nerve has no significant effect on steady-state intraocular pressure in the rabbit and a small or highly variable effect on the ability of the eye to respond to systemically administered osmotic agents. It is noteworthy that Knighton and Quigley (unpublished observations) have been unable to demonstrate any statistically significant effect of cutting the optic nerve in rabbits on the response of intraocular pressure to urea.

The hypothalamic theory forwarded by Riise and Krupin postulates that the reduced responsiveness which they found on the cut side indicates that the optic nerve carries efferent fibers between an osmoreceptor in the brain and the eye, an osmoreceptor which plays some role in the regulation of intraocular pressure. However, it seems that after all results are considered together, the effect on osmotic responsiveness is too small to be of biological significance. Furthermore, no investigator has demonstrated an effect on steady-state intraocular pressure caused by cutting the optic nerve. Finally, it is curious that previous investigators have found that cutting the optic nerve reduces the pressure-disturbing effect of an osmotic perturbation rather than increasing the effect, as if the hypothesized osmoreceptor served as a biological regulator.

We believe that the original observation of Riise and subsequent experiments can be explained more simply. It is well known that optic nerve transection results in a reduction in the number and caliber of vessels visible ophthalmoscopically at the disc. Likewise, the ganglion cell layer of the retina eventually disappears. It is possible that the number and caliber of vessels near the inner surface of the retina are reduced by cutting the optic nerve.

Since these capillary networks are nearest the bulk of water in the eye, a change in the capillary density in this origin would be very likely to reduce the speed of movement of water out of the eye in response to a hyperosmotic agent in the blood. If this were the case, we would expect to find no difference in steady-state intraocular pressure and only a small difference in osmotic responsiveness, with the lesser response being located on the cut side. Such an interpretation seems to us to be compatible with our own data and with the data of other investigators cited.

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In 33 patients with corneal or lens opacities, the VER criteria used for acuity estimates are presented. Good predictor of postoperative acuity ($r = 0.8$). The months after surgery and showed that the TVER is a predicted acuities were compared with those measured 6 months after surgery and showed that the TVER is a good predictor of postoperative acuity ($r = 0.8$). The criteria used for acuity estimates are presented.

Horowitz et al. have described a means for stimulating the retina by light delivered via an optical probe (light pipe) coupled to the lower lid, and subsequently recording the cortical evoked potentials elicited (transscleral VER, TVER). Dawson et al. have also reported the signal:noise ratios, variability, stimulus-response relationships, and subjective brightness aspects of transsclerally delivered stimuli in normal subjects. Since the VER is known to be biased for macular function, it was anticipated that the TVER might have potential value for predicting macular function in patients with opacities of the anterior segment dense enough to preclude full appreciation of the retinal state or potential acuity. The present study was undertaken to determine the prognostic value of the TVER, which has not been heretofore established.

Methods. Forty-one consecutive patients whose cornea and/or lens preoperatively was sufficiently opaque to preclude clear visualization of the posterior retina were selected for this study. The presence of obvious complicating eye diseases excluded patients, although some with macular degeneration or posterior uveitis were inadvertently included because the coexistence could not be recognized at the time of selection. In each case, the TVER was measured preoperatively with the stimuli described by Dawson et al. Briefly, the stimulating, transscleral probe was positioned at the lower lid, and cortical responses were recorded. Whenever possible, both eyes were tested, the second serving for comparison. Peak stimulus radiance at the probe tip was 340, 80, or 9 mw for white stimuli. A red stimulus ($A > 627$ nm) was also presented and had a peak radiance of 40 mw. Stimulation of each eye followed 4 min of adaptation to 0.2 troland (td). Where there was a functional fellow eye, the patient was asked to fixate a dim red light with it during the 4 min adaptation period. The lids of both the eyes were closed during flash delivery.

Preoperatively the best corrected Snellen acuity was recorded. Six to 12 months after surgical removal of the corneal or lens opacity, the visual acuity was determined once again. Of the initial 41 patients, postoperative acuity values were available in only 33.

The preoperative TVER was used to estimate the potential acuity without reference to the actual acuity data. The parameters used for the estimate from the TVER were the signal:noise ratio, the stimulus-response relationships, the amplitude of the response to red, the relationships to responses.