in our opinion, it should be used with some reservation as a prognostic test for the later appearance of glaucomatous visual field defects since the individual pressure vulnerability of the optical nerve head may vary—in this respect, even if more informative, it shares the fate of other tests for aqueous humor dynamics.

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Key words: acetazolamide test, facility of aqueous outflow, glaucoma test, intraocular hypertension, pathological and apathological aqueous circulation, weight tonography.

REFERENCES


The intraocular pressure of conscious, unanesthetized owl monkeys (Aotus trivirgatus) was measured with an applanation tonometer. Untreated eyes of the conscious animals were found to have higher values than those reported for owl monkeys anesthetized with pentobarbitone. Locally applied pilocarpine, carbachol, and oxotremorine gave concentration-related reductions in pressure, oxotremorine being the most potent and having longer duration of effect than the other compounds. Slight reductions were also observed with aceclidine and R.S. 86. These results are discussed in relation to the effects of miotics in man.

In studies on monkeys anesthetized with pentobarbitone, it was reported that locally administered pilocarpine increased the outflow facility. However, no significant reduction in intraocular pressure was induced by pilocarpine, but it is notable that under the anesthetic, the basal pressure was low even in untreated eyes. Possibly the observation of Cevario and Macri that pentobarbitone apparently reduces aqueous inflow in rhesus monkeys is significant, since pilocarpine might be unable to induce further reductions if the intraocular pressure is approaching that of the recipient veins.

The present study reports the effects of several parasympathomimetic drugs on the eyes of fully conscious owl monkeys, and it has been shown that consistent reductions in intraocular pressure can be obtained under appropriate experimental conditions.

Methods. Male owl monkeys (Aotus trivirgatus) weighing 0.8 to 1.5 kilograms were used in groups of five to seven. During tonometry each animal was loosely restrained in a cloth bag which enclosed the trunk and limbs. After thorough training, the animals accepted the experimental procedures without apparent anxiety. The pneumatic tonometer using a Digilab, Inc. (Cambridge, Mass.) floating probe was constructed in this laboratory. Oxygen was admitted to the probe at a pressure of 34.5 kPa. (5 p.s.i.) and the recordings were made using a Bell & Howell (Pasadena, Calif.) transducer (4-421-001) and transducer indicator (1-176) and an Omniscribe pen recorder (Houston Instrument Div., Bausch & Lomb, Inc., Bellaire, Texas). Open-stopcock manometric calibration was carried out on five eyes of anesthetized owl monkeys.

The parasympathomimetic drugs were dissolved in sterile physiological saline, and 10 or 20 μl of a given solution was administered topically to each

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*Pentobarbitone = pentobarbital.
Fig. 1. The concentration-effect curves for oxotremorine (■), pilocarpine (●) and carbachol (▲). Responses are expressed as the mean (± S.E.M.) of the greatest differences in intraocular pressure between the treated eyes and the untreated eyes observed after drug treatment. The number of animals receiving each treatment is shown.

eye with an Eppendorf micropipette. Local anesthesia for tonometry was induced by instillation of 0.02 ml. of an 0.5 per cent oxybuprocaine hydrochloride solution prepared in sterile saline.

Pressure values are given as the mean ± standard error. Comparisons have been made using two-sample or paired-difference t tests.

Results. In a preliminary experiment on owl monkeys treated only with local anesthetic for tonometry, it was found that the mean intraocular pressure ± S.E.M. was 25.95 ± 1.09 mm. Hg at 1000 hours Greenwich Mean Time. Observed at hourly intervals for 6 hours, the individual eyes showed physiological variation of up to 4.27 mm. Hg. However, the opposite eyes of the animals varied similarly and at no time was a significant difference detected, with the paired t test, between the right eye and the left eye values of the group. Therefore, in experiments to show drug effects, only one eye of each monkey was treated, and the responses have been expressed as the difference in pressure between the treated eye and the control opposite eye, in order to prevent confusion of any physiological variation in pressure with the drug effects.

Pilocarpine hydrochloride 0.25 to 2.0 per cent, carbachol (carbamyl choline chloride) 0.25 to 4.0 per cent, and oxotremorine 0.005 to 0.5 per cent all gave concentration-related decreases in intraocular pressure. Their effects are illustrated in Fig. 1 in which the drug concentrations are given in molar terms. Results are expressed as the mean of the greatest differences in tension observed between treated and untreated eyes after drug administration. It can be seen that oxotremorine is more potent than the other agents. With 0.5 per cent oxotremorine, systemic parasympathomimetic effects were apparent, i.e. salivation and diarrhea, in three of the seven animals tested and, therefore, higher concentrations were not tested. The time courses of responses to approximately equipotent submaximal concentrations of the three drugs are illustrated in Fig. 2 and it is seen that the duration of effect varies in this order: oxotremorine > carbachol > pilocarpine.

Two other agents were also investigated: (±)-
Fig. 2. The time course of responses to submaximal concentrations of oxotremorine (0.025 per cent), pilocarpine (0.5 per cent) and carbachol (0.5 per cent) on groups of six or seven owl monkeys. Responses are expressed as the mean difference in intraocular pressure between the treated eyes and the untreated eyes (± S.E.M. where relevant).

aceclidine hydrochloride and R.S. 86 (spiro-(N'-methyl-piperidyl-4')-N-ethyl succinimide hydrobromide, Sandoz). One hour after administration of 0.5 per cent aceclidine a significant (p < 0.02) increase of 2.29 ± 0.75 mm. Hg in the mean intraocular pressure of the treated eyes over control eyes was observed, although the values returned to control levels after 2 hours. A small but significant (p < 0.01) reduction of 2.24 ± 0.68 mm. Hg was observed 1 hour after administration of 1.0 per cent aceclidine, but pressures were again at control levels after 2 hours. R.S. 86, 0.5 per cent, gave no significant effect on intraocular pressure, although a 1.0 per cent solution caused a reduction of 3.61 ± 1.12 mm. Hg after 1 hour which was significant (p < 0.01). There was no significant effect after 2 hours. However, a 2.0 per cent solution of R.S. 86 gave a reduction which was significant after 1 hour and 2 hours, but was of similar magnitude at 1 hour (3.73 ± 0.31 mm. Hg) to that seen with 1.0 per cent R.S. 86.

Discussion. The owl monkey is of the class Simiae and has a trabecular plexus similar to that of man. Its eyes are large and this allows tonometry to be performed easily. However, one possibly relevant structural difference compared with man is that the vitreous is a viscous liquid.

The intraocular pressure of owl monkeys under pentobarbitone anesthesia has been measured by several workers. Mims and Holland obtained values of 15.7 mm. Hg by Schiotz tonometry, 13.2 mm. Hg by applanation tonometry, and 14.1 mm. Hg by manometry. Swietliczko and David obtained a mean value of 14.6 mm. Hg by manometry, with a range of 10.2 to 18.9 mm. Hg. Similar values have been obtained manometrically and tonometrically in owl monkeys anesthetized with pentobarbitone, in this laboratory (unpublished results).

There have also been reports of low intraocular pressure in other primate species under pentobarbitone anesthesia and it is interesting that Bárány found a value of 8.9 mm. Hg in Cer-
copithecus ethiops under pentobarbitone anesthesia, whereas a value of 20 mm. Hg was found in the same species under light ether anesthesia. Kitazawa and Langham\textsuperscript{6} have reported values of 18-20 mm. Hg in Macaca mulatta sedated with phencyclidine. Thus, in view of the finding of Cevario and Macri\textsuperscript{7} that pentobarbitone apparently reduces aqueous inflow, it is not considered surprising that the intraocular pressure has been found to be higher in conscious owl monkeys than in those anesthetized with pentobarbitone.

This study has demonstrated that the intraocular pressure of owl monkeys is reduced in a dose-related manner by several parasympathomimetic agents. Oxotremorine was the most potent compound tested and its effects were prolonged compared with the other drugs. It has been demonstrated\textsuperscript{8} to have a higher heptane:water partition coefficient than either pilocarpine (71 times) or R.S. 86 (12 times), and this suggests that it would penetrate membranes more easily, which might contribute to its greater potency.

Pilocarpine gives maximal reductions in intraocular pressure in many glaucoma patients at a concentration of 2.0 per cent,\textsuperscript{8} and it has been shown to have similar potency in the owl monkey. However, the duration of its effects in human beings has been reported\textsuperscript{9} to be greater than that which was observed in the monkeys. Carbachol has been shown to have slightly greater potency and duration of effects than pilocarpine in man, provided that a surfactant is incorporated in the solution.\textsuperscript{9} In the owl monkey slightly lower potency was found compared to pilocarpine, although there was no surfactant in the solution. A slightly greater duration of effect was observed, however. Aceclidine has been reported to have similar potency to pilocarpine in man,\textsuperscript{10} but it was markedly less potent in the owl monkey.

In conclusion, it may be said that the fully conscious owl monkey responds to locally applied parasympathomimetic drugs with a pattern of changes in intraocular pressure which is not dissimilar to that seen in human beings. The species would, therefore, possibly represent a valuable predictive model for the investigation of new parasympathomimetic glaucoma treatments.

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**Key Words:** owl monkey, Aotus trivirgatus, tonometry, intraocular pressure, parasympathomimetics, pilocarpine.

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**The effect of cation ionophores on intraocular pressure.** STEVEN M. Podos.

The ionophores A23187 and X537A, which increase the permeability of cell membranes to calcium and other divalent cations, produced significant elevation of intraocular pressure in rabbits. Topical instillation of these ionophores in concentrations of 1.0 and 0.1 per cent were effective. Aqueous humor protein and facility of outflow were similar in ionophore-treated and control eyes. Pretreatment with indomethacin did not block the intraocular pressure rise induced by A23187. Alterations of intracellular calcium might control cellular processes within the eye as in many other biological systems.

The secondary messenger system of cyclic nucleotides is involved in the control of aqueous humor dynamics. Changes in the cyclic adenosine 3',5'-monophosphate (cyclic AMP) level in aque-

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