Reports

Control of intraocular blood flow. III. Effect of chemical sympathectomy.

RONALD A. SCHACHAR, JOHN J. WEITER, AND J. TERRY ERNEST.

The effects of sympathetic tone on ocular blood flow have been demonstrated by both indirect and direct methods and have been shown to involve the entire uvea.[1, 2] In a previous study using nuclide-labeled spheres we demonstrated that preganglionic cervical sympathectomy increases uveal blood flow and cervical sympathetic stimulation decreases uveal blood flow to the ipsilateral side.[1] It is not known where this sympathetic tone is operating and if the sympathetic nerves present in the uvea itself are participating in ocular blood-flow control. 6-Hydroxydopamine (6-OH-DA) produces a selective degeneration of sympathetic terminals but does not affect sympathetic axons or other nerves.[3]

The purpose of the present study is to demonstrate the effect of 6-OH-DA on ocular blood flow using the nuclide-labeled microsphere technique.

In Part I of this study, eight adult cats weighing 2 to 3 kilograms and of both sexes were used. The animals were anesthetized with pentobarbital sodium, intraperitoneally, 30 mg. per kilogram. Two cats had 50 micrograms and two cats 100 micrograms of 6-OH-DA in 100 microliters injected into the vitreous through the pars plana using a 30 gauge needle. An equal amount of the 6-OH-DA diluent was injected into the opposite eye. The side of 6-OH-DA injection was alternated in the cats. As additional controls, two cats received bilateral intravitreal injections of 50 microliters of 6-OH-DA diluent and two cats received 100 microliters of diluent into both eyes. The cats were then allowed to convalesce for seven days. The cats were anesthetized a second time, a tracheotomy was performed, and the cats were maintained with a respirator. Intraocular pressure was controlled in both eyes at 17 mm. Hg by cannulating the anterior chambers at the limbus with 21 gauge needles connected to a saline reservoir.

The blood-flow measurements were obtained as previously described.[4] In brief, the left hemithorax of the cat was opened and 0.5 c.c. of labeled microspheres per kilogram of body weight were injected into the left ventricle. The eyes were enucleated and the iris, ciliary body, choroid (with and without tapetum), and retina were separated. The tissues were air dried and weighed and the radioactivity was determined.

In Part II of this study, one cat was anesthetized and received an intravitreal injection of 100 micrograms of 6-OH-DA in 100 microliters and an equal amount of diluent into the opposite eye as described above. The cat was then allowed to convalesce for seven days. The cat was then anesthetized a second time and maintained with a respirator and intraocular pressure controlled as described in Part I. The left hemithorax was then opened and 0.35 micromoles of tritiated nonepinephrine (H^3NE) with a specific activity of 1,700 microcuries per micromole was injected into the left ventricle. After 30 minutes the cat was killed by intracardiac injection of pentobarbital sodium. The eyes were then removed by rapid enucleation and were temporarily placed in crushed ice. The muscle insertions and optic nerves were cut flush with the sclera and surface blood rinsed from the globes. Using an operating microscope, each eye was then dissected into five segments: iris, ciliary body, choroid with tapetum, choroid without tapetum, and retina. All tissues were kept cool during and after dissection. Each tissue was weighed wet and then prepared and the radioactivity determined as described by Kramer and Potts.[5]

Local chemical sympathectomy obtained by intravitreal injection of 6-OH-DA produced an increased blood flow of approximately 30 per cent in the retina, choroid, and ciliary body. There was only a 10 per cent increase in the blood flow to the iris and no change in blood flow to the nictating membrane (Table I). All control animals had less than a 2 per cent difference between sides.

The uptake of H^3NE on the side of 6-OH-DA injection was decreased by 45 per cent in the choroid, 22 per cent in the ciliary body, and 11 per cent in the iris. There was equal uptake on both sides (less than 2 per cent difference between sides) for retina and nictating membrane (Table II).

Local chemical sympathectomy with 6-OH-DA produced an increase in blood flow greater than 30 per cent to the choroid, ciliary body, and retina. Thus local sympathetic terminals take part in vasomotor tone of the iris, ciliary body, and choroid. This is compatible with our previous studies of preganglionic cervical sympathectomy.[1]

6-Hydroxydopamine (6-OH-DA) produces a local chemical sympathectomy by causing sympathetic terminal degeneration.[3] This depends on the 6-OH-DA reaching the nerve terminals. In our experiment the intravitreal injection of 6-OH-DA had

Table I. The effect of 6-hydroxydopamine (6-OH-DA) on ocular blood flow*

Retina	1.43 ± 0.06
Choroid with tapetum	1.46 ± 0.24
Choroid without tapetum	1.49 ± 0.19
Ciliary body	1.31 ± 0.23
Iris	1.11 ± 0.02
Nictating membrane	0.98 ± 0.04

*Results are expressed as a ratio of the radioactivity in the experimental eye compared to the control eye with the standard error (4 cats). In the four cats which received diluent only in both eyes there was no significant difference in blood flow between the two eyes.

Table II. The uptake of tritiated norepinephrine after intravitreal 6-hydroxydopamine (6-OH-DA)*

Choroid with tapetum	0.55
Choroid without tapetum	0.51
Ciliary body	0.78
Iris	0.89
Nictating membrane	1.00
Retina	1.02

*Results are expressed as a ratio of the radioactivity in the experimental eye compared to the control eye.

no effect on the nictating membrane demonstrating that there was no significant systemic absorption. There was a small effect on the sympathetic terminals of the iris, greater on the ciliary body, and greatest on the choroid. This is probably due to the needle being pointed posteriorly during the intravitreal injection and diffusion carrying the 6-OH-DA posteriorly, or due to the much greater sympathetic nerve supply to the iris than choroid in the cat.

Since 6-OH-DA produces degeneration of sympathetic nerve terminals, it decreases the uptake of exogenous norepinephrine by these terminals. Since H^3NE uptake was reduced for the choroid, ciliary body, and iris, 6-OH-DA must be producing degeneration in the sympathetic terminals of these tissues. H^3NE was taken up on both sides equally by the sympathetic terminals of the nictating membrane. This is consistent with the lack of systemic absorption of 6-OH-DA.

The retinal circulation has no sympathetic nerve terminals as shown by the histochemical fluorescence method.[6] Therefore, the 6-OH-DA should not and in fact did not affect H^3NE uptake. There are dopaminergic endings in the retina which can take up H^3NE; however, at the dose levels of 6-OH-DA which we used (less than 20 μg 6-OH-DA per gram of eye) these endings would not be affected.[7] The increased circulation of the retina with 6-OH-DA injection may have been due to the effect of the 6-OH-DA on vessels posterior to the cribriform plate. Local retinal blood-flow control occurs by autoregulation as demonstrated by Alm and Bill.[8]

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Realignment of photoreceptors disturbed in orientation secondary to retinal detachment.

JAY M. ENOCH, JOSEPH A. VAN LOO, JR., AND EDWARD OKUN.

Laties[1] first suggested that retinal receptors are aligned with an anterior point in the eye. Several studies have appeared since then supporting the primary finding.[2-9] It was recently shown in this laboratory that human retinal receptors share this property and that the receptors are most probably aligned with a point approximating the center of the exit pupil of the eye.[6-9]

If receptors are aligned with precision toward