Effect of photocoagulation on ocular blood flow

Suresh R. Chandra, J. Terry Ernest, and Thomas K. Goldstick

The effect of panretinal photocoagulation on ocular blood flow was studied in pigmented rabbits by means of labeled microsphere impaction and in monkeys by indocyanine-green–dye clearance. In the rabbits, one eye of each animal was photocoagulated and the fellow eye of the same animal was used as the control. Twenty-six rabbits received full-scatter panretinal photocoagulation (300 ± 20 burns, one half burn apart) and an additional 32 rabbits received partial-scatter panretinal photocoagulation (150 ± 20 burns, one burn apart). After full-scatter photocoagulation there was a significant decrease in choroidal-retinal blood flow measured at 1 to 2 hr, 24 hr, 2 weeks, 4 weeks, and 3 months, but no change in iris-ciliary body blood flow. After partial scatter photocoagulation there was no consistent change. In one monkey, 100 burns were placed around the macular area and in a second monkey 100 burns were placed in the inferior half of the ocular fundus. Choroidal blood flow was significantly reduced in both monkeys for the initial hour during which it was continually measured. (INVEST OPHTHALMOL VIS SCI 22:783-787, 1982.)

Key words: uveal blood flow, photocoagulation, rabbits, monkeys, nuclide-labeled microspheres, indocyanine-green dye, choroid, choroidal blood flow

Panretinal photocoagulation has been shown to be beneficial in patients with proliferative diabetic retinopathy and is now universally employed. Closure of the choroidal vasculature after photocoagulation has been demonstrated by histopathologic studies. Panretinal photocoagulation may thus result in a decrease in uveal blood flow. To investigate this hypothesis, we studied the effects of panretinal photocoagulation on the ocular blood flow of rabbits and rhesus monkeys.

Materials and methods

Rabbits. Sixty-eight pigmented rabbits of both sexes and weighing approximately 2 to 8 kg were anesthetized with 30 mg/kg of pentobarbital sodium through an ear vein. After dilating the pupil with 2.5% phenylephrine hydrochloride, we photocoagulated alternately either the right or left eye of each animal with a xenon arc light coagulator (Clinitex, Inc., Danvers, Mass.). The treatment parameters were a 4.5 mm diameter diaphragm, a power setting of number 6 to number 10, and 0.5 to 1.0 sec exposure. Twenty-six animals received full-scatter panretinal photocoagulation (300 ± 20 burns, one half burn apart) and an additional 32 rabbits received partial-scatter panretinal photocoagulation (150 ± 20 burns, one burn apart). After full-scatter photocoagulation there was a significant decrease in choroidal-retinal blood flow measured at 1 to 2 hr, 24 hr, 2 weeks, 4 weeks, and 3 months, but no change in iris-ciliary body blood flow. After partial scatter photocoagulation there was no consistent change. In one monkey, 100 burns were placed around the macular area and in a second monkey 100 burns were placed in the inferior half of the ocular fundus. Choroidal blood flow was significantly reduced in both monkeys for the initial hour during which it was continually measured. (INVEST OPHTHALMOL VIS SCI 22:783-787, 1982.)

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burns, one half burn apart), and 32 animals received partial-scatter panretinal photocoagulation (150 ± 20 burns, one burn apart). The animals were sacrificed at 1 to 2 hr, 24 hr, 2 weeks, 4 weeks, and 3 months.

Ten rabbits did not receive any photocoagulation, and ocular blood-flow measurements were made in both eyes to determine the normal interocular variability in the same animal.

For measurement of the blood flow, the animals were anesthetized with pentobarbital sodium, tracheotomized, and artificially ventilated. Carbonized microspheres with a mean diameter of 15 ± 5 μm labeled with strontium chloride (85Sr) were used.3 The spheres were suspended in a 1% solution of saline with a small amount of the surfactant Tween-80 added to prevent aggregation and clumping. There were 7.9 × 105 spheres/ml, with a total activity of 0.21 μCi/ml. A thoracotomy was performed to expose the heart, and approximately 1 ml of the suspension was injected into the left ventricle or atrium within about 5 sec. No attempt was made to control the exact number of spheres injected. The animals were then sacrificed within 1 min by intravenous administration of potassium chloride. Both eyes were enucleated, and sample tissues were taken from the renal cortex and lung. The enucleated eyes were divided near the limbus and dissected. For each eye, samples of iris, plus ciliary body and choroid, plus retina were obtained. The samples were placed on filter papers and air dried for 12 hr. The filter papers containing the dried samples were weighed, and radioactivity was measured with a gamma spectrometer (Model 5330, Packard Instrument Co., Downers Grove, Ill.). The radioactivity of the tissue samples of the photoocoagulated eye and its fellow control eye were measured in counts per milligram of tissue, and the percent difference between the two eyes was calculated.

**Monkeys.** We anesthetized two male rhesus monkeys weighing 6 to 7 kg with 100 mg/kg of a 10% solution of alpha chloralose in polyethylene glycol administered intravenously. We then paralyzed the animals with 1 ml of a mixture of tubocurarine chloride (0.4 mg/ml) and gallamine triethiodide (Flaxedil, 2 mg/ml) administered intravenously, and intubated them with a 3 mm cuffed Foregger endotracheal tube. The animals were artificially resired and anesthesia was maintained with 2 ml increments of the alpha chloralose; paralysis was maintained with 1 ml increments of curare and Flaxedil solution. We monitored the systemic arterial blood pressure from a cannulated femoral artery with a pressure transducer (Model 1280C; Hewlett Packard, Waltham, Mass.).

In one monkey the posterior pole around the macular area and optic disc received panretinal scatter photocoagulation (100 burns, one half burn apart). In the second monkey, 100 burns were placed one half burn apart in the inferior half of the retina outside the macular area. The treatment parameters were an 8 mm diameter diaphragm, a power setting of number 3, and a 1 sec exposure.

We have previously reported our method of measuring the choroidal blood flow.6 In brief, we performed a lateral orbitotomy and exposed the superior-temporal vortex vein. Fiber-optic bundles were used to pass infrared light through it into a photodetector. To make a measurement, we injected 0.1 ml boluses of a 2.5 mg/ml solution of indocyanine-green dye in 0.2 sec into the homolateral common carotid artery. We analyzed the clearance of the dye from the choriocapillaris using a computer-generated nonlinear regression fit.

**Table I. Choroidoretinal blood flow in rabbits—control values**

<table>
<thead>
<tr>
<th>Rabbit No.</th>
<th>Eyel</th>
<th>Eye 2*</th>
<th>Difference (%)</th>
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<td>8.8</td>
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<tr>
<td>2</td>
<td>5,601</td>
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<td>2,654</td>
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<tr>
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<td>6,310</td>
<td>6,870</td>
<td>8.9</td>
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<tr>
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<tr>
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<td>21,982</td>
<td>10.2</td>
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<td>9</td>
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<td>15,464</td>
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</tr>
<tr>
<td>Mean</td>
<td>-2.3</td>
<td>± 5.5</td>
<td></td>
</tr>
</tbody>
</table>

*Alternated right eye, left eye.

**Results**

**Rabbits.** Measurements of choroidoretinal blood flow were made in 10 rabbits that did not receive photocoagulation (Table I, and control value in Fig. 1). The weight of the excised tissue ranged between approximately 20 and 60 mg. The variation between the two eyes of the same animal, however, was only about 1 mg.

The 26 rabbits that received full-scatter panretinal photocoagulation were divided into five groups, and choroidoretinal blood
photocoagulation and ocular blood flow

Fig. 1. Choroidoretinal blood flow in rabbits after partial- (150 burns) and full-scatter (300 burns) panretinal photocoagulation. The blood flow is reported as the percent difference in counts/milligram of tissue between the photocoagulated eye and its fellow control eye (mean ± S.E.). The number of animals measured at each point is shown in parentheses.

Fig. 2. Choroidal blood flow in two monkeys after photocoagulation outside the macular area. For the partial photocoagulation (open circles) the mean flows ± S.E. before and after photocoagulation were 33.0 ± 1.9 and 23.9 ± 1.3 ml of blood/min/ml of choriocapillaris; for the panretinal photocoagulation (solid circles) they were 33.7 ± 1.3 and 16.7 ± 0.6 ml of blood/min/ml of choriocapillaris.

Flow was measured at 1 to 2 hr, 24 hr, 2 weeks, 4 weeks, and 3 months. There was a significant decrease in the choroidoretinal blood flow in all the animals (Fig. 1). There was no significant change in iris–ciliary body blood flow.

In the 32 rabbits that received partial-scatter panretinal photocoagulation, there was no significant change in either the choroidoretinal blood flow (Fig. 1) or in the iris–ciliary body blood flow.

Monkeys. In the monkey receiving 100 burns around the macular area, there was a decrease of approximately 50% in choroidal
blood flow (Fig. 2). The monkey with 100 burns applied to the inferior half of the retina had an approximately 30% decrease in choroidal blood flow (Fig. 2). The control flows are about twice those reported previously in monkeys, probably because improvements in the surgical technique with experience now lead to less trauma to the preparation. This does not, however, affect the results because each eye was used as its own control.

Discussion

It is important to point out that the rabbit and monkey retinal circulations are different and our two methods of determining blood flow were also different. The labeled microsphere impaction method used in the rabbits gave flow as milliliters per minute per milligram of choroid and retina. The choroid and retina were not separated, but the rabbit retinal blood flow is less than 5% of the choroidal blood flow. The indocyanine-green-dye clearance method used in the monkeys gave choroidal blood flow as milliliters per minute per milliliter of choriocapillaris. The primate macular area has a greater blood flow than equal areas of surrounding retina because of a greater volume of choriocapillaris. Nonetheless our experimental washout curves were all monoexponential, indicating a uniform flow per unit volume. Although the macular area is not extensively photocoagulated in patients receiving the therapy, and it was not burned in the two subhuman primates in this study, its blood flow also decreased. In both the rabbit and monkey, scatter panretinal photocoagulation caused significant reductions in blood flow.

The partial recovery in the blood-flow measurement 4 weeks after photocoagulation (Fig. 1) might have been caused by recanalization of blood vessels, but it may also have been due to atrophy of the retina. In the latter case, a decrease in tissue weight would give an apparent increase in blood flow. We removed approximately equal areas from the posterior segments of the two eyes from each of the rabbits and the variation was about 1 mg. We could not, however, remove precisely equal portions of the posterior segments from all the rabbits and we did not attempt to assess the amount of functioning retina left after photocoagulation.

Our studies show that the choroidal blood flow after extensive panretinal photocoagulation is decreased. It is not clear what effects, if any, this decrease in blood flow has on the retina. The normal choroidal circulation has a relatively high blood flow and a small arterial-to-venous oxygen difference. Thus the reduction in choroidal blood flow after panretinal photocoagulation may not affect the tissue oxygen tension of the outer retina, since there may only be an increase in oxygen extraction from the blood. Moreover, photocoagulation destroys the photoreceptor-retinal pigment epithelial complex, which accounts for most of the retinal oxygen consumption.

We measured the blood flow of the tissue and choriocapillaris remaining after photocoagulation, and the blood flow was significantly reduced by full-scatter panretinal photocoagulation. This might be serious if the hypothesis is correct that the temperature of the retina is regulated by choroidal blood flow. It seems reasonable to believe that heat regulation is required, since the ocular media transmit to the retina variable amounts of electromagnetic radiation from the visible wavelengths to the near infrared wavelengths. If this is true and if photocoagulation decreases the blood flow of the choroid to an extent preventing adequate heat regulation, one might find retinal damage in photocoagulated individuals regularly experiencing either high light intensities (ophthalmoscopy) and/or elevated body temperatures (fever). It has been shown that light-induced retinal damage in normal animals is augmented by elevation of their body temperatures. Further studies are needed to determine whether, under the stress of light and heat, the decreased choroidal blood flow after photocoagulation actually does play a significant role in human retinal disease.

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REFERENCES