Effect of sympathetic stimulation on critical closure of intraocular blood vessels

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Acute common carotid occlusion in rabbits causes a reduction in ocular blood volume and ciliary artery blood pressure. At all levels of intraocular pressure, cervical sympathetic stimulation reduces these changes. The ocular blood volume reduction after acute common carotid occlusion is not linearly related to the absolute blood pressure change or to the lowest blood pressure reached in the ciliary artery; it is related to the effective perfusion pressure after occlusion. Effective perfusion pressure is equal to ciliary artery blood pressure minus intraocular pressure and it reflects the transmural pressure of ocular blood vessels. The effective perfusion pressure at which the peak ocular volume change occurs after acute common carotid occlusion reflects the critical closing pressure of the ocular blood vessels. This approaches zero in the absence of sympathetic stimulation and is 10 mm. Hg or greater in the presence of sympathetic stimulation.

Key words: critical closure, sympathetic stimulation, carotid occlusion, effective perfusion pressure, ciliary artery blood pressure.

The semilogarithmic relationship between ocular blood volume change and intraocular pressure after acute common carotid occlusion in animals has been demonstrated by both perfusion and tonographic techniques. Acute common carotid occlusion causes the greatest reduction in ocular blood volume when the intraocular pressure is between 40 and 50 mm. Hg. Above this level the effect of acute common carotid occlusion on ocular blood volume decreases rapidly.

Ocular blood volume is determined in part by the difference between intraluminal blood pressure in the ocular blood vessels and the intraocular pressure that surrounds them. This difference is termed transmural pressure, and it is affected by changes in hydrostatic pressure on either side of the blood vessel wall. Since blood vessel radius is directly related to transmural pressure within certain limits, ocular
blood volume is also directly related to transmural pressure. The reduction in intraocular blood volume caused by acute common carotid occlusion may be explained by the acute fall in transmural pressure that occurs within the ocular vascular bed. As intraocular pressure is increased from 20 to 50 mm. Hg, a larger reduction in intraocular blood volume occurs after acute common carotid occlusion, due possibly to the greater compression of the vascular bed by the higher intraocular pressure. At very high levels of intraocular pressure, however, when filling of the vascular tree is resisted by the intraocular pressure, the effect of acute common carotid occlusion will not be as great.

It is possible that acute common carotid occlusion at intraocular pressures of 40 to 50 mm. Hg reduces transmural pressure sufficiently that the critical closing pressure of intraocular vessels is exceeded. By critical closing pressure is meant the transmural pressure at which ocular blood vessels collapse and flow through them ceases.2 If critical closure of the ocular vessels occurs at this level of intraocular pressure, then the maximum effect of acute common carotid occlusion on ocular blood volume would become manifest. At intraocular pressures above this level the vascular bed will have already been reduced by the high intraocular pressure so that acute common carotid occlusion would not cause as large a reduction in ocular blood volume even if critical closure did occur.

If this analysis is correct, it would appear that the intraocular pressure at which acute common carotid occlusion causes the maximum ocular blood volume change represents the point at which critical closure of intraocular vessels occurs. The present study was designed to consider this possibility.

Materials and methods

Rabbits weighing between 2 and 3 kilograms were anesthetized with 25 mg. of intravenous pentobarbital sodium (Veterinary Somnopentyl); small additional amounts were injected as needed. Proparacaine was used topically. The perfusion technique used in this laboratory to measure ocular blood volume change after acute common carotid occlusion at controlled levels of intraocular pressure has been described previously1 and is schematically illustrated in Fig. 1. A 5 cm. length of the common carotid artery was exposed and freed of its sheath. The cervical sympathetic nerve was isolated 1 cm. below the thyroid cartilage and a stimulating electrode was attached to it at this point. A rectangular pulse 0.6 to 2.4 v. in intensity and 0.1 msec. in duration was delivered at a rate of 4 per second by an isolated dual stimulator. Intraocular pressure was controlled by an open manometric system that communicated with the anterior chamber through a 23 gauge needle so that during acute common carotid occlusion intraocular pressure was kept constant.

After disinserting the lateral rectus muscle, the temporal long posterior ciliary artery was isolated and its blood pressure was measured just posterior to its entrance into the sclera, using a PE 10 polyethylene cannula attached to a pressure transducer and a dynograph. Acute common carotid occlusion was accomplished with rubber-tipped forceps. Simultaneous measurements were made of changes in ocular volume and ciliary artery blood pressure after acute common carotid occlusion with and without sympathetic stimulation.

Results

Sympathetic stimulation reduces the intraocular blood volume change that occurs after acute common carotid occlusion at all intraocular pressures studied. Fig. 2 reflects the typical relationship between ocular blood volume change after acute common carotid occlusion and intraocular pressure with and without sympathetic stimulation.
It should be noted that the peak intraocular blood volume change during sympathetic stimulation occurs at lower intraocular pressure levels than when sympathetic stimulation is omitted. Though the slopes of the recorded curves differed in several animals, the over-all findings were similar. Fig. 3 demonstrates the finding of a sharp increase in the slope of the curve at intraocular pressures above 40 mm. Hg, both with and without sympathetic stimulation. In most animals studied, a semilogarithmic relationship was demonstrated between intraocular pressure and ocular volume change after acute common carotid occlusion for a range of intraocular pressures from 20 to 50 mm. Hg.

The ciliary artery blood pressure change after acute common carotid occlusion was similar at all levels of intraocular pressure studied. In addition, the ocular blood volume change after acute common carotid occlusion at differing levels of intraocular pressure was not linearly related to the absolute change in ciliary blood pressure or the lowest blood pressure obtained in the ciliary artery. A good correlation with the blood volume changes at each intraocular pressure is noted, however, when the effective perfusion pressure (ciliary artery blood pressure minus intraocular pressure) after acute common carotid occlusion is plotted against intraocular pressure (Fig. 4). Blood volume change increases as the effective perfusion pressure decreases and the peak blood volume change occurs when the effective perfusion pressure approaches zero. Once the effective

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Fig. 2. Ocular blood volume changes ($\Delta b$) after acute common carotid occlusion. Note that these changes are greater and peak at a higher intraocular pressure without (solid line) than with (interrupted line) sympathetic stimulation. Characteristics of stimulation are 1.9 v., 0.1 msec., four per second.

Fig. 3. Ocular blood volume changes after acute common carotid occlusion. At intraocular pressures greater than 40 mm. Hg a sharp increase in the slope of the curves occurs both with (interrupted line) and without (solid line) sympathetic stimulation. Characteristics of stimulation are 1.9 v., 0.1 msec., four per second.

Fig. 4. Ocular blood volume change after acute common carotid occlusion. Note that this volume change (solid line) is related to effective perfusion pressure (interrupted line) at each level of intraocular pressure.
perfusion pressure after acute common carotid occlusion becomes less than zero, the blood volume change begins to decrease.

Cervical sympathetic stimulation decreases the magnitude of changes that occur in ocular blood volume and in ciliary artery blood pressure after acute common carotid occlusion. Fig. 5 shows the change in ciliary artery blood pressure that occurs during acute common carotid occlusion. In the absence of sympathetic stimulation such occlusion (A) causes a rapid and sizeable fall in blood pressure with rapid recovery to the base line on release of the carotid artery. Maintained sympathetic stimulation alone (B) causes a fall in blood pressure which subsequently returns to or exceeds the original base line. Carotid occlusion during sympathetic stimulation (C) causes a much smaller fall in blood pressure than originally observed without sympathetic stimulation. When sympathetic stimulation is stopped the blood pressure gradually returns to the base line.

Sympathetic stimulation limits the fall in ciliary artery blood pressure induced by acute common carotid occlusion as shown in Fig. 6. The acute fall in ciliary artery blood pressure reaches the same level whether carotid occlusion is performed in the first few seconds after sympathetic stimulation when ciliary blood pressure is
decreasing \((B)\) or after 10 to 15 seconds when ciliary blood pressure has recovered \((C)\).

During sympathetic stimulation the ocular blood volume change after acute common carotid occlusion at varying intraocular pressures was not linearly related to the ciliary artery blood pressure fall or the lowest ciliary artery blood pressure reached. A plot of effective perfusion pressure during acute common carotid occlusion shows a good correlation with ocular blood volume change (Fig. 7). Blood volume change increases as effective perfusion pressure decreases, and the peak blood volume change occurs when the effective perfusion pressure is 10 mm. Hg or greater.

Table I lists the effective perfusion pressures at which the peak ocular blood volume changes occurred in eight animals with and seven animals without sympathetic stimulation. The difference in means is significant at a level of \(P < 0.01\).

Discussion

This study confirms that for intraocular pressures in the range of 20 to 50 mm. Hg, a semilogarithmic relationship exists between the intraocular pressure and the decrease in ocular blood volume caused by acute common carotid occlusion. The maximum ocular blood volume change usually occurs at intraocular pressures of approximately 50 mm. Hg, but occasionally occurs at intraocular pressures as high as 70 mm. Hg. Though a similar semilogarithmic relationship exists during cervical sympathetic stimulation and acute common carotid occlusion, the blood volume changes in the eye are much smaller.

The decrease in ciliary artery blood pressure after acute common carotid occlusion was similar at all intraocular pressures between 20 and 80 mm. Hg, regardless of the state of sympathetic tone. Blood pressure changes in the ciliary vessels, therefore, cannot explain the relationship between ocular blood volume change and intraocular pressure found in these and other studies.\(^1,3\) A more likely explanation lies in a consideration of the changes in the transmural pressure of the intraocular vessels at various levels of intraocular pressure.

The best estimate of transmural pressure from the data of this study is the perfusion pressure in the ciliary artery minus the intraocular pressure. We have termed this the effective perfusion pressure, and during acute common carotid occlusion it is equal to the lowest blood pressure in the ciliary artery minus the intraocular pressure. The data indicate that as the effective perfusion pressure and, therefore, the transmural pressure decrease, the ocular blood volume...
change induced by acute common carotid occlusion increases (Figs. 4 and 7). In the absence of sympathetic stimulation the maximum ocular blood volume change after acute common carotid occlusion occurs when the effective perfusion pressure approaches zero. This reflects a transmural pressure close to zero, a state in which critical closure of ocular blood vessels is likely to occur. It is quite possible, therefore, that the effective perfusion pressure at which the peak ocular blood volume change occurs is a measure of the critical closing pressure of the intraocular blood vessels.

When acute common carotid occlusion is performed during cervical sympathetic stimulation the peak ocular blood volume change occurs at an effective perfusion pressure of 10 mm. Hg or greater, indicating that critical closure occurs at higher transmural pressures when sympathetic tone is increased in the eye. This has been demonstrated for vascular beds in other parts of the body.

The smaller blood volume changes induced in the eye by acute common carotid occlusion during sympathetic stimulation, as compared to those without stimulation, are due to the smaller falls in ciliary artery blood pressure, and, therefore, larger transmural pressures. In the present study the most frequent effect of cervical sympathetic stimulation on the homolateral ciliary artery blood pressure was a fall of approximately 7 mm. Hg for eight to ten seconds followed by a recovery during the next 30 seconds to levels approximately 8 mm. Hg above the prestimulation base line (Fig. 5). The blood pressure fall induced in the ciliary artery by acute common carotid occlusion during sympathetic stimulation was noted to depend on the level of blood pressure at the time of occlusion, but its lowest level was constant and was about 18 to 20 mm. Hg higher than without sympathetic stimulation (Fig. 6). This corresponds to the finding that, in the presence of an occluded common carotid artery, subsequent stimulation of the ipsilateral cervical sympathetic chain for five minutes raises the ciliary artery blood pressure about 30 mm. Hg.

This study emphasizes that, in the consideration of ocular blood volume changes following acute common carotid occlusion, the most important variable is the effective perfusion pressure of the ocular blood vessels after occlusion. This reflects the transmural pressure of the ocular blood vessels and is important in attempts at quantifying analysis of the carotid compression tonography test. In addition, the techniques described in this investigation may offer a means of analyzing the therapeutic effects of vasodilators and ganglionic blocking agents on ocular blood volume and vasomotor tone.

REFERENCES