Acute IOP elevation with scleral suction: effects on retrobulbar haemodynamics

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Abstract

***Aims/background*—Mechanical and vascular factors may both contribute to glaucoma. This study investigated the relation of mechanical to vascular factors by examining how acute IOP elevation altered flow velocities in the central retinal and ophthalmic arteries.**

***Methods*—IOP was elevated from a baseline near 14 to approximately 45 mm Hg using suction ophthalmodynamometry. During recovery from scleral suction, IOP fell to near 8 mm Hg. At each IOP, peak systolic and end diastolic velocities (PSV and EDV) were measured in the central retinal and ophthalmic arteries using colour Doppler imaging (Siemens Quantum 2000). Eleven healthy people served as subjects.**

***Results*—Acute elevation in IOP had no effect upon PSV, EDV, or the derived resistance index in the ophthalmic artery: flow velocities in this vessel were identical at IOP of 8 mm Hg or 45 mm Hg. In contrast, in the central retinal artery, PSV and EDV fell, and the resistance index rose, in steady progression as IOP was acutely elevated (each $p<0.01$). At IOP of 45 mm Hg, EDV was virtually absent and the resistance index was very nearly 1.0.**

***Conclusion*—Ophthalmic arterial haemodynamics are unrelated to acute fluctuations of the IOP over a wide range, suggesting that ocular hypertension itself cannot induce vascular dysfunction in this artery. In contrast, flow velocities in the central retinal artery were highly IOP dependent, implying that haemodynamic and mechanical factors are closely linked in this vascular bed.**

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The aetiology of the glaucomas remains obscure. Currently two hypotheses are most credible: a mechanical theory, which proposes that excessive pressure deformation of the optic nerve head triggers cell death,[1 2] and a vascular theory, which argues that vascular insufficiency (or vasospasm) leads to optic nerve head erosion.[3 4] Clearly, mechanical and ischaemic factors may interact, since increased intraocular pressure (IOP) could potentially worsen ischaemic injury as well as inflict damage by mechanical tissue distortion.[3] In this study we investigated the interplay of mechanical and vascular factors in the retrobulbar circulation. In this region, if mechanical compression can alter vessel haemodynamics, perfusion of critical watershed zones downstream may be compromised.[5] The extant literature, while largely circumstantial,[6] finds, in primary open angle glaucoma, an association of elevated mechanical pressure with abnormal flow velocities in several retrobulbar arteries.[7] It remains unclear, however, whether vascular dysfunction is linked directly, indirectly, or at all to elevated intraocular pressure[7]; there is evidence in low tension glaucoma that vascular abnormalities may exist in the face of normal IOP.[3 4 8] To directly investigate the relation between flow velocities in two major retrobulbar vessels (the ophthalmic and central retinal arteries) and the IOP, we used scleral suction to vary IOP over a wide range in healthy eyes. We could then determine if blood velocities in these two vessels were dependent on ocular tension.

Materials and methods

SUBJECTS

All subjects had normal eye examinations, and no history of systemic or ocular hypertension. Measurements were made on the left eye; 11 volunteers were involved in studies of the ophthalmic artery, and nine other volunteers were included in investigations of the central retinal artery. Procedures were reviewed and approved by human subject protection committees at Indiana University and the University of Miami, and subjects signed informed consent before participating. All experimental procedures conformed to the tenets of the Declaration of Helsinki.

INTRAOCULAR PRESSURE

With subjects reclining at 60°, a drop of 0.5% proxymetacaine (proparacaine) hydrochloride (Alcon Laboratories, Fort Worth, TX, USA) was instilled in the eye. IOP was then measured with an electronic handheld tonometer (Tonopen XL; Mentor Inc). IOP measurements were made at each level of scleral suction. Vacuum ophthalmodynamometry was performed using a cup placed on the temporal sclera (Taberna Pro Medicum, Lüneburg, Germany). After baseline recordings were completed, suction was applied in stepwise fashion to raise IOP to approximately 40–50 mm Hg in 3–4 increments. IOP measurements were taken 2 minutes after each increase; colour Doppler recordings were completed

within 3–5 subsequent minutes. After measurement of the highest level of elevated IOP, the scleral vacuum was released. During the ensuring recovery, IOP and vascular flow velocities were recorded after 5 and 15 minutes. Baseline blood pressure was recorded using sphygmomanometry. The two experimental sequences, one devoted to ophthalmic arterial measurements, the other to central retinal arterial measurements, were identical in all other aspects.

COLOUR DOPPLER IMAGING

A Siemens Quantum 2000 (Issaquah, WA, USA) with a 7.5 MHZ linear phased transducer was used for colour Doppler imaging. Sterile ophthalmic gel was applied to the closed eyelid, and the probe gently positioned with minimal pressure.[9] To examine the ophthalmic artery, the sample volume (time segment along the transmitted beam chosen for analysis) was oriented nasally and superiorly to the optic nerve head, just lateral to and abutting the visible hyporeflective stripe representing the nerve. The sample volume marker lay about 25 mm posterior to the globe. Strong signals were routinely detectable at this site.[9 10] To examine the central retinal artery, the B-scan image of the optic nerve was used to localise the area of the optic disc. The sample volume was placed with its centre about 3 mm behind the disc surface. The probe position was adjusted until the examining beam was parallel to and essentially overlapping the optic nerve.[9]

For each vessel a peak systolic and an end diastolic velocity (PSV and EDV) were recorded. A resistance index ((PSV − EDV)/PSV) was calculated for each vessel at each IOP condition.[11]

STATISTICAL ANALYSIS

For each vessel, colour Doppler measurements of PSV, EDV, and resistance index (RI) were compared at various IOPs by using analysis of variance. Values measured at each IOP were compared with baseline using *t* tests, the p value required for significance adjusted using Bonferroni's correction for multiple comparisons.[12] Data were tested for normal distribution using the Kolmogorov–Smirnov test.

Results

The characteristics of the subjects used in the two portions of the study are shown in Table 1. None had elevated resting blood pressure or intraocular pressure (Table 1). All of the data conformed to normal distributions as determined using the Kolmogorov–Smirnov test.

Table 1 Subject characteristics (SD)

Ophthalmic artery studies:	
No of patients	11
M/F	7/4
Age (years)	23 (5)
Resting heart rate (beats/min)	67 (5)
Resting blood pressure (systolic/diastolic; mm Hg)	115 (5)/75 (4)
Central retinal artery study:	
No of patients	9
M/F	5/4
Age (years)	25 (3)
Resting heart rate	68 (3)
Resting blood pressure (systolic/diastolic; mm Hg)	117 (6)/72 (3)

Table 2 IOP during suction ophthalmodynamometry and calculated ocular perfusion pressure (2/3 MAP-IOP)

	IOP (mm Hg) (SD)	*Calculated ocular perfusion pressure (mm Hg) (SD)*
Ophthalmic artery study:		
Baseline	13.0 (0.6)	46 (3)
Stage 1	22.0 (1.2)	37 (4)
Stage 2	30.9 (1.0)	28 (3)
Stage 3	40.2 (0.7)	19 (4)
Stage 4	47.9 (1.3)	11 (5)
Recovery (5 minutes)	5.9 (0.5)	53 (5)
Recovery (15 minutes)	7.1 (0.7)	51 (5)
Central retinal artery study:		
Baseline	13.6 (1.4)	46 (4)
Stage 1	24.2 (1.7)	35 (3)
Stage 2	31.3 (1.9)	28 (3)
Stage 3	42.0 (1.2)	17 (5)
Recovery (5 minutes)	8.6 (1.4)	51 (6)
Recovery (15 minutes)	9.3 (0.9)	50 (5)

Suction ophthalmodynamometry elevated IOP progressively in stages up to averages between 42 and 48 mm Hg (Table 2). These stages were similar in the two arms of the study (Table 2), although one less stage was used in the central retinal artery experiments (Table 2). Ocular perfusion pressure (calculated as 2/3 (mean arterial pressure) − IOP) decreased as IOP was elevated (Table 2). When suction was released, IOP was briefly reduced below baseline levels in both series (Table 2), with some recovery apparent by 15 minutes (Table 2); calculated ocular perfusion pressure increased in parallel.

In the central retinal artery blood velocity characteristics were clearly dependent upon the IOP (and ocular perfusion pressure); in contrast, the ophthalmic artery was unaltered in these characteristics over the entire IOP range studied. For example, in the central retinal artery, peak systolic velocity fell progressively with IOP elevation; this velocity in the ophthalmic artery was unrelated to IOP (Fig 1). Similarly, the end diastolic velocity in the

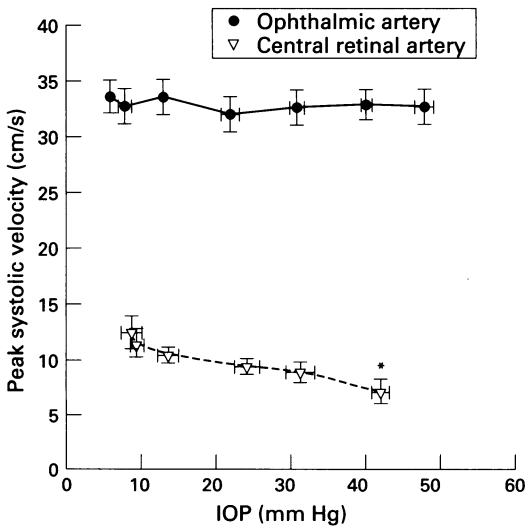

Figure 1 Effect of acute manipulation of intraocular pressure (IOP) via ophthalmodynamometry on peak systolic velocity in the ophthalmic and central retinal arteries. IOP increases left this velocity unchanged in the ophthalmic artery, while lowering it in the central retinal artery (asterisk indicates p<0.05 v baseline).

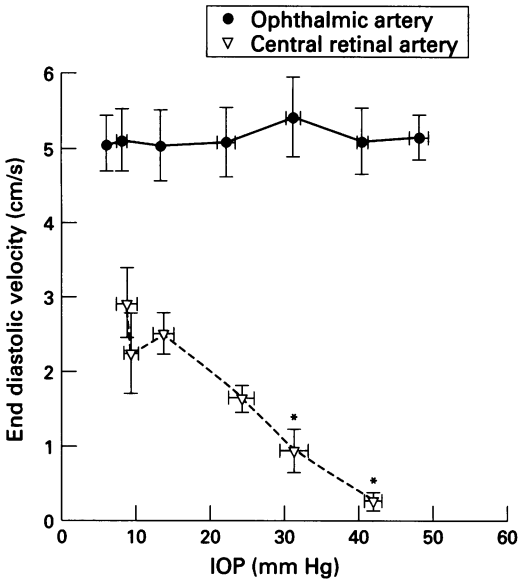

Figure 2 End diastolic velocity in the ophthalmic and central retinal arteries during acute manipulation of the intraocular pressure (IOP). IOP increases left this velocity unchanged in the ophthalmic artery, while lowering the value substantially in the central retinal artery (asterisks indicate $p<0.05$ v baseline).

central retinal artery was highly IOP dependent, while the corresponding measurement in the ophthalmic artery was, again, unrelated to IOP (Fig 2). Finally, the resistance index derived from peak systolic and end diastolic velocities (RI = (PSV − EDV)/PSV) was linked to IOP in the central retinal artery, with high IOP elevating this index to near 1.0 (Fig 3). In contrast, resistance index was unaffected by IOP in the ophthalmic artery (Fig 3).

Individual end diastolic velocity and resistance index values, measured in the central retinal artery, and expressed as a function of intraocular pressure, are shown in Figures 4 and 5. Each variable was significantly correlated with IOP ($p<0.0001$). The correlation coefficients were $r=-0.64$ for the relation of end diastolic velocity to IOP, and $r=0.68$ for the relation of end diastolic velocity to IOP.

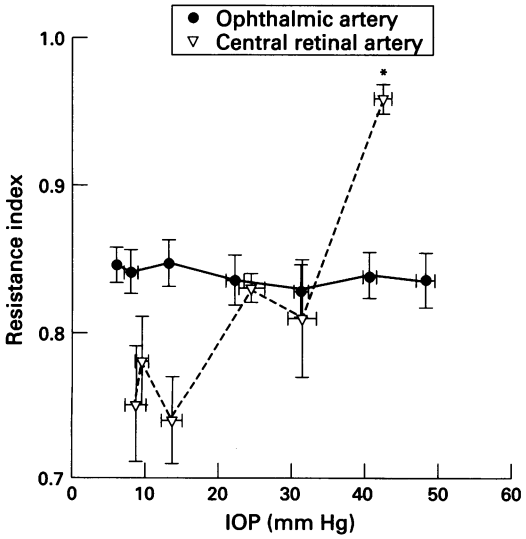

Figure 3 Resistance index ((PSV − EDV)/PSV) in two retrobulbar vessels during acute IOP manipulation using ophthalmodynamometry. IOP elevation left ophthalmic artery resistance index unchanged, as central retinal artery resistance index rose (asterisk indicates $p<0.05$ v baseline).

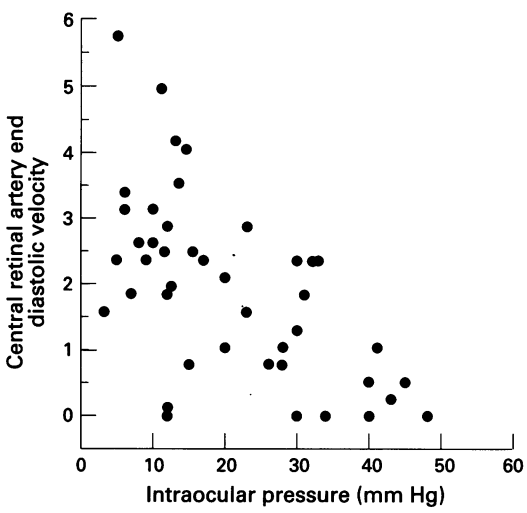

Figure 4 Individual values for central retinal artery end diastolic velocity as a function of intraocular pressure. Elevation of IOP reduced end diastolic velocity ($r=-0.64$; $p<0.0001$).

Discussion

In this study we found that blood velocity characteristics and resistance index in the central retinal artery were highly dependent upon IOP; as IOP rose peak systolic velocity fell substantially, and end diastolic velocity fell to nearly 0, causing the resistance index to rise to nearly 1.0. In contrast, elevation of IOP to 48 mm Hg or reduction to 6 mm Hg did not change these same blood velocity indices in the ophthalmic artery.

It is well established that uveal venous pressure is equivalent to the IOP (above a minimum level near 12 mm Hg[13 14]); indeed, choroidal perfusion pressure is determined by the difference between ophthalmic arterial pressure and the IOP.[13 14] Our data suggest that IOP is also a major determinant of perfusion pressure in the central retinal arterial watershed. Of course, Doppler signals provide only circumstantial evidence for changes in perfusion pressure or blood flow. None the less, the rise in resistance index in the central retinal artery with IOP elevation implies that vascular resistance is increasing downstream from the measurement site (about 3 mm behind the

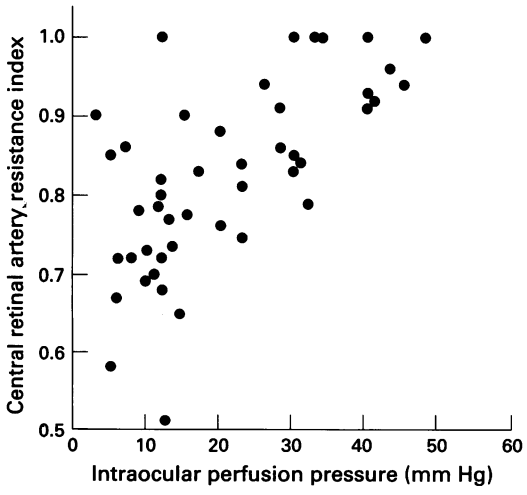

Figure 5 Individual values for central retinal artery resistance index ((PSV − EDV)/PSV), expressed as a function of intraocular pressure. Resistance indices rose as intraocular pressure was elevated ($r = 0.68$, $p<0.0001$).

bulb). Whether this resistance increase arises from arteriolar, capillary, or venous compression cannot be directly determined.

It should be emphasised that changes in calculated perfusion pressure, or changes in central retinal arterial blood velocity waveforms, are not actual blood flow changes. Unfortunately, the current 'direct' blood flow evidence on this issue is not conclusive.[15-19] While there are some reports from both healthy humans (using laser Doppler velocimetry), and non-human primate glaucoma models, that retinal and optic nerve head blood flow and to some extent choroidal blood flow, is autoregulated over a substantial range,[15-17] studies of glaucoma patients suggest a greatly reduced autoregulatory capacity.[18 19] Our results suggest, but leave unproved, the possibility that the normal human autoregulatory capacity in the critical central retinal artery watershed is severely limited.

In our study, ocular hypertension was imposed upon healthy eyes for only a few minutes. Clearly, the presence of intercurrent disease processes (for example, hypertension, diabetes, cerebrovascular disease) and chronicity characterise most situations of glaucomatous optic nerve head damage. There is evidence, for example, that acute and chronic cerebrovascular responses to perfusion pressure changes are somewhat different.[20] On the other hand, our simple model affords a clear view of these processes in an uncomplicated situation, and it seems likely that they describe the acute response to ocular hypertension in the absence of other pathological conditions. It is interesting to note in this regard that pressure reductions via trabeculectomy provide opposite effects in primary open angle glaucoma patients: an elevation in end diastolic velocity and reduced resistance index in the central retinal artery.[21]

Some recent studies suggest that primary open angle glaucoma patients, and normal tension glaucoma patients, may also be characterised by abnormal ophthalmic arterial haemodynamics. These abnormalities (defined by comparison with values measured in control subjects) include reduced end diastolic velocity, or increased resistance indices, in that vessel.[7] Of course, it remains unknown if these suspected haemodynamic alterations are cause or consequence of a more primary problem. Specifically, it is unclear to what extent these ophthalmic arterial blood velocity changes result from elevated IOP. The finding of increased resistance index in the ophthalmic artery in normal tension glaucoma patients suggests that ocular hypertension need not be a prerequisite for retrobulbar vascular abnormalities. Our results further suggest that in healthy eyes, ophthalmic artery flow velocities and resistance indices are absolutely unrelated to IOP over an extremely broad range. That range included IOP increases above the range usually experienced in chronic open angle glaucoma, and reductions below those achieved following surgical interventions for elevated pressure. Our result may be understood in light of the large watershed distal to the ophthalmic artery at its point of measurement in these experiments: elevated IOP may increase vascular resistance in only a small (though perhaps critical) fraction of that downstream vasculature.

In conclusion, our results suggest that acute intraocular pressure elevation has direct and immediate consequences for central retinal arterial, but not for ophthalmic arterial, haemodynamics. The latter finding suggests that ophthalmic arterial dysfunction in both primary open angle glaucoma and normal tension glaucoma is not directly linked to IOP. In contrast, the close relation between central retinal arterial haemodynamics and IOP implies that perfusion of the retina and optic nerve head may be vitally linked to IOP, such that the ability to withstand vascular insult is dependent upon autoregulatory capacity and vascular reserve.

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1 Morgan JE. Selective cell death in glaucoma: does it really occur? *Br J Ophthalmol* 1994;**78**:875–80.
2 Crick RP, Vogel R, Newson RB, Shipley MJ, Blackmore H, Palmer A, *et al.* The visual field in chronic simple glaucoma and ocular hypertension; its character, progress, relationship to the level of intraocular pressure and response to treatment. *Eye* 1989;**3**:536–46.
3 Carter CJ, Brooks DE, Doyle DL, Drance SM. Investigation into a vascular etiology for low-tension glaucoma. *Ophthalmology* 1990;**97**:49–54.
4 Drance SM, Douglas GR, Wijsman K, Schulzer M. Response of blood flow to warm and cold in normal and low-tension glaucoma patients. *Am J Ophthalmol* 1988;**105**:35–9.
5 Hayreh SS, Revie IHS, Edwards J. Vasogenic origin of visual field defects and optic nerve changes in glaucoma. *Br J Ophthalmol* 1970;**54**:461–7.
6 Tielsch JM, Katz J, Sommer A, Quigley HA, Javitt JC. Hypertension, perfusion pressure, and primary open-angle glaucoma. A population-based assessment. *Arch Ophthalmol* 1995;**113**:216–21.
7 Galassi F, Nuzzaci G, Sodi A, Casi P, Cappelli S, Vielmo A. Possible correlations of ocular blood flow parameters with intraocular pressure and visual-field alterations in glaucoma: a study by means of color Doppler imaging. *Ophthalmologica* 1994;**208**:304–8.
8 Stroman GA, Stewart WC, Golnik KC, Cure JK, Olinger RE. Magnetic resonance imaging in patients with low-tension glaucoma. *Arch Ophthalmol* 1995;**113**:168–72.
9 Lieb WE, Cohen SM, Merton DA, Shields JA, Mitchell DG, Goldberg BB. Color Doppler imaging of the eye and orbit. Technique and normal vascular anatomy. *Arch Ophthalmol* 1991;**109**:527–32.
10 Guthoff RF, Berger RW, Winkler P, Helmke K, Chumbley LC. Doppler ultrasonography of the ophthalmic and central retinal vessels. *Arch Ophthalmol* 1991;**109**:532–7.
11 Spencer JAD, Guissani DA, Moore PJ, Hanson MA. In vitro validation of Doppler indices using blood and water. *J Ultrasound Med* 1991;**10**:305–11.
12 Snedecor GW, Cochran WG. *Statistical methods.* 7th ed. Ames: Iowa State University Press, 1980:116.
13 Bill A. The uveal venous pressure. *Arch Ophthalmol* 1963;**69**:780–2.
14 Kiel JW, Heuven WAJ. Ocular perfusion pressure and choroidal blood flow in the rabbit. *Invest Ophthalmol Vis Sci* 1995;**36**:579–85.
15 Riva CE, Sinclair SH, Grunwald JE. Autoregulation of retinal circulation in response to decrease of perfusion pressure. *Invest Ophthalmol Vis Sci* 1981;**21**:34–9.
16 Quigley HA, Hohman RM, Sanchez R, Addicks EM. Optic nerve head blood flow in chronic experimental glaucoma. *Arch Ophthalmol* 1985;**103**:956–62.
17 Sossi N, Anderson DR. Effect of elevated intraocular pressure on blood flow. Occurrence in cat optic nerve head studied with iodoantipyrine I^{125}. *Arch Ophthalmol* 1983;**101**:98–101.
18 Schwartz B, Kern J. Age, increased ocular and blood pressures, and retinal and disc fluorescein angiograms. *Arch Ophthalmol* 1980;**98**:1980–6.

19 Namba K, Schwartz B. Nerve fiber layer and optic disk fluorescein defects in glaucoma and ocular hypertension. *Ophthalmology* 1988;**95**:1227–33.
20 Faraci FM, Baumbach GL, Heistad DD. Cerebral circulation: humoral regulation and effects of chronic hypertension. *J Am Soc Nephrol* 1990;**1**:53–7.
21 Trible JR, Sergott RC, Spaeth GL, Wilson RP, Katz LJ, Moster MR, *et al*. Trabeculectomy is associated with retro bulbar hemodynamic changes. A color Doppler analysis. *Ophthalmology* 1994;**101**:340–51.