Glaucma patients demonstrate faulty autoregulation of ocular blood flow during posture change

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Abstract

Background/aims—Autoregulation of blood flow during posture change is important to ensure consistent organ circulation. The purpose of this study was to compare the change in retrobulbar ocular blood flow in glaucoma patients with normal subjects during supine and upright posture.

Methods—20 open angle glaucoma patients and 20 normal subjects, similar in age and sex distribution, were evaluated. Blood pressure, intraocular pressure, and retrobulbar blood velocity were tested after 30 minutes of sitting and again after 30 minutes of lying. Retrobulbar haemodynamic measures of peak systolic velocity (PSV), end diastolic velocity (EDV), and resistance index (RI) were obtained in the ophthalmic and central retinal arteries using colour Doppler imaging (CDI).

Results—When changing from the upright to supine posture, normal subjects demonstrated a significant increase in OA EDV (p = 0.016) and significant decrease in OA RI (p = 0.0006) and CRA RI (p = 0.016). Glaucoma patients demonstrated similar changes in OA measures of EDV (p = 0.02) and RI (p = 0.04), but no change in CRA measures.

Conclusion—Glaucma patients exhibit faulty autoregulation of central retinal artery blood flow during posture change.

Regulation of blood flow during posture change is important to maintain proper circulating status in many organs. When in the upright posture, gravity pulls blood away from organs above the heart and towards organs below the heart. To ensure appropriate blood flow when changing from supine to upright posture, vessels below the heart constrict to block hyperaemia and oedema, while vessels above the heart dilate to offset falling perfusion pressure.

An abnormal change in blood flow during postural variation is an indication of vascular irregularity. For example, in the normal foot, vessels constrict when the foot is placed below the heart, causing blood flow to fall by 50%. However, in patients with lower limb arterial obstructive disease, blood flow increases by approximately 80% when the patient stands. In normal cerebral circulation, blood flow remains virtually constant during posture change. Middle cerebral artery blood velocity varies less than 10% in the supine compared with sitting positions. Patients with autonomic dysfunction, however, exhibit wide variation in cerebral blood flow during posture change.2 3 In these patients middle cerebral artery blood velocity falls by more than 25% when changing from a supine to upright posture.

Numerous recent studies suggest that dysfunctional ocular circulation contributes to the pathogenesis of glaucoma.4–7 Few data are available concerning the autoregulatory response of ocular blood flow to posture change in glaucoma patients. Analysis of ocular blood flow during various body positions may provide insight into the circulatory irregularity of glaucoma patients. The purpose of this study was to measure and compare the ophthalmic and central artery haemodynamics in glaucoma patients and normal subjects in both the seated and supine positions.

Subjects and methods

Paid volunteers, comprising 20 glaucoma patients and 20 normal subjects, participated in this study. This study was approved by the Indiana University institutional review board and all participants reviewed and signed informed consent statements before entering the study. Subjects and patients were examined by members of the Indiana University Medical Center Department of Ophthalmology Glaucoma Service. Both groups were free of diabetes, cardiovascular or respiratory disease, and were taking no medications for systemic hypotension. All patients had glaucomatous type optic disc appearance and/or visual field defects. The patient’s cup/disc ratios were all greater than 0.6 and the loss in visual field sensitivity (as determined by mean defect) ranged from −5.0 to −20.0 dB. No limitation was placed on the minimum level of patient intraocular pressure for study inclusion. The control group was selected to be similar for age, sex distribution, blood pressure, and heart rate to the patient group (Table 1). Normal subjects had no history of ophthalmic disorders and results of an ophthalmic examination were normal. If a patient was on a regimen of ocular hypertensive therapy for glaucoma, he or she ceased taking medication 4 weeks before the start of the experiment.

Methods

This study was performed as part of a larger study in which participants were admitted to the General Clinic Research Center (GCRC) of the Indiana University Hospital for over-
Table 2 Results for glaucoma patients and normal subjects in sitting and supine positions (mean (SD))

<table>
<thead>
<tr>
<th></th>
<th>Sit</th>
<th>Supine</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>76 (14)*</td>
<td>70 (11)*</td>
<td>0.0001*</td>
</tr>
<tr>
<td>BP sys (mm Hg)</td>
<td>132 (20)</td>
<td>130 (17)</td>
<td>NS</td>
</tr>
<tr>
<td>BP dias (mm Hg)</td>
<td>76 (10)*</td>
<td>73 (9)*</td>
<td>0.028*</td>
</tr>
<tr>
<td>IOP</td>
<td>18.4 (4)#</td>
<td>17.9 (3)##</td>
<td>0.0009#</td>
</tr>
</tbody>
</table>

*Statistically significantly different between sitting and supine position. ##Statistically significant difference between glaucoma patients and normal subjects.
Glaucoma patients demonstrate faulty autoregulation of ocular blood flow during posture change.

**Discussion**

Glaucoma patients and normal subjects demonstrate similar changes in heart rate, IOP, diastolic blood pressure, and ophthalmic artery haemodynamics during posture change. The CRA RI response to posture variation is significantly different between groups; it falls significantly in normal subjects when changing from a seated to supine position, but shows no change in glaucoma patients.

Constant intraocular pressure during posture change is contrary to the findings of many previous studies (for review see Kothe\(^1\)). Intraocular pressure has a well established circadian rhythm and is known to peak in the morning and fall during the day, reaching its lowest point in early evening before sleep.\(^2\)\(^3\)

Whereas previous studies were conducted much earlier in the day, during a time period close to the IOP peak, our study was conducted between 6 and 7 pm, a time when IOP is known to be near its diurnal trough.

The factors which control the circadian rhythm of IOP remain poorly understood. We speculate that the differences noted between the results of this study and previous studies may be related to factors that control IOP circadian rhythm. Further posture studies at different times of the day could potentially elucidate these differential diurnal IOP postural responses, if they exist.

Measures of CDI blood flow velocity and vascular resistance, as obtained in our study, cannot be used to quantitatively assess volumetric blood flow. Both vessel diameter and velocity are needed for this purpose. No technique is currently available to accurately and non-invasively measure retrobulbar vessel diameter. Nevertheless, data do indicate that changes in CDI velocity measures are highly predictive of changes in volumetric flow both in vitro\(^4\)\(^5\) and in vivo, in cerebral vessels.\(^6\)\(^7\)

Further, considerable evidence points to a close correlation between higher resistance
index and increased vascular resistance down-
stream from the point of CDI measurement.14
Consequently, our data suggest that distal vas-
cular resistance falls in the ophthalmic artery of
both normal subjects and glaucoma patients
during supination. In the CRA, only normal
subjects demonstrate such a change.

The internal carotid artery supplies the orbit
and over 80% of the cerebrum.15 Anatomically,
the ophthalmic artery exits the internal carotid
artery behind the orbit and immediately bifur-
cates into the middle cerebral and anterior cer-
bral arteries. Data from the middle cerebral
artery demonstrate a small non-significant
change in blood flow velocity during posture
change.22 This result is unlike our ophthalmic
artery data, which demonstrate a significant
increase in velocity during supination. It
appears from these data that the major feeding
vessel of the brain (that is, middle cerebral
artery) is more tightly autoregulated than the
major feeding vessel of the eye (that is, ophthalmic
artery), even though these arteries are
in very close anatomical proximity. Results
from other studies support this conclusion.
Data show that middle cerebral artery blood
velocity remains constant as blood pressure
rises during isometric exercise.17 On the
contrary, ophthalmic artery blood velocity
increases significantly during similar
conditions.17 Further, mild hypercapnia in-
duces significant elevation of middle cerebral
artery blood flow velocity, while elevated end
tidal carbon dioxide appears to have no effect
on the ophthalmic artery blood flow.19 If the
autoregulation of the ophthalmic artery is less
stringent than that of cerebral vessels, then this
suggests that the eye may be more susceptible
to vascular insult than the brain during periods
of circulatory stress.

The CRA directly feeds and is the only
source of blood supply for the retinal arteries.
These distal vessels nourish the retinal gan-
glion cells and the confluence of unmyelinated
nerve fibres anterior to the lamina cribrosa.20
Glaucoma is a disease known to cause the
death of retinal ganglion cells and erosion of
the optic nerve head. Numerous studies
indicate that glaucoma patients have altered
retinal circulation. Extensive morphological
studies describe endothelial proliferations in
the retinal vessels of glaucoma patients.21 Further,
widespread angiographic circulatory
defects appear in the retinal vasculature of
open angle glaucoma patients22 and these
patients demonstrate significantly increased
arteriovenous passage time.23 24 Such defects
could potentially increase vascular resistance in
the retinal vessels and, in turn, limit the
autoregulatory response to posture change in
retrobulbar vessels of these patients. Our data
here, taken in conjunction with these previous
studies, suggest that the failure to properly
regulate CRA blood flow during posture
change may be related to dysfunctional retinal
circulation in glaucoma patients.

A number of previous studies have demon-
strated that ocular pulsatility falls during supi-
nation in normal subjects25 26 and in patients
with chronic open angle glaucoma,27 ocular
hypertensive,28 and normal tension glaucoma.29
Ocular pulsatility is related to arterial pressure
and reflects the influx of blood into the eye
with each heart beat; the greater the pulse
amplitude, the greater the bolus of blood
entering the eye.30 The previous pulsatility
findings have been interpreted to suggest that
during supination, ocular perfusion falls, in-
creasing the potential for tissue hypoxia.31 This
interpretation is contrary to the implications
of our results. A fall in distal vascular resistance
in the retrobulbar vessels, when changing from
seated to supine posture, suggests an increase
(or minimally no change), not a decrease in
ocular perfusion during supination.

One limitation of the pulsatility measure-
ment is that it evaluates only the pulse wave in
the eye (systole) and is virtually insensitive to
the steady state non-pulsatile component
diastole) of blood flow.29 Accordingly, pulsatile
blood flow and volumetric blood flow do not
always move in concordance. Shifts in blood
flow from the sytolic to diastolic component
of the cardiac cycle can alter pulsatile flow
without changing volumetric flow, or vice versa.
For example, when perfusion pressure is
reduced in cerebral vessels due to increased
intracranial pressure, pulsatile blood flow
increases in the major feeding vessel (that is,
internal carotid artery), while volumetric blood
flow falls in this vessel.32 Further, during
hypoxic hypercapnia, cerebral volumetric
blood flow increases substantially (>50%) with
no corresponding change in pulsatile blood
flow.33 If overall ocular vascular resistance is
falling during supination, as suggested by the
CDI data here, then the reduction in ocular
pulsatility during supination shown in previous
studies may reflect not a reduction but a shift in
overall ocular perfusion but simply a shift in the blood
flow away from systole to diastole.29

In summary, unlike the middle cerebral
artery, Doppler measures of blood flow velocity
in the ophthalmic artery change significantly
during posture variation. This is true for both
glaucoma patients and normal subjects. While
the ophthalmic artery response is similar be-
tween groups, differences in measures of central
retinal artery resistance index are not. These
data indicate that posture change exposes a vas-
cular autoregulatory deficit in glaucoma pa-
tients, which appears to be most prominent in
the vessels distal to the central retinal artery.

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imaging in untreated high- and normal-pressure open-angle
imaging and spectral analysis of the optic nerve vasculature
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