Effect of Body Position on Episcleral Venous Pressure in Healthy Subjects

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Glaucosa

IOP is the most important risk factor for glaucoma and is the only variable that can currently be modified for the treatment of glaucoma. IOP is dynamic and can change rapidly on a timescale of seconds to minutes, depending on the stimulus. It is dependent on body position, increases as posture changes from sitting to supine, and increases more when a subject is inverted.1,5

Postural changes could in theory affect several variables that change the steady-state IOP. At steady state, IOP is determined by aqueous humor production (Q), outflow facility (C), uveoscleral outflow (U), and episcleral venous pressure (EVP) as described by Goldmann and later modified

\[ IOP = EVP + \frac{1}{C}(Q - U) \] (1)

Steady-state IOP can be increased or decreased by changes in any of these variables.6 IOP can also be affected transiently by deformation of the globe during eye movements, blinks, forced displacement, and changing choroidal blood volume.

The contributions of these variables to posture-induced changes in steady-state IOP have been investigated. Carlson et al.7 investigated the relationship between IOP and rate of aqueous humor formation while subjects were alternated between an upright and inverted body position. They found that body inversion increased IOP by as much as 11 mm Hg but did not change the aqueous flow rate significantly. Outflow facility also did not change between sitting and supine positions in a study by Selvadurai et al.8 A few studies have looked at the variation of episcleral venous pressure with body position,9–14 and EVP increased in supine and inverted postures compared to standing posture. However, the methods used to determine EVP did not use objective measurement end points and may have been inconsistent with pressure in episcleral veins measured directly by cannulation.15,16 The effect of body position on EVP, and its relationship to postural IOP change, therefore remains uncertain.

Understanding the mechanisms of IOP changes with posture are important for optimizing the treatment of glaucoma throughout the 24-hour period. In particular, during the nocturnal period, IOP is significantly higher than the diurnal period and is related to the recumbent position during sleep.17,18 Therapies targeted toward the mechanisms of postural IOP change may be useful in stabilizing IOP fluctuations, although evidence to support the clinical importance of postural IOP fluctuations in glaucoma pathogenesis is currently limited.

In this study, we measured EVP in sitting and recumbent postures by using semiautomated objective methods and examined the relationship between the increase in IOP and the change in EVP induced by changing from the sitting to inclined positions.

Materials and Methods

Twenty-four healthy volunteers, 15 male and 9 female, ranging in age from 24 to 73 years, were recruited from Mayo Clinic employees and students and local area residents. A medical history was obtained, and a complete dilated eye examination...
was performed. Participants were excluded if they had an IOP greater than 22 mm Hg, evidence of glaucomatous optic neuropathy or any other ocular pathology, or a history of ocular surgery or therapy. Subjects were also excluded if they had high myopia (−6 diopters [D] or more) or high hyperopia (+2 D or more). Subjects with chronic medical conditions (e.g., hypertension) were allowed to participate provided that their medical condition had been under good control over the preceding 12 months and they did not use β-adrenergic antagonists systemically. Subjects were also checked to be sure they could extend their neck while in an inclined position and maintain this posture for 7 to 10 minutes (the typical time required to obtain measurements in both eyes) as required by the protocol. On the day of the study, participants were asked to maintain a regular sleep schedule and avoid excess caffeine. Our study was conducted in accordance with the principles of the Declaration of Helsinki (1989) and was reviewed and approved by the Institutional Review Board of Mayo Clinic. All subjects gave written consent after discussion of the nature and possible risks of the study.

Measurement Techniques

IOP was measured in both eyes by using a pneumatonometer (Model 30 Classic; Reichert, Inc., Depew, NY, USA) after instilling proparacaine 0.5% in each eye. EVP was measured by using a slit-lamp–mounted, computerized venomanometer as described previously (Fig. 1). Briefly, a clear flexible membrane was placed against the surface of an episcleral vein, which was identified as being straighter and deeper than conjunctival vessels. The pressure behind the membrane was automatically and linearly increased by a computer-controlled motor drive to compress the vein. During compression, a high-definition video camera captured images of the vein as it collapsed, synchronized, and recorded with each video frame. The pressure associated with the initiation of venous collapse was assumed to be equal to the venous pressure and was determined from the video recording by using a method described previously.16

Measurement Protocol

Subjects were seated in a standard ophthalmologic examination chair. In all measurements, IOP was measured in the right eye before the left eye, and then EVP was measured in the right eye before the left eye. EVP was measured in the superior or superotemporal quadrant, and the mean of four measurements on one vein in each eye was calculated and accepted as episcleral venous pressure.

After measurements were completed with the subject in the seated position, the subject rested for 30 minutes and then assumed an inclined position on a surgery stretcher (Stryker Corp., Kalamazoo, MI, USA) with the neck extended and the chin resting on the chin rest of the slit lamp so that torso of the patient was at an angle of 45° to the ground (Fig. 2). After maintaining this posture for 5 minutes to allow for autonomic, postural, and hormonal changes to stabilize,19,20 IOP and EVP were remeasured in both the eyes.

Statistical Analysis

IOP and EVP in the seated position were compared with IOP and EVP in the inclined position. In addition, the change in IOP between positions (ΔIOP) was compared to the change in EVP (ΔEVP). Significance of all comparisons were determined by using generalized estimating equation models to account for possible correlation between eyes of the same subject. The relationship between ΔIOP and ΔEVP was examined by using Pearson correlation and significance was determined by using generalized estimating equation models. The differences between ΔIOP and ΔEVP were expressed as a function of their means according to the methods of Bland and Altman.21

The limits of agreement, which include approximately 95% of the differences, were the mean difference between ΔIOP and ΔEVP ± 2 SDs of the difference.21

RESULTS

Forty-three eyes of 24 volunteers were studied, including 15 females and 9 males, with ages ranging from 24 to 73 years (43.3 ± 15.8 years, mean ± SD; Table). Five eyes were excluded from the study because of poor-quality images of the episcleral veins, rendering accurate measurement of EVP unfeasible.

Mean IOP increased from 11.4 ± 3.0 mm Hg in the sitting position to 13.1 ± 3.4 mm Hg in the inclined position (P < 0.001). Mean EVP increased from 6.4 ± 1.4 mm Hg in the sitting position to 7.8 ± 1.7 mm Hg in the inclined position (P < 0.001; Fig. 3A).

<table>
<thead>
<tr>
<th>Table.</th>
<th>Baseline Characteristics of Study Participants</th>
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<tbody>
<tr>
<td>Age, y</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Range</td>
<td>19 to 73</td>
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<tr>
<td>CCT, µm</td>
<td>549 ± 34</td>
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<tr>
<td>Range</td>
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<tr>
<td>IOP, mm Hg</td>
<td>12.0 ± 2.1</td>
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<tr>
<td>Range</td>
<td>8 to 15</td>
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<tr>
<td>Refractive Error, D</td>
<td>–1.2 ± 1.7</td>
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<tr>
<td>Range</td>
<td>–6.0 to 1.3</td>
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The postural rise in EVP from sitting to inclined positions was 1.4 ± 1.7 mm Hg and was not significantly different from the postural rise in IOP of 1.7 ± 1.1 mm Hg ($P = 0.18$; Fig. 3B). The minimum detectable difference between the $\Delta$IOP and the $\Delta$EVP was 0.77 mm Hg ($\alpha = 0.05$, $\beta = 0.20$, $n = 43$ eyes).

The $\Delta$IOP was not correlated with the $\Delta$EVP ($r = 0.24$, $P = 0.1$; Fig. 4); the minimum detectable correlation coefficient between the two differences was $r = 0.40$ ($\alpha = 0.05$, $\beta = 0.20$, $n = 43$ eyes). The limits of agreement between $\Delta$IOP and $\Delta$EVP were from $-3.2$ to $3.8$ mm Hg (Fig. 5).

**DISCUSSION**

IOP fluctuations have been implicated as potential risk factors for glaucoma progression.\(^{22}\) Postural fluctuations in IOP are very common,\(^{23}\) but the mechanisms of these IOP fluctuations have not been fully understood. From the modified Goldmann model of IOP (Equation 1), we would expect that EVP and IOP change in a 1:1 ratio if outflow facility, aqueous humor flow rate, and unconventional outflow rate remain constant. In our study, changing from the sitting to inclined position increased both IOP and EVP by a small amount and the lack of a difference between the $\Delta$IOP and the $\Delta$EVP suggests that IOP increased, at least in part, because EVP increased. Previous studies that investigated the concordance of postural changes in IOP and EVP have reported variable results. Friberg et al.\(^{11}\) measured EVP by using a magnifying, portable transducer in supine and head down vertical position. For every 0.83 ± 0.21 mm Hg increase in EVP, IOP increased by 1 mm Hg. In contrast, Lavery and Kiel\(^{24}\) reported that EVP and IOP responses to head...
down tilt in rabbits were similar, with measurements obtained via direct cannulation. Similarly, Linnér et al.10, and Leith9 showed that both IOP and EVP increased by approximately 1 mm Hg on changing from sitting to supine positions, when they measured EVP by using variations of the pressure chamber technique described by Seidel in 1923.9,10 However, neither of these two studies reported the minimum detectable difference between the change in IOP and the change in EVP and both used subjective rather than objective measurement end points. In our study, we had an 80% chance of finding a difference as small as 0.77 mm Hg if it existed. If a smaller difference between the postural change in IOP and EVP existed, our study would not have been able to detect it. However, to detect a smaller difference between changes in these variables would be impractical; detecting a mean difference as small as 0.5 mm Hg would require 124 eyes.

Although other studies have evaluated the change in EVP with body position, we are not aware of any previous study that has evaluated EVP changes using an objective technique in living human eyes. Noninvasive measurement of EVP is based on identifying the pressure needed to collapse an episcleral vein to a specified end point.25 However, only one end point is on identifying the pressure needed to collapse an episcleral living human eyes. Noninvasive measurement of EVP is based that has evaluated EVP changes using an objective technique in

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vessels. Adequate magnification is also required to obtain images of sufficient resolution to detect changes in brightness easily. As well, the slit lamp provides an important point of stabilization at high magnification, enabling the capture of high quality videos. Although our long-term goals include the design and construction of a completely new system enabling EVP measurements in any position, this is far beyond the scope of the current study.

The changes in IOP and EVP in our study may have been greater if subjects had been positioned completely horizontal or had been inverted. Alternately, the change in EVP and IOP could have been elevated by the extended head and neck position, which has been reported to affect IOP. It is not known if the relationship between EVP and IOP is affected by alterations of the head and neck position. However, if conditions are at steady state at the time of measurements, the Goldmann equation should be valid. Nevertheless, further investigation of the elevation of EVP and its contribution to the elevation of IOP in the supine position will need to wait for the investigation of the elevation of EVP and its contribution to the nonpostural IOP fluctuations. As well, the slit lamp provides an important point of collapse using image analysis of videos and associated pressure measurements during automated episcleral vein compression.

In summary, both IOP and EVP are higher in the inclined position than they are in the sitting position. Our study suggests that postural changes in IOP are consistent with the postural changes in EVP, as indicated by the Goldmann equation. Further investigation is required to determine the contribution of EVP to nonpostural IOP fluctuations. As well, further investigation is required to understand the role of modulating EVP to reduce IOP variability.

Acknowledgments

Supported by the Bright Focus Foundation, Mayo Foundation for Medical Education and Research, and an unrestricted departmental grant from Research to Prevent Blindness.

Disclosure: N. Arora, None; J.W. McLaren, None; D.O. Hodge, None; A.J. Sit, None

References


