Effect of a β-blocker on altered body position: induced ocular hypertension

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Abstract
The intraocular pressures (IOP) were measured in both eyes of 25 healthy volunteers in various body positions. One eye was pretreated with levobunolol 0-5% or placebo applied in a masked, randomised fashion, while the other served as control. IOP changes in response to levobunolol and to changes in position were significant (p<0-0001). However, pressure rises relative to position were not significantly different in eyes treated with drug vs placebo. Levobunolol did not alter relative changes in IOP from changes in body position. However, the overall lowering effect may offer some protection to patients with glaucoma.

Changes in body position have been shown to affect intraocular pressure (IOP). Physiological changes include IOP increases of 1-4 mmHg in going from the sitting to the horizontal position, to IOP doubling on gravity inversion. These pressure changes occur rapidly in both induction and reversal and are sustained in a given position. In addition to IOP changes, gravity inversion has also been shown to cause transient changes in automated visual fields, pattern reversal electroretinograms (ERG), and visually evoked potentials (VEP).

The mechanism for IOP changes is thought to be due to decreased outflow secondary to increased episcleral venous pressure combined with vascular engorgement of the uvea. Carlson et al have shown that aqueous flow does not notably change in response to altered body position.

Exaggerated increases of IOP in the horizontal position have been shown to occur in patients with glaucoma, particularly following trabeculectomy. Anderson and Grant noted that eyes receiving miotics also showed an exaggerated response. However, this may have been due to the underlying glaucomatous state.

To our knowledge the effect of antiglaucoma medications on postural changes in IOP has not been studied in a randomised and controlled fashion. For this study, we chose the non-specific β-blocker levobunolol* as the test drug.

Materials and methods
Twenty-five healthy volunteers were enrolled after informed consent was obtained. The study was approved by the Ethics Review Board of the Toronto General Hospital.

General medical and ocular histories were obtained and a full eye examination was performed. The subjects were then randomly assigned to the right or left eye and in a double blind fashion to drug or placebo. IOP measurements were determined by Perkins tonometry. The subjects were given one drop of levobunolol 0-5% or placebo. Then measurements were taken on both the treated and untreated eyes as follows: pretreatment sitting, two hours post-treatment sitting, horizontal, 30° head down, horizontal, and a final sitting. Pressures were taken within 10–15 seconds of assuming new positions and in most instances were an average of two readings. One week later the same IOP routine was performed with the alternative drop on the same eye.

An F test analysis of variance was performed on the IOP measurements to detect differences created by position, treatment, and order (drug-placebo versus placebo-drug).

Results
There were 25 subjects, 11 male and 14 female. The age range was 13–44 years, mean 28·2 years. Four had a family history of glaucoma. All the eyes were clinically normal. Levobunolol lowered the IOP by an average of 1·65 mmHg after two hours (p<0-0001). Table 1 demonstrates IOP elevations in the horizontal and 30° head down positions. It is noteworthy that the IOP rose 1·6 mmHg in the untreated group and 1·2 mmHg in the treated group in the horizontal position.

Table 1 Elevations in intraocular pressure (mmHg) from the sitting position

<table>
<thead>
<tr>
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<th>Horizontal</th>
<th>30° Head down</th>
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<tr>
<td>Placebo</td>
<td>1·6 (SD 0·4)</td>
<td>13·7 (SD 0·8)</td>
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<tr>
<td>Drug</td>
<td>1·2 (SD 0·4)</td>
<td>13·4 (SD 0·7)</td>
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Figure 1 Positional IOP curves for drug (treat B) and placebo (treat A). S1=pretreatment sitting, S2=post-treatment sitting, H1=initial horizontal, HD=head down at 30°, H2=final horizontal, S3=final sitting.
position. Tilting the body 30° head down caused increases of 13-7 mmHg in the untreated group and 13-4 mmHg in the treated group. These results are also highly significant (p<0.0001).

The positional IOP curves for drug and placebo were parallel (Fig 1). This was also true of the control eyes (opposite eyes) for both placebo and drug (Figs 2 and 3). Levobunolol lowered the IOP in all positions but did not alter the relative IOP changes between positions.

It was interesting to note that in treated eyes the initial horizontal IOPs stayed below pretreatment sitting levels in comparison with both placebo and control.

**Discussion**

The results of this study confirm earlier reports that acute rises in IOP can be induced by changes in body position. The average rises of 1-4 and 13-6 mmHg in going from the sitting to the horizontal and 30° head down positions respectively are compatible with the 0-3 mmHg increase noted by Leonard et al and the 16 mmHg increase noted by Weinreb et al. In the latter study subjects were totally inverted, which explains the greater IOP effect.

Coakes and Brubaker have shown by fluorophotometric studies that the β-blocker timolol maleate decreases aqueous production and this is the most likely mechanism for its IOP reducing effect. We have shown that the β-blocker levobunolol has no effect on relative IOP changes with altered body position. Thus these changes appear to be insensitive to changes in aqueous production. This indirectly confirms the more recent work by Carlson and associates which showed, again by aqueous fluorophotometry, that aqueous production was not significantly altered by posturally induced elevated IOP. Therefore the mechanism for elevated IOP in the horizontal and head down positions must be due to reduced outflow, as proposed by Leonard et al.

The reduction in IOP caused by levobunolol was enough to prevent the horizontal IOP from reaching pretreatment sitting levels. This may have important therapeutic implications for patients with glaucoma, particularly those giving an exaggerated postural IOP response.

In future studies the effect of various anti-glaucoma medications on the postural IOP response in normal and glaucoma patients should be studied.

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