Effects of 0.5% apraclonidine on optic nerve head and peripapillary retinal blood flow

Tae Woo Kim, Dong Myung Kim

Abstract

Aims—To examine the effects of 0.5% apraclonidine on optic nerve head (ONH) and peripapillary retinal blood flow by scanning laser Doppler flowmetry (SLDF).

Methods—ONH and peripapillary retinal blood flow of 17 healthy subjects were measured by SLDF before and 1 hour and 3 hours after unilateral administration of 0.5% apraclonidine. The fellow eyes were treated with balanced salt solution and the examiners were masked as to which eye was treated with apraclonidine. On each occasion, three scans were obtained and haemodynamic variables (volume, flow, and velocity) were analysed at eight locations, four in the neural rim and four in the peripapillary retina, avoiding ophthalmoscopically visible vessels. The statistical significance of changes from the baseline value of variables and the differences in the measured quantities between apraclonidine treated eyes and fellow eyes at each time point were evaluated using Wilcoxon signed rank test.

Results—The intraocular pressure was reduced significantly in apraclonidine treated eyes by 15.0% (p=0.001) at 1 hour and 30.0% (p=0.000) at 3 hours after administration. In the volume, flow, or velocity of ONH and peripapillary retinal blood flow, there were no significant changes from the baseline values at 1 hour and 3 hours after apraclonidine administration in either apraclonidine treated eyes (p >0.4) or fellow eyes (p >0.2). Also, no significant differences were found in the measured quantities between apraclonidine treated eyes and fellow eyes at each time point (p >0.1).

Conclusion—A single dose of topical apraclonidine 0.5% in healthy subjects does not have adverse effects on the ONH and peripapillary retinal blood flow.


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Figure 1 Schematic diagram showing eight locations where haemodynamic variables were measured. The four retinal points were located approximately 100 µm from the edge of the optic disc.
Table 1  Cardiac responses to 0.5% apraclonidine instilled after baseline measurement (mean (SEM), n=17)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 hour</th>
<th>3 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>73 (1)</td>
<td>73 (1)</td>
<td>74 (2)</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>systolic</td>
<td>117 (4)</td>
<td>116 (4)</td>
<td>117 (4)</td>
</tr>
<tr>
<td>diastolic</td>
<td>78 (2)</td>
<td>77 (2)</td>
<td>79 (2)</td>
</tr>
<tr>
<td>mean arterial</td>
<td>91 (2)</td>
<td>90 (2)</td>
<td>91 (2)</td>
</tr>
</tbody>
</table>

Table 2  Intraocular pressure and calculated perfusion pressure responses to 0.5% apraclonidine instilled after baseline (mean (SEM), n=17)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>1 hour</th>
<th>3 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraocular pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>apraclonidine treated eyes</td>
<td>15.4 (0.7)</td>
<td>13.0 (0.6)</td>
<td>10.8 (0.4)</td>
</tr>
<tr>
<td>fellow eyes</td>
<td>15.2 (0.6)</td>
<td>14.9 (0.6)</td>
<td>14.9 (0.6)</td>
</tr>
<tr>
<td>Calculated ocular perfusion pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>apraclonidine treated eyes</td>
<td>45 (2)</td>
<td>47 (2)</td>
<td>50 (2)</td>
</tr>
<tr>
<td>fellow eyes</td>
<td>45 (2)</td>
<td>45 (2)</td>
<td>46 (2)</td>
</tr>
</tbody>
</table>

NS = not significant.

Results

The heart rate and blood pressure at each time point are summarised in Table 1. Compared with the baseline values, there were no statistically significant differences in the heart rate and blood pressure at 1 hour or 3 hours after instillation of apraclonidine (p >0.2).

The IOP was reduced in apraclonidine treated eyes by 15.0% (p=0.001) at 1 hour and 30.0% (p=0.000) at 3 hours after administration when compared with baseline values (Table 2). Calculated ocular perfusion pressure (COPP, 2/3 mean arterial pressure − IOP) was increased by 4.4% (p=0.002) at 1 hour and 11.0% (p=0.000) at 3 hours after administration. In the fellow eyes, the IOP and COPP did not vary significantly compared with baseline values.

In the volume, flow, or velocity of ONH and peripapillary retinal blood flow, there were no significant changes from the baseline values at
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1 hour and 3 hours after apraclonidine administration in either apraclonidine treated eyes (p >0.4) or fellow eyes (p >0.2). Also, no significant differences were found in the measured quantities between apraclonidine treated eyes and fellow eyes at each time point (p >0.1) (Table 3).

Discussion

Apraclonidine demonstrated ocular hypertensive, but not systemic hypertensive, actions which is in accord with previous studies.\(^1\)

Apraclonidine penetrates the eye via the conjunctival/scleral pathway because of its relatively low lipophilicity.\(^2\) The drug serves as an agonist at \(\alpha_1\) adrenoceptors in the ciliary epithelium\(^3\) and at vasoconstrictive \(\alpha_1\) adrenoceptors in all regions of the eye to which it has access. In the present study, topical administration of 0.5% apraclonidine did not significantly change the ONH and peripapillary retinal blood flow, while lowering the IOP. These results suggest three possibilities.

Firstly, apraclonidine may not penetrate posterior to the ONH and peripapillary retina to influence the haemodynamics of that area. Secondy, vasoconstrictive \(\alpha_1\) and \(\alpha_2\) adrenoceptors may be absent in ONH and peripapillary retinal vessels. Thirdly, the change in the blood flow is within the variability of measurement by SLDF.

The independence of the ocular haemodynamics from the short term or chronic application of topical apraclonidine has been reported in rabbits,\(^1\)\(^1\) cats,\(^1\) and human subjects\(^4\) with the use of corrosion casting technique, laser Doppler flowmeter imaging, or colour Doppler imaging (CDI). However, these measurements were accomplished at arterioles supplying the anterior optic nerve or ophthalmic and central retinal arteries. Using the Heidelberg retinal flowmeter, which provides physiological picture of the ONH and retinal perfusion with visualisation of capillaries, we measured the haemodynamic variables in the capillary bed. This assessment reflects the actual tissue perfusion more accurately than corrosion casting technique or CDI.

While the ONH and peripapillary retinal blood flow remain unchanged, the COPP was increased significantly as the IOP lowered after apraclonidine administration. This apparently incompatible result may be explained by the autoregulatory mechanisms of the ONH and peripapillary microcirculations that control the blood flow to be unchanged against the elevated ocular perfusion pressure. Otherwise, the possibility that vasoconstrictive activity of apraclonidine prevents blood flow from increasing in response to the increased perfusion pressure cannot be ruled out.

In conclusion, our results confirm that a single dose of topical apraclonidine 0.5% in healthy subjects does not have adverse effects on the ONH and peripapillary retinal blood flow. None the less, further studies are needed to confirm the safety of this medication in glaucomatous eyes with regard to optic nerve perfusion.

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