Effects of Hypertension and Antihypertensive Treatment on Retrobulbar Circulation Detected on Doppler Sonography

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Objective. To study the effect of antihypertensive drugs in essential hypertension and in the central retinal, posterior ciliary, and ophthalmic arteries by using Doppler sonography. Methods. Thirty patients with essential hypertension and 32 control subjects were enrolled in the study. The pulsatility and resistive indices were evaluated in the central retinal, posterior ciliary, and ophthalmic arteries before and 2 months after treatment with antihypertensive drugs as well as in the control group. The pulsatility and resistive index values for each artery in each group were compared statistically. Results. There were significant differences in the retrobulbar pulsatility and resistive index values in each artery among the patients with initially diagnosed hypertension and the control group (P < .05). There were significant reductions in the resistive and pulsatility index values of the posterior ciliary and ophthalmic arteries after treatment (P < .05). For the ophthalmic artery, posttreatment pulsatility and resistive index values did not reach the level of flow measured in the control subjects. Conclusions. The alteration of Doppler parameters of medication-free patients with hypertension may result from a peripheral vasospasm in the retrobulbar circulation, and the improvement in the Doppler parameters with oral antihypertensive drugs may indicate the importance of early diagnosis in ameliorating hypertension-induced retrobulbar circulation changes. Key words: antihypertensive drug; Doppler sonography; hypertension; ophthalmic artery; retrobulbar circulation.

Abbreviations
ACE, angiotensin-converting enzyme; BP, blood pressure; CRA, central retinal artery; EDV, end-diastolic velocity; OA, ophthalmic artery; PCA, posterior ciliary artery; PI, pulsatility index; PSV, peak systolic velocity; RI, resistive index

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The pathogenesis of essential hypertension is multifactorial, and many patients with ocular problems such as glaucoma, central retinal vein occlusion, and diabetes mellitus also have essential hypertension. Reduction of both systolic and diastolic pressure (140/90 mm Hg) with minimal side effects is the objective of hypertension management, and these patients are treated with antihypertensive drugs, including angiotensin-converting enzyme (ACE) inhibitors.

Combining color and spectral data, the Doppler signal provides physiologic information about arterial and venous hemodynamics and anatomic information about vessel walls and diameter. It also allows noninvasive examination of blood flow velocities of the ophthalmic artery (OA) and its branches in the orbit.
In this study we evaluated the effect of antihypertensive therapy in patients with newly diagnosed essential hypertension with the use of the Doppler parameters of the central retinal artery (CRA), posterior ciliary artery (PCA), and OA. We also compared these results with those in age-matched healthy control subjects. Finally, we aimed to answer the following questions: (1) do patients with newly diagnosed essential hypertension have changes in retrobulbar circulation that can be detected by Doppler sonography; and (2) if so, do antihypertensive drugs have the capability to alter these changes?

**Materials and Methods**

Thirty patients (14 male and 16 female) were selected as having mild to moderate essential hypertension with arterial hypertension defined as systolic blood pressure (BP) of 140 mm Hg or higher and diastolic BP of 90 mm Hg or higher. In all subjects, ambulatory BP monitoring was used to diagnose hypertension. A control group was composed of 32 subjects (17 female and 15 male). In the present investigation, each drug was given orally at 8 AM in a single morning dose. A questionnaire was administered to determine relevant medical histories for the patients and the control group. Subjects were not included in the study if they had any of the following: diabetes; any disease known to affect blood flow (eg, polycythemia, temporal arteritis, and systemic vascular disease); use of oral calcium channel blockers, ACE inhibitors, oral contraceptives, or hormonal therapy; astigmatism greater than 2 diopters; aphakia or pseudophakia; untreated intraocular pressure higher than 21 mm Hg; and smoking. Also, none of the patients had opacities in the cornea or vitreous. All measurements were made on a given subject with exercise prohibited before examination.

All Doppler sonographic examinations were performed by the same operator to avoid interobserver variability and with the same equipment: a linear array real-time sonography system with a 7.5-MHz transducer (LOGIQ 400 MD; GE Medical Systems, Milwaukee, WI) (Figures 1–3). The pulse repetition frequency used was 13.1 kHz, and the sample volume was 2 mm throughout the measurements. Three waveforms were analyzed and averaged for each parameter.

A preliminary sonographic examination of the orbit was performed to identify any gross abnormalities. The resistive index (RI; peak systolic velocity [PSV] – end-diastolic velocity [EDV]/PSV) and pulsatility index (PI; PSV – EDV/mean velocity) were assessed for each vessel from the Doppler signal.

The patients underwent 2 months of antihypertensive treatment (a single ACE inhibitor) to regulate BP, and the regulation was confirmed again with ambulatory BP monitoring. The essential hypertensive group had each vessel measured twice: before the treatment when the essential hypertension was first diagnosed and 2 months after treatment with the antihypertensive drug.

The PI and RI values of each artery in the control and essential hypertensive groups (before and after treatment) were compared statistically. One-way analysis of variance and a post hoc test (Tukey honestly significant difference) were used for statistical analysis. \( P < .05 \) was considered significant.

**Results**

The mean ages ± SD were 51 ± 15 years (range, 36–67 years) for the control group and 49 ± 16 years (range, 33–62 years) for the essential hypertension group. The mean PI and RI values for each artery in both groups are shown in Table 1. The PI and RI values in each artery among the patients with first-diagnosed hypertension and the control group were statistically different (\( P < .05 \)). There was significant reduction in the RI and PI values for the PCA and OA after treatment (\( P < .05 \)), but for the OA, even after the treatment, the PI and RI values did not reach the level of flow measured in the healthy control subjects (\( P > .05 \)).

**Discussion**

The OA originates from the internal carotid artery and enters the orbital cavity through the optic canal. It is a medium-sized muscular artery (1.33 ± 0.33 mm). The CRA and PCA are the ocular branches of the OA. The human eye is supplied by 2 separate vascular systems: the retinal and uveal blood vessels. The uveal vessels include the vascular beds of the iris, the ciliary body, and the choroid. The inner layers of the retina are nourished by the retinal vessels, whereas the outer retinal layers, including the photoreceptors, are nourished by the choroid. The major source of blood flow to the optic nerve
head is in most cases derived from the PCA, whereas the CRA supplies the blood flow to the retina.\textsuperscript{1}

Doppler sonography is known to be a good indicator of volumetric flow in these vessels.\textsuperscript{6,7} As in other vascular beds, ocular blood flow is given as blood flow velocity multiplied by cross-sectional area. The RI has been proposed as a measure of distal vascular resistance and is reported to be linearly related to vascular resistance in both in vitro and in vivo studies.\textsuperscript{8,9} The flow waveform of the OA is similar to that of the internal carotid artery, showing a high PSV and a low EDV. A dicrotic notch follows a steep PSV. The flow of the CRA is similar to that of the OA, with a lower systolic peak. The spectrum of the PCA is also like that of the CRA; however, the diastolic flow of the PCA is higher than that of CRA, thus reflecting low-resistance vascular channels of the choroid.\textsuperscript{10} Doppler sonography is promising in patients with CRA occlusion and obstruction, ocular ischemic syndrome, diabetes mellitus, Behçet disease, and glaucoma.\textsuperscript{11,12}

Kontos et al\textsuperscript{13} investigated the responses of cerebral precapillary vessels to changes in arterial BP. They concluded that the changes in arterial BP were size dependent; the large-surface cerebral vessels beginning with the circle of Willis changed their size with even minor changes in arterial BP, but the small-surface and intracerebral arterioles did not change size over a wide range of arterial BP, and the high degree of wall stiffness of the arterioles has been proposed as a possible explanation.\textsuperscript{13}

Several studies indicated that different sites of the vascular tree responded to effects of antihypertensive drugs in a different manner during the treatment of hypertension. Lafleche et al\textsuperscript{14} stated that carotid compliance and distensibility increased significantly, whereas little or no change was observed for the femoral artery and the abdominal aorta after the antihypertensive therapy. Benetos et al\textsuperscript{15} found that a decrease in BP was associated with a normalization of aortic compliance and distensibility, whereas no change was observed at the site of the carotid artery. Also, in essential hypertension, microcirculation (skin blood flow) has been studied, and increased peripheral vascular resistance or a peripheral vasospasm has been found. This increased peripheral vascular resistance leads to a decrease in the peripheral blood flow (skin blood flow). Antihypertensive therapy decreases this vasospasm and results in an increase in the peripheral blood flow.\textsuperscript{16,17} Steigerwalt et al\textsuperscript{1} used a duplex scanner to study the PCA and CRA of patients with hypertension and concluded that the loss of autoregulation resulted in a drop in flow velocity in the CRA and PCA; improvement in flow velocity was noted after antihypertensive therapy but did not reach the levels seen in healthy control subjects. The authors comment-

Figure 1. Time-velocity waveform of an OA from a control subject.

Figure 2. Time-velocity waveform of an OA at first diagnosis from a patient with hypertension.
ed that this finding was likely to be associated with increased peripheral vascular resistance or a vasospasm in the eye, as has been found in the peripheral circulation (skin) in patients with hypertension.16,17

In our study, we examined the retrobulbar arteries and could not directly compare our results with those of the larger and smaller arteries mentioned above. However, both the study by Steigerwalt et al1 and our study examined patients with hypertension who had no eye or fundus abnormalities, and both studies had similar findings. Hypertension causes elevation of the RI and PI, indicating increased peripheral resistance or a vasospasm. An improvement in the RI and PI of the PCA and OA after treatment with ACE inhibitors suggests that the effects of hypertension on vessels may in part be reversible, indicating the importance of early diagnosis. Of note is the finding that the PI and RI values of the PCA and OA after treatment decreased significantly, whereas those of the CRA did not. Also, the reduction of the PI and RI of the OA after treatment did not reach the levels of the healthy control subjects; therefore, these differences might be due to different vessel calibrations, as mentioned above in various investigations.14–17

The major limitation of our study was the inability to estimate the time that a patient had essential hypertension or to tell when hemodynamic changes of the retrobulbar circulation appeared during the course of the disease. The hemodynamic changes caused by the hypertension in this study occurred in patients with normal eye examination findings. Hypertension is commonly seen with coexisting systemic and ocular disease, so the PI and RI values obtained from such patient reflect the cumulative effect of disease states that affect retrobulbar circulation. This is important to note because orbital Doppler sonography may be used for diagnosis or follow-up of patients.10–12,18

In previous studies,1,19 patients were asked to suspend their medication for a period. In this study, all patients were seen at the initial diagnosis of hypertension, and even at the first diagnosis, the effect of hypertension on retrobulbar circulation already had started.

The hemodynamic alteration caused by hypertension can have begun even when eye examination findings are normal, and its effects may be partially reversed by antihypertensive drugs, at least in the PCA and OA. Early diagnosis of hypertension gains more importance because the CRA and OA are anatomically and functionally identical to similarly sized intracerebral vessels.20 All these results confirm the importance of regular health examinations and treatment with antihypertensive drugs.

### Table 1. PI and RI values for each artery, for each group: before and after antihypertensive treatment and control

<table>
<thead>
<tr>
<th>Group</th>
<th>CRA</th>
<th>PCA</th>
<th>OA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PI</td>
<td>RI</td>
<td>PI</td>
</tr>
<tr>
<td>Before treatment</td>
<td>1.30 ± 0.23</td>
<td>0.70 ± 0.04</td>
<td>1.12 ± 0.13</td>
</tr>
<tr>
<td>After treatment</td>
<td>1.21 ± 0.33</td>
<td>0.66 ± 0.10</td>
<td>0.93 ± 0.21</td>
</tr>
<tr>
<td>Control</td>
<td>1.06 ± 0.16</td>
<td>0.64 ± 0.05</td>
<td>0.90 ± 0.17</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
References


