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ORIGINAL ARTICLE

Effects of dorzolamide/timolol fixed combination on retrobulbar hemodynamics in pseudoexfoliative glaucoma

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Abstract In our study we aimed to evaluate the short-term effects of dorzolamide/timolol on ocular perfusion pressure and retrobulbar blood flow in patients with pseudoexfoliative glaucoma (PXG). This prospective observational cross-sectional study enrolled 22 eyes of 22 newly-diagnosed patients with PXG in a single center. All of the patients received a fixed combination of dorzolamide/timolol. Besides routine ophthalmologic examination, the retrobulbar hemodynamic parameters in the ophthalmic artery, central retinal artery, and short posterior ciliary arteries were measured in all participants at baseline and the 3rd month using color Doppler imaging. The mean intraocular pressure (IOP) was 22.3 ± 2.1 mmHg at baseline and reduced to 17.4 ± 2.3 mmHg at the 3rd month ($p < 0.05$). None of the retrobulbar parameters, except peak systolic velocity and resistive index in temporal short posterior ciliary arteries, changed significantly on therapy with dorzolamide/timolol fixed combination when the results were analyzed at Month 3. The drug significantly decreased the peak systolic velocity ($p = 0.044$) and reduced the resistive index in 0.04 units, 95% confidence interval 0.03–0.05, ($p < 0.001$) in the temporal short posterior ciliary arteries. This study reports that the retrobulbar hemodynamics might be affected less than expected by dorzolamide/timolol fixed combination in patients with PXG although the reduction of IOP was statistically significant.

Conflicts of interest: All authors declare no conflicts of interests.

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Introduction

Pseudoexfoliation syndrome is one of the most commonly identifiable causes of glaucoma overall [1]. Secondary chronic open-angle glaucoma as a result of blockage of the outflow channels by pseudoexfoliation material has been reported between 20% and 25% of all glaucomas [2]. Some previous studies have shown the accumulation of pseudoexfoliation material in the wall of central retinal artery, short posterior ciliary arteries, and vortex veins. A possible role in disturbance in the blood flow has been reported in patients with pseudoexfoliation syndrome.

The major role of carbonic anhydrase inhibitors (CAIs) on intraocular pressure (IOP) is reducing aqueous humor secretion by inhibition of carbonic anhydrase in the ciliary processes. In addition to IOP lowering effect of this group drugs, dorzolamide and brinzolamide also increase the retrobulbar ocular blood flow by arterial vasodilation [3–6]. Several studies, using different methods, indicated that dorzolamide reduced retrobulbar ocular blood flow [7–9].

The purpose of this study was to compare the effects of dorzolamide/timolol fixed combination on retrobulbar ocular blood flow parameters in patients with pseudoexfoliative glaucoma (PXG) using color Doppler imaging.

Materials and methods

This prospective observational cross-sectional study included 22 eyes of 22 patients (12 females, 10 males) with PXG, who are newly diagnosed at Medipol University School of Medicine, Department of Ophthalmology, Istanbul.

The inclusion criteria were having a white pupillary ruff and the presence of a manifest pseudoexfoliation deposition pattern in the anterior lens capsule, intraocular pressure (IOP) $>$ 21 mmHg with a typical glaucomatous disk, an open chamber angle, and characteristic glaucomatous visual field loss.

Exclusion criteria were eyes lacking clear corneas or those having posterior segment pathologies, previous intraocular surgery, ocular trauma or other intraocular pathology, or who were unable to understand the study or communicate. The study protocol was approved by the Ethics Committee of Medipol University. The tenets of the Declaration of Helsinki were followed and all patients provided informed consent prior to enrollment.

All patients underwent routine ophthalmic examinations including visual acuity, Goldmann tonometry, slit-lamp biomicroscopy, and fundoscopy. Color Doppler imaging measurements were performed by an experienced radiologist with a 7.5-MHz linear transducer using acoustic gel at baseline and 3rd month using Color Doppler imaging (LOGIQ P6; GE Healthcare, Milwaukee and Wisconsin, USA). For the measurements, patients were in the supine position with their eyes closed while looking straight ahead. During the examination minimal pressure was applied on the eye so as not to cause any alterations in retrobulbar blood flow measurements.

Ophthalmic artery blood flow parameters were obtained ~25 mm behind the globe, from the point where the artery crossed the optic nerve. The central retinal artery and vein were measurable ~10 mm behind the retrolaminar portion of the optic nerve. The nasal and temporal short posterior ciliary arteries were examined ~10–20 mm behind the globe just before they branched. Values for each artery, peak systolic velocity, and end diastolic velocity were obtained from the color Doppler signals. The resistive index was calculated by Pourcelot's formula [Resistive Index = (Peak Systolic Velocity − End Diastolic Velocity)/Peak Systolic Velocity]. Mean central retinal vein velocity was calculated from the color Doppler signals.

All statistical analyzes were performed using SPSS version 20 (SPSS Inc., Chicago, IL, USA). A Kolmogorov–Smirnov test was used to test for normality between samples, followed by a Levene test to assess equal variances. Wilcoxon test was used to compare the variables. All p values were two-sided and were considered statistically significant when $p < 0.05$.

Results

The mean age of patients was 63.15 ± 3.82 years (range, 52–68 years old) (12 females, 10 males). The mean IOP was 22.3 ± 2.1 mmHg at baseline and 17.4 ± 2.3 mmHg at the 3rd month. There was a significant decrease in IOP ($p < 0.05$). Retrobulbar hemodynamic variables at baseline and 3 months are given in Table 1. The mean blood flow velocities and resistance indices values, except peak systolic velocity and resistive index in temporal short posterior ciliary arteries, measured at baseline were not different from the values after 3 months of treatment with dorzolamide/timolol in patients with PXG ($p > 0.05$; Figures 1 and 2). The drug significantly reduced the resistive index in the temporal short posterior ciliary arteries from 0.60 (0.02) to 0.54 (0.02) and peak systolic velocity from 3 ± 6.8 cm/s to 2.7 ± 7 cm/s ($p = 0.001$ and $p = 0.044$, respectively).

Discussion

Pseudoexfoliation syndrome, an important cause of glaucoma, presents with an abnormal fibrillar extracellular material production and accumulation in anterior segment tissues pathologically [10]. Recent studies have described various intraocular complications associated with pseudoexfoliation syndrome [2,10–13]. According to electron microscopic investigations in autopsy specimens, pseudoexfoliation fibrils are observed not only in the eye, but also in the heart, lung, liver, gall bladder, and cerebral meninges [10]. Some studies suggested that, pseudoexfoliation syndrome seemed to extensively involve the vascular structures, causing a higher degree of decrease in orbital blood flow and circulation which presumably leads to glaucomatous damage faster than in primary open angle glaucoma patients without pseudoexfoliation [14]. In addition hemodynamic parameters in the retrobulbar vessels, especially in the central retinal artery and short posterior ciliary arteries which are the primary blood fund of the superficial nerve fiber layer, prelaminar, and laminar regions, are significantly lower in patients with PXG than in those healthy participants [14]. PXG has mostly worse outcomes compared with primary open angle glaucoma with high IOP levels, significant differences in pressure