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Original Article

Comparative Analysis of Pupil Diameters in Light and Dark Conditions After Instillation of 0.15% Brimonidine Drops in Eyes With and Without Pseudoexfoliation Syndrome

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Abstract

Objectives: This study aimed to compare pupil diameters in light and dark conditions after instillation of 0.15% brimonidine drops in eyes with and without pseudoexfoliation syndrome (PES).

Methods: Forty eyes of 40 patients in whom 0.15% brimonidine drops were instilled to their right eyes between March 2019 and June 2019 were analyzed in this study. Study groups included 20 subjects without PES (group 1) and 20 patients with PES (group 2). Pupil diameters before and 30 and 90 min after brimonidine application were recorded and analyzed.

Results: In group 1, the mean pupil diameters before brimonidine drop instillation were 4.8±1.2 mm and 5.8±1.2 mm in light and dark conditions, respectively, while those in group 2 were 4.4±1.2 mm and 4.9±1.3 mm, respectively. At 30 min after brimonidine drop instillation, the pupil diameters in light and dark conditions were 4.3±1.1 mm and 5.3±1.0 mm in group 1 and 4.1±1.1 mm and 4.5±1 mm in group 2, respectively. In group 1, the mean pupil diameters at 90 min were 4.2±1.1 mm and 5.1±1.1 mm in light and dark, respectively, and in group 2, they were 4.0±1.1 mm and 4.4±1.2 mm, respectively. In the dark, the pupil diameters before drop instillation were significantly smaller in group 2 than in group 1 ($p \leq 0.05$). A significant difference was found between the groups with respect to the measurements in the dark at 30 min ($p \leq 0.05$). When the differences at 30 and 90 min and the initial pupil diameters in light condition were compared between the groups, the change in the pupil diameter at 30 min was statistically significant ($p \leq 0.05$). At 90 min, differences in both light and dark measurements were statistically significant ($p \leq 0.05$).

Conclusion: Brimonidine causes significant miosis in eyes with PES compared with eyes without PES. Brimonidine may have positive effects on spherical aberrations, glares, and halos. However, inadequate pupillary dilation may make it more difficult to perform cataract surgery and may further increase the complication rate.

Keywords: Brimonidine, pseudoexfoliation, pupil diameter, miosis.

Introduction

Ocular pseudoexfoliation syndrome (PES), which was first described by Lindberg, (1) is characterized by progressive and extensive production and accumulation of gray-white fibrillar material, called pseudoexfoliation material (PEM), in the basement membranes and extracellular matrices in eye tissues such as in the conjunctiva, corneal endothelium, trabecular meshwork, zonules, anterior lens capsule, anterior vitreal surface, optic nerve, and extraocular muscles. Electromicroscopic studies have demonstrated the presence of

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PEM in various organs or tissues, including the kidney, lung, gallbladder, skin, myocardium, blood vessels, liver, meninx, and inner ear (2-5). PES is an important risk factor for the development of secondary open-angle glaucoma (OAG) because of the accumulation of PEM and the degeneration in the trabecular meshwork (2-7).

PES rarely occurs before age 50 years, and its incidence increases markedly with age (2-5). It has a high prevalence in Scandinavia, Ethiopia, and South Africa. In Scandinavia, more than 50% of secondary OAG cases were due to PES. Pseudoexfoliative glaucoma is the most common form of secondary OAG worldwide (2-7).

Except for glaucoma, PES is often associated with fibrillary deposits on anterior segment structures (such as the conjunctiva, lens, iris, zonules, and ciliary processes), peripapillary iris transillumination defects, iris fibrosis, increased pigmentation of the trabecular meshwork, pigmentation anterior to Schwalbe's line (Sampaolesi's line), poor pupillary dilation, and weak zonules (2-5). Especially, poor pupillary dilation and weak zonules increase the difficulty of performing anterior capsulorhexis and may lead to posterior capsular rupture and lens dislocation during cataract surgery (2-5, 8-11). Scotopic, mesopic, and low photopic pupil diameters are smaller in eyes with PES than in eyes without PES (2-5, 8,9,11,12).

Brimonidine tartrate, a selective prejunctional alpha-2 adrenergic receptor agonist, is often used in the treatment of glaucoma and ocular hypertension for the reduction of intraocular pressure and neuroprotection (13-17). Brimonidine was reported to cause a significant reduction in pupil size due to the suppression of the sympathetic nervous system under scotopic conditions, so it was used to reduce night vision difficulties, such as halos, starbursts, glares, and monocular diplopia, after refractive surgery. Briefly, brimonidine inhibits pupil dilation under scotopic vision (18,19). Brimonidine reduces norepinephrine release in the synapse.20 Pupillary size is an important indicator of patient satisfaction, as abnormal pupil size can cause deterioration of night vision quality, halos, glare, and spherical aberrations (21,22). Studies have reported that brimonidine tartrate reduces pupil diameter and thus has positive effects on visual functions (8,9,23). With this knowledge, brimonidine tartrate may have a pupil diameter-reducing effect on eyes with PES and thus may have a positive effect on the patient's visual functions. This study aimed to investigate the effect of brimonidine tartrate on the pupil diameter of eyes with PES.

Methods

Ethics and General Information

This study adhered with principles of the Declaration of Helsinki. Informed consent was obtained from the patients and volunteers. As a pilot work, this institutional controlled comparative study enrolled 40 eyes of 40 patients in whom 0.15% brimonidine were instilled to their right eyes between March 2019 and June 2019.

Clinical Examinations

All participants underwent full ophthalmologic examination including visual acuity, slit-lamp biomicroscopy, intraocular pressure measurement, and dilated fundoscopy. PES was diagnosed based on the presence of PEM deposited on the anterior lens capsule and/or pupillary borders. The demographic characteristics of the patients were recorded.

Groups

Group 1 included 20 individuals without PES, and group 2 included 20 patients with PES. Patients who have intraocular pathology that affected pupillary response, who received medication that affected the pupillary size, and who had irregular and non-symmetrical pupils, iris abnormality including rubeosis iridis, and optic nerve diseases were excluded from the study.

Measurements

Pupil diameters in both light and dark conditions before and 30 and 90 min after brimonidine instillation were recorded. The pupil diameters were measured with the ZEISS IOLMaster 500 Biometer.

Statistical Analysis

The mean pupil diameters obtained at two different amplitudes, including dark and light settings, were compared within the group using Student's t-test. Results were analyzed using IBM SPSS Statistics for Windows version 22.0 (IBM Corp., Armonk, NY, USA).

Results

The mean patient ages in groups 1 and 2 were 67.2±10.3 and 69.2±12 years, respectively. In group 1, the mean pupil diameters before brimonidine instillation were 4.8±1.2 mm and 5.8±1.2 mm in light and dark, respectively, and those in group 2 were 4.4±1.2 mm and 4.9±1.3 mm, respectively. At 30 min after brimonidine instillation, the pupil diameters in light and dark were 4.3±1.1 mm and 5.3±1.0 mm in group 1 and 4.1±1.1 mm and 4.5±1 mm in group 2, respectively. The mean pupil diameters in light and dark at 90 min were 4.2±1.1 mm and 5.1±1.1 mm in group 1 and 4.0±1.1 mm and 4.4±1.2 mm in group 2, respectively. Before brimonidine instillation, the pupil diameters in the dark were significantly smaller in group 2 than in group 1 ($p \leq 0.05$). A significant difference was found between the groups with respect to the measurements in the dark at 30 min ($p \leq 0.05$). When the differences at 30 and 90 min and the initial pupil diameters were compared between the groups, the change in pupil size

in the light at the 30 min was statistically significant (p≤0.05). At 90 min, differences in both light and dark measurements were statistically significant (p≤0.05). The mean pupil diameters in the light and dark are shown in Table 1 and Table 2, respectively.

Discussion

The characteristic pupillary findings in PES include pigment loss from the iris sphincter, irregular papillary borders, and presence of grayish PEM deposits at the pupillary border. PEMs are usually observed on the crystalline lens. PEM deposits on the iris basement membrane and bridging of the iris crypts may occur. In most cases with PES, these pupillary abnormalities result in poor or absence of pupillary dilation or miotic rigid pupil (1-7).

PEM has been histopathologically demonstrated in the pigment epithelium, stroma, smooth muscles, and vessels of the iris. Additionally, PEM deposits have been reported to be associated with degenerative changes in the vascular basement membranes, vascular smooth muscle cells, and vascular endothelial cells and loss of iris cellularity. PEM within the stroma and the muscular layer of the iris causes stiffening of the iris, posterior synechiae between the iris pigment epithelium and anterior lens capsule, mechanical restriction of pupillary movements, mechanical obstruction, muscular degeneration or atrophy in the sphincter and/or dilator muscles, and fibrotic changes in the iris sphincter muscle (2-4,12). On the contrary, the deposition in the vascular endothelium of the iris may cause iridial vascular narrowing or obliteration, which reduces the number of iris vessels, iridial ischemia and neovascularization, and vessel wall degeneration in advanced stages. Additionally, the pupils of patients with PES showed a reduced response to mydriatic agents. All the above-mentioned events may play a role in poor pupillary dilation (8-12).

PES may cause some difficulties during cataract surgery due to poor or inadequate pupillary dilation. A small pupil diameter and zonular fragility are presumed to be the most important risk factors for the desired curvilinear capsulorhexis and increased risk for anterior and posterior capsule tears, iris trauma, capsular rupture, and vitreous loss during cataract surgery (2-5,8,9,11). Additionally, PEM deposits within the iris stromal vessels can increase the risk for perioperative intraocular hemorrhage (2-5,10,11).

On the contrary, histochemical studies have demonstrated that smaller pupil diameter increases visual performance in low light by reducing high-order aberrations (24). Moreover, alpha-2 receptor agonists were shown to reduce the pupil diameter as well as lower the intraocular pressure (13,14). Although studies have shown the effect of brimonidine tartrate on pupil diameter in normal eyes, to the best of our knowledge, no study has evaluated pupil diameter in the eyes with PES.

The generalization of the results were limited by the small sample size, lack of measurement of visual function parameters, and lack of evaluation of the effects of brimonidine application after >90 min.

Although brimonidine tartrate makes significant miosis in eyes with PES compared with eyes without PES, the use of brimonidine eye drops in patients with PES may have pos-

Table 1. Mean values of pupillary diameters at the light in study groups

Group	n	Mean pupillary diameter at baseline in light (mm)	Mean pupillary diameter at 30 min in light (mm)	Mean pupillary diameter at 90 min in light (mm)
Group 1	20	4.8±1.2 mm*	4.3±1.1 mm*	4.2±1.1 mm*
Group 2	20	4.4±1.2 mm	4.1±1.1 mm	4.0±1.1 mm

*Pupillary diameters of eyes in group 2 were significantly lower than those in group 1 (p≤0.05).

Table 2. Mean values of pupillary diameters at dark in study groups

Group	n	Mean pupillary diameter at baseline in dark (mm)	Mean pupillary diameter at 30 min in dark (mm)	Mean pupillary diameter at 90 min in dark (mm)
Group 1	20	5.8±1.2 mm*	5.3±1.0 mm*	5.1±1.1 mm*
Group 2	20	4.9±1.3 mm	4.5±1 mm	4.4±1.2 mm

*Pupillary diameters of eyes in group 2 were significantly lower than those in group 1 (p≤0.05).

itive effects on unwanted visual problems, such as spherical aberrations, glares, and halos, especially on night vision functions. However, inadequate pupillary dilation may make it difficult to perform cataract surgery and may further increase complication rate. Therefore, the miotic effect of brimonidine on PES eyes should be investigated in larger case studies.

Disclosures

Ethics Committee Approval: The study was designed acoording to the Helsinki Declaration and approved by the institutional ethics committee. Informed consents were obtained from the patients and the volunteers.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Involved in design and conduct of the study (SC, CB, BT); preparation and review of the study (SC, CB, BT); data collection (SC, CB, .BT); and statistical analysis (SC, CB, BT).

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