

Administration of the fixed combination of latanoprost 0.005% and timolol 0.5% in glaucoma patients with an intraocular pressure over 30 mmHg

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Purpose: To evaluate the intraocular pressure (IOP) reducing effect of a fixed combination of 0.005% latanoprost and 0.5% timolol in patients with an IOP of 30 mmHg or higher.

Design: Prospective, randomized clinical trial.

Participants: Twenty-eight patients.

Methods: Patients had received no prior medical glaucoma treatment. Routine ophthalmic examinations and visual field tests were performed before and after treatment for each patient.

Results: Mean IOP was 32.28 ± 0.92 mmHg before treatment. Mean IOP levels were 18.75 ± 0.68 for the first day, 17.96 ± 0.90 for the first week and 17.64 ± 0.66 for the first month after treatment.

Conclusion: A fixed combination of latanoprost 0.005% and timolol 0.5% is effective in significantly reducing IOP in glaucoma patients with an IOP greater than 30 mmHg.

Keywords: latanoprost, timolol, combination, glaucoma, intraocular pressure

Introduction

Glaucoma needs to be treated in order to prevent development of additional impairment in the optic disc in the long term and to maintain the intraocular pressure (IOP) level to restrict any potential loss in the visual field or visual acuity.¹ IOP is a correctable factor in glaucoma, and a reduction in IOP can typically be achieved by medication, laser treatment or surgery. The standard approach for medication is to initiate a monotherapy with an individual agent.² The prostaglandin analogues, the most common medications indicated, can reduce IOP by up to 30%. Particularly when used in combination, instilling a drop immediately after the first drop of the other agent will result in both removal of the first agent from the field and reduced concentration of the second agent. Studies have shown that administration of more than two drops daily directly reduces patient compliance. Fixed combinations of glaucoma medications reduce the number of bottles of medication patients need to purchase, which can represent a cost saving for those whose drug plan requires a per bottle copayment.³ Fixed combinations also represent a reduction in the number of drops per day required to be instilled.³

In this study we evaluated the efficacy of a fixed combination of 0.005% latanoprost and 0.5% timolol in lowering the IOP as a first-line therapy in glaucoma patients with an IOP greater than 30 mmHg.

Materials and methods

The study included a total of 28 patients (15 females, 13 males), who had been initially diagnosed with glaucoma in the Glaucoma Unit of the Eye Clinic of the Fatih Sultan Mehmet Training and Research Hospital. Mean age was 58.64 ± 8.84 years. Patients with primary open angle glaucoma, pseudoexfoliation glaucoma or pigmentary

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Table 1 Demographic characteristics of patients

	Type of glaucoma	Primary open angle glaucoma	Pseudoexfoliative glaucoma	Pigmentary glaucoma
Female	15 (53.57%)	10 (35.71%)	4 (14.28%)	1 (3.57%)
Male	13 (46.42%)	11 (39.28%)	2 (7.14%)	
Total	28	21 (75%)	6 (21.42%)	1 (3.57%)

glaucoma were eligible for the study as well as those who had no prior glaucoma treatment, and an IOP higher than 30 mmHg at two measurements within the same day. Pre- and post-treatment measurements for visual acuity, anterior segment and fundus examination, IOP by Goldmann applanation tonometry, visual field testing (Humphrey 30–2 full threshold) and central corneal thickness were performed for each patient. The IOP measurements were obtained at 8 AM and 4 PM. At each time point, two measurements were taken to provide the mean IOP value. Patients with a contraindication for latanoprost and timolol therapy, a history of angle closure glaucoma, uveitis, surgery or any topical or systemic nonsteroidal anti-inflammatory drug and steroid use were excluded from the study. One drop of the latanoprost–timolol fixed combination was applied at 9 PM. The pre- and post-treatment IOP values at day 1, week 1 and month 1 were compared statistically using the Wilcoxon signed-rank test.

Results

Of the eyes included in the study, 21 had primary open angle glaucoma, 6 had pseudoexfoliative glaucoma, and 1 pigmentary glaucoma. Patient demographic characteristics are shown in Table 1. Treatment was discontinued in 1 patient due to lack of efficacy. IOP was diminished only 5% in this patient and was not included in the analyses. The mean pre-treatment IOP was 32.28 ± 0.92 mmHg. Following treatment, mean IOP values were: 18.75 ± 0.68 mmHg ($p < 0.05$) at day 1; 17.96 ± 0.90 mmHg ($p < 0.05$) at week 1; and 17.64 ± 0.66 mmHg ($p < 0.05$) at month 1 (Table 2). The reduction in the IOP was -13.53 ± 0.24 mmHg, 14.32 ± 0.02 mmHg, and 14.64 ± 0.26 mmHg at day 1, week 1 and month 1, respectively. A statistically significant

difference in IOP values compared to the pre-treatment period was observed for all intervals. The side effects included burning and stinging in 1 patient, redness in 1 patient, and itching in 1 patient.

Discussion

Higher concentrations of prostaglandins (PG) may elevate IOP, resulting in inflammation of the eye, whereas lower concentrations may reduce IOP by increasing the uveoscleral outflow. Latanoprost, released commercially several years ago, is an analogue of an F2 α prostaglandin and is highly selective for the FP receptor.⁴ PGs bind to the receptors on the ciliary muscles, affecting the uveoscleral outflow. By increasing the outflow of the aqueous humor through the uveoscleral pathway, latanoprost has an additive effect with agents that elevate the trabecular flow and decrease the aqueous production. It is used once daily.⁴ IOP can be significantly reduced when latanoprost is added to the regimen in patients with open angle glaucoma which could not be controlled by timolol.

Beta-blockers or prostaglandins are used in the first-line therapy for many glaucoma patients. In cases where a more effective therapy is required, fixed combination drops with two active agents should be preferred instead of a second agent. Previous studies have shown that the latanoprost–timolol fixed combination therapy is more effective than the monotherapies alone.⁵ Shin et al showed, similar to our study, that the latanoprost–timolol fixed combination is an effective and safe treatment option in reducing IOP.⁶ We found that the latanoprost–timolol fixed combination used as a first-line therapy reduced IOP by approximately 43% within a short period of time. Furthermore, it has been reported that

Table 2 Pre-treatment and post-treatment intraocular pressure (IOP) values

Pre-treatment IOP (mean mmHg $\pm$ SD)	Post-treatment IOP Day 1 (mean mmHg $\pm$ SD)	Post-treatment IOP week 1 (mean mmHg $\pm$ SD)	Post-treatment IOP Month 1 (mean mmHg $\pm$ SD)	Post-treatment IOP Month 6 (mean mmHg $\pm$ SD)	Pre-treatment visual field mean deviation (dB)	Post-treatment IOP mean deviation (dB)
32.28 ± 0.92	18.75 ± 0.68 ($p < 0.05$)	17.96 ± 0.90 ($p < 0.05$)	17.64 ± 0.66 ($p < 0.05$)	17.46 ± 0.50 ($p < 0.05$)	-3.1 ± 3.9	-3.3 ± 4.1 ($p > 0.05$)

the mean reduction obtained by a latanoprost-based fixed combination was 1.0 mmHg higher compared with a dorzolamide-based fixed combination twice a day, along a diurnal curve with three timepoints.⁶ It has been demonstrated that the latanoprost–timolol fixed combination therapy decreases IOP by more than 2.9 mmHg compared with timolol alone, and by more than 1.1 mmHg compared with latanoprost alone.⁷ Although diverse rates of iris pigmentation have been reported in previous studies,^{8,9} we believe that lack of any iris pigmentation in our cases might have been associated with the shorter study period.

We believe that our study group was preliminary, consisting of a limited number of patients, and patient adherence to the therapy was closely related to once-daily dosage. In conclusion, our short study has shown that the 0.005% latanoprost and 0.5% timolol fixed combination is effective in significantly reducing IOP in glaucoma patients with an IOP greater than 30 mmHg.

Disclosures

The authors declare no conflicts of interest.

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