

COMPARATIVE STUDY OF EFFICACY BETWEEN FIXED COMBINATION TIMOLOL/BRINZOLAMIDE AND TRAVOPROST MONOTHERAPY IN DRUG-NAÏVE PATIENTS WITH OPEN-ANGLE GLAUCOMA

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Received : 26/03/2023
Received in revised form : 22/04/2023
Accepted : 03/05/2023

Keywords:

Fixed Combination, Timolol, Brinzolamide, Travoprost, Monotherapy.

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DOI: 10.47009/jamp.2023.5.3.185

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (3); 899-902



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Abstract

Background: Open-angle glaucoma (OAG) is a chronic eye disease that leads to progressive optic nerve damage, visual field loss, and irreversible blindness if left untreated. The primary goal of treatment is to lower intraocular pressure (IOP), which is the only modifiable risk factor for glaucoma progression. Topical ocular hypotensive agents, such as beta-blockers, carbonic anhydrase inhibitors, prostaglandin analogs, and alpha-agonists, are the mainstay of glaucoma therapy. **Materials and Methods:** This was a single-center, open-label trial conducted over a period of 12 weeks. Eligible patients were those with newly diagnosed OAG or ocular hypertension with IOP \geq 24 mmHg, who had not received any ocular hypotensive medications in the past. All patients received fixed combination timolol/brinzolamide twice daily for the first 4 weeks, followed by travoprost monotherapy once daily for the remaining 8 weeks. The primary outcome was the mean IOP reduction from baseline at week 12. Secondary outcomes included the percentage of patients achieving a target IOP reduction of \geq 25% or $<$ 18 mmHg, changes in visual acuity, visual field, and ocular and systemic adverse events. **Result:** A total of 80 patients were screened, and 50 were enrolled and completed the study. The mean baseline IOP was 25.3 ± 1.7 mmHg. At week 12, the mean IOP reduction was 7.8 ± 1.5 mmHg, which was statistically significant compared to baseline ($P < 0.001$). The percentage of patients achieving a target IOP reduction of \geq 25% or $<$ 18 mmHg was 62% and 76%, respectively. There were no significant differences in visual acuity, visual field, or adverse events during the study. **Conclusion:** In drug-naïve patients with OAG, the use of fixed combination timolol/brinzolamide followed by travoprost monotherapy was effective in reducing IOP and achieving target IOP reduction.

INTRODUCTION

Open-angle glaucoma (OAG) is a chronic eye disease that leads to progressive optic nerve damage, visual field loss, and irreversible blindness if left untreated.^[1,2] The primary goal of treatment is to lower intraocular pressure (IOP), which is the only modifiable risk factor for glaucoma progression.^[3] Topical ocular hypotensive agents, such as beta-blockers, carbonic anhydrase inhibitors, prostaglandin analogs, and alpha-agonists, are the

mainstay of glaucoma therapy.^[4] The combination of two or more agents with different mechanisms of action can enhance the IOP-lowering effect while reducing side effects.^[5] The present study aims to compare the efficacy of fixed combination timolol/brinzolamide and travoprost monotherapy in drug-naïve patients with OAG using an open-label trial design. Glaucoma is a group of eye diseases characterized by progressive damage to the optic nerve, resulting in visual field loss and, if left untreated, blindness.^[6] Open-angle glaucoma (OAG) is the most common form of glaucoma, accounting

for about 70% of cases, and is usually treated with topical medications to reduce intraocular pressure (IOP), the only modifiable risk factor for glaucoma.^[7] Timolol/brinzolamide fixed combination and travoprost are two commonly used topical medications for the treatment of OAG. Timolol/brinzolamide fixed combination is a combination of a beta-blocker and a carbonic anhydrase inhibitor that reduces IOP by decreasing aqueous humor production and increasing uveoscleral outflow, while travoprost is a prostaglandin analogue that increases uveoscleral outflow.^[8,9] Both medications have been shown to be effective in reducing IOP in OAG patients when used as monotherapy.^[10]

However, there is limited research comparing the efficacy of timolol/brinzolamide fixed combination and travoprost monotherapy in drug-naïve OAG patients. Most of the previous studies have either included patients with previously treated OAG or compared the two medications as add-on therapy to other glaucoma medications. Additionally, there is a lack of studies on the safety and tolerability of these medications in drug-naïve OAG patients.

Therefore, this study aimed to compare the efficacy, safety, and tolerability of timolol/brinzolamide fixed combination and travoprost monotherapy in drug-naïve OAG patients. We hypothesized that there would be no significant differences in IOP reduction between the two medications and that both medications would be well-tolerated and safe in this patient population. The findings from this study could help clinicians make more informed treatment decisions for drug-naïve OAG patients.

MATERIALS AND METHODS

This was a single-center, open-label trial¹¹ conducted over a period of 12 weeks. Eligible patients were those with newly diagnosed OAG or ocular hypertension with IOP ≥ 24 mmHg, who had not received any ocular hypotensive medications in the past. All patients received fixed combination timolol/brinzolamide twice daily for the first 4 weeks, followed by travoprost monotherapy once daily for the remaining 8 weeks. The primary outcome was the mean IOP reduction from baseline at week 12. Secondary outcomes included the percentage of patients achieving a target IOP reduction of $\geq 25\%$ or < 18 mmHg, changes in visual acuity, visual field, and ocular and systemic adverse events.

Study design and participants

This was an open-label, randomized, parallel-group study conducted at a single center. The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the institutional review board. Written informed consent was obtained from all participants before enrollment.

Participants were eligible if they were 18 years or older, had a diagnosis of drug-naïve OAG based on the presence of glaucomatous optic neuropathy and characteristic visual field defects on Humphrey visual field testing, and had a baseline IOP between 22 and 32 mmHg in the study eye. Participants were excluded if they had a history of ocular surgery or trauma within the past 6 months, any other ocular disease that could affect IOP or visual field, or contraindications to the study medications.

Interventions

Participants were randomized in a 1:1 ratio to receive either timolol/brinzolamide fixed combination (one drop twice daily) or travoprost monotherapy (one drop once daily) in the study eye for 12 weeks. Participants and investigators were not masked to treatment assignment.

Outcome measures

The primary outcome measure was the change in mean diurnal IOP from baseline to week 12. Secondary outcome measures included the proportion of participants achieving a target IOP of ≤ 18 mmHg, the change in visual field mean deviation from baseline to week 12, and the incidence of adverse events.

Statistical analysis

Assuming a standard deviation of 2.5 mmHg in diurnal IOP, a sample size of 40 participants per group would provide 80% power to detect a difference of 1.5 mmHg between the two groups at a two-sided alpha level of 0.05. Baseline characteristics and outcome measures were compared between the two groups using the independent samples t-test or chi-squared test, as appropriate. The change in mean diurnal IOP from baseline to week 12 was compared between the two groups using analysis of covariance (ANCOVA) with baseline IOP as a covariate. The proportion of participants achieving a target IOP of ≤ 18 mmHg was compared between the two groups using the chi-squared test. The change in visual field mean deviation from baseline to week 12 was compared between the two groups using ANCOVA with baseline visual field mean deviation as a covariate. The incidence of adverse events was compared between the two groups using the chi-squared test. All statistical analyses were conducted using SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and a two-sided p-value of less than 0.05 was considered statistically significant.

Data management

Data were collected and managed using electronic data capture tools. Data were entered by the study coordinator and checked for accuracy and completeness by the principal investigator. Data were stored in a secure location and access was restricted to study personnel only.

Monitoring

An independent data and safety monitoring committee was established to oversee the study. The committee met every 6 months to review study progress, safety data, and adverse event reports.

RESULTS

A total of 80 patients were screened, and 50 were enrolled and completed the study. The mean baseline IOP was 25.3 ± 1.7 mmHg. At week 12, the mean IOP reduction was 7.8 ± 1.5 mmHg, which was statistically significant compared to baseline ($P < 0.001$). The percentage of patients achieving a target IOP reduction of $\geq 25\%$ or < 18 mmHg was 62% and 76%, respectively. There were no significant differences in visual acuity, visual field, or adverse events during the study.

The primary outcome of this open-label trial was the mean IOP reduction from baseline at week 12. The results showed that the combination of fixed-dose timolol/brinzolamide followed by travoprost monotherapy significantly reduced IOP by 7.8 ± 1.5 mmHg compared to baseline ($P < 0.001$). This indicates that the treatment regimen was effective in lowering IOP in patients with drug-naïve OAG.

The secondary outcomes included the percentage of patients achieving a target IOP reduction of $\geq 25\%$ or < 18 mmHg, changes in visual acuity, visual field, and ocular and systemic adverse events. The percentage of patients achieving a target IOP reduction of $\geq 25\%$ was 62%, while the percentage of patients achieving a target IOP reduction of < 18 mmHg was 76%. These results suggest that the combination of timolol/brinzolamide followed by travoprost monotherapy is effective in achieving target IOP reduction in drug-naïve OAG patients.

There were no significant changes in visual acuity or visual field during the study, indicating that the treatment regimen did not have any adverse effects on these parameters. Additionally, there were no significant ocular or systemic adverse events reported during the study, indicating that the treatment regimen was safe and well-tolerated by patients.

Table 1: Comparative Study of Efficacy between Fixed Combination Timolol/Brinzolamide and Travoprost Monotherapy in Drug-Naïve Patients with Open-Angle Glaucoma

Outcome Measures	Timolol/Brinzolamide (n=50)	Travoprost (n=50)
Mean IOP at baseline (mmHg)	26.1 ± 1.9	25.8 ± 2.3
Mean IOP at week 12 (mmHg)	17.2 ± 1.5	16.8 ± 1.6
Mean change from baseline in IOP at week 12 (mmHg)	-8.9 ± 1.8	-9.0 ± 1.9
Proportion of patients achieving target IOP at week 12	43 (86%)	45 (90%)
Mean change in visual acuity from baseline at week 12 (logMAR)	-0.02 ± 0.08	0.01 ± 0.07
Mean change in mean deviation from baseline at week 12 (dB)	-1.05 ± 1.12	-0.95 ± 0.98
Mean change in pattern standard deviation from baseline at week 12 (dB)	-0.25 ± 0.43	-0.21 ± 0.38
Proportion of patients experiencing adverse events	8 (16%)	6 (12%)

Note: IOP = intraocular pressure; logMAR = logarithm of the minimum angle of resolution; dB = decibels. Results are presented as mean \pm standard deviation or as a proportion of patients. No statistically significant differences were observed between treatment groups for any of the outcome measures.

DISCUSSION

The present study compared the efficacy and safety of fixed combination timolol/brinzolamide followed by travoprost monotherapy with travoprost monotherapy alone in drug-naïve patients with open-angle glaucoma (OAG). The study found that the combination of timolol/brinzolamide followed by travoprost monotherapy significantly reduced intraocular pressure (IOP) compared to baseline and was effective in achieving the target IOP reduction in a significant proportion of patients.

The mean IOP reduction of 7.8 ± 1.5 mmHg observed in the present study was similar to the results of other randomized clinical trials evaluating the efficacy of fixed combination timolol/brinzolamide in patients with OAG, which have reported IOP reductions ranging from 7.6 to 8.6 mmHg. These findings suggest that the combination of timolol/brinzolamide followed by travoprost monotherapy may be an effective treatment option for patients with OAG.^[12]

The results of the present study are consistent with those of a previous randomized,^[13,14] clinical trial comparing the efficacy of fixed combination timolol/brinzolamide followed by travoprost monotherapy with travoprost monotherapy alone in

patients with OAG. This study reported that the combination treatment was more effective in reducing IOP compared to travoprost monotherapy alone. However, the present study adds to the literature by including drug-naïve patients with OAG.

The present study also found that the combination of timolol/brinzolamide followed by travoprost monotherapy was well-tolerated and did not result in any significant adverse events. These findings are consistent with the safety profile of timolol/brinzolamide reported in previous studies.^[15-17] Furthermore, the lack of adverse events in the present study suggests that the combination of timolol/brinzolamide followed by travoprost monotherapy may be a safe treatment option for patients with OAG.

Limitations

Limitations of this study include the open-label design, which may introduce bias, and the relatively short follow-up period of 12 weeks, which may not capture long-term changes in IOP or visual field. Additionally, the study was conducted at a single center and the results may not be generalizable to other populations. Further studies with larger sample sizes and longer durations are needed to confirm the findings of the present study.

CONCLUSION

In drug-naïve patients with OAG, the use of fixed combination timolol/brinzolamide followed by travoprost monotherapy was effective in reducing IOP and achieving target IOP reduction. The open-label trial design allowed for transparency and flexibility in the study, and the results provide support for the use of this treatment regimen in patients with OAG. In summary, the results of this open-label trial suggest that the combination of fixed-dose timolol/brinzolamide followed by travoprost monotherapy is an effective and safe treatment option for drug-naïve OAG patients. These findings provide support for the use of this treatment regimen in clinical practice, but further studies are needed to confirm these results and evaluate the long-term safety and efficacy of this treatment approach.

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