

Original articles

Comparison of the efficacy and safety of bimatoprost (0.03 %) and travoprost (0.004 %) in patients with primary open angle glaucoma

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Abstract

Purpose: To compare the efficacy and safety of bimatoprost (0.03 %) and travoprost (0.004 %) in patients with primary open angle glaucoma (POAG). **Subjects and methods:** Patients with POAG were randomized to receive either bimatoprost or travoprost once daily. Detailed ocular examination was done and intraocular pressure (IOP) was measured at 9.00 am, 1.00 pm and 4.00 pm at the baseline and at 1, 2, 4, 6 and 12 weeks of therapy. **Results:** A total of 31 patients were analysed. The patients were randomly divided into two groups (Bimatoprost group = 16; Travoprost group = 15). Both the groups had a statistically significant reduction from the baseline IOP at all follow up visits at 9.00 am, 1.00 pm and 4.00 pm. The mean IOP decreased from a baseline of 25 ± 2.32 mm Hg to 15.93 ± 1.79 mm Hg after 12 weeks in the bimatoprost group ($p < 0.001$), and from 24.2 ± 1.60 mm Hg to 16.53 ± 1.56 mm Hg in the travoprost group ($p < 0.001$). A better mean reduction of IOP was obtained with bimatoprost than with travoprost at the end of the study at 12 weeks ($p = 0.03$). Mild ocular redness was the commonest side effect in both the groups but was not significant in either group. **Conclusion:** Both drugs lowered IOP effectively but bimatoprost showed a greater reduction in the mean IOP than did travoprost at 12 weeks and both are safe for ocular use.

Key-words: intra ocular pressure, bimatoprost, travoprost

Introduction

Elevated intraocular pressure (IOP) has been identified as a major risk factor for primary open-angle glaucoma (POAG) and thus drugs that reduce IOP have the potential to prevent or delay optic nerve damage and prolong vision (Cantor et al, 2006). An optimal agent is one that produces clinically significant reduction in IOP, controls diurnal fluctuations, has a favorable adverse event profile, convenient dosing schedule and exposes patients

to least number of preservatives (Higginbotham et al, 2002). The once-daily prostaglandin analogues (PGAs; bimatoprost, latanoprost and travoprost) provide significant reductions in IOP and have become the most commonly used first-line agents in glaucoma (Hedman et al, 2000; Netland et al, 2001; Van der Valk et al, 2005; McKee et al, 2005).

Bimatoprost (0.03%) is a synthetic analogue of prostamide and a potent ocular hypotensive agent (Noecker, 2003). It acts by increasing aqueous humor outflow through both the trabecular route and the uveoscleral pathway (Kammer et al, 2010; Brandt et al, 2001; Gandolfi et al, 2001). Travoprost

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0.004%, is a synthetic prostaglandin F_{2a} receptor agonist, lowers IOP by increasing uveoscleral outflow (Parrish et al, 2003). Following absorption into the eye, the free acid form of travoprost interacts with the endogenous FP prostanoid receptor, to enhance aqueous humor outflow and lower intraocular pressure (Cantor et al, 2004). The IOP Lowering efficacy of bimatoprost and travoprost monotherapy has been reported in recent clinical trials to be superior to that of timolol and roughly equivalent to that of latanoprost (Netland et al, 2001; Parrish et al, 2003; Cantor et al, 2004; Orengo et al, 2003).

The purpose of the present study was to compare the IOP lowering efficacy and safety of bimatoprost and travoprost in patients with primary open angle glaucoma and to the best of our knowledge there is no study in peer reviewed literature available on Indian eyes to compare the efficacy of travoprost versus bimatoprost.

Subjects and methods

Study design

This prospective and randomized clinical study was undertaken to compare the IOP lowering efficacy and safety of topical Bimatoprost and Travoprost in patients with POAG. It was conducted in accordance with declaration of Helsinki and was approved by the institutional Review Board. All patients received a thorough explanation of the study design and aims. Informed consent was taken from all the patients who participated in the study.

Enrolled patients were men or women of at least 18 yrs with a clinical diagnosis of POAG and whose untreated IOP in each eye was at least 21 mmHg and no more than 34 mmHg. Patients who were already using some kind of ocular hypotensive drugs completed a washout of all drugs of appropriate duration before study entry (6 weeks for prostaglandin analogues; 4 weeks for topical α blockers; 2 weeks for adrenergic agents or carbonic anhydrase inhibitors; and 1 week for miotics).

Primary exclusion criteria included history of ocular inflammation or infection within the last 3 months, history of any intraocular surgery including laser procedures, known sensitivity to Bimatoprost or Travoprost or its preservative, any ocular disease other than open angle glaucoma that would interfere with study parameters, secondary open angle glaucoma, combined mechanism glaucoma or narrow angle glaucoma, concomitant usage of any other topical drugs and use of systemic medications which may have an effect on the study parameters.

Intervention and outcome measures

After meeting all inclusion criteria and completing a washout of any ocular hypotensive agents (if needed), patients were randomized to receive either bimatoprost 0.03% once daily or travoprost 0.004% once daily. Baseline evaluations included medical and ophthalmic history and a complete ophthalmic examination (visual acuity, slit lamp biomicroscopy, visual field examination using automated perimetry, fundus examination with 90 D lens and measurement of IOP at 9.00 am, 1.00 pm and 4.00 pm).

After the baseline evaluation patients were instructed to instill one drop of the study medication in each eye once daily at 9.00 pm and were scheduled for follow-up visits at 1 weeks, 2 weeks, 4 weeks, 6 weeks and 12 weeks. IOP was measured at 9.00 am, 1.00 pm and 4.00 pm during all the follow up visits. IOP was measured using a calibrated Goldmann applanation tonometer.

Follow up study visits included an interim history and complete ocular examination. Patients were asked about adverse events and compliance, and their responses were rated on a 5 point scale of severity (0, none; 0.5, trace; 1, mild; 2, moderate; and 3, severe).

The primary outcome measures were the mean change in IOP from baseline and the percentage reduction of IOP at 9.00 am, 1.00 pm and 4.00 pm after 12 weeks. Secondary outcome measures included the incidence of adverse events.



Statistical analysis

The data for each patient was collected as per protocol and statistically analyzed. All data including demographic information, clinical examination, and both qualitative and quantitative data were entered into a database software programme. Nominal categorical variables were analysed using Chi Square test. Within group changes from baseline were analysed using the Wilcoxon signed rank test and Mann Whitney test. Continuous variables were analysed using ANOVA, and within group changes from baseline analysed using paired *t* tests with the help of SPSS (Version 15.0).

Results

Patient demographics and disposition

In all, 31 patients were enrolled in the study. The mean age of the patients in the bimatoprost group was 57.53 years and 53.60 years in the travoprost group and this difference was not statistically significant ($p = 0.375$). There was a female predominance observed in the bimatoprost group (62.5% females & 37.5% males) and male predominance in the travoprost group (46.7% females & 53.3% males) but there was no statistically significant difference between the two groups, when compared for gender distribution ($p=0.211$). There was no statistically significant difference in age and gender between the 2 groups (Table I).

Outcome measures

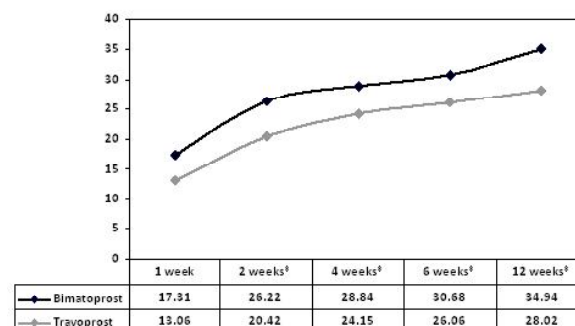
No significant differences were observed in mean baseline IOP at any diurnal time point. The mean IOP reduction from baseline to 12 weeks in the bimatoprost group was 36.28% at 9.00 am, 34.5% at 1.00 pm and 34.8% at 4.00 pm. With travoprost it was 31.6% at 9.00 am, 28.7% and 27.08% at 1.00 pm and 4.00 pm respectively. The decrease in IOP from baseline in bimatoprost group was greater than that in travoprost group at each follow

up visit. At the end of the study period (12 weeks) decrease in IOP in bimatoprost group was 34.94% whereas in travoprost group it was 28.02%. The difference was statistically significant ($p=0.03$) (Figure I).

Comparisons were also done at the various times planned in the study. Both study drugs provided significant IOP reductions from baseline at 9:00 am at all study visits ($p<0.001$), but the mean reductions in the bimatoprost group were significantly greater than those in the travoprost group. When the two groups were compared for the IOP reduction from the baseline, it was observed that at 9.00 am a better reduction was obtained with bimatoprost at each of the follow up visits as compared to travoprost. However it reached statistically significant levels only at 12 weeks ($p=0.024$) (Figure II).

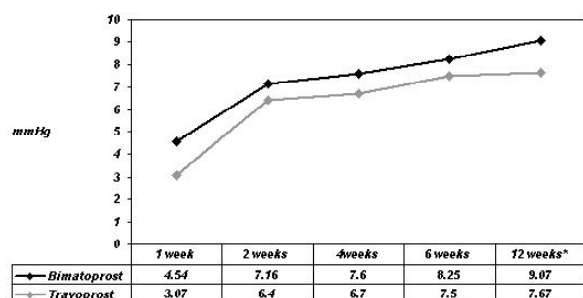
Table I: Age and gender distribution of the study groups.

Age	Bimatoprost		Travoprost	
	No. of Subjects	%	No. of Subjects	%
41-50	4	25	5	33.3
51-60	5	31.25	5	33.3
61-70	7	43.8	5	33.3
Gender				
Male	6	37.5	8	53.3
Female	10	62.5	7	46.7
Total	16	100	15	100



* = p value < 0.05

Figure I: 24-hour mean IOP reduction (%) in group I and group II.



* = p value < 0.05

Figure II: Mean reduction in IOP from baseline in study groups at 9.00 am.

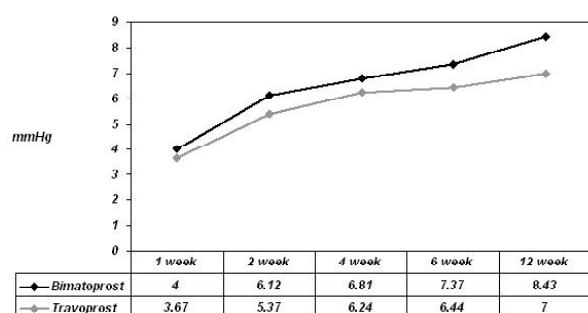
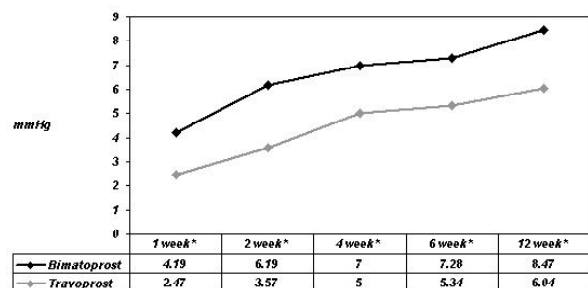


Figure III: Mean reduction in IOP from baseline in study groups at 1.00 pm.



* = p value < 0.05

Figure IV: Mean reduction in IOP from baseline in study groups at 4.00 pm.

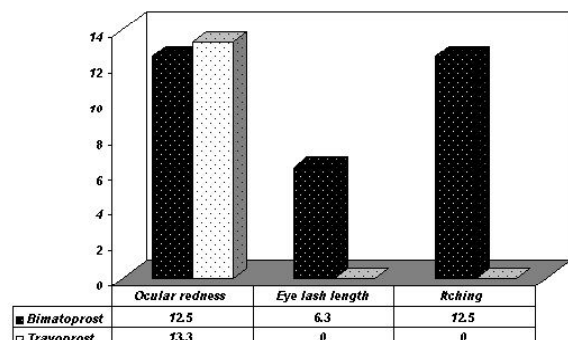


Figure V: Adverse effects in the study groups

At 1.00 pm, both study drugs provided significant IOP reductions from baseline at all study visits ($p < 0.001$). Although the mean IOP reductions in the bimatoprost group were greater than the travoprost group at 1.00 pm at every study visit, these differences were not significant at 12 weeks ($p = 0.08$) (Figure III).

Both study drugs provided significant IOP reductions from baseline at 4:00 pm at all study visits ($p < 0.001$), but the mean reductions in the bimatoprost group were significantly greater than those in the travoprost group at every study visit. The difference was statistically significant ($p = 0.03$) (Figure IV).

Ocular redness and itching were graded on a 4-grade point scale: none-to-trace (0 to 0.5), mild (1), moderate (2), and severe (3). The most common reported adverse effect was ocular redness in both the groups. In bimatoprost group, 12.5% patients complained of mild ocular redness compared to 13.3% patients in travoprost group but the difference was not statistically significant. 12.5% patients in bimatoprost group complained of ocular itching during the study period whereas no patients had such a complaint in travoprost group. In bimatoprost group 6.3 % patients had increase in the length of eye lashes which was noticed after 12 weeks of drug use whereas none of the patients in travoprost group showed it. The difference between the two groups was found to be statistically insignificant for all the adverse effects (Figure V).

Discussion

The management of POAG will evolve as we gain knowledge of the pathophysiology of glaucoma. Today, however, the primary objective of any pharmacological treatment regimen for glaucoma is the preservation of the visual field through the early and aggressive reduction of IOP. To accomplish this objective, a target IOP or upper limit IOP expected to slow or stop optic-nerve damage, should be identified,

In this study, bimatoprost provided greater IOP lowering than travoprost. Although both bimatoprost and travoprost considerably lowered IOP in patients



with glaucoma, bimatoprost provided greater mean IOP reductions from baseline than travoprost at the end of the study period of 12 weeks at every time point at every study visit, reaching statistical significance at 12 weeks at 9:00 am and at 4.00 pm bimatoprost significantly reduced IOP throughout the study (1 week, 2 week, 4 week, 6 week and 12 week) as compared to travoprost.

There are a few studies that have been done on the ocular hypotensive effect of bimatoprost and travoprost. A study by Parish et al compared the IOP lowering efficacy of bimatoprost, travoprost and latanoprost. In this large scale 3 month clinical trial, it was demonstrated that bimatoprost and travoprost were equally potent in lowering IOP. Evaluation of some other published data from the bimatoprost and travoprost trials supports the expectation that bimatoprost provides more efficacious IOP lowering than travoprost. Bimatoprost has been shown to be superior to timolol and latanoprost, whereas travoprost has been shown to be superior to timolol and equal to or superior to latanoprost (Simmons ST et al, 2004). Cantor et al, 2004 concluded that bimatoprost provided statistically significant lower mean IOP than travoprost at 9.00 am. Interestingly in our study bimatoprost provided statistically significant lower mean IOP than travoprost at 9.00 am and at 4.00 pm.

In the present study, the most common side effect of each medication was ocular redness, with a similar incidence in each treatment group. Mild to moderate ocular redness has been reported to be a common side effect of bimatoprost therapy. This is usually a transient cosmetic effect that has been shown to resolve within a month (Abelson MB et al, 2003).

Conclusion

Bimatoprost provided greater control of IOP throughout the day and significantly greater mean IOP reductions from baseline at 9:00 am and at 4.00 pm. These findings suggest that bimatoprost is an effective ocular hypotensive agent for patients with glaucoma of Indian origin.

However, current small study is certainly underpowered to show effects in a highly heterogeneous population as the one examined here. Therefore studies with more number of patients of Indian origin are needed to support our study.

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