



TO COMPARE THE EFFICACY OF TOPICAL 0.01% BIMATOPROST WITH TOPICAL 0.5% TIMOLOL MALEATE IN GLAUCOMA PATIENTS

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ABSTRACT **OBJECTIVE:** To compare the safety and efficacy of Bimatoprost 0.01% ophthalmic solution with Timolol maleate 0.5% ophthalmic solution in the treatment of Primary open angle glaucoma.

MATERIALS AND METHODS: 50 Patients with POAG were included in a prospective randomized double blinded study. Patients were divided into two groups, 25 patients each, Group A received Bimatoprost 0.01% ophthalmic solution in the study eye once daily, in the evening and Group B received Timolol maleate 0.5% ophthalmic solution in the study eye twice daily, at 12 hour interval. In all these patients Intraocular pressure was recorded at base line (day 0) and treatment scheduled follow up visits - 2wks, 6wks, 3mths, 6mths. Primary adverse effects were monitored throughout the study.

RESULTS: In this study mean reduction of IOP at 2 wks, 6 wks, 12 wks, 24 wks were 6.96 mmHg (24.71%), 9.52 mmHg (33.80%), 10.76 mmHg (38.21%), 10.96 mmHg (38.92%) for Group A (Bimatoprost group) and 4.08 mmHg (14.91%), 5.84 mmHg (21.34%), 6.96 mmHg (25.43%) and 7.2 mmHg (26.31%) for Group B (Timolol group) respectively.

CONCLUSION : Bimatoprost 0.01% ophthalmic solution was highly efficacious and well tolerated with minimal ocular side effects. It can be used as first line therapy to treat cases of POAG to reduce IOP. The only limitation for its use is regarding its cost. The topical Bimatoprost preparations are expensive when compared to the topical Timolol maleate. Considering the reduction in IOP, the modifiable factor for preventing the progression of optic nerve head damage Bimatoprost can be used to treat POAG patients.

KEYWORDS : Intraocular pressure. Primary open angle glaucoma, Bimatoprost, Timolol Maleate

INTRODUCTION:

Glaucoma is a characterized by slow progressive degeneration of the retinal ganglion cells and the optic nerve axons, leading to a progressive deterioration of the visual field. If untreated, the condition can lead to irreversible blindness. Glaucoma is classified into: 1) Primary glaucoma- Primary Open Angle Glaucoma (POAG) and Primary Angle Closure Glaucoma (PACG), 2) Secondary glaucoma – due to a specific anomaly or disease of the eye identified as the cause of increased IOP.¹

Primary open-angle glaucoma (POAG) is the most common type of glaucoma. POAG is slowly progressive, painless and usually bilateral, although it may be asymmetric. It is characterised by (a) Optic nerve damage (b) No evidence of angle closure on gonioscopy. (c) No identifiable secondary cause for glaucoma. Diagnosis of glaucoma is based on a combination of progressive characteristic vision loss (measured using VF testing) and progressive ONH damage. While an IOP is not sufficient for a diagnosis of glaucoma, but it is the greatest single risk factor for disease onset. High IOP is thought to either directly compress and damage the optic nerve or cause decreased perfusion and ischemia. The results of several studies provide strong evidence that reducing IOP slows the progression of glaucomatous optic neuropathy.²⁻³ The OHTS (Ocular Hypertension Treatment Study) concluded that IOP reduction reduced the risk of optic nerve head damage by 10% to 5% over 5yrs.⁴ Goldmann Applanation Tonometer (GAT) is considered the gold standard for IOP measurement. Prevention or control of raised intraocular pressure is the primary goal in the management of glaucoma. Target IOP may be defined as a pressure or a range of intraocular pressure levels within which the progression of glaucoma and visual field loss will be delayed or halted. Target IOP should be individualized as per patient. In medical management, the topical anti-glaucoma drugs are the mainstay of the therapy.⁵

Bimatoprost is indicated as a first line therapy or to those who are intolerant of other IOP lowering medications. Bimatoprost interacts with a prostamide receptor in the trabecular meshwork, to increase outflow facility.⁶ Reduction of IOP starts 4 hrs after first administration with maximum effect reached within 8-12 hrs. Bimatoprost produces ocular side effects - conjunctival hyperemia and foreign body sensation (most common), increased pigmentation and growth of eyelashes and increased pigmentation of the iris and periorbital tissue (eyelid). Timolol is one of the most common and most old non-selective β blocker being used worldwide today. The IOP lowering effect is due to antagonist action of the drug on the β_2 adrenergic

receptor stimulation which causes increased formation of aqueous humor. Timolol has good corneal penetration with peak aqueous humor concentrations occur within 1-2hr. The IOP lowering efficacy peaks approximately 2hrs after instillation and lasts for at least 24hrs. The pressure responsiveness of timolol decreases with continued administration

PATIENTS AND METHODS:

50 patients with POAG who presented to our tertiary care hospital in south India from December 2015 to August 2017 were included in a prospective randomized double blinded study. Patients were selected on the examination criteria of IOP recording with applanation tonometer, angle estimation with four mirror gonioscopes and visual field recording with Humphrey's analyser, from these patients diagnosed cases of POAG were taken into study. Diagnosis of glaucoma was based on baseline IOP more than 21mm of Hg with a typical glaucomatous OD change and corresponding VF defects on Humphrey's analyser. A total 50 patients with POAG, divided into two groups, 25 in bimatoprost and 25 in timolol groups respectively by systemic random sampling

INCLUSION CRITERIA:

- Patient's age above 30 yrs.
- Mean IOP > 21 mm of Hg.
- Angles wide open on gonioscopy.
- Visual fields tested on Humphrey field analyser.
- Patient has to be a primary case of POAG or OH.
- In patients with bilateral raised IOP the eye with higher IOP was selected.

EXCLUSION CRITERIA:

- Age less than 30 years old.
- H/o Chronic or recurrent severe ocular inflammatory disease.
- H/O intraocular surgery within 6 months.
- Gonioscopically closed angle.
- Presence of any systemic disease or using any medication that can affect IOP.
- One eyed patients.
- Any abnormality preventing reliable tonometry of either eye.
- Corneal abnormalities, dry eyes.
- History of trauma.
- History of severe or serious hypersensitivity to topical or systemic beta blockers or prostaglandins.
- History of severe, unstable or uncontrolled cardiovascular, hepatic or renal disease.

- History of bronchial asthma or chronic obstructive pulmonary disease.
- Pregnant and lactating women

At the screening examination, informed consent was taken from the selected patients and comprehensive medical history, general physical examination including blood pressure and pulse measurements were taken. After taking relevant history and detailed slit lamp examination, visual acuity, refraction, ophthalmoscopic examination, applanation tonometry, gonioscopy, visual field charting was done. Baseline IOP recording was first done at the time of selection at 9AM ± 1hr, 1PM ± 1hr, 5PM ± 1hr. Mean of all these values has been taken at baseline. Then the patient is instructed about the medicine, its side effects, methods of installation and asked to visit for follow up at 2wks, 6wks, 3mths, 6mths. Group A patients were instructed to instill the Bimatoprost 0.01% ophthalmic solution in the study eye once daily, in the evening. Group II patients were instructed to instill the Timolol maleate 0.5% ophthalmic solution in the study eye twice daily, at 12 hour interval. At all visits patients were asked about any side effects and IOP is recorded by Applanation tonometer at 10AM ± 1hr. At every follow-up visit slit lamp eye examination, gonioscopy, visual field testing are also done. For statistical analysis the mean values for IOP were calculated before and after treatment for both groups. IOP has been expressed in mean +/- standard deviation. Student's t-test is done to compare the differences in mean IOP between Group A and Group B at end of study period. Statistical analysis was performed between the study groups using SPSS 20.0 software (SPSS Inc., Chicago IL, USA), and P-values 0.05 or less were considered to indicate a significant difference.

RESULTS:

At the end of study a statistically significant difference in reduction of IOP was observed between Group A (Bimatoprost 0.01% QD group) and Group B (Timolol maleate 0.5% BD group) (P<0.001). The present study enrolled patients of different ages. The mean age of the Group A is 54.72 years and Group B is 55.4 years. There is no significant difference in demographic variables between the two groups.

In the present study, the IOP lowering efficacy of Bimatoprost is found to be superior to Timolol maleate. The results are evaluated at week 2, week 6, week 12 and week 24. In the present study mean reduction of IOP at 2wks is 6.96mmHg (24.71%) Group A and 4.08 mmHg (14.91%) for Group B.

- Mean reduction of IOP from baseline at 6wks is 9.52mmHg (33.80%) for Group A and 5.84mmHg (21.34%) for Group B.
- At 12wks mean reduction of IOP from baseline is 10.76 mmHg (38.21%) for Group A and 6.96mmHg (25.43%) for Group B.
- By the end of the study the mean reduction of IOP from baseline at 24wks is 10.96mmHg (38.92%) for Group A and 7.2mmHg (26.31%) for Group B.
- By the end of the study, mean reduction of IOP from baseline is 3.7mm Hg greater with Bimatoprost than with Timolol (P<0.001) drug.
- In present study 40% patients achieved IOP < 17 mmHg and 92% achieved IOP < 20mmHg with Bimatoprost as compared to 4% and 68% respectively with Timolol drug. Bimatoprost once daily enabled a greater percentage of patients to achieve lower target pressures.

Baseline mean IOP was 28.16±3(SD) mmHg in Group A and 27.36±2.87(SD) mmHg in Group B. Mean IOP after 24 wks was 17.2±1.53(SD)mmHg in Group A and 20.16±2.12(SD)mmHg in Group B. Group A showed significantly lower mean IOP at all follow up visits.

TABLE NO 1: This table shows the mean IOP that was recorded at baseline, 2wks, 6wks, 12wks and 24wks in both groups

	BIMATOPROST GROUP (mm of Hg)	TIMOLOLMALEATE GROUP (mm of Hg)
Mean IOP at baseline	28.16±3	27.36±2.87
Mean IOP at 2wks	21.2±3.11	23.28±2.57
Mean IOP at 6wks	18.64±2.14	21.52±1.94
Mean IOP at 12wks	17.4±1.58	20.4±2.18
Mean IOP at 24wks	17.2±1.53	20.16±2.12
Mean IOP difference at baseline and 24wks	10.96	7.2

Fig No 1- Comparing IOP at 24 wks in the two groups [X-Axis- Number of patients, Y Axis-IOP recorded in mmHg]

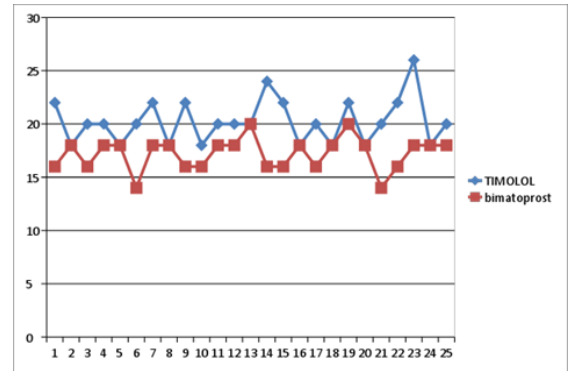


TABLE NO 2- Percentage of patients reaching Target pressure:

	BIMATOPROST	TIMOLOLMALEATE
No of patients	25	25
No of patients with IOP		
<17 mm of Hg	10(40%)	1 (4%)
17- 20 mm of Hg	13(52%)	16 (64%)
=/ > 20 mm of Hg	2 (8%)	8(32%)

DISCUSSION:

Glaucoma is the second major cause of blindness after cataract and refractive errors. In 2010 it was estimated worldwide glaucoma caused 6.6% of all blindness and 2.2% of all moderate and severe visual impairment.⁷ Topical ocular hypotensive medications are effective in delaying or preventing the onset of POAG in individuals with elevated IOP. In this regard a study has been done to compare the efficiency in controlling IOP by using the drug Bimatoprost (0.01%) once daily and Timolol maleate (0.5%) twice daily. All patients are followed till end of study. At every measurement throughout the study, mean changes from baseline IOP (primary outcome measure) is significantly greater with Bimatoprost than with Timolol (P<0.001). By the end of the study, mean changes from baseline is 3.7mm Hg greater with Bimatoprost than with Timolol (P<0.001). The clinical significance of the greater IOP lowering achieved with Bimatoprost is illustrated by an analysis of the number of patients reaching specific target pressures. The target pressure analysis in the present study suggests that Bimatoprost may reduce the risk of disease progression in glaucoma patients more than Timolol. The most commonly reported side effects with Bimatoprost is conjunctival hyperaemia (i.e. ocular surface redness), which is observed in 12% cases and is only a cosmetic phenomenon.

In the present study mean reduction of IOP from baseline at 24wks is 10.96mmHg (38.92%) with bimatoprost and 7.2mmHg (26.31%) with Timolol (P<0.001). A significantly higher percentage of patients receiving bimatoprost (40%) achieved IOPs at or below 17 mm Hg (P<0.001). Results of present study showed bimatoprost is superior to timolol in lowering IOP and in achieving low target IOPs.

CONCLUSION:

In this study Bimatoprost 0.01% ophthalmic solution was highly efficacious and well tolerated. It is systemically safe and ocular side effects are also minimal and not severe enough to withdraw the drug. Bimatoprost 0.01% ophthalmic solution can be used as first line therapy to treat cases of POAG to reduce IOP. The only limitation for its use is regarding its cost. But when considering the IOP reduction rate, which is the only modifiable factor for preventing the progression of Optic Nerve Head damage and preservation of visual function Bimatoprost can be used to treat POAG patients. Bimatoprost provides an alternative treatment for patients in whom Timolol is contraindicated. Once daily dosing of Bimatoprost also increases patient's compliance.

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