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The Comparison of Intraocular Pressure Lowering Efficacy Of 0.5% Timolol Maleate Versus 0.0015% Tafluprost in Cases of Primary Open Angle Glaucoma and Ocular Hypertension

KEYWORDS: glaucoma; IOP; ocular hypertension; POAG; tafluprost; timolol.

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ABSTRACT *Objectives: To compare the intraocular pressure lowering efficacy of 0.5% timolol maleate versus 0.0015% tafluprost in cases of primary open angle glaucoma and ocular hypertension.*

Methods and Materials: This prospective, open, randomized, parallel group study was conducted in 80 newly diagnosed primary open angle glaucoma (POAG) and ocular hypertension (OHT) cases which were randomized into two groups (I and II) of 40 cases each and received 0.5% timolol maleate and 0.0015% tafluprost respectively. Efficacy of the drugs was calculated as mmHg lowering in mean IOP observed at the end of 3 months and the observations made in both groups were compared using appropriate statistical tools.

Results: IOP at the different time points assessed during the baseline visit ranged from 24.27 to 25.10 mmHg, with a mean of 24.60 mmHg in group I and 24.65 to 25.45 mmHg, with a mean of 25.04 mmHg in group II. IOP at various time points assessed after 12 weeks ranged from 18.12 to 18.60 mmHg, with a mean of 18.36 mmHg for group I and 16.52 to 17.47 mmHg, with a mean of 16.97 mmHg for group II. Mean diurnal IOP reduction with timolol and tafluprost was 6.24 mmHg (25.37%) and 8.07 mmHg (32.23%) respectively, with the difference being statistically significant.

Conclusions: There is significant difference in IOP lowering efficacy between the two groups with tafluprost consistently achieving greater reduction in IOP as compared to timolol.

Introduction

The National Survey on Blindness 2001-2002 concluded that prevalence of blindness in India is 1.1%. Of these a substantial proportion is due to glaucoma, the second leading cause, accounting for 5.8% cases. [1] However, glaucoma is associated with reduced quality of life even before blindness occurs. [2, 3] The goal of glaucoma treatment is therefore to prevent loss of visual function so as to preserve the quality of life. [4]

Glaucomatous optic neuropathy is associated with progressive loss of visual field which can lead to total irreversible blindness if the disease is not diagnosed early and treated properly. [5] Glaucomatous optic neuropathy has multiple risk factors, the foremost being raised IOP, which may be due to an increase in the formation of the aqueous humor, a difficulty in its outflow or raised pressure in the episcleral veins. [6] Reduction of IOP using topical ocular hypotensive agents can prevent or delay the development of open-angle glaucoma [7] and slow the progression of glaucoma. [8, 9] This reduces the risk and rate of progression, even in patients with statistically normal IOP and is thus the mainstay of all current glaucoma therapy. [10, 11] Medical treatment is the first therapeutic approach while surgery is reserved for cases that cannot be controlled by drugs. [12]

Beta Adrenergic blocking agents, such as timolol, have been used extensively to treat open-angle glaucoma and ocular hypertension for years. [13] Beta Blockers reduce IOP by reducing the rate of aqueous humor formation [14] and thus provide excellent reductions in IOP, although they are known to cause cardiovascular and respiratory side effects in some patients.

Prostaglandin analogs (PGAs) were first proposed for glaucoma treatment by Camras and Brito [15] and demonstrate superiority over all current medical therapies, but they can also result in severe adverse events and high costs. [16] Prostaglandin analogues lower IOP by increasing the uveoscleral outflow of aqueous humor.

Tafluprost is a new, potent prostaglandin analogue with high affinity for the fluoro-prostaglandin (FP) receptor (PGF2 α). [17] As tafluprost is a newer drug with a recent entry into the market, there are not many studies available comparing the IOP lowering efficacy of tafluprost and timolol as well as studies on its efficacy on an Indian population.

Materials and Methods

In this prospective, open, randomized, parallel group, comparative study, 80 patients of POAG or ocular hypertension were included. Due permission from the ethical committee of the institute was obtained. The patients fulfilling the inclusion criteria and having none of the exclusion criteria were enrolled in the study after obtaining written informed consent. Patients of a minimum age of 18 years, having unilateral/ bilateral primary open angle glaucoma/ ocular hypertension with an IOP > 21 mm Hg and </= 30 mm Hg were included in the study. Exclusion criteria for patients were history of acute angle closure glaucoma, established diagnosis of secondary glaucoma, closed anterior chamber angle, ocular inflammation, ocular infection, pregnant and lactating females, patient unable to attend follow up, known sensitivity to drug, chronic use of ocular medication other than the glaucoma medications and patients having any contraindication to the

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use of beta blockers and prostaglandins analogues.

Patients requiring treatment for bilateral POAG were treated for both eyes but the right eye was the study eye. Patients selected were randomised into two groups of 40 each. Group I instilled 1 drop of timolol maleate 0.5% into study eye twice daily at 8.00 a.m. and 8.00 p.m. for 12 weeks, and Group II instilled 1 drop of tafluprost 0.0015%, into study eye once daily at 8.00 p.m. for 12 weeks. During the study patients visited the hospital on day 0, week 4, week 8 and week 12. IOP readings were taken from the study eye with the Goldmann applanation tonometer at each visit. Baseline IOP was measured on first visit at 8.00 a.m., 10.00 a.m. and 4.00 p.m. before administration of the study drugs, and then on each follow-up visit at 8.00 a.m., 10.00 a.m. and 4.00 p.m. Observations were recorded and subjected to statistical analysis at the end of the study using the student's paired t-test.

Results

Both the study groups were comparable with regards to demographic parameters. Mean age in group I was 61.55 years and in group II was 63.67 years. In our study, in group I, 47.50% of the patients were male and 52.50 were female and in group II, male and females both were 50%.

In group I, mean baseline IOP at 8:00 am was 25.10±1.15 mmHg, at 10:00 am was 24.67±1.14 mmHg, at 4:00 pm was 24.27±0.99 mmHg and mean diurnal IOP at all time points was 24.60±1.04. Mean IOP at 4 weeks, at 8:00 am was 19.45±1.13 mmHg, at 10:00 am was 19.20±1.18 mmHg, at 4:00 pm was 18.75±1.08 mmHg and mean diurnal IOP was 19.12±1.09. Mean IOP at 8 weeks, at 8:00 am was 19.10±1.08 mmHg, at 10:00 am was 18.55±1.04 mmHg, at 4:00 pm was 18.27±1.04 mmHg and mean diurnal IOP at all time points was 18.64±1.01. Mean IOP at 12 weeks, at 8:00 am was 18.60±1.08 mmHg, at 10:00 am was 18.37±0.98 mmHg, at 4:00 pm was 18.12±1.04 mmHg and mean diurnal IOP was 18.36±0.99.

In group II, mean baseline IOP at 8:00 am was 25.47±1.13 mmHg, at 10:00 am was 25.02±0.99 mmHg, at 4:00 pm was 24.65±0.92 mmHg and mean diurnal IOP at all time points was 25.05±0.98 mmHg. Mean IOP at week 4, at 8:00 am was 18.22±0.92 mmHg, at 10:00 am was 17.65±0.92 mmHg, at 4:00 pm was 17.07±0.89 mmHg and mean diurnal IOP was 17.65±0.82 mmHg. Mean IOP at week 8, at 8:00 am was 17.65±0.97 mmHg, at 10:00 am was 17.07±0.92 mmHg, at 4:00 pm was 16.72±0.93 mmHg and mean diurnal IOP was 17.15±0.89. Mean IOP at week 12, at 8:00 am was 17.47±0.93 mmHg, at 10:00 am was 16.92±0.97 mmHg at 4:00 pm was 16.52±0.96 mmHg and mean diurnal IOP at all time points was 16.97±0.87.

Mean IOP lowering with timolol at the end of 12 weeks was 6.24 mmHg (25.37 %) and with tafluprost 0.0015% at the end of 12 weeks was 8.07 mmHg (32.23%).

Discussion

The pathophysiology of open angle glaucoma includes a progressive decrease in the number of retinal ganglion cells when nerve fibers at the point where optic nerve exits the eye become pinched and die. [18] IOP levels once considered safe, do not prevent progressive visual loss in many patients. This supports increasingly aggressive efforts to get IOP as low as safely possible, especially in patients with severe or rapidly progressing disease. [19]

The results from this clinical trial of 80 patients with POAG or OHT demonstrated that both tafluprost and timolol had a substantial IOP lowering effect that was apparent after 4 weeks of treatment and was sustained throughout the 12 week assessment period. The IOP lowering effect of tafluprost was more compared to that of timolol at all visits and time points over 12 weeks. The results of the primary endpoint were supported by analyses of change from baseline in diurnal IOP, which also suggested that tafluprost was superior to timolol. The demographic data showed no statistically significant differences between the two groups regarding all parameters of the patient profile.

In the present study mean diurnal IOP lowering with timolol maleate 0.05% at the end of 12 weeks was 6.24 (25.37%). Rolle et al [20] evaluated the efficacy of timolol 0.5% and calculated that IOP reduction at trough was 23.6%. Zhao et al [21], in a comparative study, to evaluate the efficacy of timolol 0.5% with chronic angle glaucoma, concluded that the mean change in IOP from baseline to week 8 was -4.9mmHg for timolol. The reduction in IOP with timolol in our study is similar to the efficacy found in most of the previous studies.

In the present study mean diurnal IOP lowering with tafluprost 0.0015% at the end of 12 weeks was 8.07 (32.23%). Uusitalo et al [22] recorded that at the end of a 24 month study, tafluprost 0.0015% reduced the mean IOP from baseline by 7.1mmHg. Traverso et al [23] investigated the efficacy of tafluprost and found the mean IOP reduction of 9.7 mmHg from baseline in tafluprost 0.0015% group. The reduction in IOP with tafluprost 0.0015% once daily in our study is similar to the efficacy of tafluprost 0.0015% in most of the studies mentioned above.

IOP reduction at the end of 12 weeks was more with tafluprost than with timolol with mean diurnal IOP reduction with timolol maleate 0.5% and tafluprost 0.0015% being 6.24 mmHg (25.37%) and 8.07 mmHg (32.23%), respectively. Across all time points and visits during the 12 week treatment period IOP lowering produced with tafluprost was more than timolol with the difference being statistically significant. Chabi et al [24] in their randomized clinical trial also observed that IOPs ranged from 17.4 to 18.6 mm Hg for tafluprost and 17.9 to 18.5 mm Hg for timolol. There was a significant reduction in IOP after 12 weeks of treatment in both the tafluprost group (6.6-7.2) and timolol group (6.3-6.9) from the baseline.

A trial over a longer follow up period is required to elicit data comparing other outcome variables such as side – effects and cost – effectiveness of treatment between the two drug groups.

The authors reveal no conflict of interest.

Table 1 - Mean diurnal IOP changes in Group I and Group II at baseline and at subsequent visits

Visit	Group I			Group II			P value
	Mean±SD (mmHg)	Difference	% age reduction	Mean±SD (mmHg)	Difference	% age reduction	
Baseline	24.60±1.04	--	--	25.04±0.97	--	--	0.054
Week 4	19.12±1.09	5.48	-22.28%	17.65±0.82	7.39	-29.51%	0.01
Week 8	18.64±1.01	5.97	-24.27%	17.15±0.87	7.89	-31.51%	0.01
Week 12	18.36±0.99	6.25	-25.37%	16.97±0.87	8.07	-32.23%	0.01

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Fig 1 - Comparison between reduction in mean diurnal IOP in Group I and Group II

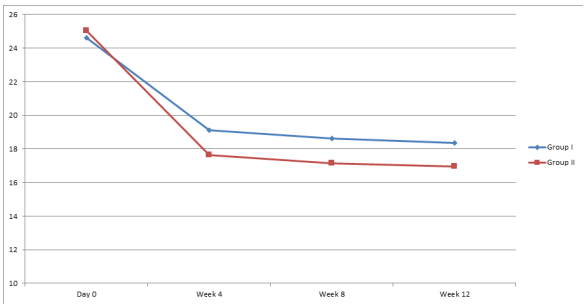
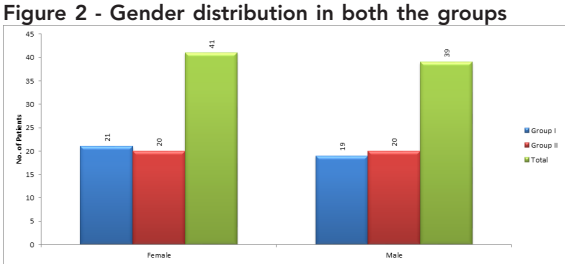


Figure 2 - Gender distribution in both the groups



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