

Original Research Article

A comparative study of the clinical efficacy and safety of timolol 0.5% and travoprost 0.004% eye drops in primary open angle glaucoma

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ABSTRACT

Background: Raised intraocular pressure (IOP) is a strong risk factor for development of glaucoma. If the condition is detected early enough it is possible to arrest the development or slow the progress with medication that lowers IOP. Travoprost is a newer prostaglandin analogue lowers IOP by facilitating outflow of aqueous humor.

Methods: This was a prospective, randomized, open labelled, parallel group study, in which sixty cases of newly diagnosed primary open angle glaucoma (POAG) were included. After baseline clinical evaluation 30 subjects of glaucoma were treated with timolol 0.5% eye drop while another 30 subjects were given travoprost 0.004% eye drop and followed for 1 month to see IOP lowering efficacy of the two drugs. Statistical analysis was done using Open Epi 2.3 version for paired t test and unpaired t test.

Results: In subjects treated with timolol eye drop mean reduction of IOP from baseline to week 4 was by 6.6mmHg while that of travoprost treated subjects was by 8.07mmHg. There was significant reduction in mean IOP of study subjects in travoprost group as compared to timolol group (P<0.05).

Conclusions: Both timolol 0.5% and travoprost 0.004% eye drops are effective in reducing intra ocular pressure in POAG. On comparison travoprost was found to be statistically superior to timolol in lowering IOP in patients with POAG.

Keywords: Primary open angle glaucoma, Timolol, Travoprost

INTRODUCTION

Glaucoma is the leading cause of irreversible blindness worldwide. It is estimated that there are more than 60 million cases of glaucoma worldwide and it will increase upto 80 million by 2020.¹

In 2013, the number of people (aged 40 to 80 years) with glaucoma worldwide was estimated to be 64.3 million, increasing to 76 million in 2020 and 111.8 million in 2040.²

There are 45 million blind persons in the world, of which 12 million blind persons are in India. In India, glaucoma

is the third major cause of blindness after cataract and refractive errors. More importantly it is the most common cause of irreversible blindness globally.³

In India, the estimated number of cases of glaucoma is 12 million, around one fifth of the global burden of glaucoma. It is estimated that more than 3 million people are blind due to glaucoma.⁴

The glaucoma's are classified, on the basis of anatomy of the anterior chamber angle of the eye, as either open angle glaucoma (OAG) or angle closure glaucoma (ACG). Raised intraocular pressure (IOP) remains a strong risk factor and it has been shown that the higher

the intraocular pressure at presentation, the greater the risk of developing POAG (primary open angle glaucoma). Untreated glaucoma leads to permanent damage of the optic disc and resultant visual field loss, which can progress to blindness. If the condition is detected early enough it is possible to arrest the development or slow the progress with medication. Several randomized controlled trials have determined that reducing IOP can reduce rate of glaucomatous nerve or field damage.^{5,6} Normal intraocular pressure ranges from 10-20mmHg. Data from early manifest glaucoma trial have shown that an additional 1mmHg of IOP lowering reduces the risk of glaucoma progression by 10%.⁷

Medical treatment is the first line of management of POAG and in that prostaglandin analogues and beta adrenergic antagonist are the most frequently used topical medications for reducing IOP in patients with glaucoma.⁸ Timolol is a nonselective beta adrenergic antagonist, decreases intraocular pressure by decreasing aqueous humor formation. Travoprost is a newer prostaglandin analogue lowers IOP by facilitating outflow of aqueous humor.

There are very few studies which compared efficacy of timolol and travoprost in patients of primary open angle glaucoma. So, this study has been done to compare the intraocular pressure lowering efficacy between timolol and travoprost in patients of primary open angle glaucoma.

METHODS

The present study was conducted from January 2015 to June 2016 on diagnosed patients of primary open angle glaucoma attending out-patient department of ophthalmology at Dr. Shankarrao Chavan Government Medical College and Hospital, Nanded. Before initiation of study, approval from Institutional Human Research Ethics committee was obtained and informed written consent of all study subjects was taken before conducting the study.

It was a prospective, randomized, open labelled, parallel group study, in which sixty cases of newly diagnosed primary open angle glaucoma of either sex, of age above 40 years and intra ocular pressure in the range of 22-32 mmHg were included in the study and divided equally into two groups based on systematic random sampling. One group was treated with timolol 0.5% eye drop twice daily and the other with travoprost 0.004% eye drop once a day.

Exclusion criteria for the study were acute angle closure glaucoma, pigmentary glaucoma, exfoliation glaucoma, secondary glaucoma, pregnant and lactating female, bronchial asthma/chronic obstructive pulmonary disease, second/third degree heart block, any ocular infection in last 3months, history of allergy to study drugs, and those with history of severe renal disease.

Primary efficacy parameter was intraocular pressure measured at 11 am at baseline and each follow up visits and primary safety parameter was adverse effect noticed at each follow up visits.

A thorough evaluation of all the study subjects was done by detailed history taking followed by general, systemic and ocular examination at baseline visit. Baseline characteristics of all study subjects of both the groups were similar. Diagnosis of primary open angle glaucoma was made by ophthalmologist based on detail ocular examination. IOP was measured using Goldman applannation tonometer.

Follow up was done at the end of 1st week, 2nd week, 3rd week and 4th week. During each follow up visits ocular examination and IOP measurement was done and also, they were assessed for any adverse effects. Visual acuity and visual field were assessed at day 0 and at the end of study period i.e. at week 4.

Subjects of one group were instructed to instil one drop of timolol 0.5% eye drop in affected eye twice daily. Subjects of other group were instructed to instil one drop of travoprost 0.004% eye drop once daily at evening. They were advised to lie down or with head tilted back, to form a conjunctival pouch and to instil the drug without the dropper touching the eye area and then close the eye gently without blinking, rubbing or squeezing. They were then instructed to apply pressure over the lacrimal puncta for one minute.

RESULTS

In this study, total sixty cases of primary open angle glaucoma were selected and divided equally into two groups. There was no lost to follow up of study subjects throughout the study period as we used to make reminder telephonic calls to subjects one day before follow up day and even if they missed any follow up visit on same day we asked them to come on next day. Our study revealed following results.

Majority of study subjects from both the groups were from age group 51-60 years. Mean age of the study subjects in both the groups was 59.62±9.46.

Majority of study subjects were male in both the groups i.e. 20 (66.67%) in timolol group and 21 (70%) in the travoprost group. Male to female ratio of study subjects was 2.16:1.

At baseline, mean IOP was similar in both the groups, Baseline mean IOP ±SD in timolol group was 26.07±2.80mmHg and that of travoprost group was 25.67±2.63mmHg (p=0.5709). There was significant reduction in mean IOP from baseline to week 4 in timolol group (p<0.0001) as well as in travoprost group (p<0.0001) (Table 1).

Table 1: Change in mean intra ocular pressure (IOP) of subjects in both groups (n = 30).

Study groups	Baseline IOP	Week 4 IOP	P value [#]
Timolol group (n=30)	26.07±2.80	19.47±2.46	<0.0001 [#]
Travoprost group (n=30)	25.67±2.63	17.60±2.25	<0.0001 [#]

#Statistical significance was considered at P<0.05

Table 2: Comparison of change in mean intra ocular pressure in subjects of both the groups (n = 60).

Timolol group (n=30)	Baseline IOP	Week 1 IOP	Week 2 IOP	Week 3 IOP	Week 4 IOP
Mean IOP ±SD	26.07±2.80	21.80±3.21	20.47±2.56	19.40±2.11	19.47±2.46
Mean change from baseline	-	4.27	5.6	6.67	6.6
Travoprost group (n=30)	Baseline IOP	Week 1 IOP	Week 2 IOP	Week 3 IOP	Week 4 IOP
Mean IOP ±SD	25.67±2.63	20.13±3.06	18.53±2.67	17.80±2.25	17.60±2.25
Mean change from baseline	-	5.54	7.14	7.87	8.07
P value [#]	0.5709	0.0440 [#]	0.0058 [#]	0.0062 [#]	0.0033 [#]

#Statistical significance was considered at P<0.05

Table 3: Adverse effects in study subjects of both the groups (n = 60).

Adverse effects	Timolol group (n=30)	Travoprost group (n=30)	Total
Conjunctival hyperaemia	2 (6.67)	3 (10)	5 (8.33)
Discomfort	1 (3.33)	1 (3.33)	2 (3.33)
Pain	1 (3.33)	0 (0)	1 (1.67)
Foreign body sensation	0 (0)	1 (3.33)	1 (1.67)
No adverse effects	26 (86.67)	25 (83.33)	51 (85)
Total	30 (100)	30 (100)	60 (100)

Table 2 shows the comparison of change in mean intra ocular pressure in subjects of both the groups, in subjects treated with timolol eye drop mean reduction of IOP from baseline to week 4 was by 6.6mmHg while that of in travoprost treated subjects was by 8.07mmHg. There was significant reduction in mean IOP of study subjects in travoprost group as compared to timolol group at week 1 (P = 0.0440), at week 2 (P = 0.0058), at week 3 (P = 0.0062) and at week 4 (P = 0.0033).

Majority of study subjects (85%) did not develop any adverse effects. Adverse effects were only ocular, there were no any systemic adverse effect seen in any of the study group. The most common adverse effect noticed was ocular hyperemia in both the groups (Table 3).

DISCUSSION

This prospective study was done to compare and evaluate efficacy of timolol 0.5% eye drops and travoprost 0.004% eye drops in management of patients of primary open angle glaucoma. The outcomes of the study are discussed as follows.

In this study mean age of study subjects in timolol group was 60.93±9.87 years and that of the travoprost group was 58.30±9.01 years. There was no significant difference in mean age of study subjects of both the

groups. Our observations regarding age distribution are consistent with the other studies done by Mehani R et al, Khan F et al and Babić N et al.^{7,9,10} However in a study by Jeffrey A et al mean age of study subjects were 63.4±12.3 and 62.7±12.4 and a study done by Giuffre I revealed the mean age of subjects as 69.52 years.^{11,12}

In our study male predominance was found which was in accordance with other observations seen in studies done by Mehani R et al, Khan F et al and Parrish RK et al.^{7,9,13}

Raised intra ocular pressure is a major risk factor for development POAG, several randomized controlled trials have determined that reducing IOP can reduce rate of glaucomatous nerve or field damage.^{5,6} In our study, in timolol group there was significant reduction in IOP from baseline to week 4. Mean reduction in IOP from baseline to week 4 was 6.6mmHg. These findings are in consistent with the other studies like study by Goldberg I et al and Netland PA et al, in which mean IOP reduction from baseline with timolol 0.5% was 6.3-7.9mmHg and 4.7 to 7.1mmHg respectively and findings of a study done by Fellman RL et al were also similar.¹⁴⁻¹⁶

In this study, mean reduction in IOP from baseline to week 4 in travoprost group was 8.07 mmHg. These observations are consistent with other studies like Mehani R et al, Goldberg I et al, Netland PA et al, Cheng JW et

al, and Deepankar UP et al.^{7,14,15,17,18} There was significant reduction in mean IOP of study subjects in travoprost group as compared to timolol group at each follow up visit.

The most common adverse effect noticed was conjunctival hyperemia (8.33%) in both the groups. Hyperemia was seen in 6.67% of subjects treated with timolol and 10% of subjects treated with travoprost eye drop. Other adverse effects seen were discomfort in eye in 1 (3.33%) subject in timolol group and 1 subject in travoprost group, pain in 1 subject of timolol group and foreign body sensation in 1 subject from travoprost group. In studies to evaluate the relative incidence of hyperemia between prostaglandins analogues, Goldberg I et al found that incidence of hyperemia caused by travoprost was 32.5% and that by timolol was 7%.¹⁴ Similar results were found in studies by, Netland PA et al, Fellman RL et al, and Mehani R et al.¹⁵⁻¹⁹

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