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Original Research Article

To Evaluate Efficacy and Safety of Latanoprost and Timolol in Patients of Primary Open Angle Glaucoma in a Tertiary Care Hospital of North India.

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Abstract:

Background: Glaucoma is a progressive disorder of eye characterized by raised intraocular pressure (IOP) leading to optic nerve damage and blindness. There is rapid shift from traditional use of beta-blockers to PG analogues for the treatment of primary open angle glaucoma (POAG) as first line of drug therapy. In this study we compared the efficacy and safety of latanoprost (PGA) with Timolol (beta-blocker).

Materials and Methods: A total of 70 newly diagnosed patients POAG who fulfilled the inclusion/exclusion criteria were enrolled and randomized into two groups. The first group (L-Group) was prescribed topical latanoprost 0.005% eye drop once daily, whereas the second group (T-Group) was prescribed topical timolol 0.5% eye drop twice a day. IOP was recorded at baseline, at the end of 1st week, 4th week and 12th week in both the groups and assessment of any adverse effects was done.

Results: The IOP lowering efficacy of latanoprost was found to be superior to timolol. In the latanoprost group, the mean reduction in IOP from baseline to final visit was 10.13±0.13 mmHg, whereas only 5.84±0.03 mmHg in the timolol group which was statistically significant (p-value <0.001). Predominant adverse effect in L-group was conjunctival hyperemia and in T-group it was dry eye.

Conclusion: Latanoprost was found to be having better efficacy and safety as compared to Timolol.

Keywords: Intraocular Pressure; Latanoprost; Timolol; Open Angle Glaucoma.

Introduction

Glaucoma is the second leading cause of blindness affecting approximately 65 million people worldwide, causing blindness in 10% of affected population. [1] Glaucoma is a chronic, progressive optic neuropathy occurring due to a group of ocular conditions, which leads to raised intraocular pressure (IOP) leading to optic nerve damage and visual function loss. Elevated IOP is the major risk factor that aggravates the course of the disease. Increase IOP results either due to increased formation of aqueous humour or its decreased outflow. IOP may also be raised due to increased pressure in the episcleral veins. [2] Other mechanisms such as neurotoxicity or impaired blood circulation may contribute to the damage. In glaucoma the only risk factor amenable to therapeutic intervention today is the IOP.

There are various classes of ocular hypotensives, which include β-blockers, carbonic anhydrase inhibitors, α-2-adrenergics, and prostaglandin analogues (PGA). Treatment is usually initiated either with a topical beta-adrenergic antagonist or a topical (PGA). [3,4,5]

Timolol is a beta-adrenergic blocking agent. It reduces IOP by decreasing aqueous humor production by acting on ciliary epithelium. [6] Maximum IOP reducing effect of timolol is seen at 2 h after initiation and lasts for 24 h. Approximately 80% of topically administered drug is reported to drain through nasolacrimal duct and absorbed systemically. This systemically absorbed timolol can cause adverse effects such as bradycardia, hypotension, bronchospasm, and respiratory failure. [7,8] Hence, it is contraindicated in patients who have a history of cardiac disease or asthma. [9]

Prostaglandin analogues are the latest therapeutic agents in glaucoma medication. [10] Latanoprost reduces IOP by stimulating aqueous humor drainage primarily through the uveoscleral outflow pathway but significant effects on trabecular

outflow have also been reported. [11,12] Prostaglandin analogues have been shown to be more effective in lowering IOP than timolol.

As new antiglaucoma drugs are being continuously added to the pharmaceutical armamentarium, the ophthalmologists are in a dilemma for selecting the best drug from the vast array of available options. The European Glaucoma Society and the Asia-Pacific Glaucoma Society guidelines and various other guidelines recommend PGA as the first line of drug in the management of glaucoma because of their efficacy, low risk of systemic side effects, and convenient once-daily dosing. [13,14,15] This article aims to compare the efficacy and safety of latanoprost and timolol in primary open angle glaucoma.

Materials and Methods

It was an open-labelled, prospective, interventional, simple randomized clinical study conducted in patients of POAG in the Department of Pharmacology in collaboration with Department of Ophthalmology in a tertiary care hospital of north India. Institutional Ethical Committee clearance was sought before initiation of the study. Study duration was 12 months.

Newly diagnosed patients of primary open angle glaucoma belonging to both genders and age above 40 years were included. A written informed consent was taken from every patient at the time of enrolment. Pregnant, lactating women and patients with any comorbidity were excluded from study.

A total of 70 patients were enrolled for the study. Demographic data (Age, Sex, Education and Locality) was recorded for each patient. Patients underwent Tonometery, Gonioscopy, Perimetery and Fundus examination at the time of enrolment. The patients were divided into two groups using simple random technique. First group the latanoprost group (L-group) and the second group timolol group (T-group). L-Group was prescribed topical Latanoprost 0.005% eye drop once daily and T-Group was prescribed topical Timolol 0.5% eye drop twice a day.

Applanation tonometer was used to record IOP. IOP reading will be taken at baseline (at time of enrolment), end of 1stweek, 4th week and 12th week. The patients were also monitored for other changes in the eyes and adverse effects during these visits.

Data collected in the study was analysed using SPSS version 23. Demographic data is presented as mean and frequency. One way ANOVA was used to compare intragroup data. Intergroup data was analysed using independent student t-test. Adverse effects recorded during the study have been presented as frequency and percentage.

Results and Observations

A total of 80 patients were enrolled in the study and divided into two equal groups (40 each). 4 patients in L-group and 6 patients in T-group were lost to follow up. Total of 70 patients completed the study. Demographic profile of the enrolled patients is presented in Table 1. Patients in both groups were similar in characteristics. Mean IOP in both groups was comparable (statistically non-significant) at the start of the study.

Table 1: Demographic profile of the participants

Variables	Latanoprost	Timolol
AGE (In Years) Mean ± S.D.	52.95 ± 9.43	51.05 ± 9.78
SEX		
Male	22	19
Female	14	15
EDUCATION		
Illiterate	12	16
Literate	24	18
LOCALITY		
Urban	23	25
Rural	13	9
Mean Baseline IOP	23.60±1.10	23.78±0.89

Table 2: Reveals a progressive decrease in mean IOP with Latanoprost therapy when the patients were compared at every subsequent follow up with the IOP of previous follow up findings. This reduction in IOP was statistically significant by one-way ANOVA. ($p<0.001$)

Table 2: Comparison of mean IOP in Latanoprost group by one- way ANOVA.

Visits	Mean	S.D.	Minimum	Maximum	F-value	P-value
Baseline	23.60	1.10	22	25	851.42	< 0.001*
1st follow up	19.31	0.83	18	21		
2nd follow up	16.30	0.70	15	18		
3rd follow up	13.47	0.97	12	15		

Table 3: Shows a decreasing trend in the mean values of IOP from first to third follow up with Timolol eye drop. This reduction in IOP was statistically significant by one-way ANOVA (p<0.001).

Table 3: Comparison of mean IOP in Timolol group by one-way ANOVA.

Follow-up	Mean	S. D	Minimum	Maximum	F-value	P-value
Base line	23.78	0.89	22	25	235.36	< 0.001*
1st follow up	21.38	1.07	20	23		
2nd follow up	19.38	1.14	17	21		
3rd follow up	17.94	0.92	16	20		

Table 4: Latanoprost produced a greater reduction in mean IOP at each follow- up as compared to Timolol (P < 0.001)

Table 4: Comparison of mean IOP reduction by latanoprost and timolol group by student independent t-test

Visits	Latanoprost	Timolol	t-Value	P-Value
	Mean± S. D	**Mean± S. D**		
Baseline	23.60±1.10	23.78±0.89	0.780	0.438#
1st follow up	19.31±0.83	21.38±1.07	9.588	< 0.001*
2nd follow up	16.30±0.70	19.38±1.14	14.009	< 0.001*
3rd follow up	13.47±0.97	17.94±0.92	19.75	< 0.001*

Table 5: Adverse effects of Latanoprost and Timolol

Adverse Effects	Latanoprost number of Patients (%)	Timolol number of patients (%)
Blurred vision	1(4.1)	3(12.5)
Burning	2(8.3)	2(8.3)
Dry Eye	1(4.1)	4(16.6)
Headache	2(8.3)	3(12.5)
Conjunctival hyperemia	4(16.6)	1(4.1)

Discussion

Glaucoma is an ocular disease having multiple causes, often insidious in onset and gradually progressive, resulting in permanent visual loss, hence, it is also called as the "silent thief of sight". Raised IOP is a significant and modifiable risk factor in the development and progression of glaucoma.[16,17] . Many randomized clinical trials have shown that reducing IOP slows the onset and progression of glaucoma. [18, 19]

Increasing age is a major risk factor for POAG. In this study, most of the patients attending the ophthalmology outpatient department were in the mean age in L- group was 52.95 ± 9.43 and in T-group was 51.05 ± 9.78 with male prepondance, males 41 (59%) and females 29 (41%). The study results were in concordance with a number of other epidemiological studies which showed that prevalence of glaucoma increases dramatically with age, especially after the age of 40 years, [20,21,22,23] whereas a study done by Sharma et al.[24] showed that the highest number of patients belonged to >60 years of age group (34%). It may be due to a decline in retinal ganglion cell number and reduced neural capacity with advancing age.

Studies of gender influence on glaucoma prevalence have been conflicting. Our study results were similar with other observations documented by Agarwal etal. [23] Das et al. [25] Mehani et al. [26] and Parrish et al. [27] and results were in contrast to a study done by Soumya et al. [28] who had more females (32) as compared to males (28) in their study subjects.

In latanoprost group there was decline in mean IOP at every follow up visit as compare to baseline. There was progressive decline in mean IOP at every follow up visit from baseline in timolol group also. When comparison between mean decline in IOP was done between Latanoprost and timolol group, it was found that latanoprost is superior to timolol at every follow up. The final reduction in the mean IOP in latanoprost group was 10.13±0.13 mmHg as compare to Timolol group which was 5.84±0.03 mmHg. The difference in IOP reduction from baseline to final follow up visit was 4.29±0.16 mmHg. This difference in IOP was also statistically significant. The study results were in agreement with other studies done by Soumya et al [28] Rao and Narayanan [29], Gulati et al. [30], and Harasyamowycz et al. [31]A meta-analysis done by Zhang et al. [32] showed that once-daily administration of Latanoprost produces a consistent reduction in IOP and stabilizes the IOP diurnal curve as well, whereas timolol has no additional benefit of stabilization of IOP compared to latanoprost. This fact again reinforces the superior efficacy of latanoprost over timolol.

In this study the adverse effect seen were local adverse effects, Conjunctival hyperemia was seen in more number of patients who received Latanoprost compared to patients who received Timolol. This result was similar to study done by Lou H.et al. [33] where Latanoprost caused conjunctival hyperemia in more patients than timolol. Dry eye, Blurred vision were mostly reported in Timolol group. There were no systemic side effects observed in both the treatment group during the study.

Conclusion

Although both Timolol and Latanoprost reduced the IOP in glaucomatous patients but Latanoprost showed higher efficacy in reducing the IOP as compared to Timolol. Once a day dosing of Latanoprost plays a major role in its better compliance and its round the clock control of IOP, added action on outflow tract and probable safer systemic side effects profile make it more preferable over Timolol eye drop.

According to the Indian scenario, management of glaucoma should be initiated with Timolol as first line drug as it is effective and affordable to the patients and Latanoprost can be used as an add on therapy in patients who show lesser response or as an alternative treatment in case of any contraindication to use of Timolol.

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