Original Article

Latanoprost 0.005% v/s Timolol Maleate 0.5% Pressure Lowering Effect in Primary Open Angle Glaucoma

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Pak J Ophthalmol 2008, Vol. 24 No. 2

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Received for publication
July' 2007

Purpose: To compare the pressure lowering effect of Latanoprost 0.005% and Timolol Maleate 0.5% in the newly diagnosed patients of primary open angle glaucoma.

Material and Method: This open label, comparative study was conducted in the department of Ophthalmology, Liaquat University of Medical & Health Sciences Jamshoro / Hyderabad, from Jan 2006 to March 2006. 58 Patients (96 eyes) who qualified at the screening examination and meet the eligibility criteria were then assessed for best corrected visual acuity, base line IOP with applanation tonometery, angle grading with gonioscopy, anterior and posterior segment examination with slit lamp bimicroscopy.The patient's base line cup / disc ratio and visual fields were also recorded for follow up assessment then the patients advised to instill latanoprost 0.005 % once daily in evening in eye that was randomly selected and timolol maleate 0.5 % twice daily in the contralateral eye of same patient to exclude all demographic systemic and ocular factors that may influence the IOP. Patients were followed on 1st week, 3rd week, 1.5 months, 2.0 months, 2.5 months and 3.0 months then compared the pressure lowering effects of both drugs.

Results: Out of 58 patients 30 (51.7%) were male and 28 (48.3%) were female and mean age was 60.5 years. During our study the base line IOP for timolol maleate was 25.8 mmHg and for latanoprost was 25.6 mmHg. During three months treatment the mean reduction in IOP was 6.55 mmHg (26.7%) timolol maleate and 7.41 mmHg (28.9%) in the patients receiving latanprost. The post-treatment IOP was 19.25 mmHg (P-value = 0.0001) in patients receiving timolol maleate and 18.18 mmHg (P-value 0.0001) in patients receiving latanoprost the difference between the values of reduction in IOP from base line IOP was 0.86 mmHg.

Conclusion: The IOP lowering effect of latanoprost was 2.2% greater than timolol maleate in newly diagnosed patients of primary open angle glaucoma.

Raised intra ocular pressure (IOP) is a risk factor, contributing to optic nerve damage and subsequent visual field loss in patient with glaucoma or ocular hypertension[1-3]. Glaucoma effects as many as 67 million people word wide and is a leading cause of vision loss and blindness[4].

To prevent the progression of glaucoma and to preserve vision, mean IOP should be reduced to a

target pressure that is patient dependent, and diurnal IOP fluctuations should be minimized. Most patients can be treated with single drug but some require multiple drug therapy. Unfortunately tachyphylaxis is common with many of currently available drugs. Since last two decades timilol maleate 0.5% has becomes first line therapy for the reduction of IOP[5], and is often used in combination with topical carbonic anhydrase inhibitors, alpha – agonist or prostaglandin analogues in those patients whose control of IOP requires more than one medication.

Though the number of available drugs has increased significantly during the last 10 years, an ideal agent has not yet been found. Because of their effectiveness and prolonged action prostaglandin analogues have recently provoked great interest.

Prostaglandin (PGF 2α) analogues comprise a new class of ocular hypotensive agents. They reduce IOP at least as effectively as β – adrenergic agonists such as timilol maleate which are the standard treatment for open angle glaucoma and ocular hypertension, but lack their undesirable systemic effects[6-8]. The PGF 2α analogue (latanoprost) after installation in the eye is hydrolyzed by esterases in the cornea to active free acid[9]. The nanomolar concentration of free fatty acid has preferential affinity and full agonist activity for the FP receptors with no meaningful affinity and activity at other receptors[10-11]. The FP receptors are abundant in the longitudinal ciliary muscle of the human eye and iris sphinter[11]. The activation of these receptors by prostaglandin PGF 2α or it's analogues triggers a cascade of events that increases the uveoscleral out flow of aqueous humour[12-13], some author suggest that activation of FP receptor has a variety of mechanism to lower the IOP, including relaxation of ciliary muscle [14], the induction of matrix metalloproteinases[15], and subsequent degradation of extracellular matrix protein, and release of endogenous prostaglandins[16].

This study was designed to compare the pressure lowering effects of latanoprost 0.005 % and timolol maleate 0.5 % in the newly diagnosed patients with primary open angle glaucoma.

MATERIAL AND METHODS

This prospective open label, comparative study was conducted on 58 patients (96 eyes) at Liaquat University Eye hospital, Hyderabad during 3 month period from 1st January to 31st March 2006. The patients selected from out patients' department of Liaquat University Eye Hospital, Hyderabad as a newly diagnosed patient of primary open angle glaucoma (POAG). The each patient screened out after getting consent and all data was recorded in a printed proforma according to following inclusion and exclusion criteria.

Inclusion criteria

Above 40 year of age, any sex and race if diagnosed as POAG, with mean IOP range from 24-36 mmHg in each eye during screening time.

Exclusion criteria

Excluded those patients having;

1. Best corrected visual acuity worse than 6/24.
2. Intra ocular pressure greater than 36 mmHg.
3. Cup / disc ratio > 0.8.
4. Severe central field loss.
5. Inability to undergo applanation tonometery.
6. Clinically significant progressive retinal diseases.
7. Ocular inflammation and infection within past three months.
8. Ocular trauma within past six months.
9. Ocular laser surgery within past three months.
10. Severe ocular pathology (like dry eye) and systemic disease (uncontrolled cardiovascular, bronchial asthma and chronic obstructive pulmonary disease) that precluded safe administration of topical β blocker, prostaglandin analogue.
11. Significant hypersensitivity to prostaglandin and it's analogue, topical or systemic β blocker.
12. Use of topical NSAID two weeks before the screening.
13. Use of glucocoriticoid therapy 2-4 week before the screening.

Patients who qualified at the screening examination and meet the eligibility criteria were then assessed for best corrected visual acuity, base line IOP with applanation tonometery, angle grading with gonioscopy, anterior and posterior segment examination with slit lamp biomicroscope.

The patient's base line cup / disc ratio and visual fields were also recorded for follow up assessment. Patients were advised to instill latanoprost once daily in evening in one eye that was randomly selected and timolol maleate twice daily in the contralateral eye of same to exclude all demographic systemic and ocular factors that may influence the IOP. Then patients were followed on 1st week, 3rd week, 1.5 months, 2.0 months, 2.5 months and 3.0 months to compare the pressure lowering effects of both drugs.

RESULTS

Out of 58 patients 30 (51.72%) were male and 28 (48.27%) were female (Table-1) and mean age was 60.5 years (Table-2). There was no statistically significant difference between age, sex and race in the study population.

During our study the base line IOP for timolol maleate was 25.8mmHg (Fig. 1) and for latanoprost was 25.6 mmHg (Fig. 2).

During three months treatment the mean reduction in IOP was 6.6 mmHg (26.7%). timolol maleate and 7.4 mmHg (28.9%) in the patients receiving latanprost (Table 4). These values of reduction in IOP from base line IOP were statistacially significant for both drugs because the post-treatment IOP was 19.25 mmHg (P-value = 0.0001) in patients receiving timolol maleate and 18.18 mmHg (P- value 0.0001) in patients receiving latanoprost (Table 3). The difference between the values of reduction in IOP from base line IOP was 0.86 mmHg that was not statistically significant.

The side effect (Table 5) of the treatment were ocular stinging in two patients with latanoprost and conjunctival congestion in two patients receiving timolol maleate 0.5%, so both treatment were well tolerated with no statistically significant difference between the two drugs.

DISCUSSION

Our study showed that the use of latanoprost has superiority over timolol maleate to reduce the IOP in newly diagnosed patients with open angle glaucoma. This is especially interesting in view of the fact that latanoprost has 2.2 times more efficacy in reducing IOP as compared with timolol maleate and was instilled once daily unlike timolol maleate which was instilled twice daily.

The value of IOP reduction in our study with timolol maleate was 6.6 mmHg (26.7%) and is comparable to the results of previous studies with timolol maleate[19-20]. A study of 391 patients with primary open angle glaucoma or ocular hypertension showed that the efficacy of timolol maleate twice daily to reduce the base line IOP was 7 mmHg (26%)[19].

Table 1: Gender distribution

Gender	Patients n (%)
Female	30 (51.7)
Male	28 (48.3)
Total	58 (100)

Table 2: Patients' age in years

Age range (years)	Patients n (%)
41 – 45	4 (6.9)
46 – 50	4 (6.9)
51 – 55	14 (24.1)
56 – 60	16 (27.6)
61 – 65	12 (20.7)
66 – 70	2 (3.4)
71 – 75	2 (3.4)
76 – 80	4 (6.9)
Total	58 (100)

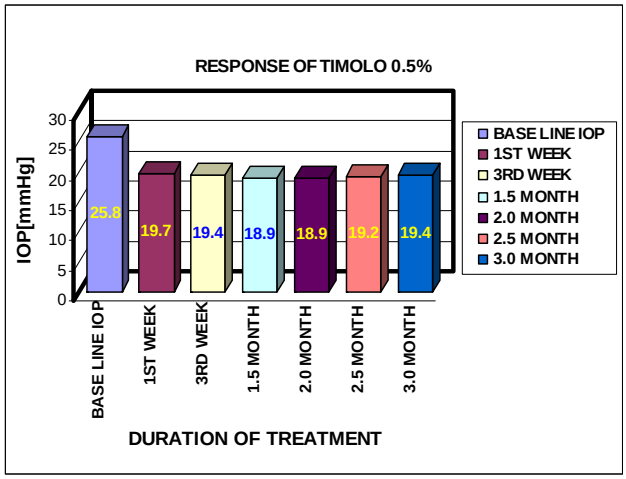

Fig. 1

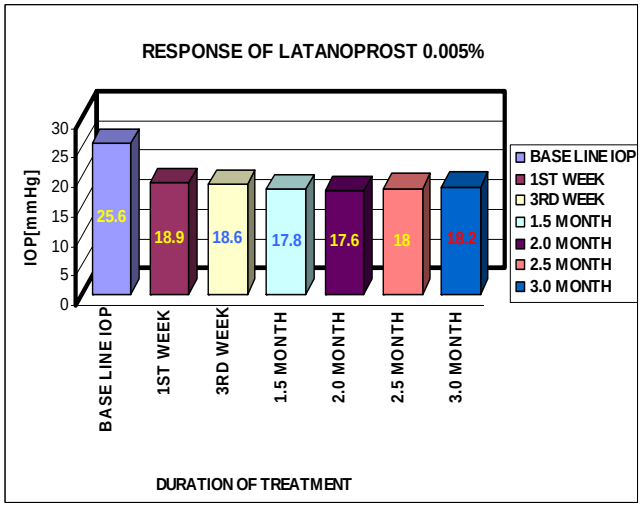

Fig. 2

Table 3: Responder analysis in IOP reduction during three months treatment

Name of Drug	Base Line IOP	IOP (mmHg) Change During Three Month Treatment						Reduction In IOP
	[Mean]	1st week	3rd week	1.5 month	2.0 month	2.5 month	3.0 month	[Mean]
Timolol 0.5%	25.8	19.7	19.4	18.9	18.9	19.2	19.4	19.3
Latanoprost 0.005%	25.6	18.9	18.6	17.8	17.6	18.0	18.2	18.2

Table 4: Values of mean IOP reduction

Name of drug	Range	Mean	%	Difference
Timolol Maleate 0.5%	6.1– 6.9 mmHg	6.6 mmHg	26.7	0.86 mmHg
Latanoprost 0.005%	6.7– 8.0 mmHg	7.4 mmHg	28.9	

Table 5: Advers effects during three month treatment

Drugs	No of cases	Side effects
Timolol Maleate 0.5%	2	Conj. Congetion
Latanoprost 0.005%	2	Ocular stinging
Total	4	

In our study results of timolol maleate (mean reduction in IOP - 6.6 mmHg) is comparatively equal with the results of Rouland JF study (mean reduction in IOP 7.0 mmHg) for timolol maleate 0.1% gel once daily versus conventional timolol maleate 0.5% solution twice daily in 210 patients with primary open angle glaucoma or ocular hypertension[17].

In our study the efficacy of latanoprost in IOP reduction was 7.4 mmHg (28.9%) that may be compared with findings with latanoprost, a prostaglandin F 2α analogue approved for use in patients with open angle glaucoma or ocular hypertension[21].

The study of Patel SS, regarding efficacy and tolerability of latanoprost reported that the installation of latanoprost in the evening were more effective that in the morning that treatment over 3-6 months lowered IOP by 27% to 35% relative to base line[6]. These results can be compared with our study results of latanoprost to reduce the base line IOP by 28.9% during three months.

A study of Halpern MT showed that the average IOP was lower for patients receiving latanoprost than timolol meleate (18.7 mmHg versus 20.5 mmHg respectively)[18] these results can support our study results that the average IOP was lower more for patients on latanoprost than patients on timolol (18.2 mmHg versus 19.3 mmHg respectively).

CONCLUSION

Our study showed that when used as primary therapy, latanoprost insitlled once daily in the evening reduced mean IOP significantly 2.2% more than timolol maleate instilled twice daily. Both the drugs were generally well tolerated and safe for use in newly diagnosed patients of primary open angle glaucoma.

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