

Role of Latanoprost in the Treatment of Primary Open Angle Glaucoma

1. Mohan Perakash Maheshwari 2. Ashok Kumar Narsani 3. Greesh Kumar
4. Kishore Kumar

1. Asstt. Prof. of Pharmacology & Therapeutics, Baqai Medical College, Karachi 2. Assoc. Prof. of Ophthalmology, Liaquat University Eye Hospital, Hyderabad, Sindh 3. Sr. Registrar, Baqai Institute of Cardiovascular Diseases, Baqai Medical University, Karachi 4. Medical Advisor, Novartis Pharma, Karachi

ABSTRACT

Objective: The aim of this study was to observe the effect of Latanoprost in lowering intraocular pressure (IOP) in primary open angle glaucoma (POAG) patients.

Study Design: Prospective, open-label, Observational Study.

Place and Duration of Study: This study was conducted at the Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute, Jinnah Post-graduate Medical Centre, Karachi from February 2008 to July 2008.

Methods and Materials: Thirty patients of POAG were enrolled and were treated with Latanoprost 0.005% eye drops for 12 weeks. The parameter examined was IOP by using Goldmann applanation tonometer.

Results: The results have been expressed as mean $\pm$ SEM. The mean IOP of both eyes decreased significantly (from 27.16 ± 0.19 mmHg to 17.94 ± 0.23 mmHg; $p < 0.001$). The average percentage reduction in IOP was -33.94% from week 0 to week 12.

Conclusion: Latanoprost 0.005% eye drops may become an important choice as a monotherapy for primary open angle glaucoma patients.

Key Words: Latanoprost, Primary open angle glaucoma, Intraocular pressure.

INTRODUCTION

Glaucoma is an optic neuropathy associated with retinal ganglion cell death that results in visual field loss¹. It is one of the leading causes of blindness worldwide², affecting about 70 million people³. Primary open angle glaucoma (POAG), the most common type, affect an estimated 2.5 million persons in the United States, 130,000 of whom will be blind as a result⁴. It usually affects both eyes and has no noticeable symptoms in most patients until the later stages of the disease, when patients lose their central vision⁵.

Epidemiological studies demonstrate that a significant proportion of typical late onset glaucoma is genetically determined. Some studies have shown the prevalence of maternal family history is six to eight times greater than a paternal history⁶.

Evidence suggests that the black population has a much higher prevalence of open-angle glaucoma than non-black population. Black patients also tend to have a more severe clinical course with onset at an earlier age, with greater severity and with more damaging results⁷⁻⁸. The exact pathophysiology of optic nerve damage in POAG is not clearly understood⁹, but there is strong evidence that elevated IOP plays an important role in the neuropathy, and it has been shown that a reduction in the level of IOP lessen the risk of visual field progression in open angle glaucoma¹⁰.

Topical ocular- hypotensive medication is considered the treatment of choice in the initial management of increased IOP in patients with glaucoma¹¹. Topical treatment aimed at decreasing IOP for the whole life of

patients¹², which might prevent optic nerve head damage and subsequent loss of visual function¹³.

Prostaglandin analogues are fast becoming the mainstay of therapy for subjects with glaucoma¹⁴. Latanoprost was the first prostaglandin approved in the United States for reduction of IOP¹⁵, offers certain advantages over other medications for the treatment of open angle glaucoma¹⁶. It is a phenyl substituted analogue of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), and is widely used for the treatment of glaucoma because of its excellent potent IOP reduction¹⁷. Studies have shown that a single dose in the evening is the most effective¹⁸. Although the mechanism of IOP reduction by latanoprost is thought to increase the uveoscleral outflow as a result of remodeling the extracellular matrix of ciliary muscle mediated by FP receptors, the details of this mechanism remain unclear^{19,20}. $PGF_{2\alpha}$ related drugs have been reported to produce endogenous prostaglandins (PGs), and several reports have suggested that induction of endogenous PGs are involved in IOP reduction^{21,22}.

The purpose of this study was to observe the effect of Latanoprost 0.005% eye drops administered once daily in patients with primary open angle glaucoma.

METHODS AND MATERIALS

Study design: This prospective, observational, open label study was conducted in the Department of Pharmacology and Therapeutics, Basic Medical Sciences (BMSI); in collaboration with Department of Ophthalmology, Jinnah Postgraduate Medical Centre (JPMC), Karachi.

Patients: Thirty patients with diagnosed primary open angle glaucoma (POAG) were initially enrolled in this study after taking informed written consent, selected from the outpatient Glaucoma Clinic. Out of these 28 patients were followed till the end of study period.

Two patients has not come for follow- up, one patient due to unknown reasons and other one patient has complaint of conjunctival hyperemia and refused to continue the study. One patient had positive family history of POAG, as shown in Table: I.

Following patients were included in the study: patients of either sex, age between 40-70 years, patients with bilateral POAG, IOP > 21mmHg, patients already on single pressure lowering drug were eligible after a wash-out period of at least 21 days for a adrenergic antagonists, 14 days for adrenergic agonists and 5days for cholinergic agonists and carbonic anhydrase inhibitors.

The patients who were excluded from the study: having angle closure glaucoma, secondary open angle glaucoma, intra-ocular surgery or argon laser trabeculoplasty within the past six months, any intra -ocular inflammation/ infection, known hypersensitivity to study drug, pregnant and nursing mothers. After inclusion in the study the patients were advised to instill Latanoprost 0.005% eye drops once daily at evening 8:00pm.

Study Procedure: At the pre-study visit, both medical and ocular histories were taken. Gonioscopy and perimetry were carried out unless recently performed. Slit lamp examination, IOP measurements, refraction, ophthalmo-scopy and visual acuity were also performed. This pre-study visit took place one month before the study started and the patients were included after these eligibility assessments. If the patients were taking a single drug glaucoma treatment, an appropriate wash-out period was allowed for before the start of the study, as out lined above.

During the study period of 12 weeks there were 4 scheduled follow-up visits: at baseline (week 0), after 4, 8, and 12 weeks. The IOP was measured with calibrated Goldmann applanation tonometer. Three measurements were performed in each eye. The mean of three measurements was used in the statistical analysis. The IOP was measured at 9.00 am, 12.00 noon, and 3.00pm at each visit.

Statistical Analysis: Our final analysis applied to 28 patients who completed the study. All values have been expressed in mean $\pm$ SEM. The observations of the parameters were recorded in a tabulated form and paired students "t" test was used to analyze the data to observe the statistical significance of results.

RESULTS

Thirty patients of both genders were enrolled. The patients demographic characteristics are presented in Table-I. All patients ranged in age between 40-69 years, 57% male and 43% female. Out of thirty patients on week 0, 28 patients were treated with study drug Latanoprost 0.005% eye drops till week 12. Mean IOP of both eyes was 27.16 ± 0.19 mmHg which decreased to 20.36 ± 0.21 mmHg on week 4, 18.69 ± 0.14 mmHg, and 17.94 ± 0.23 mmHg by the end of 8 weeks and 12 weeks respectively, as shown in Table 2 and Figure-I .

This decrease in mean IOP of both eyes were statistically highly significant ($P < 0.001$), when compared between week-0 to week 12. The average percentage change in mean IOP was – 25.03% from week-0 to week-4, –8.2% from week-4 to week -8 and – 4.01% from week-8 to week-12. The percentage reduction in mean IOP was -33.94% from week 0 to week 12 as shown in Table- 3.

Table No.1: Demographic and baseline characteristics of patients

Characteristics	Study Group (Latanoprost)	
Total patients:	30	
Remained in the study:	28	93.33%
Left out:	02	6.66%
Gender:		
Male:	16	57%
Female:	12	43%
Age:		
Mean:	52.67	years
Range:	40-69	years
Family history		
Positive:	01	4%
Negative:	27	96%
Intra-ocular pressure (mmHg)		
Mean ($\pm$ SEM)	27.16($\pm$ 0.19)	

Table- No.2: Iop Lowering Effect Of Latanoprost From Week-0 To Week-12

Parameter	Week 0	Week 4	Week 8	Week 12	P-value		
					Week 0-4	Week 4-8	Week 8-12
					Percentage change		
IOP Mean	27.16	20.36	18.69	17.94	<0.001***	<0.002**	<0.005**
IOP SEM	± 0.19	± 0.21	± 0.14	± 0.23	-25.03%	-8.2%	-4.01%

All observations were measured in mmHg Values are expressed in mean $\pm$ SEM SEM=Standard error of mean

P- Value= Probability value

*** =Highly significant

** = Moderately significant

Negative (-) sign indicates reduction in IOP

Table No.3: Percentage reduction in mean iop from week 0 to week 12

Study Group (Latanoprost)	Week 0	Week 12	%age change	P-value
(n =28)	27.16 (±0.19)	17.94 (±0.23)	-33.94%	<0.001***

n =Number of patients who completed the study

All observations were measured in mmHg

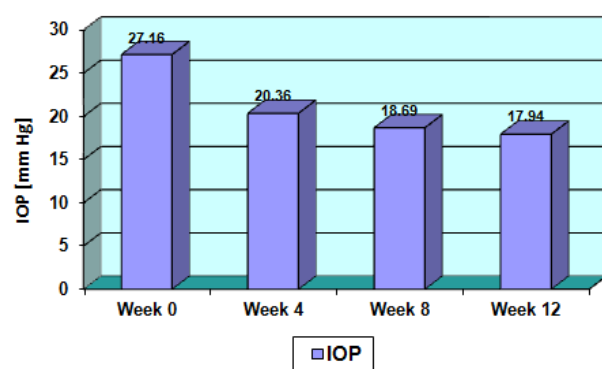
Values are expressed in mean ±SEM

SEM=Standard error of mean

P- Value= Probability value

Negative (-) sign indicates decrease in IOP

*** = Highly significant

**Figure No.1: IOP lowering effect of latanoprost from week 0 to week12**

DISCUSSION

This present study demonstrates significant reduction in mean IOP with Latanoprost 0.005% in primary open angle glaucoma patients. The results shown statistically significant ($P<0.001$) difference when compared from week 0 to week 12. Our results match with the study of Hussain et al²³, who observed 27-33% reduction in mean IOP with Latanoprost 0.005% at the end of 12 weeks of treatment.

We observed -33.94% reduction in IOP with the Latanoprost which is also in accordance with the study done by Alm A & Stjernschantz J²⁴, Scandinavian Latanoprost study group, who observed 35% reduction in mean IOP by Latanoprost 0.005% applied in the evening for six months. The study of Patel SS and Spencer CM²⁵, regarding efficacy and tolerability of Latanoprost reported that the installation of Latanoprost in the evening was more effective than in morning that treatment over 3-6 months lowered IOP by 27-35% relative to baseline. The results can be matched with our study results of Latanoprost. The results of Aquino and Luna²⁶ are in contrast to our results as they

observed 39% reduction in IOP after 12 weeks of treatment with Latanoprost 0.005% once daily.

CONCLUSION

The results of this study demonstrated that 0.005% latanoprost instilled once daily in the evening is statistically significant in reduction of IOP and may become an important choice as monotherapy for the medical management of primary open angle glaucoma. This also contributes to increase the patient compliance.

REFERENCES

1. Noecker RS, Dirks MS, Choplin N, Bernstein P, Batoosingh AL, Whitcup SM. A six months randomized clinical trial comparing the intraocular pressure lowering efficacy of bimatoprost and latanoprost in patients with ocular hypertension or glaucoma. *Am J Ophthalmol* 2003; 135:55-63.
2. Leblance RP. A Canadian glaucoma strategy. *Can J Ophthalmol* 2007; 42:60-65.
3. Aung T, Ebenezer ND, Brice G, Child A, Prescott Q, Lehmann O, et al. Prevalence of optineurin sequence variants in adult primary open angle glaucoma: implications for diagnostic testing. *J Med Genet* 2003; 4:1-4.
4. Fleming C, Whitelock EP, Beil T, Smit B, Harris RP. Screening for primary open- angle glaucoma in the primary care setting. An update for the US preventive services Task force. *Ann Fam Med* 2005; 3:167-170.
5. Kroes M and Burton H. Primary open angle glaucoma. The need for a consensus case definition. *J Epidemiol Community Health* 2003; 57:752-754.
6. Andrews R, Ressiniotis T, Tumbull DM, Birch M, Keers S, Chinnery PF, et al. The role of mitochondrial haplo groups in primary open angle glaucoma. *Br J Ophthalmol* 2006; 90:488-490.
7. Noeker RJ, Earl ML, K Thomas, Mundorf, Silverstein, Phillips MP. Comparing bimatoprost and travoprost in black Americans. *Current Medical Research and Opi* 2006;22(11):2175-2180.
8. Palmisano P, Hynes M, Mueller L. Glaucoma and race: a case for screening in Connecticut. *Conn Med* 2000; 64:75-78.
9. Kamath CA, Satyanaryana, Rodrigues CF. Ocular surfaces changes in primary open angle glaucoma with long term topical Antiglaucoma medications. *MJ AFI* 2007; 63 341-345.
10. McKinnon SJ, Gold berg LD, Peeples, Walt JG, Bramley TJ. Current management of glaucoma and the need for complete therapy. *Am J manag care* 2008; 14:S20- S27.
11. Sanchez JG, Rouland JF, Spiegel D, Pajic B, Cunliffe I, Traverso C, et al. A comparison of the fixed combination of latanoprost and timolol with the unfixed combination of brimonidine and

- timolol in patients with elevated intraocular pressure. A six month, elevator masked, multicentre study in Europe. *Br J Ophthalmol* 2004; 88:877-883.
12. Nordmann JP, Auzannean N, Ricard S, Berdeaux G. Vision related quality of life and topical glaucoma treatment side effects. *Bio Med Central* 2003; 19(75):1-9.
 13. Ressiniotis T, Griffiths PG, Birch M, Keers S, Chinnery PF. The role of Apolipoprotein E gene polymorphisms in primary open angle glaucoma. *Arch Ophthalmol* 2004; 122:258-261.
 14. Narayanaswamy A, Neog A, Baskaran M, George R, Lingam V, Desari C, et al. A randomized, crossover, open label pilot study to evaluate the efficacy and safety of Xalatan in comparison with generic Latanoprost (Latanoprost) in subjects with primary open angle glaucoma or ocular hypertension. *Indian J Ophthalmol* 2007;55: 127-131.
 15. Halpern MT, Covert DW, Robin AL. Projected impact of travoprost versus both timolol and latanoprost on visual field deficit progression and costs among black glaucoma subjects. *Trans Am Ophthalmol Soc* 2002; 100:109-118.
 16. Hylton C, Robin AL. Update on prostaglandin analogues. *Curr Opin Ophthalmol* 2003; 14:65-69.
 17. Chiba T, Kashiwagi K, Chiba N, Tsukahara S. Effect of non-steroidal anti-inflammatory ophthalmic solution on intraocular pressure reduction by latanoprost in patients with primary open angle glaucoma or ocular hypertension. *Br J Ophthalmol* 2006;90:314-317.
 18. Mandric Z, Korsia J, Bojic L. Current management of open angle glaucoma. *Acta Clin Croat* 2002; 41(S4):45-50.
 19. Lindsey JD, Kashiwagi K, Kashiwagi F, Weinreb RN. Prostaglandin action on ciliary smooth muscle extracellular matrix metabolism: implications for uveoscleral outflow. *Surv Ophthalmol* 1997; 41(Suppl 2):53-59.
 20. Weinreb RN, Kashiwagi K, Kashiwagi F, Tsukahara S, Lindsey JD. Prostaglandins increase matrix metalloproteinase release from human ciliary smooth muscle cells. *Invest Ophthalmol Vis Sci* 1997; 38:2772-2780.
 21. Kashiwagi K, Kanai N, Tsuchida T, Suzuki M, Liszukay, Tsukahara S. Comparison between isopropyl unoprostone and latanoprost by prostaglandin E₂ induction, affinity to prostaglandin transporter, and inter-ocular metabolism. *Exp Eye Res* 2002; 74:41-49.
 22. Diestelhorst, Kriegelstein GK, Lusky M, Naqasubramanian S. Clinical dose- regimen studies with latanoprost, a new ocular hypotensive PGF₂ alpha analogue. *Surv Ophthalmol* 1997; 41(Suppl 2): 77-81.
 23. Hussain I, Malik J, Khan T et al. Addictive effect of latanoprost to topical beta blockers in lowering IOP in primary open angle glaucoma and its ocular tolerance. *Pak J Ophthalmol* 2000; 16(2): 79-81.
 24. Alm A and Stjernschantz J. Scandinavian latanoprost study group. Effects on intraocular pressure and side effects of 0.005% latanoprost applied once daily, evening or morning. A comparison with timolol. *Ophthalmology* 1999; 102(12):1743-1752.
 25. Patel SS, Spencer CM. Latanoprost a review of its pharmacological properties, clinical efficacy and tolerability. *Drugs & Aging* 1996; 9(5):363-378.
 26. Aquino MV and Luna ML. The effects of latanoprost vs timolol on intraocular pressure in patients with glaucoma and ocular hypertension. *Asian J Ophthalmol* 1999; 1(3):3-7.

Address for Corresponding Author:**Dr. Mohan Perakash Maheshwari**

Assistant Professor,
Department of Pharmacology & Therapeutics,
Baqai Medical College, Karachi
Flat # C-505, 5th Floor, Alnoor Centre,
Near Ankle Saria Hospital, Randle Road,
Garden, Karachi.
E-mail: mohanpk75@yahoo.com
Cell # 0306-3346399