

# Comparison of Latanoprost and Dorzolamide in Patients with Open Angle Glaucoma

Imtiyaz Ahmad Lone, Azra Rizvi, Sheikh Sajjad Ahmad, Reyaz Ahmad Untoo

## ABSTRACT

To compare the ocular hypotensive efficacy and side effects of either latanoprost or dorzolamide in patients with open angle glaucoma, forty-four patients with open angle glaucoma were included in a randomized, double masked study for a period of 3 months. All previous glaucoma medications were stopped and the patients were randomized to receive either latanoprost 0.005% at bed time or dorzolamide 2% three times daily. After 3 months, the mean reduction in IOP was 6.8 (SD 3.1) mm Hg in the latanoprost group as compared to 4.7 (SD 2.4) mm Hg in the dorzolamide group. The difference of 2.1 mm Hg was highly significant. Both the drugs were well tolerated systemically and locally. Latanoprost was superior to dorzolamide in reducing the mean IOP and thus has the potential for becoming the first line treatment in glaucoma.

## Key Words

Latanoprost, Dorzolamide, Glaucoma, Ocular hypertension

## Introduction

Latanoprost is a prostaglandin analogue with a potent ocular hypotensive efficacy. It reduces the IOP by increasing the uveoscleral outflow. Latanoprost 0.005% used once daily (preferably bed time) reduces IOP at least as effectively as timolol 0.5% applied twice daily (1-3).

Dorzolamide is the first topical carbonic anhydrase inhibitor. When 2% dorzolamide is used three times daily, it causes a maintained reduction of IOP due to reduced aqueous production (4,5). Both latanoprost and dorzolamide are now accepted as safe and potent ocular hypotensive agents. The aim of present study was to compare the efficacy and side effects of the two drugs when used as a single agent.

## Material and Methods

To be eligible for the study, the patients had to meet the following criteria ;

- age 40 years and above.
- diagnosis of open angle glaucoma, ocular hypertension, pigmentary glaucoma or exfoliation glaucoma.
- IOP of at least 22 mm Hg on previous treatment.
- expectation by the investigator that IOP would remain adequately controlled with a single drug treatment for 3 months without optic nerve damage or progression of visual field loss.

From the Department of Ophthalmology, SKIMS Medical College, Bemina, Srinagar (J&K).

Correspondence to : Dr. Imtiyaz Ahmad Lone, Senior Resident, Department of Ophthalmology, SKIMS Medical College, Bemina, Srinagar-190011 (J&K) India.

Exclusion criteria included ; previous treatment with carbonic anhydrase inhibitor or latanoprost, narrow angles or presence of peripheral anterior synechiae, ocular surgery or argon laser trabeculoplasty carried out less than 6 months before the study, corneal abnormalities or any condition preventing reliable applanation tonometry, active eye disease other than ocular hypertension or open angle glaucoma, known hypersensitivity to any component of the study drugs, use of any oral drug known to affect the IOP, pregnant or nursing women, history of noncompliance or unreliability or inability to adhere to the protocol .

Before treatment with the study drugs, any previous glaucoma medication was washed out. The minimum wash out periods were 3 weeks for  $\beta$ -adrenergic antagonists, 2 weeks for adrenergic agonists and 5 days for cholinergic agonists.

Before the study schedule, a detailed history and examination was made. The ocular examination included determination of visual acuity, refraction, slit-lamp examination, ophthalmoscopy, perimetry and IOP measurement using Goldmann applanation tonometer.

The patients were distributed in two parallel study groups of 22 patients each. One group received latanoprost 0.005% at bed time and the other group received dorzolamide 2% three times daily.

During the study period, the patients were examined at baseline, after 2 weeks, after 4 weeks and after 3 months of treatment. Best corrected visual acuity, refraction, slit-lamp examination and IOP measurement by Goldmann applanation tonometer was performed at all visits. The IOP was determined at 11 a.m. and 4 p.m. The diurnal IOP is defined as the mean value of these two determinations. Any abnormality of the lids, conjunctiva, cornea or iris was recorded.

## Results

The results of the study were not significantly altered with regards to the age, sex, iris color or diagnosis (ocular hypertension or glaucoma).

At baseline the mean IOP was 29.3 mm Hg in the latanoprost group and 28.7 mm Hg in the dorzolamide group. After 3 months, the mean reduction in IOP was 6.8 (SD 3.1) mm Hg in the latanoprost group as compared to 4.7 (SD 2.4) mm Hg in the dorzolamide group. The difference of 2.1 mm Hg was highly significant. Both the drugs were well tolerated systemically and locally.

There were 10 adverse effects reported; 4 in the latanoprost group and 6 in the dorzolamide group. The adverse effects reported in the latanoprost group were ocular discomfort in 1, conjunctival hyperemia in 1, superficial punctate keratitis in 1 and uncontrolled IOP in 2 patients. The adverse effects reported in the dorzolamide group were ocular discomfort in 2, conjunctival hyperemia in 1, superficial punctate keratitis in 1 and uncontrolled IOP in 2 patients. No systemic adverse effects were reported during the study period.

## Discussion

The results of the study show that 0.005% latanoprost applied topically once daily is a more effective ocular hypotensive agent than 2% dorzolamide used three times daily. Latanoprost provides a stable reduction of IOP over the course of the entire 24 hr. cycle with no big peak and trough once the patient has been on it for a while. The effect of latanoprost on diurnal IOP was almost 2 mm Hg more than the effect of dorzolamide; 6.8 mm Hg compared with 4.7 mm Hg. Latanoprost has a long duration of action and is only given once a day. The shorter duration of action of dorzolamide requires administration three times a day when used as monotherapy (6).

Latanoprost (Mw 432.58) is an isopropyl ester prodrug which per se is inactive but after hydrolysis to the acid of latanoprost becomes biologically active. The prodrug is well absorbed through the cornea and all drug that enters the aqueous humor is hydrolyzed during the passage through the cornea.

The active substance latanoprost, a prostaglandin - F analogue, is a selective prostanoid FP receptor agonist which reduces the IOP by increasing the uveoscleral outflow (7). When PGs come in contact with the PG receptors, it causes the ciliary muscle cells to produce the matrix metalloproteinases, which then in turn induce degradation/remodelling of the collagen in between the muscle bundles in the ciliary muscle. Reduction of IOP starts about 3 to 4 hours after administration and maximum effect is reached after 8 to 12 hours. The pressure reduction is maintained for the entire 24 hours.

Latanoprost offers several potential advantages over currently available medications for glaucoma therapy. Unlike dorzolamide, it acts on outflow rather than formation of aqueous humor. Virtually all glaucomas result from impaired outflow, but not from excessive formation of aqueous humor.

Avascular ocular structures depend on aqueous flow for metabolic exchanges. Therefore chronic excessive reduction of aqueous humor formation may have deleterious effects. Unlike dorzolamide, latanoprost reduces IOP equally well during night and day hours (8). This represents a potential advantage because glaucomatous damage may occur during sleep when ocular perfusion pressure may be reduced because of low systemic blood pressure (9). Further more because latanoprost increases uveoscleral outflow, it can theoretically reduce IOP below episcleral venous pressure, unlike drugs that act by either reducing aqueous humor production or increasing outflow facility. This may be advantageous in patients with normal

tension glaucoma in whom progressive loss at night may develop and who may require very low IOPs.

Both study drugs were well tolerated locally and systemically. Slightly more adverse effects were seen in the dorzolamide group, 6 compared with 4 in the latanoprost group. No iris pigmentation was reported during the study based on slit-lamp examination.

In conclusion, latanoprost was found to be superior to dorzolamide in reducing the mean IOP as judged by the effect on diurnal IOP. Both drugs were well tolerated during the study period.

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