

# COMPARISON OF LATANOPROST AND DORZOLAMIDE IN THE TREATMENT OF PATIENTS WITH OPEN ANGLE GLAUCOMA

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**Background:** This study was conducted to compare the effects on intraocular pressure and side effects of monotherapy with either latanoprost or dorzolamide in patients with open angle glaucoma, pseudoexfoliation glaucoma or ocular hypertension. **Methods:** Sixty patients with open angle glaucoma or ocular hypertension were recruited to a 3-month study. Previous glaucoma medications were washed out and the patients were randomised to receive either latanoprost 0.005% once daily or dorzolamide 2% three times daily. The follow-up visits were conducted at two weeks, one month and three months of study and intraocular pressures and slit lamp examinations were carried out to look for response of therapy and detect complications. **Results:** After 3 months, latanoprost reduced mean baseline intraocular pressure from  $27.2 \pm 3.0$  mm Hg by  $8.5 \pm 3.3$  mm Hg. The corresponding figures for dorzolamide were  $27.2 \pm 3.4$  and  $5.6 \pm 2.6$  mm Hg. The difference of 2.9 mm Hg (95% CI: 2.3-3.6) was highly significant ( $p < 0.001$ ). Both drugs were well tolerated systemically and locally. **Conclusion:** Latanoprost was superior to dorzolamide in reducing the intraocular pressure, judged from the effect on mean intraocular pressure. The once daily dose in the evening ensures better compliance and the problem of hyperpigmentation of the iris were not encountered.

**Keywords:** Glaucoma, Intraocular pressure, Latanoprost, Dorzolamide.

## INTRODUCTION

Glaucoma, which causes optic nerve damage and visual field loss, is the most important cause of irreversible blindness worldwide.<sup>1</sup> The mainstay of drug treatment for glaucoma is timolol, a topical blocker. However, blockers are contraindicated in patients with cardiovascular or pulmonary disorders.<sup>2-4</sup> Pilocarpine, a cholinergic agonist, is sometimes used but it needs to be administered four times per day and causes miosis, myopia, and occasionally retinal detachment and progressive closure of the anterior chamber angle.<sup>5-6</sup> Given such problems, the search for new effective and safer antiglaucoma agents continues. Among the recently introduced agents, three are widely used as alternatives when blockers are contraindicated or fail to control intraocular pressure. Latanoprost (a prostaglandin F<sub>2</sub> analogue), dorzolamide (a topical carbonic anhydrase inhibitor), and brimonidine (a selective  $\alpha_2$  agonist). Latanoprost appears highly promising as unlike beta blockers and some other currently used medications such as carbonic anhydrase inhibitors and  $\alpha_2$  agonists, latanoprost acts on outflow rather than formation of aqueous humour.<sup>7</sup> Because latanoprost increases uveoscleral outflow,<sup>8</sup> it can theoretically reduce intraocular pressure (IOP) below episcleral venous pressure. This may be advantageous in patients with normal tension glaucoma. In fact, one trial<sup>9</sup> suggested that 0.005% latanoprost produced better lowering of ocular perfusion pressure than 0.5% timolol in normal tension glaucoma. Latanoprost may reduce IOP without reducing systemic blood pressure. In contrast, timolol may reduce both of these. Bradycardia<sup>10-12</sup> and bronchospasm<sup>13-15</sup> caused by ophthalmic timolol have been reported in patients with cardiovascular or pulmonary disorders. Therefore, caution is necessary in the use of timolol in such patients. In contrast, latanoprost does not alter heart rate and blood pressure<sup>16,17</sup> and does not affect respiratory function in asthmatic patients<sup>18</sup>.

Both latanoprost and dorzolamide are now widely used in the treatment of open angle glaucoma, and both have acceptable safety profiles. The aim of the present study was to compare the efficacy and side effects of the two drugs used as single agents on IOP in patients of primary open glaucoma in our races.

## MATERIAL AND METHODS

The study was designed as a 3 month, randomised, parallel group, open label, clinical trial comparing the efficacy and side effects of monotherapy with either latanoprost and dorzolamide, done at our department and a total of sixty patients were recruited in the trial. Patients 18 years of age or older with unilateral or bilateral primary open angle

glaucoma, capsular glaucoma, or ocular hypertension with an IOP of at least 21 mm Hg on previous treatment or 25 mm Hg without treatment were eligible for inclusion. Exclusion criteria included previous treatment with carbonic anhydrase inhibitors or latanoprost, closed or barely open anterior chamber angle, current use of contact lenses, intraocular surgery or argon laser trabeculoplasty within the past 3 months, any ocular inflammation or infection within the past 3 months, known hypersensitivity to any component of the study drugs, or any condition preventing reliable applanation tonometry.

During the pre study visit (done three weeks for the study), a medical and ocular history was taken and any concomitant medications were recorded. A thorough ocular examination was performed including determination of visual acuity, refraction, a slit lamp examination, ophthalmoscopy, automated perimetry, and IOP measurement. Also any previous glaucoma drugs were washed out. After washout, the patients were randomised to two parallel study groups: one group received latanoprost 0.005% once daily in the evening, the other group received dorzolamide 2% twice daily. The patients were instructed to instill latanoprost at 10 pm and dorzolamide at 9 am, 2 pm and 10 pm.

During the study, the visits were conducted at baseline, after two weeks, one month, and at three months of treatment. At baseline and at the three month visit IOP was determined at 9 am, 11 am, and 5 pm. The IOP was measured with a calibrated Goldmann tonometer. The mean value of these three determinations was taken as the reading for the statistical analysis. Best corrected visual acuity and refraction were determined and a slit lamp examination was performed at all visits. Flare, if present, was graded as mild, moderate, or severe and cells present in a 2 mm slit were counted and graded as none (0-2 cells), mild (3-5 cells), moderate (6-20 cells), or severe (>20 cells). Any abnormalities of the conjunctiva, cornea, or iris were described and the severity graded as mild, moderate, or severe.

A final follow up visit, 2-4 weeks after the end of the study, was scheduled for all patients to follow up any previously noted adverse events or to detect late adverse events.

The difference in mean IOP reduction from baseline was used as the main response variable. Student's paired t-test was performed to test significance of differences in IOP between the groups.

## RESULTS

There were thirty seven males and twenty-three females in the study that were equally distributed between the two groups. The mean age was 56 (SD 4.4, range: 35-77) years. The most common diagnoses were primary open angle glaucoma seen in thirty-four cases and capsular glaucoma in thirteen. Both eyes were treated in forty-seven cases and only one eye in thirteen. There were forty-six patients on treatment at the pre study visit that had to undergo washout before randomisation. Of these, thirty-two were on only one drug before the study, ten on two drugs and four on three drugs. The most common drugs used were timolol, betaxolol, levobunolol and pilocarpine. At baseline the mean diurnal IOP was 27.9 (SD 2.6) mm Hg in the latanoprost group and 27.9 ( $\pm$ 3.1) mm Hg in the dorzolamide group. After three months, latanoprost had reduced the diurnal IOP by 8.9 ( $\pm$ 2.4) mm Hg compared with 6.6 ( $\pm$ 2.1) mm Hg for dorzolamide). The difference of 2.3 mm Hg (95% CI: 1.4-3.2) was highly significant ( $p < 0.001$ ). A pressure reduction of at least thirty percent was obtained in forty-nine percent of the patients treated with latanoprost compared with sixteen percent cases of the patients treated with dorzolamide. A diurnal pressure of twenty-one mm Hg or lower after three months of treatment was observed in seventy-nine percent of patients treated with latanoprost compared with forty percent of patients on dorzolamide. Ocular adverse events, grouped according to symptoms/signs, are presented in figure-1. Most adverse events were graded as mild or moderate. There were no serious systemic effects of the drugs. Two patients from the dorzolamide group were withdrawn from the study because of non-serious adverse events. In one case the reason was episodes of facial edema and irritation and in one case, metallic taste and nausea after eye drop administration. Iris changes that occurred in one case of latanoprost group consisted of lightening in colour of a small patch of iris not amounting to atrophy or heterochromia.

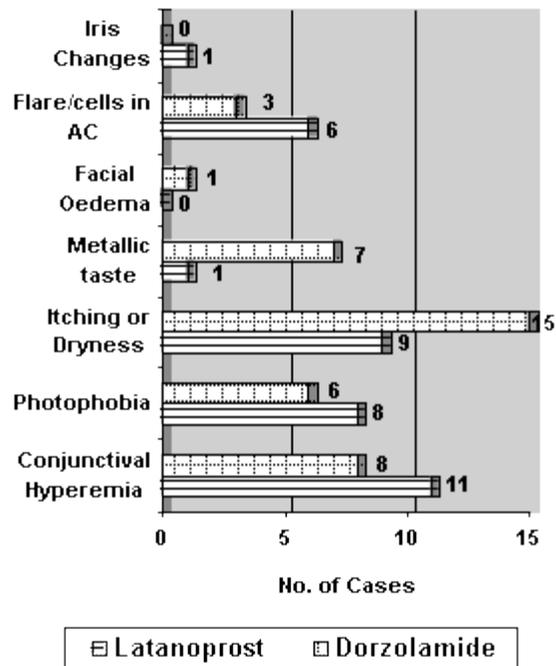
**Table-1: Comparison with a study abroad**

Parameters	Donoghue EP et al <sup>39</sup>	This study
No. of Cases	224	60

Duration of Study	3-months	3-months
Drugs used	.005% Latanoprost-HS 2% Dorzolamide-BD	.005% Latanoprost-HS 2% Dorzolamide-BD
Mean IOP reduction with Latanoprost( $\pm$ SD)	8.5 mm of Hg (3.3)	8.9 mm of Hg (2.4)
Mean IOP reduction with Dorzolamide( $\pm$ SD)	5.6 mm of Hg (2.6)	6.6 mm of Hg (2.1)
Withdrawals form study	8	1
Systemic Complications	66	09
Ocular Complications	107	67

## DISCUSSION

About 66.8 millions people have glaucoma, 6.7 million of whom are bilaterally blind.<sup>19</sup> Pharmacological treatments for glaucoma aim to lower IOP and thereby reduce the risk of optic nerve damage. Studies have shown that reduction of IOP prevents development of glaucoma or visual field loss<sup>20-22</sup> and indeed if the IOP is substantially lowered through treatment, the rate of progression of glaucoma is reduced even among those patients with normal tension glaucoma.<sup>23</sup> Latanoprost is one of the first prostaglandins to be used on a chronic basis in glaucoma patients. It is shown to reduce intraocular pressure effectively in normal, ocular hypertensive and glaucomatous eyes.<sup>24-31</sup> The main mode of action of PGF2 and latanoprost is an increase in uveoscleral outflow of aqueous humour<sup>32,33</sup>. No significant effect on aqueous humour production has been found. The efficacy of latanoprost has previously been compared with 0.5% timolol in three 6 months studies<sup>34-36</sup>. In two of these three studies the IOP reducing effect of latanoprost on diurnal IOP was significantly larger than the effect of timolol<sup>34-36</sup>. The effect of dorzolamide on IOP, on the other hand, is less than that of timolol<sup>37</sup> which is explained by its weaker aqueous suppressive effect compared with timolol<sup>38</sup>. Thus, one might expect that latanoprost should be the more effective drug of the two in terms of IOP reduction, an assumption which was confirmed in our study. The effect of latanoprost on diurnal IOP was almost 3 mm Hg more than the effect of dorzolamide, 8.5 mm Hg compared with 5.6 mm Hg. Latanoprost has a long duration of action and is only given once a day. The shorter duration of dorzolamide requires administration three times a day when used as monotherapy.



**Figure-1: Complications**

Both study drugs were well tolerated locally and systemically. There were no major differences between the groups. No iris pigmentation was reported in our study based on slit lamp examination. Conjunctival hyperaemia was the most frequent event encountered alongwith burning sensation, that subsided by itself with the passage of time. A comparison of our study with another recent study<sup>39</sup> is shown in Table -1.

## CONCLUSION

Latanoprost proved to be a superior drug than dorzolamide in controlling the intraocular pressure. Both drugs were well tolerated, and there was no serious systemic complication observed.

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