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Original Research Article

Efficacy of Latanoprost (0.005%) and Dorzolamide (2%), in Primary Open-Angle Glaucoma (POAG) Patients, as Monotherapy: A Comparative Study

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Abstract

Background: In India as well as the rest of the globe, glaucoma is the second most frequent cause of blindness, and its incidence is rising. The most significant factor and a direct cause of the development of primary open-angle glaucoma is increased intraocular pressure (IOP) (POAG). In order to compare the effectiveness of latanoprost and dorzolamide for lowering IOP in POAG as monotherapy, the current study was conducted. The following are the objectives: To compare the effectiveness of topical latanoprost (0.005%) and topical dorzolamide (2%), both used as monotherapies for POAG, and to assess the negative effects of each drug.

Methods: Eighty patients; 40 males and 40 females with a POAG diagnosis were randomly chosen for the current prospective, open-label trial and split into two groups. One group received topical latanoprost eye drops (0.005%) once day, while the other received dorzolamide eye drops (2%), three times daily. Three follow-up visits were made with each participant at two, four, and eight weeks. IOP was measured using a Perkins Handheld Tonometer before to beginning the baseline phase of treatment. IOP was once more recorded at every subsequent visit in order to track the impact of medications. All patients provided their freely given informed permission.

Results: The mean IOP reduction for latanoprost group was 9.5 ± 3.56 and dorzolamide group was 7.89 ± 3.56. Both medications were successful in lowering IOP. Latanoprost and dorzolamide reduced IOP in different ways, and this difference was statistically significant (P = 0.02). Both medications were well tolerated over the course of the research, with latanoprost group (n = 9) experiencing more adverse effects than dorzolamide group (n = 7).

Conclusion: The results of this study show that topical eye drops containing latanoprost (0.005%) and dorzolamide (2%) both significantly lower IOP in POAG. In terms of lowering IOP, latanoprost is more effective than dorzolamide.

Keywords: Glaucoma; Intraocular Pressure; Latanoprost; Dorzolamide.

Introduction

Glaucoma is a chronic, progressive optic neuropathy brought on by a number of ocular diseases that harm the optic nerve and impair vision.[1] In India as well as the rest of the world, glaucoma is the second most common cause of blindness after cataracts.[2] The number of glaucoma sufferers worldwide is thought to be over 65 million.[2-4] It is estimated that 11.2 million people in India have glaucoma.[5] Over the age of 40, 2.25 million Americans are thought to have primary open-angle glaucoma (POAG), according to estimates. [6]

Out of all the many varieties of glaucoma, POAG is the one that is more common.[5] A multifocal optic neuropathy with distinctive optic nerve atrophy is a potential definition of POAG (adapted from the American Academy of Ophthalmology Preferred Practice Pattern Guidelines, 2005).[7] 6.48 million people in India are affected by PAOG, a form of glaucoma.[5] The prevalence of POAG may rise to 16 million by 2020 as the frequency of the condition rises with age.[5]

As the primary risk factor for glaucoma and glaucoma development, lowering intraocular pressure (IOP) is the major goal of treatment for POAG.[8] Currently, a wide variety of medications, including cholinergic agonists, adrenergic agonists, beta-blockers, carbonic anhydrase inhibitors, and prostaglandin analogues, are available to reduce IOP.[7] Prostaglandin analogues are employed both singly and in combination with other treatments.[7] Latanoprost is the most effective of these medications, has a longer duration of action, and also lessens diurnal IOP variability.[9] According to a research by Gupta *et al*., prostaglandin analogues are the first-line treatment for POAG.[3]

The most significant contributing factor to glaucoma is an increase in IOP, and this variable affects how the disease progresses.[8] Latanoprost is a prostaglandin analogue medication that lowers IOP by enhancing uveoscleral outflow. This is accomplished by relaxing the ciliary muscle and modifying the ciliary muscle extracellular matrix. Latanoprost also reduces the IOP's nocturnal fluctuations [7,10]. A carbonic anhydrase inhibitor, dorzolamide lowers IOP by lowering aqueous production. This is accomplished by restricting the ciliary epithelium's ability to produce bicarbonate ions. As a result, its mode of action is distinct from latanoprost's [7]. According to certain research, dorzolamide lowers IOP by 22.8% of elevated IOP. [11,12] Its effectiveness is comparable to pilocarpine's while having less side effects.[11]. Both the Singh and Shrivastava study and the Thomas *et al*. study demonstrated that latanoprost significantly lowers IOP near normal value and stabilises the diurnal curve in variation of IOP.[8,10] Therefore, we chose a comparative trial to see which medication was more effective at lowering IOP when applied topically to POAG patients: latanoprost or dorzolamide.

Materials and Methods

Patients were chosen from the outpatient Department of Ophthalmology at JLNMCH, Bhagalpur, Bihar from June 2022 to December 2022 for the prospective type, open-labeled, randomised study that was conducted on patients with POAG at the Department of Pharmacology, Jawaharlal Nehru Medical College, Bhagalpur, Bihar. In this study, both sexes of selected patients with IOP > 21 mmHg, POAG, and ocular hypertension affecting one or both eyes and age 40 and above were included. Whose patients narrow angle or presence of peripheral anterior synechiae, ocular surgery or argon laser trabeculoplasty carried out <6 months before the study, corneal abnormalities or any condition preventing reliable Perkins Tonometer used to measure IOP, active eye disease other than open-angle glaucoma, known hypersensitivity to any

component of the study drugs (latanoprost or dorzolamide), use of any drug (e.g., pilocarpine and neostigmine) known to affect the IOP, pregnant or nursing women, history of noncompliance or unreliability or inability to adhere to the protocol, normal-tension glaucoma (IOP <21 mmHg) were excluded.

There were 80 POAG patients in the research. According to the inclusion and exclusion criteria, all patients were chosen. Each subject was given an informed consent after being educated about the study's specifics. The prior study's findings were used to determine the sample size.[9]

A thorough medical history was taken of the patient's general and ocular complaints, including blurred vision, difficulty reading or working up close, ocular allergies, history of recent ocular surgery, drug allergy, history of hypertension, diabetes, chronic obstructive pulmonary disease, asthma, liver dysfunction, smoking and alcohol use, history of other medications, family history of glaucoma, and condition which in the past has resulted in glaucoma.

Quantitative variables were analysed statistically, and mean and standard deviation were used to summarise them. The student's unpaired test was used to compare the means of the two groups, with a significance level of $P < 0.05$. The difference in IOP reduction between the latanoprost group and the dorzolamide group is compared using the Mann-Whitney U-test.

Results

The study compared the efficacy of latanoprost and dorzolamide medication solutions when used as topical monotherapy on POAG patients over the age of 40. Eight additional people dropped out of the study, leaving a total of 80 participants. Of these, 72 persons finished the study. Out of the eight dropouts, two were not found for follow-up, four got combination therapy, one switched to a more affordable drug regimen, and one underwent eye surgery (trabeculoplasty).

Statistical Package for the Social Sciences software was used to compare the demographic information for the latanoprost and dorzolamide groups. Analyses of effectiveness were performed for each protocol population.

The descriptive statistics (mean, standard deviation, and median) for the efficacy variables were computed at baseline and the third follow-up for each treatment group. The Mann-Whitney U-test was used to determine the difference between the mean IOP reductions between the latanoprost and dorzolamide groups.

The demographic breakdown of the participants is provided in Tables 1 and 2. Based on inclusion and exclusion criteria, a total of 80 patients with ages above 40, including both males and females, were included for the study. The mean age for the dorzolamide group was 65.61± 9.44 and 63.11± 10.46 for the latanoprost group. The majority of patients in both categories are between the ages of 61 and 70. In the latanoprost group, there were 19 men and 21 women, but in the dorzolamide group, there were 23 men and 17 women [Table 2]. The total number of males and females in the studied population was 42 males and 38 females.

Table 3 lists the risk variables that are connected to POAG. In the current study, 12 patients had a history of smoking, 25 patients had hypertension, and 14 patients had diabetes mellitus.

Table 1: Age distribution in study group

Age in years	Dorzolamide groupno. of patients=40	Latanoprost group no. of patients=40
41-50	4	7
51-60	9	10
61-70	17	13
71-80	10	10

Table 2: Sex distribution Latanoprost and Dorzolamide group

Age in years	Dorzolamide group no. of patients=40	Latanoprost group no. of patients=40	Total n=80
Male	19	23	42
Female	21	17	38

Table 3: Number of diabetic patients, hypertensive patients, and smoking risk factors in both drug groups

Risk Factor	No. of patient with risk factor n=51(%)
Diabetes mellitus	14/80(17.5%)
Hypertension	25/80(31.25%)
Smoking history	12/80(15%)

IOP was 29.78± 5.1 for the latanoprost group and 30± 4.06 for the dorzolamide group at baseline. As a result, the starting mean IOP for both drug groups was similar. The mean IOP for the latanoprost group was 20.28± 2.45 and for the dorzolamide group it was 22.11±2.83 during the third follow-up. The variations in the mean IOP at baseline and the third follow-up were indicators of the medications' efficacy. For the latanoprost group, the difference between the mean IOP at baseline and the third follow-up was 9.5± 3.56, while for the dorzolamide group, it was 7.89± 2.29 [Table 4]. Both medication groups' mean IOP reductions were statistically significant ($P < 0.05$).

Table 4: Baseline mean IOP and third follow-up mean IOP value for Latanoprost and Dorzolamide group

Characteristics	Dorzolamide group Mean±SD	Latanoprost group Mean±SD
Baseline IOp	30±4.06	29.78±5.1
Third Follow up IOP	22.1±2.83	20.28±2.45
Difference in IOP	7.89±2.29	9.5±3.56

Because neither drug group's difference in IOP reduction followed a normal distribution (Shapiro-Wilk, $P<0.05$), statistical analysis is conducted using the non-parametric Mann-Whitney U-test. In the latanoprost group, the median IOP decrease was 10, while in the dorzolamide group, it was 8. The difference in IOP decrease between the two groups was determined using the Mann-Whitney U-test, and the difference was statistically significant ($P = 0.02$) [Table 5]. Therefore, compared to the dorzolamide group, the IOP decrease in the latanoprost group was superior.

Table 5: Difference in IOP reduction between Latanoprost and Dorzolamide group according to Mann-Whitney U-test

Variable	Group	Median	Interquartile range	P-value	Significance
Difference IOP reduction	Dorzolamide	8	2	0.027	P<0.05
	Latanoprost	10	4		

Nine participants in the latanoprost group experienced negative side effects, including conjunctival hyperemia in two and a foreign body sensation in seven. Seven participants in the dorzolamide group experienced negative side effects: two experienced a feeling of a foreign body, two experienced conjunctival hyperemia, and the other participants experienced stinging, headaches, and dry eyes [Table 6].

Table 6: Adverse effects of Latanoprost and Dorzolamide solution

Adverse effects	Dorzolamide group	Latanoprost group
Foreign body sensation	7	2
Conjuctival hyperemia	2	2
Stinging sensation	0	1
Headache	0	1
Dryness of eye	0	1

Discussion

The second most frequent cause of blindness in the world is glaucoma. Racial characteristics, ageing, increased IOP, family history of glaucoma, a thinner cornea, and decreased corneal thickness are risk factors that can lead to the onset and progression of glaucoma.[2,7,13] The most significant risk factor is elevated IOP because it is directly associated to the onset of glaucoma and can be controlled to a normal level to stop the disease's progression.[7,8,14] Currently, both medication and surgical therapies are available to treat glaucoma.[8] The most popular form of treatment for glaucoma is medical therapy.[15] In the current study, both pharmacological groups' majority of patients are between the ages of 61 and 70. Glaucoma risk rises with advancing age. [16]

Male patients made up 52% of the study's participants, while female participants made up 48%. IOP in the 20–40-year-old age range does not appear to be significantly impacted by gender overall.[7] In older age groups, the menopause is when the apparent rise in mean IOP is larger in women than in males.[7] Baseline IOP, which is the IOP measured on the initial visit prior to the start of study medications, namely topical eye drops containing latanoprost and dorzolamide. IOP at baseline was 29.78± 5.1 for the latanoprost group and 30± 4.06 for the dorzolamide group, respectively. As a result, there is no significant difference between the two groups' baseline means for IOP (P>0.05).

The patients were then given topical eye drops containing latanoprost and dorzolamide as a monotherapy. Then, during the 2-week, 4-week, and 8-week visits, the follow-up IOP was noted. For comparison purposes between the two medication groups, the third follow-up IOP was collected at 8 weeks after the trial started. The mean IOP at the third follow-up was 20.28± 2.45 for the latanoprost group and 22.11± 2.83 for the dorzolamide group. The difference between the mean IOP at baseline and the mean IOP at the third follow-up was used to compute IOP reduction. IOP decrease was 7.89± 2.29

for the dorzolamide group and 9.5±3.56 for the latanoprost group. According to this result, topical latanoprost eye drop reduced IOP more effectively than topical dorzolamide eye drop. IOP reduction in both the groups was statistically significant ($P < 0.05$).

Both latanoprost and dorzolamide were well tolerated in the current study throughout the testing period. The two drug groups' most frequent side effects were conjunctival hyperemia and the sensation of a foreign body; the latanoprost group had the greatest number of individuals experiencing this side effect (n = 7). Other less frequent side effects observed in the dorzolamide group included headache, stinging, and dry eyes. Although there were more adverse effects in the latanoprost group than the dorzolamide group, this difference was not statistically significant ($P > 0.05$).

In a population-based Japanese investigation, there were no gender differences in IOP. IOP was higher in women than in males in the Barbados eye research, which included a mixed group of participants.[7] Numerous research have revealed that POAG is more common in men.[17,18] However, research by Alieja *et al*. and Possner and Schlossman indicated that both males and females had the same prevalence of POAG.[19,20] In the current study, 12 patients had a history of smoking and 14 POAG patients had diabetes mellitus and 25 POAG patients had hypertension. Immediately after smoking, tobacco use induces a brief increase in IOP, probably as a result of vasoconstriction and increased episcleral venous pressure.[7]

Comparing the results of the current study to those of O'Donoghue study[27] (5.6±2.6), Khizar and Raja study[24] (6.6±2.1), and Imtiyaz *et al*. study[9] (4.7±2.4), it can be seen that the dorzolamide group saw a greater IOP reduction (7.89±2.29). There was a statistically significant difference in IOP reduction between the latanoprost and dorzolamide groups ($P<0.05$). Imtiyaz *et al*.,[9] Khizar and Raja study,[24] and O'Donoghue study all came to the same conclusion.[27] As a prodrug, latanoprost is hydrolyzed during absorption to produce "active acid latanoprost," which acts on the prostanoid FP receptor to release matrix metalloproteinase, causing the collagen between the muscle bundles in the ciliary muscle to degrade or remodel, ultimately increasing uveoscleral outflow.[6,9]

In many forms of glaucoma, increased IOP is caused by impeded outflow rather than by an excessive amount of aqueous humour production.[9] Latanoprost is therefore superior to dorzolamide in managing IOP. IOP reduction caused by latanoprost begins about 3–4 hours after topical medication application, and its full impact is felt about 8–12 hours later. For the full 24 hours, the pressure reduction is maintained.[27] Dorzolamide works by reducing the production of aqueous humour. A vital source of sustenance for avascular structures like the cornea and lens is aqueous fluid. Therefore, inhibiting the development of aqueous humour may have negative consequences.[9] The effects of dorzolamide start to take effect right away and reach their peak after two hours.[27]

In addition to lowering IOP, dorzolamide offers the benefit of increasing blood flow to retinal nerve fibres, preventing IOP-related neuronal damage. [28] Timolol is superior to dorzolamide in terms of IOP lowering.[27] Due to its less potent suppression of aqueous humour than timolol, dorzolamide is less effective at lowering IOP.[27] In comparison to latanoprost monotherapy, the fixed medication combination of timolol and dorzolamide significantly reduced IOP.[29] Therefore, when compared to timolol monotherapy, this combination is more effective.[29,30] In the Imtiyaz *et al*. study,

side effects associated with latanoprost included conjunctival hyperemia, conjunctivitis, superficial punctate keratitis, and uncontrolled IOP, while side effects associated with dorzolamide included conjunctival hyperemia, conjunctivitis, superficial punctate keratitis, and uncontrolled IOP. [9]

In the O'Donoghue research, the dorzolamide group experienced more adverse effects than the latanoprost group; conjunctival hyperemia was the most prevalent side effect in both groups.[27] Timolol is typically seen of as the gold standard medication for lowering IOP, but a meta-analysis research found that latanoprost is more effective at doing so than timolol.[31]

IOP decrease for latanoprost is 6.7±3.4 mmHg and for timolol is 4.9±2.9 mmHg because latanoprost is more effective at reducing IOP than timolol.[31] An independent risk factor for glaucomatous damage is high diurnal fluctuations. Therefore, glaucoma progression can be stopped by stabilising IOP for 24 hours. Diurnal fluctuation is considerably reduced by the medication latanoprost.

Latanoprost has a lengthy duration of action, therefore one dose of 0.005% controls IOP for 24 hours. According to a research by Zhang *et al*., once-daily injection of latanoprost consistently lowers IOP and stabilises the IOP diurnal curve.[31] Timolol, in contrast, does not outperform latanoprost in terms of stabilising IOP.[24,26] Latanoprost is therefore a first-line treatment option for POAG.[7,9,24]

Conclusion

This study compared the effectiveness of 2% dorzolamide and 0.005% latanoprost when applied topically to treat POAG. Dorzolamide and latanoprost are both effective glaucoma treatments because they both dramatically lower IOP. When used alone, latanoprost (0.005%) is more effective than dorzolamide (2%). Neither latanoprost nor dorzolamide cause any severe side effects, and they are both well tolerated. Growing older is a risk factor for glaucoma development.

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