e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(7); 1141-1146

Original Research Article

Comparative Study of Efficacy of Latanoprost and Dorzolamide in Primary Open-Angle Glaucoma (POAG) Patients as Monotherapy

Avani Raj[1], Trishla[2], Iftekhar Ahmed[3]

[1,2]Tutor, Department of Pharmacology, Government Medical College and Hospital, Purnea, Bihar
[3]Professor, Department of Pharmacology, Government Medical College and Hospital, Purnea, Bihar

Received: 15-05-2023 / Revised: 11-06-2023 / Accepted: 05-07-2023
Corresponding author: Dr. Trishla
Conflict of interest: Nil

Abstract:

Background: Glaucoma is the second most common cause of blindness worldwide, and its prevalence is increasing in India. Increased intraocular pressure (IOP), primary open-angle glaucoma (POAG) is the most important factor and a direct cause of the development of POAG. The current study aimed to examine the efficacy of latanoprost and dorzolamide for decreasing IOP in POAG as monotherapy. The following goals are set forth: To evaluate the side effects of each medication and compare the efficiency of topical latanoprost (0.005%) and topical dorzolamide (2%), both administered as monotherapies for POAG.

Methods: For the current prospective, open-label trial, 40 patients, 20 males and 20 females with a POAG diagnosis were randomly selected and divided into two groups. Topical latanoprost eye drops (0.005%) were administered to one group once daily while dorzolamide eye drops (2%), were administered to the other group three times daily. At two, four, and eight weeks, each participant underwent three follow-up visits. Prior to starting the baseline phase of treatment, IOP was assessed using a Perkins Hand Held Tonometer. At each following appointment, IOP was once more measured in order to monitor the effects of drugs. Each patient gave their informed consent voluntarily.

Results: The mean IOP decrease for the dorzolamide group was 7.89±3.56 and the latanoprost group was 9.5±3.56. IOP was successfully decreased by both drugs. There was a statistically significant difference between how latanoprost and dorzolamide lowered IOP (P = 0.02). Throughout the study, both drugs were well tolerated, however the latanoprost group (n = 5) had higher side effects than the dorzolamide group (n = 4).

Conclusion: The findings of this study demonstrate a significant reduction in IOP in POAG caused by topical eye drops containing latanoprost (0.005%) and dorzolamide (2%) respectively. Latanoprost is more efficient than dorzolamide at lowering IOP.

Keywords: Glaucoma; Intraocular Pressure; Latanoprost; Dorzolamide.

Introduction

Numerous eye illnesses that damage the optic nerve and impair vision can lead to glaucoma, an optic neuropathy that is chronic and progressive.[1] Glaucoma, after cataracts, is the second most prevalent cause of blindness both in India and the rest of the world.[2] Over 65 million people are thought to be affected with glaucoma worldwide.[2-4] Glaucoma affects 11.2 million people in India, according to estimates.[5] Estimates suggest that 2.25 million Americans over the age of 40 have primary open-angle glaucoma (POAG). [6]

POAG is the most prevalent type of glaucoma out of all the different subtypes.[5] One possible diagnosis of POAG is a multifocal optic neuropathy with significant optic nerve atrophy (derived from the American Academy of Ophthalmology Preferred Practice Pattern Guidelines, 2005).[7] PAOG, a kind of glaucoma, affects 6.48 million persons in India.[5] As the incidence of the ailment increases with age, the prevalence of POAG may reach 16 million by 2020.[5]

Lowering intraocular pressure (IOP) is the main goal of treatment for POAG because it is the main risk factor for glaucoma and the development of glaucoma.[8] There are several different drugs that can be used right now to lower IOP, including cholinergic agonists, adrenergic agonists, beta-blockers, carbonic anhydrase inhibitors, and prostaglandin analogues.[7] Prostaglandin analogues can be used alone or in conjunction with other therapies.[7] The most successful of these drugs is latanoprost, which also has the longest duration of action and reduces diurnal IOP variations.[9] Prostaglandin analogues are the first-

line treatment for POAG, claims a study by Gupta et al.[3] An increase in IOP is the main cause of glaucoma, and this element has an impact on how the condition develops.[8] The prostaglandin analogue drug latanoprost reduces IOP by improving uveoscleral outflow. The ciliary muscle is relaxed, and the extracellular matrix of the ciliary muscle is altered, to achieve this. Additionally, latanoprost lessens nocturnal oscillations in the IOP [7,10]. Dorzolamide, a carbonic anhydrase inhibitor, reduces IOP by reducing aqueous generation. By limiting the ciliary epithelium's capacity to create bicarbonate ions, this is achieved. Its mode of action differs from latanoprost's as a result [7].

Dorzolamide decreases IOP by 22.8% of increased IOP, according to certain studies.[11,12] It is as effective to pilocarpine but has less adverse effects.[11]. Latanoprost has been shown in studies by Singh and Shrivastava and Thomas et al. and others to dramatically drop IOP around normal levels and stabilize the diurnal curve in IOP variation.[8,10] In order to determine which drug was superior in lowering IOP when administered topically to POAG patients, latanoprost or dorzolamide, we decided to conduct a comparative experiment.

Materials and Methods

The prospective type, open-labeled, randomised study was carried out on patients with POAG at the Department of Pharmacology, GMCH, Purnea, Bihar, from November 2022 to April 2023. Patients were chosen from the outpatient Department of Ophthalmology, Government Medical College and Hospital, Purnea, Bihar. Both sexes of chosen individuals aged 40 and older with IOP > 21 mmHg, POAG, and ocular hypertension affecting one or both eyes were included in this study.

Patients with a narrow angle or peripheral anterior synechiae, ocular surgery or argon laser trabeculoplasty performed less than six months prior to the study, corneal abnormalities or any condition that makes it impossible to reliably measure IOP with a Perkins Tonometer, active eye disease other than open-angle glaucoma, known hypersensitivity to any study drug (latanoprost or dorzolamide), use of any medication (such as 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.

40 POAG patients participated in the study. All patients were chosen based on the inclusion and exclusion criteria. Each participant was informed about the details of the study before providing their consent. The sample size was established using the results of the previous study.[9] The patient's general and ocular complaints, such as blurry 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 that has previously resulted in glaucoma, were thoroughly recorded in the medical history.

The statistical analysis of quantitative data was summarized using the mean and standard deviation. With a significance level of $P < 0.05$, the student's unpaired test was employed to compare the means of the two groups. The Mann-Whitney U-test is used to compare the difference in IOP reduction between the latanoprost group and the dorzolamide group.

Results

The effectiveness of latanoprost and dorzolamide pharmaceutical solutions when applied topically to POAG patients over the age of 40 was compared in the study. There were now 40 participants in the trial after four more volunteers withdrew. 36 of them completed the research. One of the four dropouts is untraceable for follow-up, two had combination therapy, and one had trabeculoplasty eye surgery. The demographic data for the latanoprost and dorzolamide groups were compared using the statistical package for the social sciences. For each protocol population, efficacy analyses were carried out. At baseline and the third follow-up for each treatment group, the descriptive statistics (mean, standard deviation, and median) for the efficacy variables were calculated. The mean IOP reductions between the latanoprost and dorzolamide groups were compared using the Mann-Whitney U-test. Tables 1 and 2 present the participant's demographic breakdown. A total of 40 patients, including both males and females, with ages above 40 were enrolled for the study based on the inclusion and exclusion criteria. The mean age for the latanoprost group was 63.11±10.46 and 65.61±9.44 for the dorzolamide group. Between the ages of 61 and 70, patients in both categories predominate. There were 12 men and 8 women in the dorzolamide group compared to 9 men and 11 women in the latanoprost group (Table 2). In the population under study, there were 19 females and 21 males overall. The risk factors associated with POAG are listed in Table 3. In the current study, 13 patients had hypertension, 7 patients had diabetes mellitus, and 6 patients had a history of smoking.

Table 1: Age distribution in study group

Age in years	Dorzolamide group no. of patients=20	Latanoprost group no. of patients=20
41-50	2	4
51-60	5	5
61-70	8	6
71-80	5	5

Table 2: Sex distribution Latanoprost and Dorzolamide group

Age in years	Dorzolamide group no. of patients=20	Latanoprost group no. of patients=20	Total n=40
Male	12	9	21
Female	8	11	19

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=26(%)
Diabetes mellitus	7/40(17.5%)
Hypertension	13/40(32.5%)
Smoking history	6/40(15.0%)

IOP was 29.78±5.1 for the latanoprost group at baseline versus 30.0±4.06 for the dorzolamide group. As a result, both medication groups' initial mean IOPs were comparable. During the third follow-up, the mean IOP was 20.28± 2.45 for the latanoprost group and 22.11±2.83 for the dorzolamide group. The changes in the mean IOP between the first and third follow-up were signs of the effectiveness of the drugs. The difference between the mean IOP at baseline and the third follow-up for the latanoprost group was 9.5±3.56, whereas for the dorzolamide group, it was 7.89±2.29 [Table 4].

IOP decreases were substantially significant in both treatment groups ($P < 0.05$).

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

The non-parametric Mann-Whitney U-test is used in statistical analysis because neither drug group's difference in IOP reduction followed a normal distribution (Shapiro-Wilk, $P<0.05$). The median IOP drop was 10 in the latanoprost group and 8 in the dorzolamide group. Using the Mann-Whitney U-test, the difference in IOP drop between the two groups was identified, and the difference was statistically significant ($P = 0.02$) [Table 5]. As a result, the IOP decrease in the latanoprost group was superior to that of the dorzolamide group.

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 subjects received latanoprost, and two of them developed conjunctival hyperemia and seven of them felt like a foreign body. Seven individuals in the dorzolamide group experienced adverse side effects: stinging, headaches, dry eyes, and a feeling of a foreign body in two cases and conjunctival hyperemia in two other cases (Table 6).

Table 6: Adverse effects of Latanoprost and Dorzolamide solution

Adverse effects	Dorzolamide group	Latanoprost group
Foreign body sensation	4	1
Conjuctival hyperemia	1	1
Stinging sensation	0	0
Headache	0	1
Dryness of eye	0	1

Discussion

Glaucoma is the second most common cause of blindness in the world. The incidence and progression of glaucoma can be influenced by racial traits, aging, elevated IOP, family history of glaucoma, a thinner cornea, and decreasing corneal thickness.[2,7,13] Elevated IOP is the most important risk factor since it causes glaucoma to develop and can be managed to a normal level to halt the disease's progression.[7,8,14] Currently, glaucoma can be treated surgically or with medications.[8] Medical therapy is the most widely used glaucoma treatment method.[15] The bulk of patients in the current study for both pharmacological groups range in age from 61 to 70. The risk of glaucoma increases with age. [16]

52% of the study's participants were male patients, while 48% were female patients. Overall, gender does not appear to have a substantial effect on IOP in the 20–40 year age group.[7] In older age groups, the menopause is when women appear to experience a greater increase in mean IOP than men do.[7] Baseline IOP, which is the IOP recorded during the first visit before the study's prescribed drugs, mainly topical eye drops containing latanoprost and dorzolamide, were started. For the latanoprost group at baseline, IOP was 29.78±5.1 while for the dorzolamide group, it was 30.0±4.06. As a result, there is no significant difference in the baseline averages of IOP between the two groups (P>0.05).

The patients were then administered topical eye drops as a monotherapy that contained latanoprost and dorzolamide. The subsequent IOP was noticed at the 2 week, 4 week, and 8 week visits. Eight weeks following the trial's beginning, the third follow-up IOP was taken in order to compare the two drug groups. At the third follow-up, the latanoprost group's mean IOP was 20.28± 2.45 while the dorzolamide group's was 22.11±2.83. IOP decrease was calculated using the difference between the mean IOP at baseline and the mean IOP at the third follow-up. IOP reductions for the latanoprost group were 9.53.56 and 7.892.29 for the dorzolamide group, respectively. This finding showed that topical latanoprost eye drop significantly lowered IOP compared to topical dorzolamide eye drop. IOP decrease was statistically significant in both groups (P <0.05).

In the current study, latanoprost and dorzolamide were both well tolerated during the testing phase. Conjunctival hyperemia and the feeling of a foreign body were the two side effects that occurred most frequently in both treatment groups; the latanoprost group had the most people experience these side effects (n = 4). The dorzolamide group also experienced headache, stinging, and dry eyes on a less frequent basis. Despite the fact that the latanoprost group experienced greater side effects than the dorzolamide group did, this difference was not statistically significant (P > 0.05).

There were no gender differences in IOP in a population-based Japanese study. In the mixed-gender Barbados eye study, IOP was higher in female individuals than in male participants.[7] Numerous studies have shown that POAG is more prevalent among men.[17,18] The prevalence of POAG was the same in both sexes, according to studies by Alieja et al. and Possner and Schlossman.[19,20] In the present study, 13 POAG patients had hypertension, 7 POAG patients had diabetes mellitus, and 6 patients had a history of smoking. Tobacco use causes a short rise in IOP after smoking, most likely as a result of vasoconstriction and elevated episcleral venous pressure.[7]

The dorzolamide group experienced a bigger IOP reduction (7.89±2.29) when compared to the findings of the 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). The difference in IOP decrease between the latanoprost and dorzolamide groups was statistically significant (P <0.05). The studies by Imtiyaz et al.,[9] Khizar and Raja,[24] and O'Donoghue reached the same conclusion.[27] As a prodrug, latanoprost is absorbed and hydrolyzed to create "active acid latanoprost," which then interacts with the prostanoid FP receptor to release matrix metalloproteinase, causing the collagen between the muscle bundles in the ciliary muscle to break down or remodel and ultimately boosting uveoscleral outflow.[6,9]

Increased IOP is frequently brought on by blocked outflow rather than by excessive aqueous humour formation in many types of glaucoma.[9] In treating IOP, latanoprost is consequently superior to dorzolamide. IOP reduction brought on by latanoprost starts to take effect from 3 to 4 hours after topical medicine administration and peaks between 8 and 12 hours afterwards. The pressure drop lasts the entire 24 hours.[27] By decreasing the generation of aqueous humor, dorzolamide works. Aqueous fluid is an essential source of nutrition for avascular structures like the cornea and lens. Therefore, preventing the production of aqueous humour can have unfavorable effects.[9] Dorzolamide's effects begin to manifest immediately and peak two hours later.[27]

Dorzolamide has the advantage of raising blood flow to retinal nerve fibers, avoiding IOP-related neuronal injury in addition to lowering IOP.[28] In terms of decreasing IOP, timolol is superior to dorzolamide.[27] Dorzolamide is less successful at lowering IOP than timolol due to its weaker suppression of aqueous humour.[27] The fixed medicine combination of timolol and dorzolamide

effectively decreased IOP as compared to latanoprost monotherapy.[29] Consequently, this combination is more successful than timolol monotherapy.[29,30] Conjunctival hyperemia, conjunctivitis, superficial punctate keratitis, and uncontrolled IOP were side effects of latanoprost in the Imtiyaz et al. study, whereas conjunctival hyperemia, conjunctivitis, superficial punctate keratitis, and uncontrolled IOP were side effects of dorzolamide. [9]

Conjunctival hyperemia was the most common side effect in both groups in the O'Donoghue study, which found that the dorzolamide group had more negative side effects than the latanoprost group.[27] Although latanoprost is more effective than timolol at lowering IOP, timolol is still widely regarded as the gold standard drug for this purpose.[31] Due to latanoprost's superior ability to lower IOP compared to timolol, the IOP decrease for latanoprost is 6.7±3.4 mmHg and 4.9±2.9 mmHg.[31] High diurnal fluctuations are an independent risk factor for glaucomatous damage. Therefore, stabilizing IOP for 24 hours can arrest the progression of glaucoma. The drug latanoprost significantly lessens dilatory fluctuation. One dose of 0.005% of latanoprost controls IOP for 24 hours due to its long duration of action. Latanoprost injections given once daily reliably lower IOP and stabilize the IOP diurnal curve, according to studies by Zhang et al.[31] In contrast, timolol does not perform better than latanoprost at stabilizing IOP.[24,26] As a result, latanoprost is a first-line therapy for POAG.[7,9,24]

Conclusion

In order to treat POAG, this study assessed the efficacy of 0.005% latanoprost and 2% dorzolamide when used topically. Both dorzolamide and latanoprost significantly reduce IOP, making them both efficient glaucoma therapies. Latanoprost (0.005%) is more efficient when taken alone than dorzolamide (2%). Both latanoprost and dorzolamide are well tolerated medications that don't have any serious adverse effects. Age is a risk factor for developing glaucoma.

References

1. Sihota R, Tandon R. Parson’s Diseases of the Eye. 21st ed. New Delhi: Elsevier Publication. 2011;20.
2. Ramesh S, Pradeep PG, Ronnie G, Mani B, Arvind H, Raj MV, *et al*. Determinants of glaucoma awareness and knowledge in urban Chennai. Indian J Ophthalmol. 2009; 57:355-60.
3. Gupta SK, Galpalli N, Agrawal SS, Srivastava S, Saxena R. Recent advances in pharmacology therapy of glaucoma. Indian J Pharmacol. 2008; 40:119-208.
4. Quigley HA. Number of people with glaucoma worldwide. Br J Ophthalmol. 1996; 80:389-93.
5. Yadav AK, Patel V. Drug use in primary open angle glaucoma. A prospective study at a tertiary care teaching hospital. Indian J Pharmacol. 2013; 45:117-20.
6. Robert SL, Marc LF, Michael DV. Becker Shaffer’s Diagnosis and Therapy of the Glaucoma’s. 8th ed. New York: Elsevier Publication; 2010; 1-3.
7. Allingham RR, Damji KF, Freedmam S, Moroi SE, Rhee DJ. Shields Textbook of Glaucoma. 6th ed. Philadelphia, PA: Wolters Kluver Publisher; 2010. p. 176-85.
8. Thomas R, Parish R, Muliyil J, George R, Paul P, Abraham LM. Comparison between latanoprost and brimonidine efficacy and safety in Indian eyes. Indian J Ophthalmol. 2003; 51:123-8.
9. Imtiyaz LA, Azra R, Sheikh AS, Reyaz UA. Comparison of latanoprost and dorzolamide in patients with open angle glaucoma. JK Sci. 2003; 5:26-8.
10. Singh K, Shrivastava A. Medical management of glaucoma: Principle and practice. Indian J Ophthalmol. 2011; 59:88-92.
11. Adamsons IA, Polis A, Ostros CS, Boyle JE. Two year safety study of dorzolamide as monotherapy and with timolol and pilocarpine, dorzolamide safety study group. J Glaucoma. 1998; 7:395-401.
12. Wilkerson M, Lippa EA, Esposito D, Deasy D, Panebianco D, Fazio R, *et al*. Four week safety and efficacy study of dorzolamide, novel active topical carbonic anhydrase inhibitor. Arch Ophthalmol. 1993; 11:1343-50.
13. Navid N, Mehdi Z, Taher RM, Ghasem F. Primary open angle glaucoma risk factors. Iran J Ophthalmol. 2008; 20:25-31.
14. Comparison of glaucomatous progression between untreated patient with normal tension glaucoma and patient with therapeutically reduced intraocular pressures. Collaborative normal tension glaucoma study group. Am J Ophthalmol. 1998; 126:487-97.
15. Laurence BL, Bruce CA, Bjorn KC. Goodman and Gliman’s, The Pharmacology Basis of Therapeutics. 12th ed. China: McGraw Hill Companies; 2011. p. 1785-8.
16. Kahn HA, Milton RC. Revised Framingham eye study prevalence of glaucoma and diabetic retinopathy. Am J Epidemiol. 1980; 111:769-76.
17. Martinez GS, Campbell AJ, Reinken J, Allen BC. Prevalence of ocular disease in a population study of subjects 65 years and older. Am J Ophthalmol. 1982; 94:181-9.

18. Richler M, Werner EB, Thomas D. Risk factors for progression of visual field defects in medically treated patients with glaucoma. Can J Ophthalmol. 1982; 17:245-8.
19. Alieja RR, Shahrul ML, Christopher OG, Derek CG, Deborch A. Variations in primary open-angle glaucoma prevalence by age, gender and race: A meta-analysis. Invest Ophthalmol Vis Sci. 2006; 47:4254-61.
20. Possner A, Schlossman A. The clinical course of glaucoma. A review of 474 cases from private practice. An J Ophthalmol. 1948; 31:915-34.
21. Shephard RJ, Ponsford E, Basu PK, LaBarre R. Effect of cigarette smoking on intraocular pressure and vision. Br J Ophthalmol. 1978; 621:682-7.
22. Tielsch JM, Katz J, Quigley HA, Javitt JC, Sommer A. Diabetes, intraocular pressure and primary open angle glaucoma in the Baltimore eye survey. Ophthalmology. 1995; 102:48-53.
23. Mitchell P, Smith W, Chey T, Stat M, Healcy PR. Open angle glaucoma and diabetes. The Blue Mountains eye study, Australia. Ophthalmology. 1997; 104:712-8.
24. Khizar NM, Raja N. Comparison of latanoprost and dorzolamide in the treatment of patients with open angle glaucoma. J Ayub Med Coll Abbottabad. 2004; 16:50-3.
25. Indian Latanoprost Study Group. Open label, prospective, multicenter Indian study of latanoprost in primary open angle glaucoma and ocular hypertension. Asian J Ophthalmol. 2002; 4:2-5.
26. Ravi T, Rajul P, Sood D, Vijaya L, Chandrasekhar G, Sood NM, *et al*. Efficacy and safety of latanoprost for glaucoma treatment: A three-month multicentric study in India. J Pharmacol Ther. 2005; 53:23-30.
27. O'Donoghue EP, The UK and Ireland Latanoprost Study Group. A comparison of latanoprost and dorzolamide in patients with glaucoma and ocular hypertension: A 3 month, randomized study. Br J Ophthalmol. 2000; 84:579-82.
28. Siesky B, Harris A, Cantor LB, Kagemann L, Weitzman Y, Mc Cranor L, *et al*. A comparative study of the effects of brinzolamide and dorzolamide on retinal oxygen saturation and ocular microcirculation in patients with primary open-angle glaucoma. Br J Ophthalmol. 2008; 92:500-4.
29. Januleviciene I, Harris A, Kagemann L, Siesky B, McCranor L. A comparison of the effects of dorzolamide/timolol fixed combination versus latanoprost on intraocular pressure and pulsatile ocular blood flow in primary open-angle glaucoma patients. Acta Ophthalmol Scand. 2004; 82:730-7.
30. Jason Y, Daniel K, Braian F. Rational use of the fixed combination of dorzolamide, timolol in the management of raised intraocular pressure and glaucoma. Clin Ophthalmol. 2008; 2:389-99.
31. Zhang WY, Po AL, Dua HS, Azuara-Blanco A. Meta-analysis of randomized controlled trials comparing latanoprost with timolol in the treatment of patients with open angle glaucoma or ocular hypertension. Br J Ophthalmol. 2001; 85:983-90.