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Timolol 0.5% versus Latanoprost 0.005% as A Single Hypotensive Drug in Glaucoma Patients: A 2-year Follow-up

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Abstract

Background: Glaucoma is a progressive optic nerve disease that, despite its treatment, is associated with retinal ganglion cell damage. However, timely treatment hinders the progression of visual field damage and preserves visual function. Our study aimed to evaluate the treatment outcomes and adverse effects in glaucomatous patients of using a single anti-glaucomatous agent, 0.5% timolol maleate, or 0.005% latanoprost, for 24 months.

Methods and Results: This prospective, single-arm, open-label study included 87 patients (47.13% men and 52.87% women) with open-angle glaucoma treated with a single hypotensive agent. The patients were divided into two groups. Group 1 patients (n=43) were treated with 0.5% timolol, and Group 2 patients (n=44) were treated with 0.005% latanoprost. We assessed the intraocular pressure (IOP) in 7 visits for 24 months, the cup-to-disc ratio (CDR), and the drug's side effects.

At baseline (Visit 1), Group 1 showed an IOP(OD) of 26.46±1.99 mmHg and an IOP(OS) of 26.34±2.14 mmHg. Group 2 showed an IOP(OD) of 26.18±1.98 mmHg and an IOP(OS) of 26.18±2.03 mmHg. There were no significant differences between the two treatments at the initial stage. At the second follow-up visit, the mean IOP(OD) and IOP(OS) significantly decreased from baseline in both groups. There was no significant difference between the two treatments at this stage. By the third follow-up visit, IOP continued to decrease effectively in both groups, and no significant difference was observed between the two treatments at this stage. At Visits 4 and 5, in Group 1, the IOP remained without significant dynamics compared to Visit 3. At the same time, in Group 2, the IOP continued to decrease slightly. However, no significant difference was observed between the two treatments at these stages. Latanoprost appears to result in slightly lower IOP levels overall. By the sixth follow-up visit, IOP continued to decrease effectively in both groups. Although latanoprost provided lower IOP values, there was no significant difference between groups. By Visit 7, the difference between the two treatments becomes more noticeable. Group 1 has an IOP(OD) of 16.09±1.26 mmHg and IOP(OS) of 16.00±1.38 mmHg, while Group 2 continued to show lower IOP levels: IOP(OD) of 14.18±1.04 mmHg and IOP(OS) of 14.13±1.09 mmHg. The differences between the groups became significant (P=0.029), indicating that latanoprost was more effective in reducing IOP in the long term.

Changes in the CDR used to assess the optic nerve were assessed before and after 24 months of treatment. In Group 1, CDR before treatment was 0.451±0.112 and slightly increased by the end of treatment to 0.484±0.123. In Group 2, CDR before treatment was 0.436±0.138 and slightly increased to 0.452±0.15.

With timolol therapy, side effects were found in 11(25.58%) patients, and with latanoprost therapy only in 7(15.9%) patients. Although the differences were not statistically significant, latanoprost had a slightly more favorable safety profile than timolol.

Conclusion: The consistently lower mean IOP values for latanoprost treatment suggest it may be more effective in reducing IOP than timolol. However, the lack of statistically significant differences indicates that while one may perform slightly better on average, both treatments are generally effective and may be chosen based on individual patient needs and tolerability.**(International Journal of Biomedicine. 2024;14(4):626-631.)**

Keywords: glaucoma • intraocular pressure • timolol • latanoprost • cup-to-disc ratio • adverse effects

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Abbreviations

CDR, cup-to-disc ratio; **GAT**, Goldman applanation tonometer; **IOP**, intraocular pressure; **OD**, right eye; **OS**, left eye; **POAG**, primary open angle glaucoma.

Introduction

Glaucoma is a progressive optic nerve disease that, despite its treatment, is associated with retinal ganglion cell damage.[1] However, timely treatment hinders the progression of visual field damage and preserves visual function.[2-4] Topical medications remain one of the main treatment methods for ocular hypertension.[5] The main goal of this conservative treatment is to lower the intraocular pressure (IOP). In most cases, a single hypotensive topical drug is the first-line therapy. However, more than 40% of patients respond positively to a combined treatment with two or more hypotensive agents.[6] Latanoprost, a prostanoid selective FP receptor agonist, reduces the IOP by increasing the outflow of the aqueous humor. In contrast, timolol reduces the formation of the aqueous humor in the ciliary body in the eye. The level of the IOP is directly related to the damage to the optic nerve and to loss in the visual field: The higher the IOP, the greater the damage to the optic nerve and visual field.[7] Timolol and latanoprost are efficient in lowering the IOP and, therefore, are considered first-line therapies for glaucoma.[8-10]

Our study aimed to evaluate the treatment outcomes and adverse effects in glaucomatous patients of using a single anti-glaucomatous agent, 0.5% timolol maleate, or 0.005% latanoprost, for 24 months.

Materials and Methods

This prospective, single-arm, open-label study, conducted in the Clinic of Ophthalmology at the University Clinical Center of Kosovo, included 87 patients (47.13% men and 52.87% women) with open-angle glaucoma treated with a single hypotensive agent: 0.5% timolol maleate or 0.005% latanoprost. The patients were divided into two groups. Group 1 patients (n=43) were treated with 0.5% timolol, and Group 2 patients (n=44) were treated with 0.005% latanoprost.

Data Collection

Eligible patients for the study were 30 years or older and diagnosed as having unilateral or bilateral primary open-angle glaucoma (POAG). Patients were expected to visit the clinic according to the observation schedule determined in the study protocol.

The exclusion criteria included any corneal abnormalities or other diseases that could interfere with accurate IOP measurement with a Goldmann applanation tonometer (GAT); a history of corneal refractive surgery; corrected visual acuity of 0.6; advanced visual field defects; active extraocular disease, or ocular or eyelid inflammatory or infectious diseases; a history of anterior or intraocular surgery; a history of glaucoma surgery, including laser treatment; allergy to the ingredients used in this study; pregnancy, lactation, possibly pregnancy, a wish to become pregnant during the study period or unable to conduct appropriate contraception during the study; scheduled medications or therapies prohibited during the study period; contraindications to beta-blockers, such as bronchial asthma or poorly controlled cardiac failure; anyone the principal or other investigators considered ineligible for enrollment. During the study period, the patients were prohibited from using anti-glaucoma eye drops other than the study drugs, oral or intravenous IOP-lowering agents, or corticosteroid drugs. Ocular laser surgery and invasive surgery were also prohibited.

Glaucoma diagnosis was established following European Glaucoma Society (EGS) Guidelines. Primary open-angle glaucoma diagnosis was based on abnormal visual field testing and corresponding disk changes with open angles on gonioscopy.

All participants underwent a complete ophthalmic examination during the eligibility visit, including best-corrected visual acuity (BCVA), slit-lamp examination, and optic disc examination through a dilated pupil. Each patient was followed up for 24 months, completing seven visits in total. During the treatment period, scheduled visits were performed at baseline and at the end of weeks 4, 8, 12, 24, 48, and after 24 months of treatment. Apart from the IOP, the main variable, we also evaluated the drug's side effects in each patient and the cup-to-disc ratio (CDR), which was assessed using optical coherence tomography. All data were inserted in a specific database designed specifically for this study.

Statistical analysis was performed using the statistical software package SPSS version 27.0 (SPSS Inc, Armonk, NY: IBM Corp). Baseline characteristics were summarized as frequencies and percentages for categorical variables and mean (M) ± standard deviation (SD) for continuous variables. The unpaired and paired t-tests were used to compare two groups. Multiple comparisons were performed with one-way ANOVA. A probability value of $P<0.05$ was considered statistically significant.

Results

The demographic characteristics of patients included in the study are presented in Table 1. The mean age of the respondents was 67±7.64 years, with ranges from a minimum of 47 to a maximum of 81 years.

Table 1.

General characteristics of the patients.

Variable	Mean	SD	Min	Max
Age	66.966	7.635	47	81

Gender	n	Percent	Cum.
Male	41	47.13	47.13
Female	46	`52.87	100.00
Total	87	100.00	

Timolol was used by 43 participants, accounting for 49.43% of the total sample, while latanoprost was slightly more prevalent, with 44 participants, representing 50.57% of the sample. This nearly equal distribution between the two *Cum.*s suggests that both were used with similar frequency in the study (Table 2).

Table 2.

Treatment regimens in study groups.

Pharmacological agent	n	Percent	Cum.
Timolol (0.5%)	43	49.43	49.43
Latanoprost (0.005%)	44	50.57	100.00
Total	87	100.00	

At baseline (Visit 1), the IOP for both groups was very similar (Table 3). Group 1 showed an IOP(OD) of 26.46±1.99 mmHg and an IOP(OS) of 26.34±2.14 mmHg. Group 2 showed an IOP(OD) of 26.18±1.98 mmHg and an IOP(OS) of 26.18±2.03 mmHg. There were no significant differences between the two treatments at the initial stage.

Table 3.

Changes in IOP during scheduled visits in the study groups.

Visit	Group 1				Group 2				P-value
	IOP(OD)		IOP(OS)		IOP(OD)		IOP(OS)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
VISIT 1	26.46	1.99	26.34	2.14	26.18	1.98	26.18	2.03	0.703
VISIT 2	20.67	1.78	20.34	2.06	20.29	1.83	19.97	1.88	0.549
VISIT 3	19.07	1.58	18.80	1.56	18.50	1.71	18.09	1.73	0.507
VISIT 4	18.46	1.36	18.48	1.54	17.70	1.50	17.84	1.41	0.553
VISIT 5	18.53	1.31	18.62	1.34	17.61	1.10	17.63	1.22	0.257
VISIT 6	17.34	1.25	17.11	1.13	14.86	1.13	14.79	1.30	0.378
VISIT 7	16.09	1.26	1600	1.38	14.18	1.04	14.13	1.09	0.029

At the second follow-up visit, the mean IOP(OD) and IOP(OS) significantly decreased from baseline in both groups. In Group 1, IOP(OD) dropped to 20.67±1.78 mmHg and IOP(OS) to 20.34±2.06 mmHg (P<0.05 in both cases). In Group 2, IOP(OD) dropped to 20.29±1.83 mmHg and IOP(OS) to 19.97±1.88 mmHg (P<0.05 in both cases). However, no significant difference (P=0.549) was observed between the two treatments at this stage, indicating that both drugs were equally effective in reducing IOP.

By the third follow-up visit, IOP continued to decrease effectively in both groups, and no significant difference (P=0.507) was observed between the two treatments at this stage.

At Visits 4 and 5, in Group 1, the IOP remained without significant dynamics compared to Visit 3. At the same time, in Group 2, the IOP continued to decrease slightly. However, no significant difference was observed between the two treatments at these stages (P=0.553 and P=0.257). Latanoprost appears to result in slightly lower IOP levels overall.

By the sixth follow-up visit, IOP continued to decrease effectively in both groups. Although latanoprost provided lower IOP values, there was no significant difference between groups (P=0.378). However, the clinical trend suggested that latanoprost may be more effective in further lowering IOP at this stage of treatment.

By Visit 7, the difference between the two treatments becomes more noticeable. Group 1 has an IOP(OD) of 16.09±1.26 mmHg and IOP(OS) of 16.00±1.38 mmHg, while Group 2 continued to show lower IOP levels: IOP(OD) of 14.18±1.04 mmHg and IOP(OS) of 14.13±1.09 mmHg. The differences between the groups became significant (P=0.029), indicating that latanoprost was more effective in reducing IOP in the long term.

Changes in the CDR used to assess the optic nerve were assessed before and after 24 months of treatment (Table 4). In glaucoma, increased CDR may indicate damage to the optic nerve. In Group 1, CDR before treatment was 0.451±0.112 and slightly increased by the end of treatment to 0.484±0.123. The minimum and maximum values remained unchanged before and after treatment, ranging from 0.3 to 0.7, indicating that the treatment did not significantly change the range of values but had a modest effect on the mean values. In Group 2, CDR before treatment was 0.436±0.138 and slightly increased to 0.452±0.15. However, the maximum value increased from 0.9 to 1, indicating that the treatment increased CDR in some patients, signaling damage to the optic nerve.

Table 4.

CDR before and after treatment in the study groups.

Treatment agent	Variable	n	Mean	SD	Min	Max
Timolol (0.5%)	Before treatment	43	0.451	0.112	0.3	0.7
	After treatment	43	0.484	0.123	0.3	0.7
Latanoprost (0.005%)	Before treatment	44	0.436	0.138	0.3	0.9
	After treatment	44	0.452	0.15	0.3	1

We also compared the treatment results by gender (Table 5). Before treatment, in Group 1, IOP was 19.497±0.975 mmHg in men and 19.545±0.95 mmHg in women. In Group 2, IOP was 18.536±0.967 mmHg in men and 18.429±0.821 mmHg in women. The differences between the groups were not significant. By the end of treatment, despite the decrease in IOP in men and women in both groups, there were no significant differences between two groups (P=0.461), indicating the absence of a significant gender difference in the response to both treatment regimens. Overall, the lower mean IOP values for latanoprost indicate some advantages in reducing IOP compared to timolol. However, the lack of significant differences indicates that both treatments are

generally effective and can be selected based on individual patient needs and tolerability.

Table 5.

Comparison of the study data according to gender.

Gender	Group 1			Group 2			*P*-value
	IOP			IOP			
	n	Mean	SD	n	Mean	SD	
Visit 1 Male	21	19.497	0.975	20	18.536	0.967	0.909
Female	22	19.545	0.95	24	18.429	0.821	
Total	43	19.522	0.951	44	18.477	0.881	
Visit 2 Male	21	19.333	1.058	20	18.386	0.887	0.461
Female	22	19.461	1.06	24	18.375	0.868	
Total	43	19.399	1.048	44	18.38	0.866	

During the observation, we summarized all side effects in the two groups (Table 6).

Table 6.

Side effects in the study groups.

Side Effects	Yes		No		Total	
	n	%	n	%	n	%
Timolol (0.5%)	11	25.58	32	74.42	43	100
Latanoprost (0.005%)	7	15.9	37	84.1	44	100
Total	18	41.48	69	158.52	87	

With timolol therapy, side effects were found in 11(25.58%) patients, and with latanoprost therapy only in 7(15.9%) patients. Although the differences were not statistically significant, latanoprost had a slightly more favorable safety profile than timolol. In the timolol group, the most frequently reported side effects were burning sensation and conjunctival hyperemia, followed by blurred vision, dry eyes, and headache (Figure 1). Thus, the most common side effects associated with timolol included sensations that may affect visual comfort.

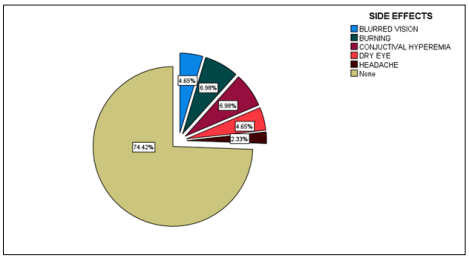

Fig. 1. *Side effects in the timolol (0.5%) group.*

In the latanoprost group, conjunctival hyperemia and dry eye were the most frequently reported adverse events, followed by blurred vision, burning, and headache. Thus, with latanoprost therapy, adverse events were primarily associated with eye health (Figure 2).

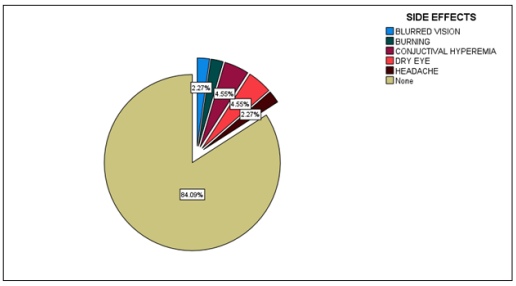

Fig. 2. *Side effects in the latanoprost (0.005%) group.*

Discussion

Many clinical studies support the conclusion that more significant reductions in IOP are associated with delays in glaucoma progression. [11,12] Literature data suggest that for many patients, monotherapy is insufficient to achieve the target IOP, necessitating the use of multiple medications.[13,14] However, researchers suggest that the addition of a second drug plays a major role in decreased compliance with anti-glaucoma therapy.[1,15,16] Current clinical treatments for glaucoma include topical medication (eye drops) and surgery; however, topical medications remain the first choice of treatment.[17] Latanoprost ophthalmic solution 0.005% is characterized by high compliance and persistence among patients; thus, it is widely used as a first-line therapy for glaucoma patients.[18,19]

Timolol (0.5%) and latanoprost (0.005%) effectively reduce IOP over time; however, latanoprost shows a slightly greater reduction in IOP, particularly in the later visits, which could suggest a potential long-term advantage in managing the IOP. Similarly to our results, in their study on the efficacy of latanoprost versus timolol, Varma et al.[20] concluded that compared to timolol, treatment with latanoprost results in significantly fewer patients with a high IOP fluctuation. The efficacy of latanoprost used either as a single agent or as an additional agent is also supported by Konstas et al.[21] Their results show that latanoprost and timolol maleate, both given once daily in the morning or evening, effectively reduce the IOP for the 24-hour diurnal curve when compared with timolol maleate twice daily.

Although both latanoprost and timolol have been shown to be efficient hypotensive agents in open-angle glaucoma treatment, latanoprost has proven to be superior.[7] The changes in the CDR in our study were slight in both groups, regardless of the treatment agent used; however, they were not statistically significant.

Side effects were reported in seven patients treated with latanoprost and 11 patients treated with timolol. The most frequent side effects were conjunctival hyperemia and burning sensation. Despite the higher number of patients who reported

having side effects in the timolol group in our study, results from other studies comparing timolol 0.5% to omidenepag isopropyl show that the rate of adverse effects was lower in patients using timolol than in patients using omidenepag isopropyl.[22]

Conclusion

The consistently lower mean IOP values for latanoprost treatment suggest it may be more effective in reducing IOP than timolol. However, the lack of statistically significant differences indicates that while one may perform slightly better on average, both treatments are generally effective and may be chosen based on individual patient needs and tolerability.

Ethical Considerations

The study was conducted in accordance with the ethical principles of the WMA Declaration of Helsinki (1964, ed. 2013) and approved by the Ethics Committee of the University Clinical Center of Kosovo (Ref. Nr.11389 dated 10.28. 2022). Written informed consent was obtained from all participants.

Study Limitations

The major limitation of the present study is that the sample is small due to the low patient compliance with follow-up visits.

Competing Interests

The authors declare that they have no competing interests.

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