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Research Article

AN EVALUATION OF EFFICACY OF COMMONLY USED FIRST LINE DRUGS IN TERMS OF INTRA OCULAR PRESSURE, OCULAR PERFUSION PRESSURE, AND FIELD OF VISION IN PATIENTS OF PRIMARY OPEN ANGLE GLAUCOMA OF NORTH KARNATAKA

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ABSTRACT

Objective: The objective of the study was to measure the efficacy of commonly used timolol and latanoprost as first line drugs in terms of intra ocular pressure (IOP) and ocular perfusion pressure (OPP).

Methods: This was an open-labeled, randomized, and prospective study conducted in the outpatient department of ophthalmology. Newly diagnosed patients were recruited into the study. A total of 60 patients were recruited into our study and were randomized in a 1:1 ratio into two groups of 30 each to receive either timolol 0.5% eye drops twice daily (Group 1) or latanoprost 0.005% eye drops once daily in the evening for a period of 6 weeks (n=30/group). A baseline general ophthalmic examination was done, and the patients were followed up at week 4 and week 6.

Results: Latanoprost has a greater IOP lowering effect in patients with primary open angle glaucoma as compared to timolol and also concurrently increases Ocular perfusion pressure to a larger extent as compared to timolol.

Conclusion: Latanoprost (left eye: 18.47 and right eye: 18.36) has a greater IOP lowering effect in patients with primary open angle glaucoma as compared to timolol (left eye: 20.4 and right eye: 20.7). Latanoprost (left eye: 57.13 and right eye: 57.20) also concurrently increases ocular perfusion pressure to a larger extent as compared to timolol (left eye: 54.15 and right eye: 55.33).

Keywords: Intraocular pressure, Beta blocker, Prostaglandin analogue, Primary open angle glaucoma, Intra ocular pressure, Ocular perfusion pressure.

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INTRODUCTION

Glaucoma, a chronic, progressive optic neuropathy caused by a group of ocular conditions, leads to the damage of the optic nerve with corresponding visual field defects. Its incidence is gradually increasing throughout the world, and it is the second most important cause of blindness [1]. It is characterized by an increase in the intra-ocular pressure (IOP), which happens to be the single most important risk factor of glaucomatous optic neuropathy [2]. Hence, its measurement is vital in the initial diagnosis and management of glaucoma. The other risk factors for its occurrence include older age, thinner cornea, lower corneal hysteresis, systemic hypotension, and low ocular perfusion pressure (OPP) [3].

OPP, an estimate of optic nerve head (ONH) perfusion, is calculated by incorporating systemic blood pressure (BP) and IOP [4]. OPP is directly proportional to BP, whereas it is inversely proportional to IOP [5]. Glaucoma, associated with increased IOP, causes a decrease in OPP, leading to ONH and retinal ganglion cell damage [3]. Ophthalmologists routinely evaluate only the IOP to screen and evaluate the patients for glaucoma of the patients without estimating OPP. In our present study, we have estimated the OPP of the patients, which gives a better insight into the diagnosis and prognosis of glaucoma.

The ultimate goal in the management of primary open angle glaucoma (POAG) is directed at lowering the elevated IOP using medications, laser or surgery [2]. Medical management forms the most commonly used modality, and others are reserved in cases where medical therapy fails [6,7].

Beta- adrenergic blockers that reduce the aqueous formation and prostaglandin analogues that increase uveoscleral outflow constitute the most commonly used drugs in the management of POAG [2].

Timolol, a prototype ocular β blocker, which has been a first line drug in the management of POAG, has been presently questioned on its efficacy and its effect on blood pressure, ocular perfusion pressure, adverse effect profile and associated non-compliance that could be a potential limitation for its use [8,9].

Prostaglandin analogue latanoprost, which is more potent and longer acting, decreases IOP with higher efficacy in comparison to timolol [10]. Latanoprost, in comparison to timolol, also reduces nocturnal IOP, achieves target IOP in more patients, and has lesser systemic side effects and lesser non-responder rate with the convenience of once daily dosing [11-14]. In view of these features, latanoprost has become a popular ocular hypotensive agent in clinical practice these days.

The objective of the present study was to compare the IOP lowering efficacy and OPP enhancing ability of latanoprost with timolol in patients with POAG.

METHODS

This was an open-labeled, randomized, and prospective study conducted in the Outpatient Department of Ophthalmology attached to Shri B. M. Patil Medical College Hospital and Research Centre, Vijayapura.

After obtaining institutional ethics committee clearance, the patients visiting the outpatient department of ophthalmology who fulfilled the inclusion/exclusion criteria and who gave written informed consent were recruited into our study.

The inclusion criteria included newly diagnosed patients of POAG above 18 years.

The exclusion criteria included patients suffering from active ocular disease, amblyopia, legal blindness (6/60 or less) in either eye, acute angle closure glaucoma, optic nerve disease, advanced cataract, dry eye, and ocular infection or inflammation within the previous 3 months. Patients with previous intraocular surgery, severe trauma and hypersensitivity or any systemic contraindications to study medications were also excluded from the study.

Patients using other ocular medications or other therapies that might have a substantial effect on IOP, and those who were pregnant and lactating were also excluded from our study.

The sample size was determined to be 60 in each group using the formula [1]:
$N = 2\sigma^2 (Zcrit + Zpwr)^2/D^2$
N – Sample size in each group.
σ – Assumed SD of each group.
Zcrit – Desired significance criterion.
Zpwr – Desired statistical power.
D – Minimum expected difference between the two means.

A total of 60 patients were recruited into our study and were randomized in a 1:1 ratio into two groups of 30 each to receive either timolol 0.5% eye drops twice daily (Group 1) or latanoprost 0.005% eye drops once daily in the evening (Group 2).

At baseline visit (visit 1), demographic data, ocular history, medical history, concomitant medications and details of general, systemic, and ophthalmological examination were recorded.

The evaluations included the following parameters:

Best Corrected Visual Acuity, IOP, Gonioscopy, Fundus Examination, Slit Lamp Examination, Visual Field Examination, Ultrasound Biomicroscopy (UBM), BP, Ocular Perfusion Pressure (OPP).

The patients were followed-up at 4 weeks (visit 2) and 6 weeks (visit 3) after administering the respective study drugs. At each follow-up visit, blood pressure, IOP, slit lamp examination and visual acuity were observed.

Statistical analysis
Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) software. Statistical analysis was performed on patients who had completed the 12 weeks of treatment period. Drug effect in terms of change in IOP was compared using Independent sample test. $p<0.05$ was considered statistically significant.

RESULTS

Best corrected visual acuity
The best corrected visual acuity examined in all the visits showed the following results (Table 1).

Mean IOP
The mean IOP was estimated at all the visits. The mean IOP observed, and its percentage decrease is depicted in Table 2 and Fig. 1, respectively.

Gonioscopy
The gonioscopy grades observed are depicted in Table 3.

Fundus examination, UBM
The fundus examination depicting the Cup: Disc (C: D) Ratio and the UBM Examination that depicts the angle of the anterior chamber showed the mean values as depicted in Table 4.

Slit lamp examination
Slit lamp examination was normal in all the patients, with none showing any abnormalities.

Table 1: Best corrected visual acuity of the study participants

	Timolol		Latanoprost	
	Left eye	Right eye	Left eye	Right eye
6/6	4	4	3	3
6/9	4	2	2	6
6/12	14	6	18	3
6/18	2	14	4	16
6/24	3	2	2	1
6/36	3	1	1	1
6/60	0	1	0	0

Table 2: Intra ocular pressure values of the study participants at week 4 and week 6 with timolol and latanoprost

	Day 1		Week 4		Week 6	
	Left eye	Right eye	left eye	Right eye	Left eye	Right eye
Timolol	25.47	25.63	22.22	22.4	20.4	20.7
Latanoprost	24.4	24.33	20.5	20.33	18.47	18.36

Table 3: Gonioscopy values of the study participants with timolol and latanoprost

Grade	Timolol		Latanoprost	
	Left eye	Right eye	Left eye	Right eye
I	1	0	0	0
II	1	1	0	0
III	26	26	22	19
IV	2	3	8	11

Table 4: Fundus examination and UBM values of the study participants with timolol and latanoprost

	Timolol		Latanoprost	
	Left eye	Right eye	Left eye	Right eye
Fundus examination Cup: Disc (C: D) Ratio	0.66	0.67	0.66	0.67667
UBM	28.8	30.6	29.9333	30

UBM: Ultrasound Biomicroscopy

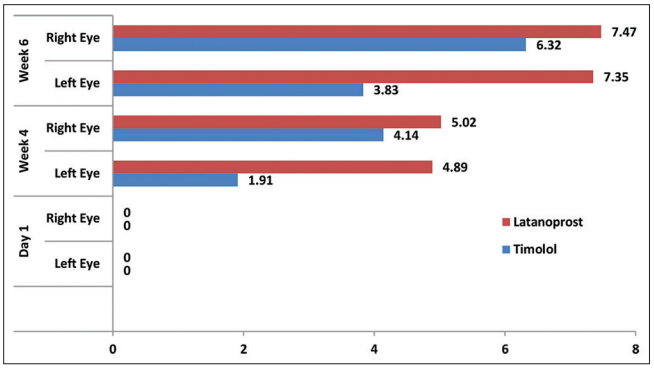

Fig. 1: Percentage decrease of IOP in the study participants at week 4 and week 6 with timolol and latanoprost

Visual field examination
Visual field examination done in all the visits depicted the following values (Table 5). The readings were as follows, with no changes in their values from their baseline visits.

Mean ocular perfusion pressure

The mean ocular perfusion pressure calculated through their standard formulae with both drugs is depicted in Table 6. The percentage decrease in the mean ocular perfusion pressure with timolol and latanoprost at week 6 and week 8 is depicted in Fig. 2.

DISCUSSION

Best corrected visual acuity

The best corrected visual acuity showed no changes in subsequent visits. For changes in visual acuity to be appreciated, a longer period of time is needed. Hence, there was no change seen in its value even after the end of 6 weeks [15].

Mean IOP

It was seen that there was a statistically significant ($p<0.05$) decrease in the IOP at both the subsequent visits with latanoprost showing a greater percentage decrease in the IOP in comparison with Timolol. Our results are in comparison with the study done by Rao *et al*. [1]. This can be attributed to the potent and longer acting activity of latanoprost.

Gonioscopy

Gonioscopy carried out in both eyes at subsequent visits, showed no change in its values in comparison to their baseline values. For its effect to be appreciable, a longer study period is needed [15].

Fundus examination, UBM, visual field examination

A longer period of time is needed for the changes to be produced in these parameters. Hence, there was no change in these parameters seen.

Table 5: Visual field examination values of the study participants with timolol and latanoprost

	Timolol		Latanoprost	
	Left eye	Right eye	Left eye	Right eye
SS	9	8	7	6
SAS	4	4	6	6
NFD	15	16	15	16
DAS	2	2	1	1
BAS	0	0	1	1

SS: Siedels scotoma, SAS: Superior arcuate scotoma, NFD: No field defects, DAS: Double arcuate scotoma, BAS: Bi arcuate scotoma

Table 6: Mean ocular perfusion pressure values of the study participants with timolol and latanoprost

	Day 1		Week 4		Week 6	
	Left eye	Right eye	left eye	Right eye	Left eye	Right eye
Timolol	52.15	52.044	53.15	54.1996	54.15	55.3329
Latanoprost	53.18	53.2244	55.78	55.8911	57.1356	57.2022

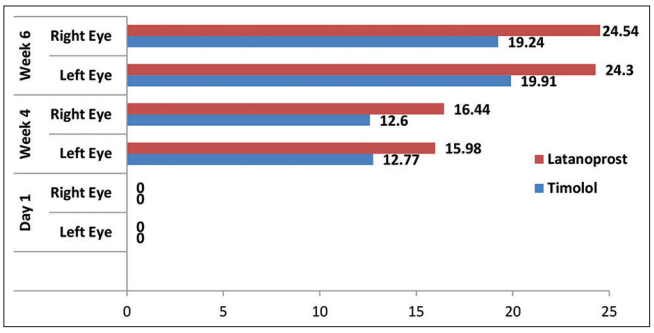

Fig. 2: Percentage increase in mean ocular perfusion pressure of the study participants with timolol and latanoprost at the end of week 4 and week 6

Mean ocular perfusion pressure

The mean ocular perfusion pressure was significantly ($p<0.05$) increased with both the drugs with latanoprost showing a greater percentage increase as compared to timolol [3].

Limitations of our study

As the study was carried out in a limited number of patients (n=30/ study group), the results cannot be generalized to the whole population. A study with a larger number of participants can yield a much appropriate result.

Furthermore, the study was carried out for a shorter duration of time (6 weeks). No parametric changes can be inferred in this duration as some of the parameters take a much longer time (almost years) for a change to be appreciated. A study with a longer period of time can draw a much more logical conclusion on the activity of the study drugs.

CONCLUSION

Latanoprost has a greater IOP lowering effect and ocular perfusion pressure increasing ability than timolol in primary open angle glaucoma.

Timolol, on account of its lesser price can still be used among patients who cannot afford latanoprost.

AUTHOR'S CONTRIBUTIONS

All the authors have equally contributed to the collection and analysis of the data, designing and preparation of the manuscript.

CONFLICT OF INTEREST

Nil.

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