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## Original Research Article

## Travoprost versus latanoprost or timolol in primary open angle glaucoma- Efficacy and safety profile

Abhishek Ranjan<sup>1</sup>, Satapathy K Sugyani<sup>2</sup>, Mukta Prasad<sup>3,\*</sup><sup>1</sup>Dept. of Ophthalmology, Nalanda Medical College, Patna, Bihar, India<sup>2</sup>MKCG Medical College, Berhampur, Odisha, India<sup>3</sup>Dept. of Ophthalmology, Patna Medical College, Patna, Bihar, India

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## ABSTRACT

**Background:** Glaucoma is progressive optical neuropathy which is challenging to treat despite advances in medical and interventional mode of treatments. Primary open angle glaucoma (POAG) is generally associated with diabetes mellitus and hypertension. Any ocular topical pharmacological agent which is to be used in POAG to maintain intraocular pressure have to be very efficacious with good safety profile. We conducted a study comparing travoprost with latanoprost and timolol as single therapeutic agent having favorable outcome.

**Materials and Methods:** Seventy five patients were included in the study for a period of two years. After ethical clearance, patients were randomly allocated to three groups of treatment arm having 25 patients in each group. IOP was noted at 8 A.M, 10 A.M, 4 P.M on two eligibility visits for the same eye. Data collected included demographic data, blood pressure, visual acuity, ocular hyperaemia, Slit lamp finding, IOP & fundus examination.

**Result:** Travoprost treated patients had minimum IOP significantly lower at all visits than those using timolol ( $p < 0.0001$ ) and latanoprost ( $p < 0.004$ ). Also, Travoprost treated patient had maximum IOP records significantly lower at all visits than those using timolol ( $p < 0.0001$ ) and those using latanoprost ( $p < 0.02$ ). No significant difference was found between travoprost and latanoprost treated patients ( $p < 0.25$ ) while patients treated with timolol had on average a higher IOP variance ( $p < 0.004$ ) suggesting a lower peak control during the day.

**Conclusion:** TRAVOPROST 0.004% once daily or in combination with other agents is the most effective and safest topical agents for patients of primary open angle glaucoma with the best safety profile.

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### 1. Introduction

Glaucoma is a potentially blinding, multifactorial optical neuropathy characterized by progressive loss of optic nerve tissue with associated visual field loss. Elevated IOP is often observed in glaucomatous eyes and is a strong risk factor for the development and progression of glaucoma.<sup>1</sup> Therapeutically, reducing IOP, medically or surgically or both is the only proven way to reduce the risk of developing as well as slow down the progression of the disease once it is

present.<sup>2</sup> Medication either topical, oral or intervention by laser trabeculoplasty, trabeculectomy or deep sclerectomy are available options. Prostaglandin analogues are recently added to the armamentarium of glaucoma medication. Topical application of prostaglandin was shown to reduce the IOP effectively without sign of tachyphylaxis by novel mechanism of enhanced uveoscleral outflow. In this group, Latanoprost and Travoprost have been extensively studied. We conducted this study comparing efficacy and safety profile of travoprost with latanoprost and timolol to be used as single therapeutic agent.

\* Corresponding author.

E-mail address: [dr Mukta98@gmail.com](mailto:dr Mukta98@gmail.com) (M. Prasad).

## 2. Materials and Methods

This study is a pharmacological trial comparing three drugs based on their efficacy and safety profile after assigning cases in a randomised manner. After getting approval from Institutional ethical committee, a group of seventy-five patient were selected from among the patients attending the outpatient department of Ophthalmology, Patna Medical college after they went through a detailed screening procedure from November 2017 to September 2019. Consent for photography and publication of data for research were obtained from each patient. Fifty seven of these patients were diagnosed primary open angle glaucoma cases on medication who had come for follow-up whereas the rest 18 patients were detected incidentally while undergoing routine ophthalmic examination. History taking of all cases followed by pre-randomization of cases acted as the baseline data for future follow up. Data collected included demographic information like age, sex and color of the iris, ocular and systemic medical history; resting pulse and blood pressure measurement; visual acuity assessment; assessment of ocular hyperaemia. Slit lamp biomicroscopy for aqueous inflammatory cells and flare; intraocular pressure measurement; gonioscope; dilated fundus examination with an indirect ophthalmoscope followed by fundus photography; iris and eyelash photography; urine pregnancy test for females of childbearing potential.

Criteria for inclusion age of more than 18yrs, Indian origin, IOP measurement between 21 and 36 mm Hg recorded at 8 A.M on two eligibility visits 7 days apart with the same eye qualifying at both visits and IOP in neither eye exceeding 36 mm Hg at any of the IOP measurements taken at 8 A.M, 10 A.M and 4 P.M on the two eligibility visits. Gonioscopy demonstrating open angle & Fundus examination revealing cup-disc ratio $>0.6$ ; localized rim loss, disc hemorrhage or cup-disc asymmetry $>0.2$ . Perimetry showing characteristic glaucomatous visual field defect were excluded.

Patients who met the inclusion criteria at the screening visit and who were currently using topical IOP lowering therapy were instructed to stop all medication for a variable period of washout based upon the agent being used prior to the start of the study. After eligibility was confirmed at a screening visit and two eligibility visit, patients were randomly distributed into there groups of twenty-five each. Group I received timolol maleate (0.5%) twice daily at 8 A.M and 8 P.M. Group II received latanoprost (0.005%) once daily at night time. Group III received travboprost (0.004%) once daily at night time.

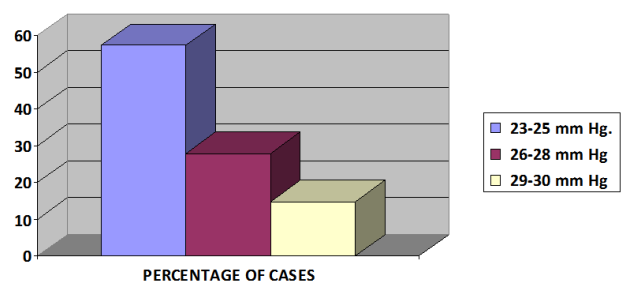
Patients were called for re-examination and follow up at 2<sup>nd</sup> week, 12<sup>th</sup> week, 24<sup>th</sup> week and 48<sup>th</sup> week. At all the follow –up visits, mean IOP was measured at 8 A.M. 10 A.M, noon, 4 P.M. IOP used for analysis at each time point was the mean of 2 measurements if these were within 4mm Hg of one another. If the difference between these two

measurements was greater than 4 mm Hg, a third reading was taken and the IOP value used for analysis was the mean of all three, if the three differed from one another by equal amounts or the mean of 2 measurements closest to each other if the three differed by unequal amounts.

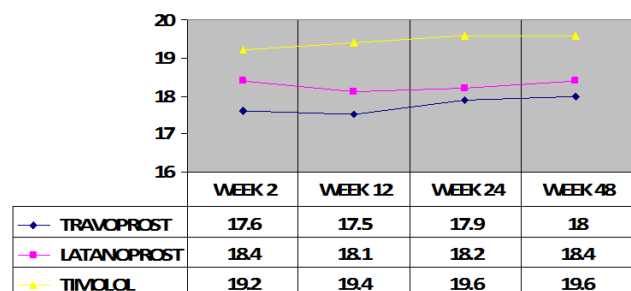
## 3. Results

Around 21 out of seventy-five patients were of age more than 70 years followed by 24% in the range of 61-70 years. Only about 6.7% cases were young ( $< 40$ years). Visual acuity of the participants showed the majority of the participants had an acuity of 6/12. Baseline intraocular pressure was measured. Patients already on medication were advised a suitable duration of washout period depending on the class of drugs being used after which IOP was recorded on the eligibility visits.

Intraocular pressure of the participants.



All the participants were found to be comparable with regard to the confounding factor of primary open angle glaucoma. Six patients discontinued the study. Four in the timolol group and one each in the latanoprost and travoprost group. In the timolol group, 2 participants dropped out because of sudden exacerbation of respiratory distress while the other two had to be advised filtering surgery because the intraocular pressure failed to reduce and visual acuity showed a fall. In the latanoprost group, the reason for dropout was persistent burning and stinging sensation. In the travoprost group, the patient decided to discontinue because of long- lasting ocular hyperemia and financial constraints. Average IOP (least square mean values) measured for each treatment group.



**Table 1:** Following ocular & systemic side effects were charted in all three groups.

Side effects	Travoprost		Latanoprost		Timolol	
	Number	Percent	Number	Percent	Number	Percent
Foreign body sensation	3	12%	2	8%	5	20%
Watering	1	4%	1	4%	1	4%
Punctate epithelial keratopathy	1	4%	0	0%	3	12%
Dry eye	0	0%	0	0%	1	4%
Stinging	0	0%	2	8%	2	8%
Conjunctival hyperaemia	8	32%	3	12%	2	8%
Blurred vision	0	0%	0	0%	1	4%
Pruritus	2	8%	3	12%	3	12%
Increased iris pigmentation	3	12%	5	20%	0	0%
Blepharitis	0	0%	0	0%	1	4%
Headache	1	4%	0	0%	3	12%
Flu syndrome	0	0%	0	0%	4	16%
Malaise	0	0%	0	0%	1	4%
Depression	0	0%	0	0%	2	8%
Hypertension	0	0%	0	0%	4	16%
Hypotension	0	0%	0	0%	3	12%
Bradycardia	0	0%	0	0%	2	8%
Diarrhoea	0	0%	1	4%	0	0%
Nausea	1	1%	1	4%	1	4%
Dyspepsia	0	0%	1	4%	2	8%
Gastritis	0	0%	0	0%	0	0%
Hyperglycaemia	0	0%	0	0%	2	8%
Respiratory distress	0	0%	0	0%	2	8%

Statistical analysis was performed by MINITAB 16 (Minitab Inc., State College, Pennsylvania, USA).

Travoprost treated patients had average IOPs significantly lower at all visits than those using timolol (-1.3 mm of Hg,  $p < 0.0001$ ) and those using latanoprost (-0.3 mm of Hg,  $p < 0.001$ ). Average IOP (in mm Hg.) after treatment in different groups at different visits were significantly less in Travoprost group. (Travoprost/Timolol  $p < 0.0001$  & Travoprost/Latanoprost  $p < 0.001$ ).

Travoprost treated patients had minimum IOP significantly lower at all visits than those using timolol (-1.3 mm Hg,  $P < 0.0001$ ) and latanoprost (-0.3 mm Hg,  $P < 0.004$ ). Also, Travoprost treated patient had maximum IOP records significantly lower at all visits than those using timolol (-1.5 mm Hg,  $P < 0.0001$ ) and those using latanoprost (-0.3 mm Hg,  $P < 0.02$ ).

No significant difference was found between travoprost and latanoprost treated patients ( $P < 0.25$ ) while patients treated with timolol had on average a higher IOP variance ( $P < 0.004$ ) suggesting a lower peak control during the day. It was observed that prostaglandin analogues, travoprost and latanoprost maintained the reduced value of IOP throughout the day as well in night. Additionally travoprost showed consistently lowest IOP at 4 P.M. among the three drugs. Timolol, on the other hand showed a night rise in IOP level.

#### 4. Discussion

Medical management of primary open angle glaucoma requires thorough investigation, meticulous planning and lifelong frequent follow-up. The mainstay of the treatment is to lower intraocular pressure as close as possible to the target pressure, maintain it at this level and also prevent diurnal fluctuation. Besides that the ocular and systemic side-effects of the drugs should be such so as not to pose any safety concern to the overall health of the patient.

In the present study travoprost was compared with latanoprost and timolol. The average IOP at 2<sup>nd</sup>, 12<sup>th</sup>, 24<sup>th</sup> and 48<sup>th</sup> week were 17.6, 17.5, 17.9 and 18.0 mm Hg respectively with average IOPs significantly lower at all visits than those using timolol (-0.3 mm Hg ;  $P < 0.0001$ ) and those using latanoprost (-0.3 mm Hg,  $P < 0.001$ ). A study comparing travoprost and timolol suggested 30% decrease in IOP by travoprost as compared to 26% by timolol.<sup>3</sup> Similarly another study comparing with latanoprost had similar result to the present study.<sup>4</sup> The minimum IOP readings were also significantly lower in the travoprost group than timolol group (-1.3 mm Hg;  $P < 0.0001$ ) and latanoprost group (-0.3 mm Hg;  $< 0.001$ ) which was compared to other study.<sup>5,6</sup>

The maximum IOP readings were also significantly lower in the travoprost group as compared to timolol (-1.5 mm Hg;  $P < 0.0001$ ) and latanoprost group (-0.3 mm Hg;  $P < 0.02$ ). The variance in IOP however did not show

significant difference between Travoprost and latanoprost ( $P < 0.25$ ) while the difference between travoprost and timolol was significant ( $P < 0.004$ ) meaning therapy that the prostaglandin analogues maintain IOP at a reduced level throughout the day while timolol is not as effective in controlling circadian fluctuation as described by other researchers like Frank et al & Shoji T et al.<sup>7,8</sup> The mean  $\pm$  S.D readings of IOP for the travoprost group at various time points were  $16.5 \pm 2.7$ ,  $15.8 \pm 3.0$  and  $15.5 \pm 3.0$  mm Hg at 8 A.M, Noon and midnight respectively. These values of IOP were lower in the travoprost group than the corresponding values in the latanoprost and timolol group – also these recordings showed that travoprost maintained IOP at reduced level through out 24 hrs. even at midnight unlike timolol.<sup>7</sup> Comparable results were noted as of study by Pfeiffer et al<sup>9</sup> among the ocular side effects, conjunctival hyperemia was the most common. (8 patients; 32%). This was also responsible for discontinuation by one of the participants. Besides this, other ocular side effects were foreign body sensation, increased iris pigmentation, watering and superficial punctate keratopathy as stated in other research article.<sup>10,11</sup> These were mild in nature and did not require any treatment. No serious systemic side effects were reported. There was only one complaint of headache and nausea throughout the study period which were very mild in nature.<sup>12</sup>

## 5. Conclusion

A greater proportion of patients achieve lower IOP on monotherapy with travoprost. Reduction of IOP by travoprost is significantly lower than latanoprost and timolol. It provides IOP control consistently throughout the day and this stabilization in the long term helps to prevent optic nerve damage and visual field damage. Latanoprost is equally efficacious but timolol fails to maintain reduced IOP in the midnight. Travoprost act by improving uveoscleral outflow even after 2 year of treatment. Travoprost 0.004% once daily with or without combining other agents of varying mode of action is the most effective and safest topical agents for patients of primary open angle glaucoma with the best safety profile.

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## 7. Source of Funding

None.

## 8. Conflicts of Interest

All contributing authors declare no conflict of interest.

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## Author biography

**Abhishek Ranjan**, Assistant Professor

**Satapathy K Sugyani**, Senior Resident

**Mukta Prasad**, Senior Resident

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