

A Comparative Study between Timolol and Timolol in Combination with Newer Anti Glaucoma Drugs in the Treatment of POAG

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Abstract: The aim of study was to compare the IOP lowering efficacy of timolol and timolol with fixed combination therapy with latanoprost and dorzolamide. Study was undertaken in 60 patients attended to ophthalmology OPD, GGH, Guntur. They were randomly divided into three groups. 20 patients in Group I treated with timolol. 20 patients in Group II treated with fixed combination of timolol with latanoprost. 20 patients in Group III treated with fixed combination of timolol with dorzolamide. Thorough history was taken and patients underwent a comprehensive ocular examination i.e , visual acuity recording, slit lamp examination, gonioscopy, fundus examination with +78 D, +90 D lens, Goldmann applanation tonometry, visual fields recording on Humphrey's field analyser. All the patients were followed up to six months. Percentage of reduction in IOP from baseline to 12th week was observed as: Group I- 26%(timolol), Group II-38%(timolol+ latanoprost), Group III-35%(timolol+ dorzolamide)

Keywords: POAG, IOP, target pressure, combination therapy.

1. Introduction

Glaucoma is a chronic, progressive optic neuropathy comprising of raised IOP, optic disc changes due to death of retinal ganglion cells and associated visual field defects. The only modifiable risk factor in POAG is raised IOP. (1)

2. Aims & Objectives

A total number of 120 eyes of 60 patients who attended ophthalmic O.P.D, GGH, Guntur were included in the study. Of them 20 patients were treated with only timolol eyedrops, 20 patients with latanoprost and timolol, 20 patients with dorzolamide and timolol. We set a target pressure for each individual patient. Our aim is to compare the IOP-lowering efficacy of timolol maleate and fixed combinations, with latanoprost and dorzolamide in patients with primary open angle glaucoma.

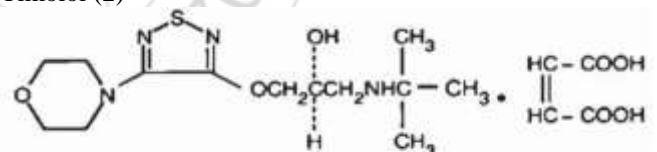
3. Pathogenesis of Poag:

Risk factors for the pathogenesis of POAG are Age above 40 yrs, Heredity, Myopia, Diabetes mellitus. Usually most of the patients will have an elevated IOP>21mmHg on more than two occasions. Quigley and Addicks speculated that elevated intra ocular pressure induced backward bowing of lamina cribrosa and pinching of axons resulting in obstruction of axoplasmic flow. Anderson proposed that elevated IOP interferes with vascular supply. An insult to axons can trigger ganglion cell death by apoptosis.

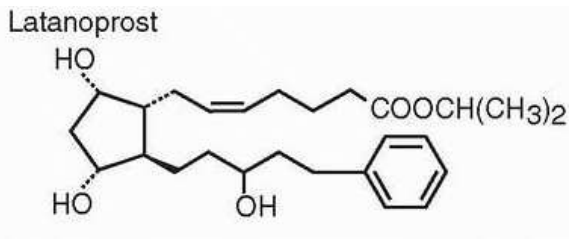
4. Mechanism of Action of Anti Glaucoma Drugs

1. Timolol maleate(0.25-0.5%) is a non selective beta blocker, administered twice daily. Timolol reduces IOP by reducing aqueous humor production. It blocks beta 2 adrenergic receptors on non pigmented epithelial cells of ciliary body and hence reduces IOP. It acts for 24 hrs and is contraindicated in heart disease and bronchial asthma. It may Cause side effects like dry eye, allergy etc.

Timolol (2)



2. Latanoprost (0.005%):-is a prostaglandin F2 α analogue. It decreases IOP by increasing aqueous outflow by increasing uveoscleral outflow by binding to F2 receptors, - PGF2 α in ciliary muscle and PGE2 α in sphincter muscle.it lowers IOP at night and during the day providing uniform round the clock IOP reduction when administered once daily singly or in combination with timolol.(2). It causes side effects like conjunctival hyperaemia, burning, stinging, blurred vision, itching, foreign body sensation and iris pigmentation. They are to be used cautiously in contact lens users, inflammation, macular edema and Neovascular glaucoma.



3. Dorzolamide(2%):-is a carbonic anhydrase inhibitor. It is administered two times a day, potent inhibitor of carbonic anhydrase II, decreases aqueous production by increasing H⁺ ions and decreasing pH. It improves ocular blood flow, macular & paramacular perfusion. The Side effects include allergy, dryness, superficial punctate keratopathy, induced myopia. The Dorzolamide-Timolol combination exhibited greater IOP lowering than Timolol during the daytime but not at night. (2)



Systemic absorption of the topical anti-glaucoma drugs is decreased and local action is increased by following the technique of digital pressure over inner canthus for a few minutes after instillation.

5. Materials and Methods

The comparative study between Timolol and combination drugs was done on patients attending the Ophthalmology O.P.D, GGH, Guntur. This is a hospital based Prospective study to compare the IOP lowering efficacy of 0.5% Timolol with 0.005% Latanoprost + 0.5% Timolol and 2% Dorzolamide+ 0.5% Timolol combination on POAG patients.

Inclusion Criteria

Male/female patients, between 40 and 65 years with POAG with IOP of atleast 22mmHg on more than two occasions

Exclusion Criteria

1. Patients with previous eye surgeries/laser.
2. Patients with history of ocular trauma.
3. Patients with corneal infection in preceding 6 months..
4. Patients with bronchial asthma, COPD, heart disease, drug allergies.
5. Patients with angle closure glaucoma, advanced glaucoma with optic atrophy, other forms of glaucoma.
6. One Eyed patients.

6. Methodology

After taking informed consent, complete evaluation is done with detailed history taking, followed by systemic and ocular examination. Patients with previous history of

antiglaucoma medication were allowed after a wash out period of 3 weeks.

7. Examination

Visual acuity was recorded with snellen's chart, a comprehensive eye examination by slit lamp, anterior chamber depth measurement with Van-Herrick's method done, pupillary reflexes were examined, angle of anterior chamber with gonioscopy was evaluated, IOP was measured with Goldmann applanation tonometry, examination of optic disc with +78D, +90D lens was done. Direct and indirect ophthalmoscopy was done. Visual field examination was done by Humphery's field analyzer. Physician's consultation was taken in all the patients to rule out any systemic contra-indications.

Management of POAG

There are three possible treatment options- 1.) to decrease IOP 2.) to increase perfusion to optic nerve head, 3.) neuroprotection

8. Initiation of Treatment

We included both the eyes of sixty patients. 30% reduction in initial IOP is taken as target IOP. (3)
 Target IOP was calculated for every patient.
 Target IOP = (1 - [baseline IOP+ VF score] / 100) x baseline IOP (4)

AAO Guidelines for Target IOP:

Start treatment with one drug in worse eye, usually beta blocker or prostaglandin analogue. After the peak IOP reduction ability is reached, diurnal variation is evaluated.
 Early glaucoma- beta blocker

Moderate to severe- prostaglandin analogue.

Normotensive glaucoma- prostaglandin analogue, because beta blocker may be absorbed systemically and reduce ONH perfusion pressure.

If first drug fails to reduce IOP by 20%, from base line, or produces side effects, switch to another class of drug.

If first drug reduces IOP by 20%, from base line, but target IOP is not reached, second drug is added (Brimonidine) is best additive. If third drug cannot reduce IOP, filtering surgery is considered.

- 1) Early stage-- reduction of IOP by 20%-30% from baseline
- 2) Advanced Stage -- reduction of 40% or more from baseline
- 3) NTG-reduction 30%
- 4) Ocular hypertension-20% from baseline
- 5) OAG with IOP in mid to high 20s-target IOP range 14-18mmHg
- 6) Advanced glaucoma-target IOP range<15mmHg
- 7) Ocular HTN- IOP>30 with no signs of optic nerve damage. target IOP range<20mmHg

Follow-Up:-

Patients were followed up after 1st month, 3rd month and after 6 months

9. Observation and Results

All the Patients belonging to three groups were followed up after 1st month, 3rd month and after 6 months. Mean baseline IOP was noted in all the three groups. IOP & visual fields were recorded in every visit. Percentage reduction in IOP from baseline to 12th week.

- Group I- 26%(timolol)
- Group II-38%(timolol+ latanoprost)
- Group III-35%(timolol+ dorzolamide)

	Mean base line IOP	Mean IOP after 1month	Mean IOP after 3months	Mean IOP after 6months	% reduction in IOP
Group I	25.9 mmHg	22.67 mmHg	20.06 mmHg	18.43 mmHg	26%
Group II	26.6 mmHg	20.06 mmHg	19.21 mmHg	16.50 mmHg	38%
Group III	26.8 mmHg	22.45 mmHg	19.06 mmHg	17.4 mmHg	35%

There is statistically significant difference in the reduction of IOP ($p < 0.001$) between group I & other two groups. No significant difference ($p > 0.05$) between group II & group III. At the end of the study, there is no much difference in the BCVA, Optic nerve head and Visual fields.

Complications

The most common complications are conjunctival hyperemia, irritation, and watering which are seen in all three groups.

	% reached target IOP	% failed to reach target IOP
Group I	85%	15%
Group II	96%	4%
Group III	94%	6%

10. Conclusion

Timolol, by reducing the production of aqueous humor, 4⁵ and 6 exhibits additive effects when combined with other ocular hypotensive agents. 7, 8, 9 and 10. According to present study the combination therapy is very much effective in reducing IOP to a preset target IOP than timolol monotherapy.

Among two combinations, latanoprost-timolol & dorzolamide-timolol; latanoprost-timolol has proven to be more effective with advantages like once a day dosing play a major role in compliance. And also it is preferred due to its potency, efficacy, mechanism of action, additivity with aqueous humour suppressants and probable safer systemic side-effect profile.

In conclusion in Indian scenario an especially patient from lower socio-economic group, management of glaucoma with timolol is affordable and effective. In case when

Timolol fails as a single drug to reach target IOP, combination therapy was proved to be are more effective.

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