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A Comparative Study of Timolol Maleate 0.5% v/s Latanoprost 0.005% In the Treatment of Primary Open Angle Glaucoma

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ABSTRACT

Glaucoma is an optic neuropathy associated with retinal ganglion cell death that results in visual field loss. Elevated intraocular pressure (IOP) is a primary risk factor for the disease. Glaucoma is the second leading cause of blindness worldwide. Primary open angle glaucoma alone accounts for about 75% of all primary glaucoma. Timolol maleate (non selective β adrenergic antagonist) and Latanoprost (prostaglandin analogue) are commonly used drugs. Our aim of study is to compare the ocular hypotensive effect and safety of topical Timolol maleate (0.5%) and Latanoprost (0.005%) in patients of primary open angle glaucoma. A total of 60 patients with primary open angle glaucoma were included and studied for 6 months. One group of patients were given 0.5% timolol maleate eye drops twelve hourly and other group were given 0.005% latanoprost eye drops once a day. In our study both drugs were significantly effective in lowering the intraocular pressure. The mean fall in IOP in Timolol group was 6.69mmHg (26.10%) and in Latanoprost group was 7.20mmHg (28.5%) from pretreatment values. The difference between the values of mean of reduction in IOP from baseline IOP of the two groups was 0.512 mmHg that was statistically insignificant. The systemic and ocular side effects observed in two groups were comparable and both groups were well tolerated. Timolol maleate and Latanoprost both drugs are effective significantly in lowering the IOP, well tolerated and safe with negligible systemic side effects and comparable ocular side effects.

Keywords: Timolol maleate, Latanoprost, Safety, Efficacy

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INTRODUCTION

The most fundamental fact concerning glaucoma is that is not a single disease process. Rather, it is a large group of disorders that are characterized by widely diverse clinical and histopathological manifestations. It is an important public health problem and is responsible for causing temporary or permanent impairment in vision and discomfort to the patient. Glaucoma is an optic neuropathy associated with retinal ganglion cell death that results in visual field loss. Elevated intraocular pressure (IOP) is a primary risk factor for the disease and demonstrated that the risk of progression of glaucomatous visual field loss is reduced at lower IOPs. In addition, results from Ocular Hypertension Treatment Study[1] showed that a 20% IOP reduction from baseline decreased the risk of developing optic disc cupping and/ or visual field loss in ocular hypertension patients from 9.5% to 4.4%.Glaucoma is potentially blinding disease and is the second leading cause of blindness worldwide. Primary open angle glaucoma (POAG) alone accounts for about 75% of all primary glaucoma with an incidence of 1-2% in general population above 40 years of age.[2] World Health Organization (WHO) has estimated that globally there are 12.5 million people blind from glaucoma with total number affected by this condition around 66 million.[3] Raised intraocular pressure is the only known factor that can be therapeutically manipulated. Reducing IOP in glaucoma patients limits disease progression and slows visual field loss. It is said that for every 1mmHg drop in IOP, a reduction in risk of glaucomatous progression is observed. Therefore, the primary goal in management of glaucoma is to lower the first and the most obvious target that is IOP to a predetermined level (target IOP) which is based on patient needs. Many schools of medicine are still of view that POAG is basically a medical disease with surgery and laser reserved for cases that could not be controlled by medical therapy. Beta blockers have been traditionally used as first line agents. However, nonselective ones cause pulmonary, cardiovascular and CNS adverse effects. With long term timolol treatment about 20-25% of patients will experience tachyphylaxis. James A Nathanson (1981)[4] is of the opinion that human ciliary processes have primarily β_2 adrenergic receptors but a small percentage of β_1 receptors cannot be ruled out. Timolol maleate is a non selective β adrenergic antagonist. Topical β adrenergic antagonist reduce IOP by decreasing the aqueous humor production at ciliary epithelium.[5] Latanoprost, a prostaglandin analogue, is a novel drug in glaucoma therapy. Increased uveoscleral outflow is responsible for IOP lowering effect of topical prostaglandin analogue.[6] Prostaglandin analogue are fast becoming as first line agents for treatment of POAG but much costly than beta blockers. So its efficacy has to be proved for it to be included under the first line therapy of primary open angle

glaucoma. Our aim of study is to compare the ocular hypotensive effect and safety of topical Timolol maleate (0.5%) and Latanoprost (0.005%) in patients of primary open angle glaucoma.

MATERIALS AND METHOD

A total of 60 patients with a clinical diagnosis of primary open angle glaucoma were included in the study and randomly divided into two groups. One group of patients were given 0.5% timolol maleate eye drops twelve hourly and other group were given 0.005% latanoprost eye drops once a day.

Inclusion Criteria:

1. IOP more than 21mmHg during screening examination.
2. Open anterior chamber angle on gonioscopy.
3. With glaucomatous disc change and/ or field change.

Exclusion criteria:

1. Advance glaucoma with risk of progression during washout period.
2. Active ocular infection/ inflammation.
3. Hypersensitivity to any of study drugs or components of it.
4. Any pulmonary or cardiovascular disease.
5. Pregnancy and lactation.
6. Current use of systemic beta blockers.

Materials:

IOP was measured with applanation tonometer and progression was monitored with automated perimetry.

Method:

All patients were followed up regularly for 6 months at 1st week, 2nd week, 4th week, 3rd month and 6th month and were examined.

RESULTS AND DISCUSSION:

The basic approach in a case of glaucoma is to prevent loss of visual fields and in turn loss of visual acuity and visual function in general. Various drugs and their combinations have been tried in treating primary open angle glaucoma. Timolol maleate and latanoprost are used most commonly either singly or in combination with any other drug, to control the intraocular pressure effectively. Patients included in our study are of 38-75 years of age with diagnosis of POAG. Our study shows that chronic simple glaucoma is prevalent in both men (56.66%) and women (43.33%) with a higher prevalence among men, in consonance with studies carried out by Segal,[(7)]

Kahn, Leibowitz et al[2]. The pretreatment clinical data of the two groups were more or less similar. In our study both groups were significantly effective in lowering the intraocular pressure. At the end of 6 months the mean fall in IOP in Timolol group was 6.69mmHg (26.10%) and in Latanoprost group was 7.20mmHg (28.5%) from pretreatment values (Table- 1, 2). This is comparable to results of Arshad Ali Lodhi et al[8] who reported 26.7% and 28.9% reduction of IOP with Timolol and Latanoprost respectively in a 3 month study of 58 patients of POAG. When used as primary therapy Latanoprost instilled once daily in the evening reduced mean IOP 2.25% more than Timolol Maleate instilled twice daily in consonance with studies of Arshad Ali Lodhi et al.(8) But the difference between the values of mean of reduction in IOP from baseline IOP of the two groups was 0.512 mmHg that was statistically insignificant (t test, p value=0.090), this was supported by study by Mishima Hk et al.[9] As regards the long term effect of timolol, there was no short term escape or long term drift as proposed by Boger WPIII[10] in our study. In our study there was no significant change in blood pressure and pulse rate at the end of study in consonance with studies by Berry et al(11) but differ from study by Van Buskirk[12] that timolol causes slight reduction in blood pressure and pulse rate. Regarding local ocular side effects in our study, timolol did not alter basal tear secretion, lacrimation was reported in 1(2.8%) eye, burning sensation in 2(4.76%) and conjunctival hyperemia in 2(4.76%) eyes in timolol group in consonance with studies by Stewart et al(13) and Mishima Hk et al[9]. In Latanoprost group conjunctival hyperemia was reported in 3(7.14%) of eyes, burning sensation in 2(4.76%) eyes and diminished corneal sensation in 2(4.76%) eyes (Table- 3). According to Mishima Hk et al[9] the main ocular side effects observed were conjunctival hyperemia and smarting in both groups which were also seen in our study. Both the groups were well tolerated in our study.

Table- 1 Change in mean IOP (mmHg) with duration of treatment

Drugs	Base line IOP^{+}	IOP at 1st week	2nd week	4th week	3rd month	6 month
Timolol 0.5%	25.64	19.81	18.80	18.21	18.64	19.23
Latanoprost 0.005%	25.41	19	18.41	17.59	17.8	18.21

$^{+}$- Intraocular pressure

Table- 2 Group statistics

Drugs	Range of reduction in IOP^{+} (mmHg)	Mean of reduction in IOP	Percentage	Difference in mean of reduction in IOP
Timolol 0.5%	5.8-7.4	6.694	26.10%	
Latanoprost 0.005%	6.41-7.81	7.206	28.35%	0.512 mm Hg(2.25%)

$^{+}$- Intraocular pressure

Table- 3 Side Effects

Side Effects	Timolol 0.5% Group (n= 42 eyes)	Latanoprost 0.005% Group (n= 42 eyes)
Superficial Punctate Keratopathy	0	0
Conjunctival hyperemia	2	3
Burning sensation	2	2
Itching	0	1
Foreign body sensation	0	0
Allergic conjunctivitis	0	0
Conjunctival follicles	0	0
Blepharitis/ Lids swelling	0	0
Blurred vision	0	0
Lacrimation	1	0
Cell in Anterior chamber	0	0
Iris color change	0	0
Diminished corneal sensitivity	3	2
Total	8 (19.04%)	8 (19.04%)

CONCLUSION

Timolol maleate and Latanoprost both drugs are effective significantly in lowering the IOP, well tolerated and safe with negligible systemic side effects and comparable ocular side effects. Latanopost can be considered to be safe and effective agent for treating primary open angle glaucoma with advantage of single dosing but its main draw back is its cost as compared to timolol maleate.

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