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A COMPARATIVE STUDY OF CLINICAL EFFICACY OF BIMATOPROST 0.03% AND TIMOLOL 0.5% IN NORMAL TENSION GLAUCOMA.

Ophthalmology

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ABSTRACT

BACKGROUND: Glaucoma is a potentially blinding condition that causes an irreversible optic neuropathy with accelerated retinal ganglion cell death leading to sight threatening complication due to a specific pattern of progressive visual field loss. Elevated intraocular pressure(IOP) is an important risk factor for glaucoma. Normal tension glaucoma(NTG) is a unique condition in which optic nerve damage and vision loss have occurred despite a normal pressure inside the eye related to abnormal vasoregulation. However, IOP still is a part of the pathogenesis in NTG, and lowering IOP is effective in reducing the progression of damage. In the last decade, several new ocular hypotensive drugs have become available. Present study is done to compare clinical efficacy of Bimatoprost 0.03% and Timolol 0.5% in Normal Tension Glaucoma.

MATERIALS AND METHODOLOGY: This prospective interventional study was conducted in ophthalmology department at tertiary care hospital for a period of 2 years. 50 cases of NTG were selected and divided in 2 groups based on simple random sampling. One group treated with 0.5% Timolol eye drops and the other with 0.03% Bimatoprost eye drops. Ocular improvement and effect of the drug were assessed by a follow up done at 1st week, 1st month, 3rd month and 6th month wherein IOP was measured using Applanation tonometer and Non-contact tonometer. 30% reduction of baseline IOP was targeted in this study.

CONCLUSION: Aim of glaucoma treatment is to prevent further visual loss and blindness by reduction in the IOP.
Bimatoprost(0.03%) is more efficient in IOP reduction than timolol(0.5%). Both the drugs are well tolerated with more ocular side effects with bimatoprost which was not statistically significant and can be minimized with low concentration(0.01%) with similar efficacy1. patient's compliance is better with Bimatoprost due to once daily dose. Therefore, Bimatoprost is preferred over timolol, because the ultimate goal in NTG is to reduce the IOP.

KEYWORDS

Normal tension glaucoma, Bimatoprost, Timolol

INTRODUCTION

- Glaucoma is third most common cause of vision impairment worldwide.[2] Clinically, the two most common types of glaucoma are primary open angle glaucoma(POAG) and primary angle closure glaucoma(PACG). POAG is characterized as a multifactorial optic neuropathy with 'a characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons' developing in the presence of open anterior chamber angles, and manifesting characteristic visual field abnormalities.[3]
- The most important risk factor in POAG is raised IOP secondary to reduced aqueous outflow through the trabecular meshwork at the filtration angle. In general population, the mean IOP is 16mmHg(11-21 mmHg). POAG with baseline IOP in normal range is referred to as Low pressure glaucoma or more commonly, Normal tension glaucoma(NTG).
- Pathogenesis of normal tension glaucoma is still not clear. Patients with NTG have been noted to have a higher prevalence of hemodynamic crises; hypercoagulability; abnormal ophthalmodynamometry; hypertension; hypotension; increased blood viscosity; elevated blood cholesterol and lipids; carotid artery disease; slowed parapapillary, choroidal, and retinal circulations; peripheral vasospasm, and migraine.[3] NTG is more common in women than in men. It usually affects adults of an average age of 60 years.
- Lowering IOP to reduce glaucomatous optic nerve damage is current goal of therapy.[4] In the last decade, several new ocular hypotensive drugs have become available. Bimatoprost(0.03%) is a member of new class of agents called prostamides.[5] It lowers the IOP by increasing the uveoscleral outflow from the eye.[5] Timolol Maleate(0.5%) is a non-selective beta adrenergic receptor blocker. It reduces aqueous humor secretion by inhibiting cyclic adenosine monophosphate production in ciliary epithelium.[6] Present study is done to compare clinical efficacy of Bimatoprost 0.03% and Timolol 0.5% in Normal Tension Glaucoma.

METHODOLOGY

A hospital based prospective interventional study was conducted in ophthalmology department at tertiary care hospital for a period of 2 years. 50 cases of NTG were selected and divided in 2 groups based on simple random sampling.

INCLUSION CRITERIA:

- IOP must be less than or equal to 21 mmHg without treatment
- Gonioscopically open angles
- Typical glaucomatous optic disc changes: rim thinning, cupping, rim notching, disc hemorrhage, nerve fiber layer defect, vertical cup/disc asymmetry 0.2 or more
- A reproducible visual field defect on at least three prior visual fields as observed in standard automated perimetry from the Humphrey Visual Field Analyzer using the 30-2 test pattern
- Willing and able to provide informed consent
- Able to adhere to treatment/visit plan

EXCLUSION CRITERIA:

- Subjects with visual field defect attributable to organic causes other than glaucoma
- Occludable narrow angles, angle closure glaucoma and secondary glaucoma
- Prior filtration surgery
- Prior laser iridotomy
- Laser trabeculoplasty < 6 months prior to enrollment or for an IOP >21 mmHg
- History of chronic inflammatory eye disease
- History or signs of intraocular trauma
- Current use of any ophthalmic, dermatologic or systemic steroid
- Therapy with another investigational agent within past 30 days
- Subjects who can not complete follow-up
- Subjects who are unable to provide informed consent
- History of severe or serious hypersensitivity to topical or systemic prostaglandins or beta-blockers
- Women of child bearing age , nursing mothers, pregnancy

PATIENT EVALUATION AND DATA COLLECTION:

All patients provided informed consent before undergoing the study. Data was collected in a pre-tested questionnaire containing details about demographic profile with history and other ocular associations

like myopia, DM, family history of glaucoma. Detailed clinical history was collected.

This was followed by a detailed ophthalmic examination which included torch light examination, visual acuity, complete anterior segment examination by slit lamp and dilatation of pupil for detailed stereoscopic fundus examination using 90 diopter lens and with indirect ophthalmoscope using 20 diopter lens.

IOP was measured with Goldman's Applanation Tonometer and Non-contact Tonometer, diurnal variation is taken into consideration to rule out ocular hypertension and early POAG. Gonioscopy was done for analysis of angle structures. Pachymetry was done to measure central corneal thickness(CCT) to calculate corrected IOP. Humphrey's automated perimetry SITA standard stimulus size III 30-2 programme was used for visual field analysis.

MANAGEMENT:

25 patients were treated with 0.5% Timolol eye drops 2 times a day and another 25 patients with 0.03% Bimatoprost once a day for 6 months. Ocular improvement and effect of the drug were assessed by follow-up at 1st week, 1st month, 3rd month ad 6th month wherein visual acuity, IOP, and visual field were examined. Based on the results of the CNTGS study we aimed to reduce IOP about 30% from the baseline.[7]

STATISTICALANALYSIS:

The data collected was tabulated and analyzed using descriptive statistical tool, mean and standard deviation. Comparison between groups was done by using independent 't' test. Complete analysis was carried out using SPSS software.

RESULTS AND DISCUSSION

- There were 28 males and 22 females out of 50 patients. In each group, there were 14 males and 11 females.

Table 1: central corneal thickness (CCT)

	Mean CCT±SD(Micron)
Group B	538.4±27.45
Group T	547.94±36.54
Average(all cases)	543.17±33

The mean CCT observed in the study was 543.17±33 micron ranging from 479 to 697 micron.

MEAN IOP REDUCTION:

Table 2: Mean IOP at baseline and on follow up visits

	Mean Baseline IOP(mmHg)	1st week	1st month	3rd month	6th month
Group B	16.53	13.73	13.68	13.73	13.55
Group T	16.63	14.65	14.67	14.69	14.65

As per Table 2, The reduction of IOP at 6 months with Bimatoprost (0.03%) was from 16.53 to 13.55mmHg and with Timolol(0.5%) it was from 16.63 to 14.65 mmHg. The mean overall reduction in IOP for Bimatoprost(0.03%) was 2.98 mmHg(P=0.0014) and for Timolol(0.5%) it was 1.98 mmHg(P=0.00853). The reduction in IOP with both drugs is consistent but more reduction is seen with Bimatoprost.

Table 3: Response rates

	Group B		Group T	
Target % of IOP reduction	No. of eyes achieved target IOP reduction	%	No. of eyes achieved target IOP reduction	%
>20%	21	42	4	8
>15%	27	54	14	28
>10%	38	76	36	72

Response rates for all target IOPs were higher with Bimatoprost once daily regimen. A higher percentage of patients in the Bimatoprost groups achieved low target pressure as compared to Timolol.

SAFETY EVALUATION

Table 4: Adverse effects

Adverse effects	Bimatoprost	Timolol
Redness	5(20%)	1(4%)
Ocular pain	2(8%)	0
Blurring of vision	1(4%)	0

Table 4 represents that adverse effects occurred more with the Bimatoprost group when compared to the Timolol group, but statistically not significant($p>0.05$)

Both treatment regimens were safe and well tolerated during the study. Patients in the bimatoprost group had a higher incidence of conjunctival hyperemia, pain and blurring of vision. Importantly, conjunctival hyperemia was not associated with intraocular inflammation or any other sequelae. These adverse effects of Bimatoprost 0.03% can be reduced by Bimatoprost 0.01% without change in efficacy as per a pivotal, 12 months randomized controlled trial that showed Bimatoprost 0.01% to be equivalent in efficacy to Bimatoprost 0.03% for the once daily treatment of glaucoma. Both preparations reduced mean IOP approximately same after 12 months.[1] In contrast with the decrease in heart rate found in Timolol patients, there were no clinically significant systemic adverse effects of Bimatoprost.

Visual acuity and the field of vision at the end of 6 months; was the same in both groups, as what was recorded at the baseline visits.

The results of this trial indicate that Bimatoprost provides excellent IOP control. It was highly efficacious, well tolerated and systemically safe. Bimatoprost given once daily in the evening was statistically and clinically superior to Timolol 0.5% in IOP lowering throughout the visits. Importantly, patients receiving Bimatoprost once daily were significantly more likely than Timolol patients to achieve substantial IOP reductions and reach low target pressures.

As per a randomized, clinical trial, subjects of POAG and ocular hypertension who were treated either with Bimatoprost 0.01% or Timolol 0.5% showed that Bimatoprost 0.01% is more effective than Timolol 0.5% in IOP reduction throughout the day($p=0.0003$). Timolol reduced mean 24h systolic BP, diastolic BP in day hours, and reduced heart rate and ocular perfusion pressure.[8]

CONCLUSION

- Aim of glaucoma treatment is to prevent further visual loss and blindness by reduction in the IOP.
- Bimatoprost(0.03%) is more efficient in IOP reduction than timolol(0.5%). Both the drugs are well tolerated with more ocular side effects with bimatoprost which was not statistically significant and can be minimized with low concentration(0.01%) and similar efficacy[1]. patient's compliance is better with bimatoprost due to once daily dose. Therefore, Bimatoprost is preferred over timolol, keeping in mind that the ultimate goal in NTG is to reduce the IOP, to prevent further damage to the optic nerve causing loss of vision.

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