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IJPBS |Volume 5| Issue 2|APR-JUN|2015|288-292

Research Article
Pharmaceutical Sciences

DORZOLAMIDE, A BETTER CHOICE IN PRIMARY OPEN ANGLE GLAUCOMA (POAG) IN COMPARISON WITH TIMOLOL

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ABSTRACT

Objective: *To compare the IOP reducing efficacy and safety of 0.5% timolol and 2% dorzolamide in primary open angle glaucoma.* ***Material and methods:*** *In this prospective, open labelled, randomised comparative study, 60 patients received either 0.5% timolol twice daily (n=30) or 2% dorzolamide twice daily (n=30) for 6 months. IOP was measured every fortnight.* ***Results:*** *The mean IOP reduction from baseline was 15.55mmHg for dorzolamide group and 13.45 for timolol group, but not statistically significant (p = 0.028). Dorzolamide group had higher incidence of adverse effects like ocular irritation compared to timolol group, but not statistically significant (p=0.097).* ***Conclusion:*** *0.5% timolol eye drops twice daily is non inferior in IOP lowering efficacy compared to 2% dorzolamide eye drops twice daily in patients with POAG. Incidence of adverse effects like ocular irritation was higher in dorzolamide group compared to timolol group.*

KEY WORDS

dorzolamide, timolol, POAG

INTRODUCTION

Glaucoma, a chronic, progressive and most often asymptomatic disease, is ranked as the leading cause of irreversible blindness worldwide by the World Health Organization(1). Primary open angle glaucoma (POAG) is defined as a chronic optic neuropathy with characteristic changes in optic disc and visual field (2). POAG is estimated to affect about 6.48 million people. With an increase in life expectancy, this figure will increase to 16 million 2020 (3). These numbers highlight the importance of understanding the disease, its natural history, and its underlying pathophysiology, so that we may try to establish effective methods of treatment and preventive measures to delay, or even arrest disease progression, thereby reducing visual morbidity. At present, all resources are directed towards reduction of intraocular pressure (IOP), the only known causal and treatable risk factor for glaucoma. Topical drugs are commonly used to reduce IOP in the medical management of POAG.

The purpose of this study was to compare the IOP reducing efficacy and safety of 0.5% timolol and 2% dorzolamide in POAG.

MATERIALS AND METHODS

This prospective open labelled randomised comparative study was carried out in out patient department of ophthalmology at Dr.B.R.Ambedkar Medical College and Hospital during November 2009 and October 2010. It was approved by the Institutional Ethics Committee. Informed consent was taken from each patient before they enrolled in the study. Patients>40years of age of either sex who were newly diagnosed cases of POAG atleast in one eye were included in the study. Patients with acute angle closure glaucoma or narrow angle, pigmentary/exfoliation glaucoma, pregnant and lactating females, h/o hypersensitivity to study drugs, bradycardia, second or third degree heart block, bronchial asthma, COPD, CHF, severe renal impairment, PVD were excluded from the study. 60 cases of POAG were selected and divided equally into two groups based on simple random sampling. Detailed history was taken and a thorough examination of their general and systemic conditions was done. 30 patients were treated with 0.5% timolol eye drops twice daily and another 30 patients with 2% dorzolamide eye drops twice daily for 6 months. Ocular improvement and effect of the drug were assessed by follow up every fortnight for 6 months. Each time IOP was measured using Perkins hand held tonometer and Schiotztonometer. Two readings were taken to establish the gradual reduction and final IOP. The visual field defect was documented by Octopus and visual acuity by Snellen's chart both at the baseline and at the end of the study. All these details were recorded in a well designed Performa. The data was analyzed using descriptive statistical tool and comparison between the groups by student's T-test.

RESULTS

60 patients were included in the study. 40(66.6%) were male and 20(33.3%) were Females. They were classified into four age groups i.e. 41-50, 51-60, 61-70 and 71-80 years. Maximum numbers of patients (33.3%) were in the age group of 51-60years.The mean IOP across various time points is shown in table 1. There was no much difference in efficacy between the two treatment groups. The mean IOP reduction from baseline is shown in table 2. It was 15.55mmHg for dorzolamide group and 13.45 for timolol group, but not statistically significant (p= 0.028) Dorzolamide group had higher incidence of adverse effects like ocular irritation compared to timolol group, (table 3) but not statistically significant (p = 0.097).

Treatment group	Baseline	4th week	12th week	24th week
Timolol	28.83	26.70	20.98	15.37
Dorzolamide	31.67	30.87	25.18	16.12

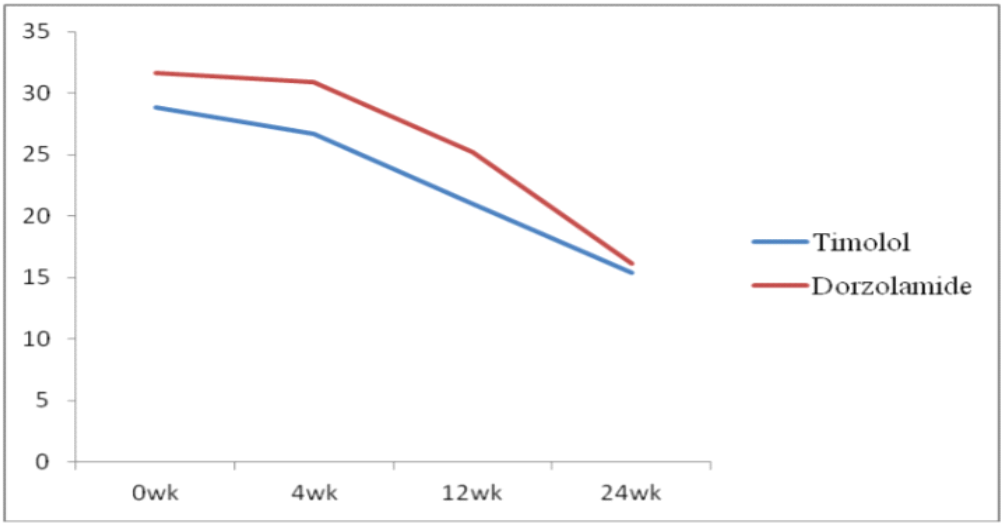
[Table -1]: Mean IOP (mm Hg) across time points

Treatment group	12th week	24th week
Timolol	7.85	13.46
Dorzolamide	6.49	15.55

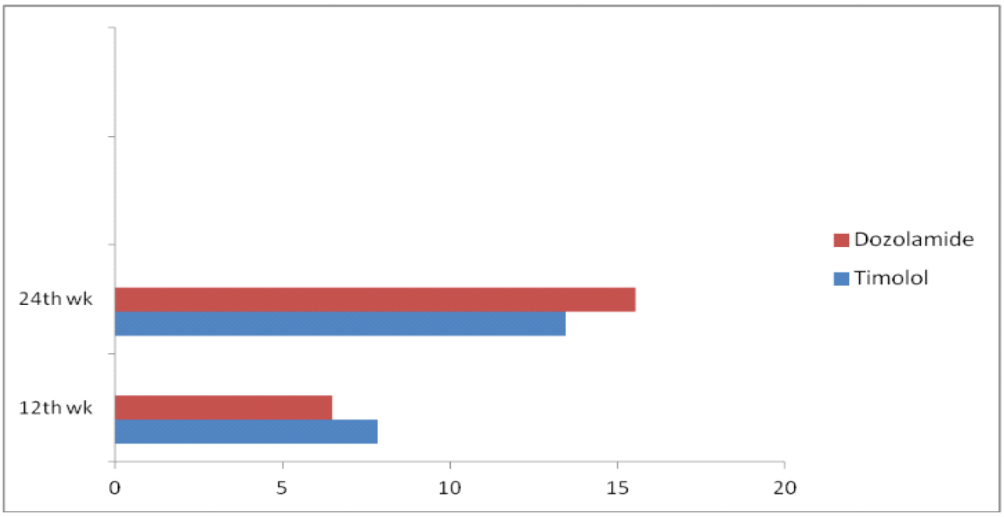
[Table-2] :Mean IOP change from baseline

Adverse effect	Timolol (%)	Dorzolamide (%)
Ocular irritation	1 (3%)	7 (23%)
Ocular pain	0	3 (10%)
Blurring of vision	0	1 (3%)

[Table-2]: Comparative evaluation of safety



[Figure-1]: Mean IOP (mm Hg) across time points



[Figure-2]: Mean IOP change from baseline (mmHg)

DISCUSSION

Timolol is a non-selective beta-blocker being used extensively world wide as a first line agent for the treatment of POAG and ocular hypertension. It acts by blocking beta-2 receptors in the ciliary processes and thus reducing aqueous production. Dorzolamide is a topical carbonic anhydrase inhibitor. It slows the production of bicarbonates and thus decreases sodium and fluid transport which in turn reduces the secretion of aqueous humor (4). The mean IOP reduction from

baseline is shown in table 2. It was 15.55mmHg for dorzolamide group and 13.45 for timolol group, but not statistically significant (p= 0.028).Visual acuity and field of vision at the end of 6 months was same in both the treatment groups as recorded at the baseline.Dorzolamide group had higher incidence of adverse effects like ocular irritation compared to timolol group (table 3), but not statistically significant (p = 0.097). These findings are consistent with other studies conducted by Strahlman etal (5) and Fuchsjager G etal(6). There are studies which indicate that dorzolamide, but not timolol, increases optic nerve head and choroidal blood flow in patients with POAG or ocular hypertension(6).This effect may be associated with a preservation of visual fields in patients with glaucoma. Monotherapy is frequently not sufficient for reaching the preset target IOP. Therefore ophthalmologists prescribe combination therapy to achieve adequate reduction in IOP (7). It also improves patient compliance. Most fixed dose combinations contain timolol as it can be dosed either once/twice daily and can be combined with prostaglandin analogues, adrenergic agonists and carbonic anhydrase inhibitors(8). The combination of timolol and dorzolamide significantly improves retinal haemodynamics in POAG (9). Therefore FDCs if rational offer benefits of convenience, cost and Safety.

CONCLUSION

0.5% timolol eye drops twice daily is non inferior in IOP lowering efficacy compared to 2% dorzolamide eye drops twice daily in patients with POAG. Incidence of adverse effects like ocular irritation was higher in dorzolamide group compared to timolol group. Dorzolamide increases optic nerve head and choroidal blood flow in patients with POAG or ocular hypertension. This effect may be associated with a preservation of visual fields in patients with glaucoma.

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