ORIGINAL ARTICLE

Timolol and Bimatoprost in Primary Open Angle Glaucoma-A Comparative Study

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Abstract

The present study evaluated safety and intraocular pressure lowering efficacy of ocular antiglaucoma drugs timolol maleate 0.5% and bimatoprost 0.03% as monotherapy for 12 weeks on 50 patients divided in two groups with established primary open angle glaucoma. Higher incidence (72%) was found in patients aged 50 years and above and 60% were males. In both the groups, significant fall in mean intraocular pressure was observed. The mean reduction in intraocular pressure was 29.9% for timolol group and 36% for bimatoprost group. Bimatoprost o.d. was statistically and clinically superior to timolol b.d. in lowering intraocular pressure.

Key Words

Primary Open Angle Glaucoma, Intraocular Pressure, Conjunctival Hyperemia, Timolol, Bimatoprost

Introduction

Primary open angle glaucoma (POAG) is a progressive, chronic optic neuropathy in adults where intraocular pressure (IOP) and other currently unknown factors contribute to damage and in which, in the absence of other identifiable causes, there is characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons. This is associated with an anterior chamber angle that is open by gonioscopic appearance (1). In India, glaucoma is emerging as a major cause of blindness. The National Survey on Blindness (2001-02) conducted in the country estimated the prevalence of glaucoma to be about 5.8% (2). The risk of developing glaucoma consistently appears to be greater with progressively higher levels of baseline intraocular pressure. Older age, family history of glaucoma, African or Latino ancestry and thinner central corneal thickness are risk factors for POAG. Among these, IOP is best known and most studied factor. Kitawaza and Horie reported definite causal relationship between the level of IOP and damage to the optic nerve with resultant change in visual field (3). The mainstay of treatment in POAG is medical. The IOP is lowered medically either by reducing the production of aqueous entering the eye or by increasing the facility of aqueous outflow from anterior chamber. In the present study, the safety and efficacy of timolol maleate 0.5% ophthalmic solution, a non-selective -blocker and bimatoprost 0.03%, a prostamide were compared in the treatment of patients with POAG.

Material and Methods

Twelve week prospective study was conducted on 50 patients, divided in two groups of 25 each, comparing safety and efficacy of timolol 0.5% ophthalmic solution and bimatoprost 0.03% in the treatment of patients with POAG.

The inclusion criteria for patients were: age >21 years of either sex, untreated IOP between 22-35 mmHg in atleast one eye i.e. study eye with glaucomatous optic disc change with or without perimetric evidence of glaucomatous visual field defects and anterior chamber angle is open and normal on gonioscopy. Also, patients

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with bilateral glaucoma, in whom both eyes fulfilled the above criteria, eye with higher IOP was chosen for study.

The exclusion criteria for patients included: history of hypersensitivity or poor tolerance of any component of the preparation used in the study; patients with significant medical conditions like cardiopulmonary diseases, cerebrovascular disease or pulmonary diseases; patients with corneal abnormalities that will interfere with tonometry; patients that require chronic use of ocular medication other than the study medications during the study; patients with functionally significant visual loss within the past year; pregnant, lactating females; and patients with history of recent ocular surgery.

At the screening examination, informed consent was taken from the selected patients and comprehensive medical history, general physical examination including blood pressure and pulse measurements were taken.

Detailed ocular examination including Snellen visual acuity, fundus examination, IOP, slit lamp examination, gonioscopy and visual field charting was done.

Patients were divided into two treatment groups of 25 each. Group I patients were instructed to instill the timolol maleate 0.5% ophthalmic solution in the study eye twice daily, at 12 hour interval for 12 weeks. Group II patients were instructed to instill the bimatoprost 0.03% ophthalmic solution in the study eye once daily, in the evening, for 12 weeks. Efficacy and safety was evaluated at baseline, week 1, week 3, week 6 and week 12.

Stastistical Analysis

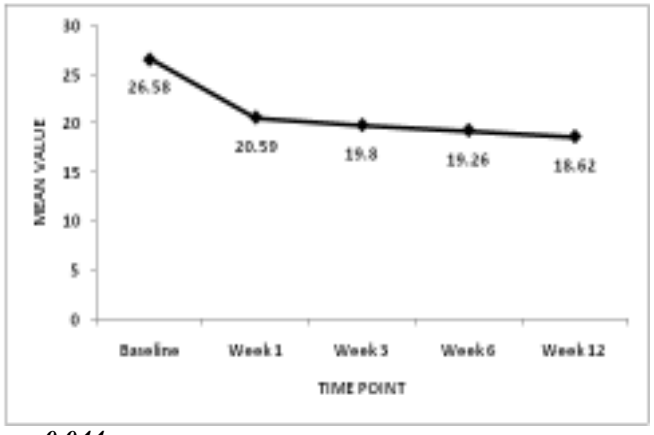
Data was expressed as mean and standard deviation. Paired and unpaired 't' test was used to assess statistical significance of the data. A level of $p<0.05$ was accepted as statistically significant result.

Results

In the present study, majority of the patients (72%) were over 50 years of age, with 60% being males. Most of the patients had more than one symptom related to diseased eye. However, the commonest complaint was painless diminution of vision seen in 33 (66%) patients.

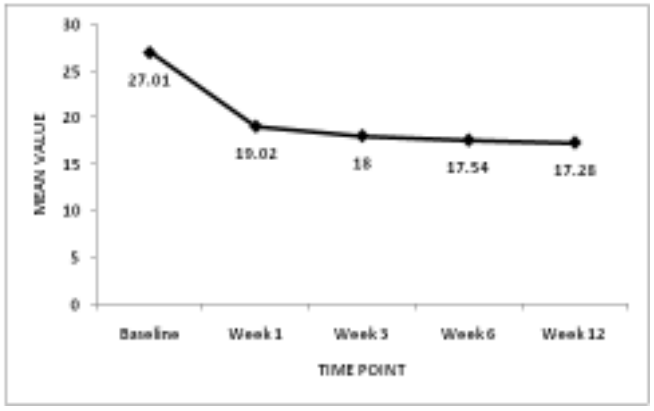
In Group I, 15 patients (60%) and in Group II, 17 patients (68%) had vertical cup:disc (C:D) ratio of more than 0.6.In Group I, baseline mean IOP was 26.58 ± 3.15 mmHg, whereas in Group II, baseline mean IOP was 27.01 ± 3.33 mmHg, the comparison between the

Fig. 1 IOP (mmHg) During Treatment with Timolol Group I Patients



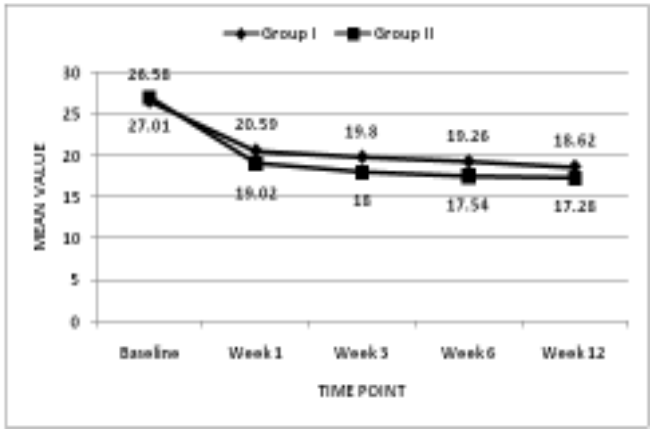
p < 0.044

Fig. 2 IOP (mmHg) During Treatment with Bimatoprost in Group II Patients



p < 0.043

Fig. 3 IOP (mmHg) During Treatment with Timolol in Group I and Bimatoprost in Group II Patients



two was statistically non-significant (p<0.461).In Group I during treatment with timolol, baseline IOP fell from average of 26.58 ± 3.15 mmHg to 20.59 ± 2.95 mmHg at week 1. This mean reduction of IOP was maintained throughout the study and it was 18.62 ± 1.20 mmHg at week 12 (*Fig. 1*). The mean reduction in IOP was statistically significant (p<0.044).

In Group II during treatment with bimatoprost, the baseline IOP fell from average of 27.01 ± 3.33 mmHg to 19.02 ± 2.41 mmHg at week 1 and this mean reduction of IOP was maintained at all follow-up visits and it was 17.28 ± 1.20 mmHg at week 12 (*Fig. 2*). This mean reduction in IOP was also statistically significant (p<0.043).

The changes in pulse rate and systolic and diastolic blood pressure was clinically as well as statistically non-significant in both the groups (*Fig 3*).

Discussion

Traditional studies for the treatment of glaucoma, for more than a century, have focused on reducing and controlling IOP with topically applied ocular hypotensive medication. In the present study, hypotensive efficacy and safety of bimatoprost 0.03% was compared to that of timolol maleate 0.5%. The results were evaluated at week 1, week 3, week 6 and week 12. No patient was lost to follow-up and no patient was removed from the study because of adverse reaction or inadequate IOP control.

The present study enrolled patients of different ages. High incidence i.e. 72% of glaucoma was found over 50 years of age, followed by 22% in age group of 41-50 years. Klein et al. in the Beaver Dam Eye Study reported an increased incidence of open angle glaucoma with increase in age from 0.9% in people 43-57 years of age to 4.7% in people 75 years of age or older (4).

The present study observed preponderance of POAG in males (60%) as compared to females (40%). Ramakrishnan et al. also found POAG more in males (54.5%) than in females (45.5%) (5). The Rotterdam Eye Study carried out by Dielemens et al. observed that men were at three times higher risk than women in developing POAG (6). Family history of glaucoma was observed in 2 (4%) patients in the present study. Teikari reported a 10.2% inheritance for chronic open angle glaucoma (7).

In the present study, no significant improvement or deterioration in visual acuity (i.e. upto two Snellen's line) in any treatment group was observed. However, one patient in Group I and two patients in Group II showed improvement of vision by one Snellen line at the end of study period. Cohen et al. conducted a 2-year trial and found no significant improvement in visual acuity in patients with POAG after treatment with bitamatoprost 0.03% and timolol 0.5% (8).

In the present study, the baseline IOP for Group I was 26.58 ± 3.15 mmHg. The mean IOP fell from the baseline to 20.59 ± 2.95 mmHg at week 1 and 18.62 ± 1.20 mmHg at week 12 (*Fig. 1).* It was found that at week 1, the mean IOP reduction was 22.2% and at week 12 it was 29%. The mean reduction in IOP was statistically significant at all follow-up visits (p<0.001).

In Group II, the baseline mean IOP was 27.01 ± 3.33 mmHg and it reduced to 19.02 ± 2.66 mmHg at week 1 followed by 17.78 ± 1.20 mmHg at week 12 (*Fig. 2*). It was observed that mean IOP reduction was 29% at week 1 and 36% at week 12. The mean reduction in IOP was statistically significant (p<0.001).

It was observed that mean reduction in IOP for bimatoprost was 1.57 mmHg more at week 1 as compared to timolol. This pattern was maintained till week 12 where the difference was 1.34 mmHg (*Fig. 3*).

Sherwood and Brandt conducted a 6 month comparison study of bimatoprost once daily and twice daily with timolol twice daily. At 6 months, the mean IOP reduction from baseline was 8.1 mmHg (33%) with bimatoprost o.d., 6.3 mmHg (26%) with bimatoprost b.d. and 5.6 mmHg (23%) with timolol (9). Higginbotham et al. in a 1-year double-masked clinical trial comparing the effect of bimatoprost 0.03% and timolol 0.5% in patients with POAG observed that mean IOP reduction ranged from 7.6 to 8.3 mmHg (30.2-32.9%) in bimatoprost group and from 5.1 to 5.8 mmHg (20.4-23.3%) in timolol group (10).

In the present study, mean reduction in heart rate in Group I patients was from 75.52 ± 4.51 per minute at baseline to 73.36 ± 4.34 per minute at week 12. In Group II patients, mean heart rate remained constant i.e. 74.4 ±

3.55 per minute at baseline to 74.48 ± 3.57 per minute at week 12. The changes in both the groups was statistically non-significant.

Higginbotham *et al.* (10) in his 12 months study found no clinically significant changes in the heart rate of 700 patients divided in two groups, one group receiving timolol 0.5% b.d. and other bimatoprost 0.03% o.d (10). Laibovitz et al. on comparing the effect of bimatoprost 0.03% with timolol 0.5% also found no clinically significant effect on heart rate between the two treatment regimens (11).

In the present study, relatively stable systolic and diastolic blood pressure was observed in both, Group I and Group II patients. There were minimal mean changes in blood pressure from baseline in both the groups. These changes were statistically non-significant.

Cohen *et al*. (8) and Witcup *et al.* (12) also observed minimal mean changes from baseline in systolic and diastolic blood pressure in both timolol and bimatoprost treatment groups throughout the study period.

In the present study, ocular burning / stinging sensation was found only in 12% and 4% in Group I and Group II patients, respectively. Conjunctival hyperemia was found in no patient in Group I and 36% patients in Group II. However, these adverse events did not necessitate discontinuation of the drugs.

Higginbotham *et al.*(10) observed conjunctival hyperemia in 44.7% patients in bimatoprost group compared to 13% patients in timolol group (10). Noecker *et al.* (13) and Konstas *et al.*(14) also reported a high incidence of conjunctival hyperemia of 44.4% and 34%, respectively in the bimatoprost treated patients

Conclusion

It was concluded that bimatoprost o.d. is statistically and clinically superior to timolol in lowering intraocular pressure and except for mild hyperemia the drug is safe and well tolerated in patients of primary open angle glaucoma.

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