Original Article

Primary Open Angle Glaucoma Pak Armed Forces Med J 2012; 62 (3): 409-12

COMPARISON OF PRESSURE LOWERING EFFECTS OF TIMOLOL/DORZOLAMIDE COMBINED PREPARATION VERSUS LATANOPROST IN PRIMARY OPEN ANGLE GLAUCOMA

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ABSTRACT

Objective: To compare the intraocular pressure (IOP) lowering effect of Timolol/Dorzolamide combined preparation to that of Latanoprost in eyes with primary open angle glaucoma.

Design: Randomized control trial (RCT).

Place and duration of study: The Eye department, Military Hospital, Rawalpindi, over six months, from 9th June 2008 to 8th December 2008.

Patients And Methods: Eighty Six patients included were divided into two equal groups. Initial IOP measurement was taken for every patient using Goldmann Applanation Tonometer with Fluorescein. Topical Antiglaucoma therapy was started in patients of either group. Group A patients were administered timolol/dorzolamide combined preparation where as latanoprost was administered to group B patients. Follow up IOP measurements were recorded at 4 week and 8 week interval for every patient and findings were endorsed on a pre-designed proforma. Data were analyzed using SPSS version 11.0.

Results: Eight week follow up IOP of Group A (14.51 ± 2.54) was significantly lower than the initial IOP (19.37± 2.49) (p<0.05). For Group B, difference between initial IOP (19.53 ± 2.69) and 8 week follow up IOP (14.09 ±2.23) was also statistically significant. The difference between mean IOP of the two groups at 4 week (p=0.284) and at 8 week (p=0.419) follow up was not statistically significant. Frequency of cases with ≥4 mm Hg drop at 4 week follow up was 26 (60.46%) in group A as against 29 (67.44%) in group B (p=0.50), whereas at 8 week follow up it was 31 (72.09%) for group A and 34 (79.07%) in group B (p=0.451).

Conclusion: The results suggest that latanoprost monotherapy and timolol/dorzolamide combined therapy is equally effective in controlling IOP in patients with POAG.

Keywords: Primary Open Angle Glaucoma, Timolol, Intraocular pressure.

INTRODUCTION

Primary open angle glaucoma (POAG) is an acquired condition, with onset typically after 40 years of age[1]. It affects both eyes but often asymmetrically. In early and even in moderate stages, the patient is usually asymptomatic. Abnormalities of the visual field occur insidiously and initially involve the midperiphery. In more advanced stages, the patient may become aware of an enlarging scotoma, particularly when it encroaches on fixation [2].

POAG is the most common subtype of glaucoma in the world[3]. It features acquired loss of optic nerve fibers and abnormality in the visual field with an open anterior chamber angle and raised IOP at some point in the course of disease[4,5]. POAG is a major worldwide health concern, because of its usually silent, progressive nature, and because it is one of the leading preventable causes of blindness in the world[6].

IOP is the only clinical risk factor that has been successfully manipulated to control the progression of the disease. Initially medical treatment is tried and if indicated surgical options are resorted to[7,8].

Currently there are five major classes of medications that are used to lower the IOP including beta adrenergic antagonists, alpha adrenergic agonists, parasympathomimetics, prostaglandin analogues, and carbonic anhydrase inhibitors[6,8]. Dorzolamide

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Received: 25 Mar 2011; Accepted: 18 Oct 2011

hydrochloride/timolol maleate ophthalmic solution is a combined preparation of a topical carbonic anhydrase inhibitor and a topical beta-adrenergic receptor blocking agent, each reducing IOP by a different mechanism[8]. Latanoprost is a prostaglandin F2α (PGF2α) analogue that is believed to reduce IOP by increasing the outflow of aqueous humour[9].

The purpose of this study was to compare the effect of timolol/dorzolamide combined preparation to that of latanoprost in lowering the intraocular pressure in patients with primary open angle glaucoma presenting at Eye Department, Military Hospital, Rawalpindi.

PATIENTS AND METHODS

This Randomized control trial as carried out at the Department of Ophthalmology Military Hospital Rawalpindi. From 9th June 2008 to 9th December 2008. Approval from hospital ethics committee was obtained. An informed consent was taken from all participants. The study included 86 patients divided into two equal groups by random number table.

GroupA:Patients on Timolol(0.5%)/Dorzo-lamide(2%) combined preparation administered B.D.

Group B: Patients on Latanoprost (0.005%) administered H.S.

Complete ocular examination, including visual acuity, refraction, slit lamp biomicroscopy, gonioscopy, IOP measurement and fundus examination with special attention to optic nerve head changes, was performed in all eyes. After initial assessment, patients from each group were started on their respective treatment. Confounding variables were controlled by excluding patients with glaucoma other than POAG. The patients were followed up in OPD at 4 and 8 week intervals. On each follow up visit IOP was measured and recorded on study proforma. Changes in IOP of at least 4 mm of Hg were considered significant.

Data were analyzed using SPSS version 11.0. Mean and standard deviation (SD) were calculated for age, height, weight and IOP at each visit. Frequencies and percentages were calculated for gender. Chi-square test was used to compare gender between groups. Paired't' test was used to compare mean IOP within each group. Independent't' test was used for comparison of quantitive variables between groups. p value < 0.05 was taken as significant.

RESULTS

There were 86 cases in the study; 43 each in both treatment groups A and B. There was no drop outs from because they were included after detailed work up and laboratory investigations as out patients. Mean age of the patients in group A was 54.16 ± 7.90 years and group B it was 55.65 ± 8.103 years. Majority of patients in both the groups were between 51-60 years of age (Fig.1) (p=0.645).

Gender distribution across both treatment groups was the same with the proportion of men slightly higher than the proportion of women (p= 0.829) (Fig.2). The mean initial IOP of group A was not significantly different from the mean initial IOP of group B (Table) 1.

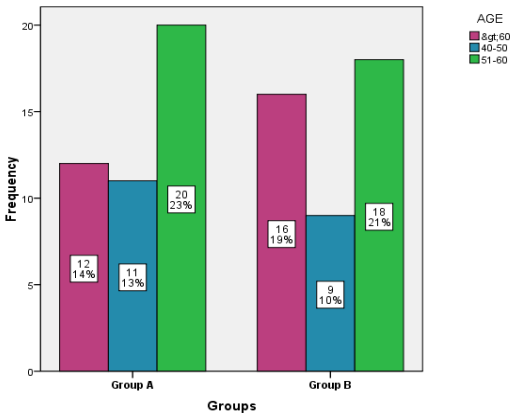

Fig 1: Description of age in both the groups

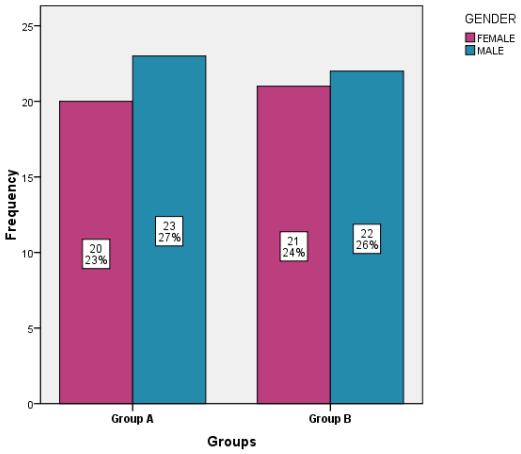

Fig. 2: Comparison of gender in both the groups

Comparison of changes in IOP in two groups at 4 and of weeks follow up are given in table 1 & 2.

Average IOP drop in group A was 4.86+2.47 mm of Hg while in group B it was 5.44+2.62 mm Hg. This difference was statisticially insignificiant (p=0.293) (Table-1).

Table 1: Comparison of IOP before and after treatment

IOP (mm Hg)	GROUP A (n=43)	GROUP B (n=43)	P value
Initial exam	**19.37± 2.49**	19.53 ± 2.69	0.772
4 wk follow up	15.37 ± 2.64	14.81 ±2.13	0.284
8 wk follow up	14.51 ± 2.54	14.09 ±2.23	0.419

(Values are given as mean ± SD)

Table-2: Comparison of frequency of IOP drop between group A and Group B

Drop in IOP	GROUP A (n=43)	GROUP B (n=43)	P value
At 4 wks			
≥ 4 mm Hg	26 (60.47%)	29 (67.44%)	0.500
< 4 mm Hg	17 (39.53%)	14 (32.56%)	
At 8 wks			
≥ 4 mm Hg	31 (72.09%)	34 (79.07%)	0.451
< 4 mm Hg	12 (27.90%)	9 (20.93%)	

DISCUSSION

The hypothesis for this study was that there is a significant decrease in IOP with the use of Timolol/Dorzolamide combined preparation as compared to Latanoprost alone in patients of primary open angle glaucoma. The results were contrary to this hypothesis and revealed that, the mean IOP level was slightly lower in latanoprost-treated patients as compared to patients on timolol-dorzolamide combined preparation. Compliance to Latanoprost was better than fixed-combination dorzolamide and timolol because of its once daily administration.

As POAG is a disease of old age, the diagnosis of POAG before the age of 40 years is unusual[10]. Studies have also been conducted in other countries of the region to evaluate the prevalence of POAG. A study from south India shows prevalence of 1.62% in individuals over the age of 40 years[11]. In a study conducted on 40 years-old or above population in China, the prevalence of POAG was 1.97% in rural men, 2.07% in urban men, 1.04% in rural women and 1.42% in urban women[12]. In an international study estimated prevalence for age 40-89 years in mainly white Caucasian people was 1.2%, rising from 0.2% for those in their 40s to 4.3% for those in their 80s[13]. Incidence rates have also been estimated from age-specific prevalence rates in the Framingham Study[14].

In a study conducted in India, male dominance was seen for POAG[15]. Our study did not reveal male predominance for POAG. The male to female ratio is approximately 1:1.

Review of the published literature shows that a lot of work has been done to compare the effects of topical Beta blockers, Carbonic anhydrase inhibitors and Prostaglandin analogues on IOP in patients of POAG. Sussana et al[16], in their study to compare the efficacy and tolerability of latanoprost with that of the fixed combination of dorzolamide and timolol over 8 weeks, found that the mean baseline diurnal IOP values were similar between the 2 groups[16]. Mean (SD) diurnal IOP reductions at week 8 before the water-drinking test were 6.9 (3.0) mm Hg for the latanoprost group and 6.4 (3.2) mm Hg for the dorzolamide/timolol group. Latanoprost was better tolerated than fixed-combination dorzolamide and timolol.

Two 3-month, parallel group, randomized, observer-masked and patient-masked, multicentre, clinical trials were performed in patients with ocular hypertension or open-angle glaucoma by COSOPT versus XALATAN Study Groups Glaucoma Division, New Jersey Medical School[17]. Study 1 (n=256) was conducted in the United States and Study 2 (n=288) was conducted in Europe/Israel. Both treatments were equally effective at lowering

IOP and were well tolerated over 3 months, although ocular stinging occurred more frequently with the dorzolamide/timolol combination. Tamer et al compared the 24-hour efficacy of dorzolamide and timolol maleate administered twice daily to POAG patients whose IOP could not be adequately controlled with latanoprost monotherapy. The successful reduction rates were 86% for the dorzolamide group and 61% for the timolol group. Both of the combinations were effective in lowering IOP, the exact amount and percentage of reduction was greater with the latanoprost+ dorzolamide regimen, especially at night-time[18].

One of the limitations of this study was the relatively short follow up period. Long term follow up was not possible in our setup because of frequent patient turnover. Another difference between published data and our work is that most of the previous studies were retrospective whereas this was a prospective study.

CONCLUSION

By the measures used in this study, the results suggest that a switch to latanoprost monotherapy is an alternative to combined treatment with timolol and dorzolamide in patients with primary open angle glaucoma. Both the drug significantly reduced IOP in comparison with baseline. The differences in mean IOP were not statistically significant when latanoprost was compared with timolol/dorzolamide. However further evaluation in larger groups of patients and over longer periods of time is required in our region.

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