Original Article

A comparative study of efficacy of 0.5% timolol maleate versus 1% brinzolamide in case of primary open angle glaucoma and ocular hypertension

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Abstract

Background: Glaucoma is the second largest cause of bilateral blindness in the world, after cataracts. In India, glaucoma accounts for 5.8% cases of blindness. Medical treatment is the first therapeutic approach for the treatment of glaucoma to lower raised IOP. Though the number of drugs have been used over years, an ideal agent has not yet been found. The present study was undertaken to compare the efficacy of 0.5% timolol maleate versus 1% brinzolamide in case of primary open angle glaucoma and ocular hypertension. **Material and Methods:** This was a prospective, randomized comparative study conducted on 50 patients of POAG or ocular hypertension. Patients were randomized into two equal groups as Group A and B. Group A received 0.5% timolol maleate and Group B received 1% brinzolamide. Patients were followed on day 0, week 4, week 8 and week 12for IOP measurements. **Results:** The baseline IOP readings taken at Day 0 were 24.63 ± 0.82 and 24.80 ± 1.06 for Group A and B respectively. When IOP readings were compared between the two groups, it was observed that across all visits during the 12 weeks treatment period IOP lowering produced with timolol maleate 0.5% was more as compared to brinzolamide 1%. **Discussion:** Treatment with timolol 0.5% was more effective in lowering the raised IOP than brinzolamide 1%.
Key Words: Glaucoma, lOP, Timolol, Brinzolamide, efficacy.

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INTRODUCTION

Glaucoma affects over 67 million people worldwide (1) and is the second largest cause of bilateral blindness in the world, after cataracts (2). According to National Survey on Blindness 2001- 2002, prevalence of blindness in India is 1.1%. In India, glaucoma accounts for 5.8% cases of blindness[2]. The most common form of glaucoma is primary open angle glaucoma (POAG). It is defined by three criteria which are, an IOP consistently above 21 mmHg in at least on eye, an open, normal appearing anterior chamber angle with no apparent ocular or systemic abnormality that might account for elevated IOP, and typical glaucomatous visual field and/or optic nerve head damage. Ocular hypertension is defined as an intraocular pressure consistently above 21 mmHg in the absence of the other two criteria[3]. Elevated IOP, increasing age, family history and thin central corneal thickness are the major risk factors for the development of glaucomatous optic nerve damage. However, IOP remains the only risk factor readily amenable to therapy. Therefore, almost all currently used strategies for the treatment of glaucoma are aimed at lowering or preventing a rise in IOP. Medical treatment is the first therapeutic approach while surgery is reserved for cases that cannot be controlled by drugs[4]. Currently, there are five major classes of drugs used for the treatment of glaucoma which are cholinergic agonists, alpha adrenergic- receptor agonist, beta adrenergic- receptor antagonists, topical and systemic carbonic anhydrase inhibitors and hypotensive lipids i.e. prostaglandin analogues and prostamides[5]. Timolol maleate, whichbinds

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to beta-adrenergic receptors non selectively, is a potent antagonist of the catecholamine-stimulated synthesis of cyclic AMP. It reduces IOP by decreasing aqueous humor formation without changing the outflow pathway. Timolol enters the eye rapidly; following topical administration, IOP begins to fall in 30–60 minutes, becomes lowest in 2 hours, and then in 24-48 hours, returns to normal[6]. Brinzolamide is a carbonic anhydrase inhibitor indicated in patients with ocular hypertension or open- angle glaucoma for the treatment of elevated intraocular pressure. It is a highly specific, reversible, non-competitive and potent inhibitor of carbonic anhydrase II (CA-II)[9], because of which it is able to suppress formation of aqueous humour and thus decrease IOP. Following topical administration, brinzolamide is absorbed into the systemic circulation where due to its affinity for CA-II, brinzolamide distributes extensively into the RBCs and exhibits a long half-life of approximately 111 days[7]. Though the number of available drugs has increased significantly during the last 10 years, an ideal agent has not yet been found. The present study was undertaken to compare the efficacy of 0.5% timolol maleate versus 1% brinzolamide in case of primary open angle glaucoma and ocular hypertension.

MATERIAL AND METHODS

This was a prospective, randomized comparative study conducted on 140 patients of POAG or ocular hypertension attending the Outpatient Department of Ophthalmology at a tertiary care hospital. The patients fulfilling the inclusion criteria were enrolled in the study after obtaining written informed consent. Institutional ethical committee permission was obtained. Patients of a minimum age of 18 years, having unilateral/bilateral primary open angle glaucoma/ ocular hypertension with an IOP > 21 mm Hg and </= 30 mm Hg were included in the study. Patients with history of acute angle closure glaucoma, secondary glaucoma, closed anterior chamber angle, ocular infection or inflammation, known sensitivity or contraindication to use of drug, pregnant and lactating femalesand patients unable to attend follow up were excluded from the study. Patients requiring treatment for bilateral POAG were treated for both eyes but the right eye was the study eye. After inclusion in the study, the first patient was divided into group A and group B by lottery methodand the subsequent patients were consecutively placed in the respective groups. Group A received a drop of timolol 0.5%twice daily and B received a drop of brinzolamide 1% twice daily for 12 weeks. During the study, patients visited the hospital on day 0, week 4, week 8 and week 12. IOP readings were taken from the study eye with the Goldmann applanation tonometer at each visit. IOP was measured on day 0 before administration of the study drugs to get the baseline IOP and then on each follow-up visit to record the peak and trough of each medication.

RESULTS

A total of 140 (70 in each group) patients were included in the study. In Group A, mean age was 52 years with standard deviation ±11.34 whereas in Group B, mean age was 56 years with standard deviation ±12.26. In Group A 42 (%) patients were male and 28 (%) patients were female, whereas, in Group B 38(%) patients were male and 32 (%) patients were female. The two groups were comparable and no statistically significant differences regarding all the parameters of patient profile observed.

Table 1: Mean IOP in Group A and Group B at Different Points of Time

	Group A (Timolol maleate 0.5%)	Group B (Brinzolamide 1%)
Visit	Mean±SD (mmHg)	Mean±SD (mmHg)
Day 0	24.63 ± 0.82	24.80 ± 1.06
Week 4	18.69 ± 1.12	19.48 ± 1.14
Week 8	18.71 ± 1.16	19.56 ± 1.12
Week 12	18.82 ± 1.04	19.63 ± 1.02

In present study, the baseline IOP readings taken at Day 0 were 24.63 ± 0.82 and 24.80 ± 1.06 for Group A and B respectively. At all follow up visits it was observed that timolol maleate 0.5% showed a consistent reduction in IOP when compared to baseline values, including both peak and trough readings. All the values were extremely significant when compared with baseline readings. Maximum fall in IOP was observed at the first follow-up visit at 4 weeks followed by a slight rise in readings at the final visit. Thus, at the end of 12 weeks IOP reduction with timolol maleate was 18.89% for peak and 23.47% for trough readings (Table 1). Brinzolamide 1% also demonstrated a constant lowering of IOP values compared with the baseline. All the readings being extremely significant compared to the baseline. Treatment with brinzolamide also produced maximum IOP lowering at 4 weeks followed by slight raise seen at 12 weeks. Final readings taken at 12 weeks showed IOP lowering of 20.14% for peak and 20.26% for trough readings (Table 1). When IOP readings were compared between the two groups, it was observed that across all visits during the 12 weeks treatment period IOP lowering produced with timolol maleate 0.5% was more as compared to brinzolamide 1%. At the end of the study period, IOP lowering with timolol 0.5% was significantly more than brinzolamide 1% for both peak readings (p=0.0045) and for trough readings (p=0.003). Thus there was a statistically significant (p value < 0.05) difference between the IOP reduction with timolol maleate 0.5% and

brinzolamide 1%.

DISCUSSION

In recent years, many new medications have become available for glaucoma that have permitted less frequent dosing, fewer local and systemic side-effects and superior IOP control. The advent of these new medicationsmight have reduced the need forglaucoma surgery inmany patients. Reduction of IOP to the normal range significantly reduces the risk of damage to the nerve fibres for the individual and consequent visual loss. It may even prevent further damage[4]. Medications lower IOP either by reducing the production or by increasing outflow of aqueous humour. There is a scarcity of studies comparing brinzolamide with timolol maleate as monotherapy in cases of POAG and ocular hypertension especially in the Indian population. Our study aimed to compare the efficacy of these two drugs in such a population as monotherapy. The efficacy of brinzolamide 0.3%–3% BD has been evaluated in several clinical trials[8-13]. When diurnal IOP was measured, brinzolamide 1% or 3% reduced IOP significantly better than brinzolamide 0.3%[9]. At the end of our study, brinzolamide 1% showed reduction in IOP of 4.90 mmHg (20.14%) for peak and 4.84 mmHg (20.26%) for trough readings. Wang *et al* concluded that a significant decrease in mean IOP was found after 6 weeks of treatment in both the brinzolamide group (- 17.0%) and the timolol group (- 19.7%), with no significant between-group difference in the control of IOP. When used twice a day, topical brinzolamide is as effective as 0.5% timolol in lowering IOP in patients with open angle glaucoma[13]. In our study, we also observed significant IOP lowering with both timolol 0.5% and brinzolamide 1% at each visit, but the IOP lowering with timolol 0.5% was significantly more than that produced with brinzolamide 1%. In a meta-analysis study of randomized clinical trials of intraocular pressure– lowering effects of all commonly used glaucoma drugs, IOP reduction with timolol 0.5% [peak, 27% (29% to 25%), and trough, 26% (28% to 25%)] was more than that with brinzolamide 1% [peak, 17% (19% to 15%), and trough, 17% (19% to 15%)]. Thus the findings of their meta-analysis are in concordance with the results observed at the end of our present study[14]. In our study, comparison between the two groups showed that across all visits during the 12 week treatment period IOP lowering produced with timolol maleate 0.5% was more as compared to brinzolamide 1%. There was a statistically significant (p value < 0.05) difference between the IOP reduction with timolol maleate 0.5% and brinzolamide 1%. Thus, in our study we concluded that treatment with timolol 0.5% was more effective than brinzolamide 1%.

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