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Original Research Article

A Randomized Comparative Study to Assess the Intraocular Pressure Lowering Efficacy of 0.5% Timolol Maleate Versus 1% Brinzolamide in Cases of Primary Open Angle Glaucoma and Ocular Hypertension

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Abstract

Aim: The aim of this study to study the intraocular pressure lowering efficacy of 0.5% timolol maleate versus 1% brinzolamide in cases of primary open angle glaucoma and ocular hypertension.

Material and methods: Patients selected were randomised into two groups of 50 each. Group I and Group II instilled 1 drop of timolol 0.5% and brinzolamide 1% respectively, into study eye twice daily at 8.00 a.m. and 8.00 p.m. 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 at 8.00 a.m. and 10.00 am before administration of the study drugs to get the baseline IOP and then on each follow-up visit at 8.00 a.m. and 10.00 a.m. to record the peak and trough of each medication.

Results: Comparison between the two groups showed that across all time points and visits during the 12 week 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 ($p = 0.004$). Thus there was a statistically significant (p value < 0.05) difference between the IOP reduction with timolol maleate 0.5% and brinzolamide 1%.

Conclusion: We concluded that treatment with timolol 0.5% was more effective than brinzolamide 1%.

Keywords: 1% brinzolamide, 0.5% timolol maleate , intraocular pressure

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, which binds 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), 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 extensiv-ely. Into the RBCs and exhibits a long half-life of approximately 111days. [7] Though the number of available drugs has increased significantly during the last 10 years, an ideal agent has not yet been found.

Material and methods

This prospective observational study was carried out in the Department of Ophthalmology, N.M.C.H, Patna, Bihar, India for 1 year.

In this prospective, open, randomized, parallel group, comparative study, 100 patients of POAG or ocular hypertension attending the Outpatient Department of Ophthalmology, were included.

Inclusion criteria

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.

Exclusion criteria

Patients were history of acute angle closure glaucoma, established diagnosis of secondary glaucoma, closed anterior chamber angle, ocular inflammation, ocular infection, pregnant and lactating females, patient unable to attend follow up, known sensitivity to drug, chronic use of ocular medication other than the glaucoma medications and patients having any contraindication to the use of beta blockers and carbonic anhydrase inhibitors.

Methodology

Patients who were already on any other anti-glaucoma treatment were taken up for

study after a washout period of 7 days for miotics and carbonic anhydrase inhibitors, 14 days for alpha- and beta-adrenergic agonists and 21 days for beta blockers, prostaglandin analogues and combination drugs. Patients requiring treatment for bilateral POAG were treated for both eyes but the right eye was the study eye. Patients selected were randomised into two groups of 50 each. Group I and Group II instilled 1 drop of timolol 0.5% and brinzolamide 1% respectively, into study eye twice daily at 8.00 a.m. and 8.00 p.m. 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 at 8.00 a.m. and 10.00 am before administration of the study drugs to get the baseline IOP and then on each follow-up visit at 8.00 a.m. and 10.00 a.m. to record the peak and trough of each medication.

Results

There were no statistically significant differences between the two groups regarding all the parameters of patient profile. In the 100 patients included in the study the mean age was 61.77 years. Mean age in group I was 58.2 years and in group II was 65.3 years. Overall in the study 59% of the patients were male and 41% were female.

In our study, timolol maleate 0.5% showed a consistent reduction in IOP when compared to baseline values at all follow-up visits, including both peak and trough readings, taken at 4 weeks (6.97 mmHg and 6.73 mmHg), 8 weeks (6.80 mmHg and 6.77 mmHg) and 12 weeks (6.77 mmHg and 6.70 mmHg). 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 24% for peak and 24% for trough readings IOP values compared with the baseline with brinzolamide 1% also demonstrated a constant lowering at the end of 4 weeks (6.03 mmHg and 5.97 mmHg), 8 weeks (5.90 mmHg and 5.94 mmHg) and 12 weeks (5.90 mmHg and 5.84 mmHg) with all 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% for peak and 18% for trough readings.

Comparison between the two groups showed that across all time points and visits during the 12 week 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 ($p = 0.004$). Thus there was a statistically significant (p value < 0.05) difference between the IOP reduction with timolol maleate 0.5% and brinzolamide 1%.

Table-1: Sex Distribution of Patients in Group I and Group II

	Group I		**Group II**	
	Timolol Maleate 0.5%		**Brinzolamide 1%**	
Gender	**No. of Patients**	**%age**	**No. of Patients**	**%age**
Female	23	46%	18	36%
Male	27	54%	32	64%
Total	50	100%	50	100%

Table-2: Mean IOP in Group I and Group II at Different Points of Time

	GROUP I (TIMOLOL MALEATE 0.5%)		GROUP II (BRINZOLAMIDE 1%)	
Visit	At 8:00 am Mean±SD (mmHg)	At 10:00 am Mean±SD (mmHg)	At 8:00 am Mean±SD (mmHg)	At 10:00 am Mean±SD (mmHg)
Day 0	25.50 ± 1.18	25.30 ± 0.89	25.57 ± 0.87	25.33 ± 0.86
Week 4	19.77 ± 1.27	19.33 ± 1.26	20.60 ± 0.83	20.30 ± 1.16
Week 8	19.73 ± 1.18	19.50 ± 1.29	20.63 ± 0.89	20.43 ± 0.87
Week 12	19.80 ± 1.32	19.53 ± 1.32	20.73 ± 1.21	20.43 ± 1.24

Discussion

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.[8][10] Medicat-ions lower IOP either by reducing the production or by increasing outflow of aqueous humour. There are very few 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 randomized double-blind, multicentre comparative clinical trials.[9-17] A dose-response study comparing brinzolamide in concentrations of 0.3%, 1%, 2%, and 3% demonstrated mean IOP reductions of 3 mmHg (11.3%), 4.3 mmHg (16.1%), 4.4 mmHg (16.1%), and 4.2 mmHg (15.4%), respectively. When diurnal IOP was measured, brinzolamide 1% or 3% reduced IOP significantly better than brinzolamide 0.3%.[11] At the end of our study, brinzolamide 1% showed reduction in IOP of 5.90 mmHg (20%) for peak and 5.84 mmHg (18%) for trough readings.

In their study Wang et al. [17] (2004) 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. 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% across all time points.

Van der Valk et al.[18] (2005) in their meta-analysis of randomized clinical trials of intraocular pressure– lowering effects of all commonly used glaucoma drugs, ranked IOP reduction with timolol 0.5% [peak, 27% (29% to 25%), and trough, 26% (28% to 25%)] 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.[19]

In the present study, IOP reduction with timolol maleate 0.5% and brinzolamide 1% was 6.77 mmHg (24%) and 5.90 mmHg (20%), respectively at peak readings; and 6.70 mmHg (24%) and 5.94 mmHg (18%), respectively for trough readings. Comparison between the two

groups showed that across all time points and 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%.

Conclusion

We concluded that treatment with timolol 0.5% was more effective than brinzolamide 1%.

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