Journal homepage: www.ijcbr.com

INTERNATIONAL JOURNAL OF CLINICAL AND BIOMEDICAL RESEARCH

Research article

A COMPARATIVE STUDY OF DORZOLAMIDE+TIMOLOL VS. BRIMONIDINE+TIMOLOL FIXED COMBINATION THERAPY IN THE MANAGEMENT OF PRIMARY OPEN ANGLE GLAUCOMA

Dr. PRATIK RAMNIKLAL SAVALIA

AUTHOR DETAILS

Received: 12th Aug 2016
Revised: 9th Sep 2016
Accepted: 31st Dec 2016

Author details:
Third year Resident Doctor, M & J Institute of Ophthalmology, Civil Hospital, Ahmedabad, Gujarat.
Corresponding author:
Dr. Pratik Ramniklal Savalia
Third year Resident Doctor, M & J Institute of Ophthalmology, Civil Hospital, Ahmedabad, Gujarat.
Email: pratiksvl2@gmail.com

ABSTRACT

Background: To compare the efficiency of dorzolamide + timolol fixed combination vs. the Brimonidine + timolol fixed combination in the management of primary open-angle glaucoma **Materials and methods**: A prospective study conducted over a period of 6 months with a total of 69 patients having primary open angle glaucoma (POAG) who completed a follow up of 6 months at a tertiary care hospital. Detailed history of the patient was obtained and patients were assessed for best corrected visual acuity, base line IOP with Goldmann applanation tonometer and detailed anterior and posterior segment examination. They were categorized into two groups according to the combinations prescribed by the ophthalmologist as follow: group 1-dorzolamide+timolol and group 2-brimonidine+timolol. A follow up evaluation of each patient was done at 1, 3 and 6 months after baseline visit. **Results:** During our study the baseline IOP for dorzolamide + timolol group was 25.7 ±4.25 mm Hg and for brimonidine + timolol group was 26.3 ±5.86 mm Hg. During 6 months treatment, the mean reduction in IOP was 7.83 mm Hg (29.4%) in dorzolamide + timolol group and 9.39 mm Hg (35.6%) in brimonidine + timolol group. **Conclusion:** Our study showed that brimonidine + timolol combination has superiority over dorzolamide + timolol to reduce the IOP in newly diagnosed patients with POAG The value of IOP reduction in our study in brimonidine + timolol group was 9.39 mm Hg (35.6%) and 7.83 mm Hg (29.4%) in dorzolamide + timolol group.

KEYWORDS: Primary open angle glaucoma, brimonidine, timolol, dorzolamide

INTRODUCTION

Glaucoma is a group of disorders characterized by progressive optic neuropathy resulting in characteristic appearance of optic disc and specific pattern of visual field defects that are associated frequently but not invariably with raised intra ocular pressure (IOP). Glaucoma affects as many as 67 million people worldwide and is a leading cause of vision loss and blindness[1]. Normal IOP ranges between 10-20 mm Hg. The aetiology of glaucoma is multi factorial, but, to date, reduction of intraocular pressure (IOP) is the only evidence-based therapy for glaucoma.

POAG (primary open angle glaucoma) results due to decrease in the aqueous outflow facility due to increased resistance to aqueous outflow as a result of thickening and sclerosis of trabecular meshwork, narrowing of inter trabecular spaces and deposition of amorphous material in juxtra canalicular space[2]. It is characterized by slowly progressive raised intraocular pressure (IOP), open appearing anterior chamber angle, characteristic optic disc cupping and specific visual field defects [3].

IOP reduction is achieved by the use of topical medications. Fixed combinations of IOP-lowering medications have been developed by combining different pharmacologic classes of ocular hypotensive drugs commonly prescribed for the treatment of elevated IOP in patients affected by open-angle glaucoma or ocular hypertension[4,5]. Modern fixed combinations pair beta-adrenoceptor antagonists (beta-blocker) with either prostaglandin analogues or carbonic anhydrase inhibitors or alpha adrenergic agonists[6]. Potential benefits of fixed combinations include better compliance, reduction in exposure to preservatives, and elimination of the washout effect.

Vision lost as a result of glaucoma cannot be recovered. The goal of treatment therefore is to prevent further optic nerve and visual field damage by adequately lowering the IOP. An approach to the treatment of primary open angle glaucoma is outlined below:

Counsel the patient: on the nature and natural history of disease, drug compliance and probability of life time treatment.

Define target IOP: usually at least 20% reduction from the baseline IOP; target IOP should be lower if there is advanced damage or if the disease continues to progress[7].

Aim: To compare the efficiency of dorzolamide + timolol fixed combination vs. the brimonidine + timolol fixed combination in the management of primary open-angle glaucoma.

MATERIALS & METHODS

Study design: A prospective analytical study

Ethical approval: The study was approved by the IRB and patients fulfilling the selection criteria were enrolled and written informed consent was taken.

Sample size: A total of 69 patients with POAG completed a follow up of 6 months at a tertiary care hospital.

Inclusion criteria: The population comprised of men and women above the age of 15 years. It included patients diagnosed as having glaucoma and on anti-glaucoma medications.

Exclusion criteria: Those with a history of ocular inflammation or infection within last 3 months of baseline, known to be sensitive to vehicle or drug, pregnant or lactating women psychiatric patients, patients younger than 15 years and those who refused to participate were excluded from the study.

Grouping: They were categorized into two groups according to the combinations prescribed by the ophthalmologist as follow: group 1: Dorzolamide + timolol (n=35) and Group 2: Brimonidine + timolol (n=34).

Drug administration: Eye drops twice a day.

Methodology: Detailed history of the patient was obtained and recorded in a pre-tested Case Record Form along with findings from general examination, laboratory investigations, if any, and treatment given. All patients were assessed for best corrected visual acuity, base line IOP with Goldmann applanation tonometry, angle grading with gonioscopy, detailed anterior and posterior segment examination.

A follow up evaluation of each patient was done at 1, 3 and 6 months after baseline visit. At each subsequent visit, IOP measurement and direct ophthalmoscopy was repeated. Efficacy was assessed by the degree of reduction in intraocular pressure and change in cup disc ratio. Additionally, the patients were asked for adverse drug reactions (ADRs), if any, and the details were noted in an ADR reporting form[8-10].

Statistical analysis: Analyses were performed for both the groups of group 1 & group 2 [11,12]. Analysis of variance (ANOVA) was used to test between-group differences in mean IOP at baseline and analysis of covariance (ANCOVA) with baseline IOP as the covariate was used to test between group-differences in mean IOP at follow-up visits. Results were qualitatively similar when ANOVA rather than ANCOVA was used for these analyses. Other continuous variables were analyzed using t-tests. Categorical variables were analyzed using the chi-square test. All statistical tests were two-tailed with the level for significance set at 0.05.

RESULTS

Out of 69 patients 30 were male and 39 were female and mean age was 60 years.

Table 1. **Showing gender wise distribution of the patients.**

Gender	**No. of Patients**
Male	30
Female	39
Total	69

The IOP was noted at day 0 and 1, 3 and 6 months. The difference in IOP reduction in two treatment groups from baseline to 6 months was the main outcome measure.

During our study the baseline IOP for dorzolamide + timolol group was 25.7 ±4.25 mm Hg and for brimonidine + timolol group was 26.3 ±5.86 mm Hg.

During 6 months treatment the mean reduction in IOP was 7.83 mm Hg (29.4%) in dorzolamide + timolol group and 9.39 mm Hg (35.6%) in brimonidine + timolol group.

The post treatment IOP was 17.87 ±4.25 mm Hg in dorzolamide + timolol group and 16.91 ±5.86 mm Hg in brimonidine + timolol group.

Table 2. Responder analysis in IOP (mm Hg) reduction during 6 months treatment.

Group	Baseline IOP	**IOP (mm Hg) change during 6 months follow up**		
		1month	3 months	6 months
Group 1	25.7±4.3	23.0±3.6	20.2±3.7	17.9 ±4.4
Group 2	26.3 ±5.9	21.3±4.6	18.8±4.6	16.9±5.9

Table 3. Adverse effects during 6 months treatment.

Gender	**No. of Patients**	**Side effects**
Male	3	Conjunctival congestion
Female	3	Itching
Total	6	

DISCUSSION

This study was designed to compare the efficacy, safety, and ocular tolerability of brimonidine-timolol with dorzolamide-timolol.

The fixed combination of Brimonidine tartrate 0.2% and timolol maleate 0.5% combines a highly selective alpha 2 adrenergic agonist (Brimonidine) with a nonselective beta blocker (timolol)[13].The fixed combination of Dorzolamide 2% and timolol maleate 0.5% combines a carbonic anhydrase inhibitor dorzolamide) with a nonselective beta blocker (timolol). They act by reducing aqueous production and enhancing uveo scleral outflow.

Our study showed that brimonidine + timolol combination has superiority over dorzolamide + timolol to reduce the IOP in newly diagnosed patients with POAG.

The value of IOP reduction in our study in brimonidine + timolol group was 9.39 mm Hg (35.6%) and 7.83 mm Hg (29.4%) in dorzolamide + timolol group. This showed that brimonidine + timolol combination is more efficacious in reducing the IOP than dorzolamide + timolol combination.

Numerous clinical trials have demonstrated the importance of IOP lowering in minimizing glaucomatous progressions. Most recently, the Canadian Glaucoma Study demonstrated that every 1mm Hg rise in IOP was associated with a 19% increase in the risk of progression. Therefore, the primary consideration in selecting a medical regimen in glaucoma and OHT remains achieving maximum IOP lowering to a target IOP[7]. For patients who need additional IOP lowering, the number of additional medication ideally should be limited as the addition of a third or fourth IOP-lowering agent to a medication regimen is often unsuccessful for reasons of efficacy, safety or compliance. In patients on antiglaucoma therapy requiring further IOP reduction, the addition of a fixed-combination therapy may provide significant IOP lowering while adding only one bottle and two drops to the patient's daily regimen [6]. In this study, both the brimonidine-timolol fixed combination and the dorzolamide-timolol fixed combination provided substantial IOP lowering (29.3% with brimonidine-timolol and 23.5% with dorzolamide-timolol).

CONCLUSION

Both brimonidine-timolol and dorzolamide-timolol effectively lowered IOP in patients with glaucoma or OHT. Better IOP reduction and overall ocular comfort was reported in those patients on the brimonidine-timolol combination.

REFERENCES

1. Resnikoff S, Pascolini D, Etya'ale D, Kocur I, Pararajasegaram R, Pokharel GP, et al. Global data on visual impairment in the year 2002. Bull World Health Organ. 2004;82:844–51.
2. Allingham, R.R., Shields, B.M. & Freedman, S. (2005) Shield textbook of glaucoma.5th edition.
3. Kanski JJ. Glaucoma, Clinical Ophthalmology a systemic approach, 6th edition. Butterworth & Heinmann Elsevier Saunders publisher, 2007; 372-439.
4. Fechtner RD, Realini T. Fixed combinations of topical glaucoma medications. Curr Ophthamol 2004; 15:132-5
5. Khouri AS, realini T, Fechtner RD. Use of fixed –dose combination drugs for the treatment of glaucoma. Drugs Aging 2007; 24:2007-16.
6. Lesk-MR, Koulis T, Sampalis f. Effectiveness and safety of dorzolamide+timolol alone or combined with latanoprost in open angle glaucoma or ocular hypertension. Ann Pharmac other 2008; 42:498-504
7. Jampel HD, target pressure in glaucoma therapy. J Glaucoma 1997;6:133-8.
8. Sall KN, Greff IJ, Johnson-Pratt LR. Dorzolamide/timolol combination versus concomitant administration of brimonidine and timolol: six month comparison of efficacy and tolerability. Ophthalmology 2003;110:615-24.
9. Solish AM, DeLucca PT, Cassel DA. Dorzolamide/timolol fixed versus concomitant administration of brimonidine and timolol in patients with elevated intraocular pressure: a 3-months comparison of efficacy, tolerability and patient-reported measures. J Glaucoma 2004;13:149-57.
10. Chan K, Testa M, McCluskey P. Ocular comfort of combination glaucoma therapies: brimonidine 0.2% timolol 0.5% compared with dorzolamide 2% timolol o.5% J Ocul Pharmacel then 2007;23:372-6.
11. Arcieri ES, Arcieri RS, Periera AC. Comparing the fixed combination brimonidine-timolol versus fixed combination dorzolamide-timolol in patients with elevated intraocular pressure. Curr Med Res Opin 2007;23:683-9.
12. KatzLJ, Simmous ST, Craven ER. Efficacy and safety of brimonidine and dorzolamide for intraocular pressure lowering in glaucoma and ocular hypertension. Curr Med Res Opin 2007, 23.2971-83.
13. Crichton ACS. Timolol/ brimonidine combination therapy in glaucoma management. Clin Surg J Ophthalmol 2005; 23:356-9.