Journal of Advanced Medical and Dental Sciences Research

@Societv of Scientific Research and Studies

Journal home page:www.jamdsr.com doi:10.21276/jamdsr Index Copernicus value [ICV] =82.06

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Original Research

Comparison of efficacy of Dorzolamide 2 percent timolol 0.5 percent fixed combination versus brinzolamide 1 percent brimonidine 0.2 percent fixed combination therapy in patients of primary open angle glaucoma

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ABSTRACT:

Background: Glaucoma is a chronic and progressive optic neuropathy that can be differentiated from other types of acquired optic neuropathies by the distinctive morphology of the optic nerve. Hence; the present study was conducted for comparing the efficacy of Dorzolamide 2 percent timolol 0.5 percent fixed combination versus brinzolamide 1 percent brimonidine 0.2 percent fixed combination therapy in patients of primary open angle glaucoma (POAG). **Materials & methods:** A total of 50 patients of POAG were enrolled. Complete demographic and clinical details of all the patients was obtained. Patients selected were then be randomised into two groups of 25 each. Baseline IOP was recorded at morning time. Fixed drug combination of Dorzolamide2%/ Timolol 0.5% (DTFC) dosed twice daily in morning time and in evening time after twelve hours among patients of group 1.Fixed drug combination of Brinzolamide 1%/ Brimonidine 0.2% (BBFC) dosed twice daily in morning time and in evening time after twelve hours among patients of group 2. Patients was then be called for follow up at 2ndweek, 4thweek and 6thweek during the study period and IOP was recorded. All the results were analyzed by SPSS software. **Results:** Mean age of the patients of group 1 and group 2 was 41.5 years and 42.9 years. Majority proportion of patients of both the study groups were males. Among patients of group 1, mean IOP at baseline, 2nd week follow-up, 4th week follow-up and 6th week follow-up was 28.3 mm of Hg, 17.3 mm of Hg, 16.9 mm of Hg and 15.9 mm of Hg respectively. Among patients of group 2, mean IOP at baseline, 2nd week follow-up, 4th week follow-up and 6th week follow-up was 27.9 mm of Hg, 16.5 mm of Hg, 16.1 mm of Hg and 16.9 mm of Hg respectively. Non-significant results were obtained while comparing mean IOP among the two study groups at different time intervals. Also while comparing the incidence of adverse events among the two study groups, non-significant results were obtained. **Conclusion:** Increased intraocular pressure (IOP) is a significant risk factor for primary open-angle glaucoma; the principal therapeutic strategy to mitigate the progression of glaucoma and ocular hypertension involves the reduction of IOP. Both the drugs were equally effective in managing patients with POAG.

Key words: Dorzolamide, Brinzolamide, Glaucoma

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This article may be cited as: Bang R. Comparison of efficacy of Dorzolamide 2 percent timolol 0.5 percent fixed combination versus brinzolamide 1 percent brimonidine 0.2 percent fixed combination therapy in patients of primary open angle glaucoma. J Adv Med Dent Scie Res 2016;4(2):300-303.

INTRODUCTION

Glaucoma is a chronic and progressive optic neuropathy that can be differentiated from other types of acquired optic neuropathies by the distinctive morphology of the optic nerve. In cases of glaucoma, the neuroretinal rim of the optic nerve experiences a gradual thinning, leading to an increase in the size of the optic nerve cup, a process known as optic nerve cupping. This condition arises from the degeneration of retinal ganglion cell axons, along with the associated glial cells and vascular structures.[1, 2] Notably, the remaining neuroretinal rim maintains its typical pink hue. In contrast, other forms of optic neuropathy are characterized by a loss of this pink coloration and do not exhibit cupping, with the exception of arteritic anterior ischemic optic neuropathy, where cupping may also be present. Patients suffering from glaucoma often experience a decline in peripheral vision, which can progress to complete vision loss if left untreated. While glaucoma can occur in the absence of elevated intraocular pressure, it is typically categorized based on variations in the anterior segment that may lead to increased intraocular pressure. The anterior segment of the eye possesses its own circulatory system, which provides nourishment to the crystalline lens and

cornea, both of which are avascular. The ciliary body produces aqueous humor, which circulates within the anterior chamber and is drained through the trabecular meshwork located at the iridocorneal angle, the junction between the iris and cornea. Elevated intraocular pressure is primarily attributed to a decrease in aqueous humor outflow rather than an increase in its production.[3, 4]Fixed-combination therapies for glaucoma facilitate the administration of multiple mechanisms of action through a single topical formulation, thereby enhancing intraocular pressure (IOP) reduction without complicating the treatment regimen or heightening the risk of drug washout. The combination of brinzolamide 1% and timolol 0.5% integrates a carbonic anhydrase inhibitor (CAI) with a β-blocker, demonstrating an IOP-lowering effectiveness that surpasses that of the individual monotherapies.[5- 7]Hence; the present study was conducted for comparing the efficacy of Dorzolamide 2 percent timolol 0.5 percent fixed combination versus brinzolamide 1 percent brimonidine 0.2 percent fixed combination therapy in patients of primary open angle glaucoma.

MATERIALS & METHODS

The present study was conducted for comparing the efficacy of Dorzolamide 2 percent timolol 0.5 percent fixed combination versus brinzolamide 1 percent brimonidine 0.2 percent fixed combination therapy in patients of primary open angle glaucoma. A total of 50 patients of POAG were enrolled. Complete demographic and clinical details of all the patients was obtained. Patients selected were then be randomised into two groups of 25 each. Baseline IOP was recorded at morning time. Fixed drug combination of Dorzolamide2%/ Timolol 0.5% (DTFC) dosed twice daily in morning time and in evening time after twelve hours among patients of group 1.Fixed drug combination of Brinzolamide 1%/ Brimonidine 0.2% (BBFC) dosed twice daily in morning time and in evening time after twelve hours among patients of group 2. Patients was then be called for follow up at 2ndweek, 4thweek and 6thweek during the study period and IOP was recorded. All the results were analyzed by SPSS software. Chi- square test and Mann-Whitney U test were used for assessment of level of significance.

RESULTS

Mean age of the patients of group 1 and group 2 was 41.5 years and 42.9 years. Majority proportion of patients of both the study groups were males. Among patients of group 1, mean IOP at baseline, 2nd week follow-up, 4th week follow-up and 6th week follow-up was 28.3 mm of Hg, 17.3 mm of Hg, 16.9 mm of Hg and 15.9 mm of Hg respectively. Among patients of group 2, mean IOP at baseline, 2nd week follow-up, 4th week follow-up and 6th week follow-up was 27.9 mm of Hg, 16.5 mm of Hg, 16.1 mm of Hg and 16.9 mm of Hg respectively. Non-significant results were obtained while comparing mean IOP among the two study groups at different time intervals. Also while comparing the incidence of adverse events among the two study groups, non-significant results were obtained.

Table 1: Comparison of Mean IOP of Both Groups

Visit	Groups	N	Mean	SD	p value
Baseline	Group 1	25	28.3	1.82	0.711
	Group 2	25	27.9	1.32	
2nd week	Group 1	25	17.3	1.45	0.125
	Group 2	25	16.5	1.65	
4th week	Group 1	25	16.9	1.78	0.663
	Group 2	25	16.1	1.61	
6th week	Group 1	25	15.9	1.28	0.258
	Group 2	25	16.9	1.63	

Table 2: Adverse effects

Adverse effects	Group 1		Group 2	
	Number	Percentage	Number	Percentage
Conjunctival Hyperemia	5	20	2	8
Eye Irritation	1	4	2	8
Taste Perversion	2	8	2	8

DISCUSSION

Primary open-angle glaucoma is a progressive optic neuropathy and is arguably the most prevalent type of glaucoma. Given that the condition is manageable and the visual deficits resulting from glaucoma are permanent, early identification is crucial. The timely diagnosis relies on the assessment of the optic disc, the retinal nerve fiber layer, and the visual field. Advances in imaging techniques and psychophysical assessments can enhance both the detection and monitoring of disease progression. Recent long-term clinical trials have provided compelling evidence that reducing intraocular pressure can halt disease progression in both early and advanced stages. The extent of neuroprotection correlates with the level of intraocular pressure reduction achieved.

Enhancements in treatment options include the development of more effective and better-tolerated medications for lowering intraocular pressure, as well as improved surgical interventions. Additionally, novel therapies aimed at directly treating and safeguarding the retinal ganglion cells affected by glaucoma are currently under investigation.[7- 9]

A diverse range of intraocular pressure (IOP)-lowering medications, each with distinct mechanisms of action, is currently available. These include β-blockers such as timolol, prostaglandin analogs like latanoprost, carbonic anhydrase inhibitors (CAIs) such as brinzolamide, and α2-adrenergic agonists like brimonidine. These pharmacological agents lower IOP by either decreasing the production of aqueous humor, increasing its outflow, or employing a combination of both strategies. Specifically, β-blockers and CAIs diminish aqueous production by restricting blood flow to the iris root and ciliary body or by inhibiting specific carbonic anhydrase isozymes that are sensitive to sulfonamides, respectively. Conversely, prostaglandin analogs facilitate a reduction in IOP by enhancing the outflow of aqueous humor through both the uveoscleral and trabecular meshwork pathways, while α2-adrenergic agonists not only decrease aqueous production but also promote aqueous outflow via the uveoscleral route.[8- 10]Hence; the present study was conducted for comparing the efficacy of Dorzolamide 2 percent timolol 0.5 percent fixed combination versus brinzolamide 1 percent brimonidine 0.2 percent fixed combination therapy in patients of primary open angle glaucoma.

Mean age of the patients of group 1 and group 2 was 41.5 years and 42.9 years. Majority proportion of patients of both the study groups were males. Among patients of group 1, mean IOP at baseline, 2nd week follow-up, 4th week follow-up and 6th week follow-up was 28.3 mm of Hg, 17.3 mm of Hg, 16.9 mm of Hg and 15.9 mm of Hg respectively. Among patients of group 2, mean IOP at baseline, 2nd week follow-up, 4th week follow-up and 6th week follow-up was 27.9 mm of Hg, 16.5 mm of Hg, 16.1 mm of Hg and 16.9 mm of Hg respectively. Centofanti M et al. conducted a study to evaluate the acute intraocular hypotensive effects of brimonidine tartrate 0.2%, a highly selective α2-adrenergic agonist, in comparison to dorzolamide 2%, a topical carbonic anhydrase inhibitor, as adjunctive therapy to topical β-blockers in patients diagnosed with primary open-angle glaucoma. The study involved one eye from each of 28 patients who were receiving various β-blocker treatments. Intraocular pressure (IOP) was measured two hours post-instillation of the β-blocker, after which one of the two medications was randomly administered, and an IOP diurnal curve was established. Both brimonidine 0.2% and dorzolamide 2% demonstrated significant ocular hypotensive efficacy, effectively reducing IOP compared to β-blocker therapy alone throughout the entire diurnal curve. The maximum mean percentage decrease in IOP from baseline was recorded at 22.0±15.7% (4.0±2.9 mmHg) for dorzolamide 2% six hours post-instillation, and 35.5±16.4% (7.0±4.1 mmHg) for brimonidine 0.2% eight hours after administration. When comparing the two treatments, brimonidine 0.2% exhibited a greater hypotensive effect than dorzolamide 2% at both four and eight hours. The findings of this study suggest that the combination of 0.2% brimonidine with β-blockers represents a promising new therapeutic approach for the management of glaucoma.[10]

In the present study, non-significant results were obtained while comparing mean IOP among the two study groups at different time intervals. Also; while comparing the incidence of adverse events among the two study groups, non-significant results were obtained.Ines Lanzl and colleagues conducted a study to evaluate the effectiveness and tolerability of the newly introduced fixed-combination (FC) brinzolamide 1%/timolol 0.5% in a real-world clinical setting. The analysis specifically included patients who switched from other FC therapies to brinzolamide/timolol. The study encompassed data from 14,025 patients across 1,161 medical centers. Following a transition period of four to six weeks to brinzolamide/timolol, patients exhibited an average intraocular pressure (IOP) reduction of 3.9 ± 4.3 mm Hg. Notably, all predefined patient subgroups, categorized by their prior treatments, showed a significant decrease in mean IOP after switching to brinzolamide/timolol. Furthermore, patients rated the tolerability of brinzolamide/timolol more favorably compared to their previous therapies, with favorable assessments at 87.2% versus 53.7%, and reported a high satisfaction level of 93.4% with the new treatment. The preference for brinzolamide/timolol over previous therapies was nearly 9:1. Among patients transitioning from dorzolamide/timolol (n = 2,937), there was a significant reduction in mean IOP, with 88.9% rating brinzolamide/timolol as more tolerable compared to dorzolamide/timolol (28.9%), and a preference ratio exceeding 9:1. Similarly, patients switching from brimonidine/timolol (n = 209) also experienced a significant IOP decrease, rated brinzolamide/timolol as more tolerable (86.5% vs 32.1%), and preferred it at a ratio of 11.5:1. Overall, the FC brinzolamide 1%/timolol 0.5% demonstrated superior IOP control compared to all previously analyzed therapies, alongside favorable tolerability and high satisfaction ratings.[11]

CONCLUSION

Increased intraocular pressure (IOP) is a significant risk factor for primary open-angle glaucoma; the principal therapeutic strategy to mitigate the progression of glaucoma and ocular hypertension involves the reduction of IOP. Both the drugs were equally effective in managing patients with POAG.

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