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Comparison of efficacy of Dorzolamide 2% timolol 0.5% 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: The glaucomas are a group of optic neuropathies characterized by progressive degeneration of retinal ganglion cells. These are central nervous system neurons that have their cell bodies in the inner retina and axons in the optic nerve. The purpose of this study was to compare the efficiency of the new brinzolamide/brimonidine fixed combination vs the dorzolamide/timolol fixed combination.

Materials & methods: This was randomized, open label, comparative, parallel group study to be conducted on 40 patients of POAG. Patients selected were then be randomised into two groups of 20 each as follows: Group 1 in which fixed drug combination of Dorzolamide2%/ Timolol 0.5% (DTFC) dosed twice daily and Group 2 in which fixed drug combination of Brinzolamide 1%/ Brimonidine 0.2% (BBFC) dosed twice daily. Patients were then being called for follow up and IOP were recorded. IOP readings were taken from the study eye at each visit. All the results were analyzed by SPSS software.

Results: Mean IOP among patients of Group 1 at visit 1, visit 2, visit 3 and visit 4 was 28.69, 19.36, 18.46 and 17.11 mm of Hg respectively. Mean IOP among patients of Group 2 at visit 1, visit 2, visit 3 and visit 4 was 27.15, 19.12, 18.69 and 17.96 mm of Hg respectively. Non-significant results were obtained while comparing the mean IOP at different time intervals in between the two study groups.

Conclusion: Both the modalities are equally good in treating patients with primary open angle glaucoma.

Key words: Dorzolamide, Timolol, Primary open angle glaucoma

INTRODUCTION

The glaucomas are a group of optic neuropathies characterized by progressive degeneration of retinal ganglion cells. These are central nervous system neurons that have their cell bodies in the inner retina and axons in the optic nerve. Glaucoma affects more than 70 million people

worldwide with approximately 10% being bilaterally blind, making it the leading cause of irreversible blindness in the world. The two most common forms of glaucoma are primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PACG), with the former approximately seven times more common than the latter in the United States and Europe.1 When POAG and PACG are left untreated, the typical disease course is chronic, progressive, and irreversible visual field loss, which may progress to tunnel vision and, ultimately, loss of central vision. Treatment that reduces intraocular pressure has been shown to improve outcomes in randomized clinical trials.[1- 3]

Many patients with glaucoma remain asymptomatic, even as the disease advances, because progressive visual field loss is peripheral and typically asymmetric, which allows for compensation from the overlapping, less-affected visual field of the other eye. As a result, POAG is often found incidentally on ocular examination.[4, 5]

IOP is one of the most important parameters in the diagnosis and treatment of glaucoma. Topical β-blockers such as timolol have been widely used since the 1970s and they reduce IOP by decreasing aqueous humor secretion. The precise mechanism of action is presumed to be mediated via blockade of the β2 adrenergic receptors found in the ciliary body. Since then, newer treatments have become available, including carbonic anhydrase inhibitors such as dorzolamide and brinzolamide, prostaglandins such as latanoprost and travoprost, and α2 adrenergic agonists such as brimonidine. As these drugs reduce IOP through different pathways, they are often given as combinations, for example, the combination of dorzolamide 2% and timolol 0.5%, which is available in a fixed single-dose preparation, which is more effective at reducing IOP than either of its components given alone.[6] The purpose of this study was to compare the efficiency of the new brinzolamide/brimonidine fixed combination vs the dorzolamide/timolol fixed combination.

MATERIALS & METHODS

This was randomized, open label, comparative, parallel group study to be conducted on 40 patients of POAG. Patients selected were then be randomised into two groups of 20 each as follows: Group 1 in which fixed drug combination of Dorzolamide2%/ Timolol 0.5% (DTFC) dosed twice daily and Group 2 in which fixed drug combination of Brinzolamide 1%/ Brimonidine 0.2% (BBFC) dosed twice daily. Patients were then being called for follow up and IOP were recorded. IOP readings were taken from the study eye at each visit. All the results were analyzed by SPSS software. Chi- square test and Mann-Whitney U test were used for assessment of level of significance. P- value of less than 0.05 was taken as significant.

RESULTS

Mean age of the patients of Group 1 and group 2 was 38.4 years and 39.4 years respectively. There were 19 males and 21 females in group 1 while there were 21 males and 19 females in group 2. Mean IOP among patients of Group 1 at visit 1, visit 2, visit 3 and visit 4 was 28.69, 19.36, 18.46 and 17.11 mm of Hg respectively. Mean IOP among patients of Group 2 at visit 1, visit 2, visit 3 and visit 4 was 27.15, 19.12, 18.69 and 17.96 mm of Hg respectively. Non-significant results were obtained while comparing the mean IOP at different time intervals in between the two study groups.

Table 1: Comparison of IOP pressure at different time intervals

Visits	Mean Diurnal IOP of Group 1	Mean Diurnal IOP of Group 2	p- value
Visit 1	28.69	27.15	0.265
Visit 2	19.36	19.12	0.125

Visit 3	18.46	18.69	0.445
Visit 4	17.11	17.96	0.339

DISCUSSION

Many patients with glaucoma remain asymptomatic, even as the disease advances, because progressive visual field loss is peripheral and typically asymmetric, which allows for compensation from the overlapping, less-affected visual field of the other eye. As a result, POAG is often found incidentally on ocular examination. Although the prevalence of glaucoma increases with age, most patients with undetected glaucoma are younger than 60 years, which represents an opportunity to diagnose the disease earlier.3 This article reviews the pathophysiology of and risk factors for glaucoma, and emphasizes the role of family physicians in the care of affected patients.[6-9] The purpose of this study was to compare the efficiency of the new brinzolamide/brimonidine fixed combination vs the dorzolamide/timolol fixed combination.

Mean age of the patients of Group 1 and group 2 was 38.4 years and 39.4 years respectively. There were 19 males and 21 females in group 1 while there were 21 males and 19 females in group 2. Mean IOP among patients of Group 1 at visit 1, visit 2, visit 3 and visit 4 was 28.69, 19.36, 18.46 and 17.11 mm of Hg respectively. Mean IOP among patients of Group 2 at visit 1, visit 2, visit 3 and visit 4 was 27.15, 19.12, 18.69 and 17.96 mm of Hg respectively. Feldman et al in 2016 conducted a study to evaluate the safety and efficacy of adding fixed combination brinzolamide 1%/brimonidine 0.2% (BBFC) as adjunctive therapy to travoprost 0.004%(TRAV) in patients with open angle glaucoma. The results of the study suggested that mean diurnal IOP at week 6was 17.6±0.4 mm Hg and 20.7±0.4 mmHg in the BBFC+TRAV and vehicle+ TRAV groups respectively (between group difference -3.2±0.5 mm Hg; p<.0001). Superiority of BBFC+TRAV over vehicle+TRAV was established. Mean and percent diurnal IOP change from baseline were significantly greater with BBFC+ TRAV compared with vehicle+TRAV (p<.0001 for both). Conjunctival hyperemia was the most common treatment related adverse event in either group (BBFC+TRAV, 12.8%; vehicle+TRAV,6.0%). It was concluded that adjunctive treatment with BBFC added to TRAV resulted in lower mean diurnal IOP after 6 weeks of treatment compared with vehicle added to TRAV; this difference was both statistically and clinically significant.[9]

In the present study, non-significant results were obtained while comparing the mean IOP at different time intervals in between the two study groups. Lee NY et al (2016) conducted a prospective, interventional, randomized, single-blinded, crossover design study to assess the noninferiority of a dorzolamide-timolol fixed combination (DTFC) versus latanoprost in terms of intraocular pressure (IOP) and to compare blood pressure (BP), ocular perfusion pressure (OPP) and diastolic ocular perfusion pressure (DOPP) between the latanoprost and DTFC groups in patients with normal-tension glaucoma (NTG). Patients with newly diagnosed NTG that had not been treated with a glaucoma medication in the most recent 2 months were recruited. In total, 44 patients with NTG were randomly allocated to one of two groups. Patients in group A were treated with DTFC, lubricant, and latanoprost for 4 weeks each, whereas patients in group B were treated with latanoprost, lubricant, and DTFC for 4 weeks each. Patients were examined on day 1 (without medication), week 4 (under medication), week 8 (without medication), and week 12 (under medication). At weeks 4 and 12, diurnal IOP, systolic and diastolic BP, and OPP were measured at 8:00 AM, 10:00 AM, 12:00 PM, 4:00 PM, and 8:00 PM.Baseline demographic characteristics showed no difference in terms of age, sex, centralcorneal thickness, spherical equivalent, or stage of glaucoma between the groups. Thebetween-group difference was -0.19 ±

0.18 mmHg (mean ± SE, upper bound of one-sided 95% CI, 0.12). Diurnal IOP showed no difference between the groups with an average IOP reduction of 13.1%using latanoprost and 12.3% using DTFC. Diurnal systolic and diastolic BP were lower in the DTFC group than the latanoprost group; however, the difference between the groups was not statistically significant. Diurnal OPP and DOPP also showed no statistically significant difference between the groups.[10] Hartleben et al (2017) conducted a study to evaluate the efficacy and safety of triple fixed-combination bimatoprost 0.01%/brimonidine 0.15%/timolol 0.5% (TFC) versus dual fixed-combination brimonidine 0.2%/timolol 0.5% (DFC) in primary open-angle glaucoma and ocular hypertension. Patients with intraocular pressure (IOP) ≥23 and ≤34 mmHg were randomized to twice-daily TFC or DFC. The primary variable is the change in worse eye mean IOP from baseline at week 12 (modified intent-to-treat (mITT) population). Secondary endpoints are mean IOP and mean change from baseline at weeks 1, 2, 4, 8, and 12 (mITT population). TFC superiority was demonstrated if the primary variable favored TFC. Sensitivity analyses were conducted, and safety was assessed at all visits. TFC provided greater IOP reductions from baseline than DFC () at week 12 (treatment difference, 0.85 mmHg;) and all other visits. TFC was also superior to DFC in patients with high baseline IOP (i.e., IOP ≥ 25 mmHg. Conjunctival hyperemia, ocular irritation, and dry eye were reported more often with TFC; however, discontinuations for ocular adverse events were similar between treatments. TFC demonstrated IOP-lowering benefits that outweigh the risk of predominantly mild ocular side effects, which may be particularly relevant in patients who require greater IOP lowering to prevent/delay disease progression.[11]

CONCLUSION

From the above results, the authors conclude that both the modalities are equally good in treating patients with primary open angle glaucoma.

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