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Original Research Article

Comparison of Efficacy and Tolerability of Fixed Drug Combination of Brimonidine and Timolol with Timolol Monotherapy

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Abstract

Aim: The purpose of this study is to assess and contrast the efficacy and tolerability of 0.5% timolol delivered as monotherapy and a fixed medication combination of 0.2% brimonidine and **0.5%** timolol in patients with POAG.

Material and Methods: The included 120 patients were divided into two different groups as follows: group A included 60 patients in Fixed dose combination of Brimonidine Timolol group; taken as study group and group B with 60 patients who received For a period of 12 weeks, timolol 0.5% eye drops were administered morning and evening as the control group. Each patient had their own case record form and was registered as a POAG case. Following enrollment in the trial and the start of the study medicines, follow-up was conducted at 2, 4, 8, and 12 weeks. Change in intraocular pressure (IOP) from the starting point to the target pressure served as the main efficacy end point. The assessment of tolerability included both subjective and objective evaluation of adverse ocular and systemic effects.

Results: At the conclusion of the trial, group A experienced a considerable reduction in intraocular pressure when compared to group B. Unpaired "t" test statistical analysis is carried out.

Conclusion: For the treatment of primary open angle glaucoma, brimonidine-Timolol fixed combination is more efficient and secure in decreasing IOP than Timolol monotherapy. Additionally, the neuroprotective properties of brimonidine may prove useful in long-term halting the disease's progression.

Keywords: Brimonidine, Intraocular Pressure, Primary Open Angle Glaucoma, Timolol.

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Introduction

Greek for "clouded," glaucoma originally referred to either a fully developed cataract or chronically increased pressure-induced ocular edema. The definition of glaucoma is a disturbance of the anatomical or functional integrity of the optic nerve that is typically

halted or reduced by a sufficient reduction in IOP. The term "glaucoma" refers to a wide range of disorders rather than a single disease process, each of which is characterized by a distinctive pattern of irreversible visual field defects as the damage to the eye progresses, a potentially progressive optic neuropathy, and elevated intraocular pressure (IOP), which is a major modifiable factor [1-3].

The rate at which the ciliary body produces aqueous humor and the resistances to aqueous outflow at the angle of the anterior chamber dictate the intraocular pressure. The barrier to aqueous fluid outflow causes a rise in IOP [4,5].

The second-leading cause of blindness in the world, glaucoma has a disproportionately high morbidity rate for Asians and women. With an about 3:1 ratio, POAG affects more people than angle closure glaucoma (ACG) on a global scale. A third of all glaucoma cases worldwide are caused by primary open-angle glaucoma (POAG), which is more common than primary angle closure glaucoma (PACG) [6] In general, glaucoma ranks second to cataract and refractive errors as the leading cause of blindness. More importantly, it is the leading global cause of permanent blindness. More than 3 million people are thought to be blind from glaucoma. Twelve million instances of glaucoma, or around one-fifth of all cases worldwide, are thought to exist in India [1,7].

In the Ocular Hypertension Treatment Study, after four years, more than 41% of the patients required two or more drugs to reach the desired IOP. 80% of the patients in the Collaborative Initial Glaucoma Treatment Study needed two or more drugs after two years [6,7]. Therefore, the purpose of this study is to compare and assess the effectiveness and safety of a fixed medication combination of 0.2% brimonidine and 0.5% timolol with that of 0.5% timolol used as monotherapy in POAG patients.

Materials and Methods

The present study is the comparative study conducted in the department of ophthalmology tertiary care teaching hospital. The study period of the analysis was around 6 months. The aim and objective of the research analysis was explained to the ethical committee of the institute and the ethical clearance certificate was obtained prior to the start of the study. The inclusion and exclusion criteria followed in the study were as follows:

Inclusion criteria:

Patients diagnosed with Primary Open-Angle Glaucoma with IOP of 22 mmHg at presentation and above, patients having IOP range above 25 - 30 mmHg, patients of both sexes (male and female), and patients were included if they were within the age range of 30-65 years.

Exclusion criteria:

patients who are older than 65 but younger than 30 years Patients with anterior synechiae, clinically evident dry eye syndrome, active ocular infection, inflammation, and significant ocular trauma; patients taking additional systemic or ocular medications that may have a significant impact on intraocular pressure; patients with other medical conditions; patients who have had prior eye surgery; female patients of childbearing age who do not use medically approved contraceptives; and patients who do not wish to participate in the study.

The study included patients who meet the inclusion and exclusion criteria and who are willing to provide informed consent for participation. The study involved 120 patients in all. The patients who were included were split into two groups, according to the following: In group A, 60 patients received a fixed dose combination of brimonidine and timolol eye drops for 12 weeks; this group served as the study group.

In group B, 60 patients received timolol 0.5% eye drops twice a day for 12 weeks; this group served as the control group.

The outpatient ophthalmology department at Medical College Hospital served as the recruitment site for the study's participants. According to the inclusion criteria, informed written consent was obtained from the qualified patients. The participants were given information about the study, and informed consent was obtained in their Vernacular language. The following medications were utilized in this study:

1. Fixed drug dose combination 0.2% Brimonidine-0.5% Timolol eye drop.
2. 0.5% Timolol eye drop.

Each patient had their own case record form and was registered as a POAG case. The patient underwent a thorough ocular examination, which included measuring intraocular pressure, visual acuity, direct ophthalmoscopy, slit lamp examination and visual field testing. To measure the intraocular pressure, Goldman applanation tonometry was used.

During each visit, the patient's pulse, systolic and diastolic blood pressure were recorded. Administration of medication: Patients were instructed on how to apply eye drops topically and the value of maintaining good hand hygiene was emphasized.

Following enrollment in the trial and the start of the study medicines, follow-up was conducted at 2, 4, 8, and 12 weeks. The patients were followed up with at the ophthalmology department after a 12-week trial period.

Adverse reactions: The study medications were secure and were not known to cause any life-threatening adverse reactions. Following administration of the research medicines, participants were instructed to report any side effects, including irritation, itching, redness, dryness, etc. They were told to show up right away to the study center. Compliance: The patients were informed and given instructions on how to follow the treatment schedule. The patient kept a compliance diary, which was checked on each visit.

The patients were free to leave the trial at any moment during the research period for their own reasons or if any negative medication effects materialized. The difference between the intraocular pressure at baseline and the goal pressure served as the major efficacy endpoint. The assessment of safety included both subjective and objective evaluation of adverse ocular and systemic effects. At each appointment, the patient was questioned to determine whether they were experiencing subjective symptoms including stinging, itching, dry mouth, or headaches. The patient was thoroughly examined using clinical and visual examinations to get objective signs.

Statistical Analysis

Data were expressed as mean ± standard deviation. Quantitative data from the two groups were compared using the students independent t-test. While the Chi-square test was used to assess the qualitative data about the frequency of adverse events, the paired t-test and unpaired t-test were used to analyze the quantitative data.

Results

In order to assess the effectiveness of Brimonidine-Timolol fixed-dose combination therapy with Timolol monotherapy in patients with Primary Open-Angle Glaucoma for reaching Target Intra Ocular Pressure, study analysis was conducted. Following the first assessment of 134 patients, selection criteria led to the exclusion of 14 patients (6 patients refused to participate in the trial, 8 patients had a history of DM and hypertension), and 120 patients with POAG-like symptoms were ultimately enrolled in the study.

There are 60 patients in each group. Patients in Group A received a fixed dose combination of brimonidine-timolol eye drops that were administered twice daily. Timolol 0.5% eye drops were administered twice daily to participants in group B as their treatment. Patients were administered study medicines at the initial appointment for 4 weeks, and their progress was monitored at 2 weeks, 4 weeks, 8 weeks, and 12 weeks. The patients' compliance, subjective improvements, adverse events, and the administration of drugs until the completion of the 12-week period were all tracked during each appointment.

At the conclusion of the study, demographic parameters like age and gender were evaluated and analyzed. comprehensive patient eye examination, including measurement of intraocular pressure, visual acuity, and slit-lamp examination. At the beginning and end of the trial, gonioscopy, vision field, pachymetry, and direct ophthalmoscopy were evaluated. During each visit, the patient's pulse, systolic and diastolic blood pressure were recorded. At the conclusion of the trial, adverse effects of the study medicines were assessed and examined.

Table 1 compares the IOP levels between the FDC BT group and the Timolol group at the conclusion of the trial. Unpaired "t" test statistical analysis is carried out. At the conclusion of the trial, group A experienced a considerable reduction in this parameter when compared to group B.

Table 1: IOP in comparison between group A and B

End of treatment	Group A		Group B		Unpaired t test
	Mean	SD	Mean	SD	P= 0.0001
IOP in mmHg	17.58	2.48	21.38	2.69	

Discussion

The largest global cause of vision loss and blindness is glaucoma. It is connected to the degeneration of retinal ganglion cells and increased intraocular pressure, both of which are modifiable glaucoma risk factors. More than 60 million people are estimated to be affected by glaucoma worldwide75. More than 8% of global total blindness is brought on by it. There are 20 million glaucoma patients in India, according to estimates [8-10].

The most prevalent form of glaucoma, primary open angle glaucoma (POAG), is characterized by a chronically increased IOP, ocular neuropathy, and distinctive visual field abnormalities.

The major goal of the treatment plan is to lower IOP in order to stop vision loss. Patients with POAG typically receive their therapy with topical anti-glaucoma medications. To reach the goal IOP, two or more medications are needed. Fixed drug combinations have recently received approval for this use. In addition, a different strategy such as neuroprotection is required to stop RGC mortality in people with chronic glaucoma [11,12].

Two or more drugs are required to reach the goal IOP after two to four years of glaucoma care, according to the Ocular Hypertension Treatment Study and Collaborative Initial Glaucoma Treatment studies [7,13,14].

At the conclusion of treatment, the mean IOP in both groups is lower than it was at the start. The FDC brimonidine-timolol combination considerably decreased the mean IOP by an

average of 12.70 1.09 mmHg as compared to the baseline value. At the conclusion of the treatment, the FDC BT group's mean IOP is significantly lower than it was in the timolol group (p 0.05).

The brimonidine-timolol fixed combination has two additional possible advantages in addition to decreasing IOP. First, because benzalkonium is frequently used as a preservative in ocular drugs and because treating glaucoma is a lifelong process, it may have adverse effects on the corneal surface that are dose-related. When FDC BT is used twice daily, the daily preservative exposure to the eyes is reduced by one third compared to when the two component medications are used separately.

Four participants in the FDC BT group and eleven in the Timolol group in this trial experienced burning or stinging. 9 individuals in the Timolol group and 6 patients in the FDC BT group experienced an eye-related alien body sensation. 6 patients in the Timolol group and 2 individuals in the FDC BT group both experienced allergic pruritus. The Timolol group had two patients with dry eyes and two patients with hyperemia. Patients in the FDC BT group experienced less adverse effects than those in the Timolol group. No significant side effects were observed in either group.

Conclusion

As a result, brimonidine-timolol fixed combination is safer and more successful at lowering IPO than Timolol monotherapy for the treatment of primary open angle glaucoma, according to the findings of our study. Additionally, the neuroprotective properties of brimonidine may prove useful in long-term halting the disease's progression.

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