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Original Article

# Evaluation of the Use of Brinzolamide-Brimonidine Fixed Combination in Maximum Medical Therapy

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## Abstract

**Objectives:** To investigate the intraocular pressure (IOP)-lowering efficacy, safety, and treatment tolerability of brinzolamide/brimonidine fixed combination (BBFC) in maximum medical therapy.

**Materials and Methods:** The medical records of 92 patients with glaucoma or ocular hypertension who had previously been treated with a different antiglaucomatous regimen and were switched to a treatment regimen that included BBFC were retrospectively analyzed. Patients were divided into 4 groups including 22, 20, 27, and 23 patients based on previous glaucoma treatment. All patients received maximum medical treatment regimen by adding a combination of beta blocker-prostaglandin analogue therapy along with BBFC. IOP values at baseline and month 1, month 3 and month 6 after starting BBFC and ocular adverse effects at follow-up visits were evaluated.

**Results:** The mean age of all patients was 62.7±16.6 years (range: 18-90). Fifty-two patients (56.5%) were women and 40 (43.5%) were men. Forty-eight (52.2%) patients had primary open-angle glaucoma, 35 (38.0%) had pseudoexfoliation glaucoma, and 9 (9.8%) had ocular hypertension. The IOP of the all eyes was 21.1±4.8 mmHg (range: 17-25) before and 17.6±3.7 mmHg, 17.3±3.4, and 17.0±3.5 mmHg at month 1, 3, and 6 after the introduction of BBFC, respectively ($p<0.001$ for all time points compared to baseline). In all 4 groups, a significant decrease in IOP was observed at month 1, 3, and 6 follow-ups compared to baseline after the introduction of BBFC. The mean number of antiglaucoma drops was significantly reduced from 2.5±0.6 at baseline to 2 after BBFC ($p<0.001$). The most frequent ocular adverse event was ocular allergic reactions reported in 8 patients (8.7%), conjunctival hyperemia in 5 patients (5.4%), and ocular discomfort in 2 patients (2.5%).

**Conclusion:** Maximum medical therapy with BBFC provides significant IOP reduction and antiglaucoma therapy simplification with a favorable safety profile in patients with glaucoma.

**Keywords:** Brimonidine, brinzolamide, fixed combination, glaucoma, intraocular pressure

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## Introduction

Glaucoma is a chronic optic neuropathy characterized by progressive optic nerve head atrophy, retinal ganglion cell degeneration, and typical visual field losses.[1] As many glaucoma patients have severe vision loss at diagnosis and the damage caused is irreversible, early diagnosis and monitoring progression accurately and objectively are important. Intraocular pressure (IOP) is the main parameter used in the diagnosis, treatment, follow-up, and classification of glaucoma. IOP is the best known risk factor for glaucomatous damage and is considered the most important modifiable factor for the prevention of progressive glaucomatous injury.[2,3] Multicenter, large-scale clinical studies have shown that reducing IOP can prevent or delay the progression of visual field defects caused by glaucoma and preserve visual function.[4,5] Determining the target IOP is important in the treatment of glaucoma. Initial glaucoma treatment aims to lower elevated IOP by using one or more topical antiglaucoma drugs to reduce the production of aqueous humor and/or increase aqueous outflow.[6]

Antiglaucoma agents with different mechanisms of action are available. Beta-blockers and carbonic anhydrase inhibitors reduce IOP by reducing aqueous humor production; prostaglandin (PG) analogs increase uveoscleral and trabecular outflow; and alpha-2 agonists lower IOP by both reducing aqueous secretion and increasing uveoscleral flow.[4,6] In a large proportion of glaucoma patients, IOP cannot be lowered to within the target range with a single drug, and a second or third drug must be added to treatment to control glaucoma. In maximum medical therapy, the use of three or more different classes of antiglaucoma agents is required to achieve a sufficient reduction in IOP.[7] In the treatment of glaucoma, two, three, or four-component glaucoma therapies can be applied separately, or they can be used as fixed combinations of two drugs in a single bottle to improve ease of use and reduce the adverse effects associated with preservatives. The use of fixed combinations is known to be more comfortable and more advantageous than the use of multiple drugs in terms of patient compliance, posology, ease of use, and adverse effects.[8,9] Frequently used combinations include the topical beta-blocker timolol 0.5% combined with a PG analog, an alpha-adrenergic receptor agonist, or a topical carbonic anhydrase inhibitor. Although fixed combinations containing beta-blockers generally provide effective IOP reduction, they should not be selected for patients with conditions such as asthma, chronic obstructive pulmonary disease, sinus bradycardia, impotence, and depression.[10]

Brinzolamide 1% and brimonidine 0.2% fixed combination (BBFC) was the first fixed combination produced that did not include a beta-blocker. It can be used alone or together with timolol, PG analogs, and combinations thereof. To the best of our knowledge based on the literature, no studies have been conducted in Turkey to evaluate the efficacy and safety of this fixed combination in IOP control. The aim of this study was to investigate the IOP-lowering effect, adverse effect profile, and treatment adherence in glaucoma patients who receive BBFC therapy.

## Materials and Methods

The data of patients who were treated and followed up in the glaucoma unit of the Ankara University Faculty of Medicine Department of Ophthalmology between September 2019 and November 2020 were retrospectively reviewed. The study was approved by the Ankara University Faculty of Medicine Clinical Research Ethics Committee (date: 23.10.2019, decision no: İ8-549-20). Written informed consent was obtained from the patients in the study. The study sample included patients who received different antiglaucoma treatments for glaucoma and ocular hypertension (OHT) and were switched to a maximum medical therapy regimen to achieve target IOP by adding BBFC for reasons such as failure to adhere to the use of 3-4 different glaucoma drugs. All patients received brinzolamide 10 mg/mL (1%) and brimonidine 2 mg/mL (0.2%) fixed combination (Simbrinza®, Novartis Pharma AG, Basel, Switzerland) twice daily. The patients were divided into four groups according to the antiglaucoma treatment used before switching to BBFC therapy:

Group 1: Brinzolamide/beta-blocker fixed combination + PG analog therapy

Group 2: Brinzolamide + beta-blocker/PG fixed combination therapy

Group 3: Brimonidine + brinzolamide/beta-blocker fixed combination + PG analog therapy

Group 4: Brimonidine + brinzolamide + beta-blocker/PG fixed combination therapy

All patients were administered a maximum medical therapy regimen of BBFC with a beta-blocker/PG fixed combination once daily. Each patient received the beta-blocker/PG fixed combination containing the same PG analog used before initiating BBFC.

Inclusion criteria for the study were:

1. Age 18 years or older
2. IOP ≤25 mmHg in both eyes (mean of the last 3 measurements before adding BBFC)
3. For patients with glaucoma, presence of glaucomatous visual field losses and presence of glaucomatous optic nerve head damage on fundus examination (vertical enlargement of the optic pit and thinning of the neural rim; vertical cup/disc ratio >0.6, cup/disc asymmetry >0.2 between the two eyes)
4. For patients with OHT, IOP >21 mmHg in at least two measurements and no glaucomatous visual field defect or optic nerve head damage
5. Angle open in all quadrants on gonioscopic examination
6. No optic media opacity (e.g., corneal opacity, substantial cataract, substantial vitreous opacity) or marked retinal pathology
7. No history of ocular trauma or intraocular surgery other than cataract

In the initial examination of all patients, a detailed history was obtained, followed by best corrected visual acuity measurement, slit-lamp anterior segment examination, dilated fundus examination, IOP measurement with Goldmann applanation tonometer (the average of three consecutive measurements made between 9 and 11 AM by another ophthalmologist not involved in the study), angle examination with an Ocular Instruments 4-mirror goniolens, central corneal thickness measurement by ultrasonic pachymeter, visual field analysis (Humphrey Field Analyzer, Carl Zeiss Meditec, Dublin, CA, USA) and retinal nerve fiber layer and ganglion cell complex measurements by spectral domain optical coherence tomography (Carl Zeiss Meditec, Dublin, CA, USA). The patients' records were reviewed to collect the following data: IOP measurements at the last follow-up before and at 1, 3, and 6 months after initiating BBFC, routine ophthalmological examinations, time since treatment modification, topical antiglaucoma treatment regimen used before and after switching to BBFC, total number of drops used, and local and systemic adverse effects associated with BBFC use.

### Statistical Analysis

The data were analyzed using SPSS for Windows version 11.5 (SPSS Inc, Chicago, IL, USA) software package. Descriptive statistics were expressed as mean ± standard deviation for normally distributed variables and as number (n) and percentage (%) for nominal variables. After importing the IOP values to the SPSS program, paired samples t-test was used to determine the statistical significance of the differences between baseline and values measured at 1, 3, and 6 months to determine the effect of drug use in the three different periods. Results with $p<0.05$ were considered statistically significant in statistical analyses.

## Results

A total of 92 patients were included in the study. Four patients discontinued BBFC at 1-month follow-up because of adverse effects and were not included in the analysis. The mean follow-up period after initiation of BBFC for all patients was 8.7±4.5 months (range: 5-11). The demographic and clinical characteristics of the patients in the four groups are shown in Table 1. There were 22 patients (23.9%) in group 1, 20 (21.7%) in group 2, 27 (29.3%) in group 3, and 23 (25.0%) in group 4. Of all the patients in the study, 52 were women (56.5%) and 40 were men (43.5%). There was no statistically significant difference between the groups in terms of gender distribution ($p>0.05$) (Table 1). The mean age of all patients was 62.7±16.6 years (range: 18-90). Mean age did not differ significantly between the groups ($p>0.05$) (Table 1). In the whole patient group, 48 patients (52.2%) were diagnosed with primary open-angle glaucoma (POAG), 35 (38%) with pseudoexfoliation glaucoma (PEG), and 9 (9.8%) with OHT. There was no statistically significant difference between the groups in terms of glaucoma types ($p>0.05$) (Table 1).

The mean IOP of all patients in the study was 21.1±4.8 mmHg (range: 17-25) before treatment and decreased to 17.6±3.7 mmHg at 1 month, 17.3±3.4 mmHg at 3 months, and 17.0±3.5 mmHg at 6 months ($p<0.001$). The IOP values of patients in all groups before BBFC and at 1, 3, and 6 months after BBFC are shown in Table 2 and Figure 1. In group 1, the mean IOP was 22.1±3.1 mmHg before BBFC and 16.8±3.0 mmHg at 6-month follow-up ($p<0.01$). In group 2, the mean IOP was 21.7±3.2 mmHg before BBFC and 16.9±2.8 mmHg at 6-month follow-up ($p<0.01$). In group 3, the mean IOP was 20.6±5.7 mmHg before BBFC and 17.1±3.6 mmHg at 6-month follow-up ($p<0.01$). In group 4, the mean IOP was 20.3±4.8 mmHg before BBFC and 17.3±3.9 mmHg at 6-month follow-up ($p<0.01$). IOP values measured at 6 months were below 18 mmHg in 82% (18/22) of group 1 patients, 85% (17/20) of group 2 patients, 85% (23/27) of group 3 patients, and 86% (20/23) of group 4 patients. At the end of treatment, IOP was 18 mmHg or lower in 45 (93.7%) of the POAG

**Table 1. Evaluation of demographic and clinical characteristics by group**

| | Group 1 (n=22) | Group 2 (n=20) | Group 3 (n=27) | Group 4 (n=23) | p |
|---|---|---|---|---|---|
| Age (years), mean ± SD | 64.5±11.9 | 64.2±12.2 | 61.8±13.6 | 64.1±18.2 | 0.360 |
| Gender, n (%) | | | | | 0.170 |
| Female | 13 (%59.0) | 12 (%60.0) | 14 (%52.0) | 13 (%57.0) | |
| Male | 9 (%41.0) | 8 (%40.0) | 13 (%48.0) | 10 (%43.0) | |
| Lens status, n (%) | | | | | 0.240 |
| Pseudophakic | 4 (%18.2) | 4 (%20.0) | 5 (%19.0) | 5 (%22.0) | |
| Phakic | 18 (%81.8) | 16 (%80.0) | 22 (%81.0) | 18 (%78.0) | |
| Glaucoma type, n (%) | | | | | 0.270 |
| POAG | 11 (%50) | 8 (%40.0) | 15 (%55.5) | 14 (%60.9) | |
| PEG | 9 (%40.9) | 9 (%45.0) | 10 (%37.0) | 7 (%30.4) | |
| OHT | 2 (%9.1) | 3 (%15.0) | 2 (%7.4) | 2 (%8.7) | |
| CCT (µm), mean ± SD | 529±38.2 | 531.3±30.3 | 538±44.3 | 536±40.5 | 0.720 |

SD: Standard deviation, POAG: Primary open-angle glaucoma, PEG: Pseudoexfoliation glaucoma, OHT: Ocular hypertension, CCT: Central corneal thickness

patients, 32 (91.4%) of the PEG patients, and all (100%) of the OHT patients. At last follow-up, IOP was in the 12-18 mmHg range in 31 (64.6%) of the POAG patients, 22 (62.8%) of the PEG patients, and 7 (77.7%) of the OHT patients, and was 12 mmHg or lower in 14 (29.2%) POAG patients, 10 (28.6%) PEG patients, and 2 (22.2%) OHT patients.

The mean IOP changes of the patients in the four groups after starting BBFC are shown in Table 2. Among all patients in the study, the mean IOP change from baseline was -3.5±3.4 mmHg at 1 month, -3.8±3.5 mmHg at 3 months, and -4.1±3.8 mmHg at 6 months after starting BBFC. The mean percent changes in IOP from baseline to 1 month after BBFC in all patients and in the four groups are shown in Figure 2. In all patients, the mean IOP values decreased by 16.6% at 1 month, 18% at 3 months, and 19.3% at 6 months compared to baseline after BBFC (Figure 2). The mean IOP changes and percent decrease at 6 months by glaucoma diagnosis can be seen in Figure 3. After 6 months, the mean change in IOP from baseline was -4.1±3.4 mmHg (19.5%) in POAG patients, -4.0±3.2 mmHg (18.9%) in PEG patients, and -4.1±3.3 mmHg (19.3%) in OHT patients. There was no statistical difference between glaucoma types in terms of IOP changes or percent decrease compared to baseline.

Before BBFC, patients in groups 1 and 2 used a total of two topical antiglaucoma drugs, and those in groups 3 and 4 used three topical antiglaucoma drugs. The mean number of topical antiglaucoma drugs used in all patients was 2.5±0.6 before BBFC and decreased to 2 after BBFC was initiated ($p<0.001$).

Drug-induced ocular adverse effects were observed in 15 (16.3%) of the patients who received BBFC treatment continuously during the 6-month follow-up period, and 13 (14.1%) of these patients discontinued treatment due to the adverse effects. BBFC therapy was not discontinued in 2 patients with mild ocular irritation. The most common adverse event was allergic reaction to the drug within the first 2 weeks of BBFC (n=8, 8.7%), followed by conjunctival hyperemia in (n=5, 5.4%) and ocular irritation/discomfort (n=2, 2.5%) (Table 3). There was no statistical difference between the groups in terms of the frequency of adverse effects ($p>0.05$). Two patients who had not previously used brimonidine reported systemic hypotension after starting BBFC.

**Table 2. Mean IOP and change in IOP values after treatment with brinzolamide/brimonidine fixed combination, by group**

| | Group 1 (n=22) | | Group 2 (n=20) | | Group 3 (n=27) | | Group 4 (n=23) | |
|---|---|---|---|---|---|---|---|---|
| | Mean IOP ± SD (mmHg) | Mean IOP change (mmHg) | Mean IOP ± SD (mmHg) | Mean IOP change (mmHg) | Mean IOP ± SD (mmHg) | Mean IOP change (mmHg) | Mean IOP ± SD (mmHg) | Mean IOP change (mmHg) |
| Initial | 22.1±3.1 | | 21.7±3.2 | | 20.6±5.7 | | 20.3±4.8 | |
| 1 month | 17.8±3.0 | -4.4±2.9 | 17.7±4.0 | -4.0±2.9 | 18.1±4.1 | -2.5±2.8 | 16.8±3.6 | -3.5±3.1 |
| 3 months | 17.3±2.6 | -4.8±2.7 | 17.2±3.6 | -4.5±3.9 | 17.4±3.9 | -3.2±3.0 | 17.2±3.6 | -3.1±2.9 |
| 6 months | 16.8±3.0 | -5.3±3.2 | 16.9±2.8 | -4.8±3.7 | 17.1±3.6 | -3.5±3.2 | 17.3±3.9 | -3.0±2.9 |

IOP: Intraocular pressure, SD: Standard deviation

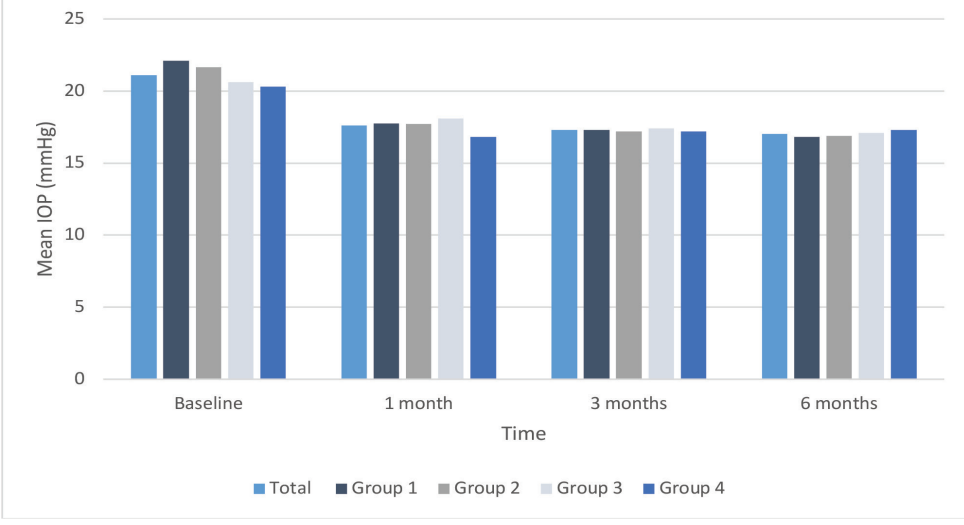


**Figure 1.** Mean intraocular pressure (IOP) values during follow-up after treatment with brinzolamide/brimonidine fixed combination, all patients and by group

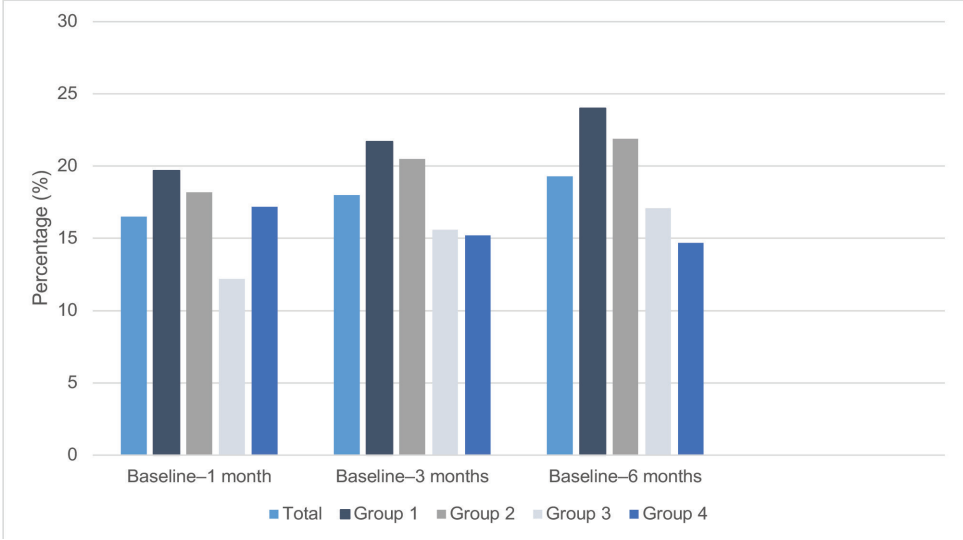


**Figure 2.** Mean percent change in intraocular pressure (IOP) during follow-up after treatment with brinzolamide/brimonidine fixed combination, all patients and by group

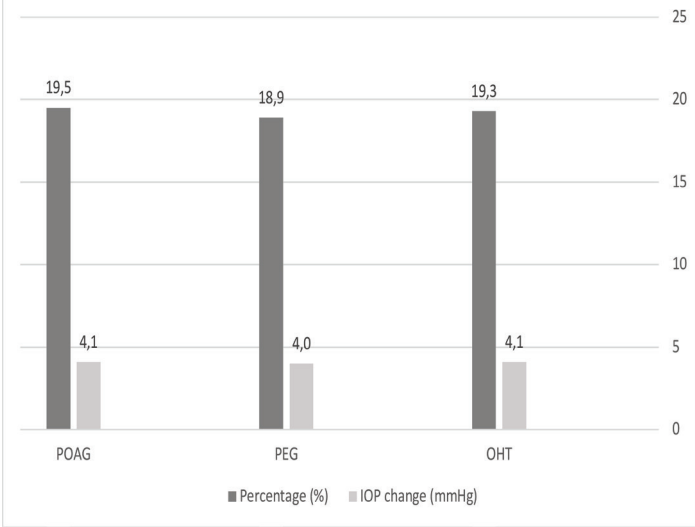


**Figure 3.** Mean intraocular pressure (IOP) change and percent change at 6 months according to glaucoma diagnosis. POAG: Primary open-angle glaucoma, PEG: Pseudoexfoliative glaucoma, OHT: Ocular hypertension

| **Table 3. Adverse effects observed after treatment with brinzolamide/brimonidine fixed combination, by group** | | | | |
|---|---|---|---|---|
| | **Group 1 (n=22)** | **Group 2 (n=20)** | **Group 3 (n=27)** | **Group 4 (n=23)** |
| Systemic AE | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Ocular AE | | | | |
| Allergy | 2 (9.1%) | 2 (10.0%) | 3 (11.1%) | 2 (8.7%) |
| Hyperemia | 2 (9.1%) | 1 (4.0%) | 2 (7.4%) | 0 (0%) |
| Irritation, pain | 1 (4.5%) | 0 (0%) | 0 (0%) | 1 (4.3%) |
| AE: Adverse effect | | | | |

## Discussion

Currently, the first-line treatment of glaucoma is mainly based on the topical application of one or more antiglaucoma drugs to lower IOP. Before resorting to surgical treatment, multidrug regimens must be initiated to achieve target IOP. Studies have shown that using more than two drops a day negatively affects patient compliance and the resulting treatment success.[11,12] Therefore, drugs that act with fewer drops or fixed combinations that contain two drugs in a single bottle are preferred. The fixed-dose combination of 1% brinzolamide (a carbonic anhydrase inhibitor) and 0.2% brimonidine tartrate (an alpha-2 adrenergic receptor agonist) was approved by the U.S. Food and Drug Administration in April 2013 as a new treatment option for patients with POAG or OHT.[13] The drug entered the market for patients in Turkey in September 2019. There is no study conducted in Turkey examining the efficacy and reliability of BBFC in the literature to date.

Our study examined the efficacy of BBFC in 92 patients with POAG, PEG, or OHT who required maximum medical therapy. In this study, BBFC with beta-blocker/PG combination therapy was administered to patients in groups 1 and 2 when a triple therapy with a beta-blocker, PG analog, and carbonic anhydrase inhibitor was insufficient, and a statistically significant decrease in IOP was observed in both groups at 1, 3, and 6 months after switching treatment. In addition, there was a statistically significant decrease in IOP at 1, 3, and 6 months after initiating BBFC and beta-blocker/PG combination therapy in group 3 patients, who previously received brimonidine, combined brinzolamide/beta-blocker, and PG analog therapy in 3 different bottles, and in group 4 patients, who previously received brimonidine, brinzolamide, and beta-blocker/PG combination therapy in 3 different bottles. We believe the significant IOP lowering observed after switching to BBFC in groups 3 and 4, which received four-component antiglaucoma therapy prior to initiating BBFC, can be attributed to improved treatment adherence due to fewer drug bottles and less preservative exposure, as well as reduced potential for the drugs to wash each other out.

Kóthy and Holló[14] studied the effects of BBFC in 52 POAG and OHT cases and reported significant IOP reduction in the majority of eyes included in the study. However, 19 patients (36.5%) in that study had to discontinue treatment due to BBFC-related adverse effects. BBFC therapy was discontinued due to systemic adverse effects in 6 patients (11.5%) and ocular adverse effects in 13 patients (25%).

Gandolfi et al.[15] compared treatment regimens using brinzolamide 1% and brimonidine 0.2% administered as a fixed combination and in separate bottles in patients with POAG and OHT and found that BBFC was as effective in lowering IOP as separate treatment. Based on the results of their study, the authors suggested that BBFC is an effective alternative for patients in whom IOP is not adequately controlled with brinzolamide or brimonidine alone, or in patients with contraindications to PG analog and beta-blockers. Similarly, Wang et al.[16] compared treatment regimens including BBFC and separate brinzolamide and brimonidine drops together in patients with POAG and OHT and found both treatment regimens to have similar efficacy and safety. Kozobolis et al.[17] compared the efficacy of BBFC and a dorzolamide/timolol fixed combination in 44 patients and reported a comparable IOP-lowering effect and safety profile. In this study, they proposed that BBFC is a safe and effective option in patients in whom beta-blocker therapy is contraindicated.

Previous studies in the literature have mostly evaluated the efficacy of BBFC alone in glaucoma patients. In a few recent studies, patients received a maximum medical therapy regimen of BBFC together with a beta-blocker/PG combination. Lerner et al.[7] evaluated maximum medical therapy by investigating the additive efficacy of BBFC with travoprost/timolol fixed combination in 67 open-angle glaucoma and OHT patients and observed a statistically significant reduction in IOP in the group to which BBFC was added. Joh and Jin[18] divided patients who received maximum medical therapy into two groups, triple (dorzolamide-timolol combination + brimonidine + latanoprost) and double (tafluprost/timolol combination + BBFC) maximum therapy. No statistically significant difference was found between the double and triple maximum medical therapy groups in terms of IOP reduction rate, but the rate of ocular adverse effects such as conjunctival hyperemia and dry eye was significantly lower in the double maximum therapy group. Similarly, Wy et al.[19] examined POAG patients who switched from triple maximum medical therapy (dorzolamide/timolol combination + brimonidine + latanoprost) to double maximum medical therapy (tafluprost/timolol combination + BBFC). Although IOP reduction rates were similar between the double and triple maximal medical therapy groups, the dry eye rate was significantly lower in the double maximal therapy group.

Lowering IOP is the only glaucoma treatment option proven to be effective in maintaining visual function. The results of the Early-Onset Glaucoma Study showed that each 1 mmHg decrease in IOP reduced glaucoma progression by 10%.[5] In our study, there was a mean IOP reduction of 4.1 mmHg in the entire patient group according to data obtained at 6 months after the initiation of BBFC. The greatest reduction was 5.3 mmHg in group 1, followed by 4.8 mmHg in group 2, 3.5 mmHg in group 3, and 3.0 mmHg in group 4. Studies have demonstrated that IOP values below 18 mmHg reduce visual impairment.[3] In our study, IOP values measured at 6 months were below 18 mmHg in 82% of patients in group 1, 85% of patients in group 2 and group 3, and 86% of patients in group 4.

The number of topical antiglaucoma drugs used in all patients decreased from an average of 2.5±0.6 before BBFC to 2 after BBFC was initiated. The lower drop number makes use easier and decreases the number of bottles the patient needs to buy, thus decreasing the cost of treatment. We think the increased treatment adherence and lower likelihood of the drugs washing

each other out when using fewer drops played a role in the significant IOP reduction after BBFC. After fixed combination treatment, adverse effects such as ocular surface damage and dry eye associated with the toxic effects of preservatives such as benzalkonium chloride decrease and drug tolerance increases.[15,16]

In our study, the rate of ocular side effects after BBFC was reported to be 16.3%. These included allergic reaction, irritation, and conjunctival hyperemia, which are known side effects of brinzolamide and brimonidine. No serious adverse effects or systemic adverse effects were observed. Previous studies in the literature reported adverse drug reactions similar to those in our study after BBFC.[7,15,16,17,18,19,20] Similar to our study, Lerner et al.[7], reported that the rate of ocular adverse effects was 11.9% in patients who received maximum medical therapy in the form of BBFC and a beta-blocker/PG analog. In the same study, ocular adverse effects were observed in 7.5% of the control group given the beta-blocker/PG analog combination alone.

In previous studies in the literature, it is seen that the majority of patients treated with BBFC are diagnosed with POAG.[15,16,17,18,19] In contrast, our study included 48 patients with POAG (52.2%) and 35 patients with PEG (38.0%). BBFC provided effective IOP reduction in both POAG and PEG patients. At 6 months, IOP decreased from baseline by 4.12±3.37 mmHg (19.5%) in patients with POAG and 4.02±3.17 mmHg (18.9%) in patients with PEG, with no statistical difference in mean IOP change or percent change from baseline between the groups.

### Study Limitations

Limitations of our study include the relatively short follow-up period due to the recent introduction of BBFC in Turkey, the lack of a treatment compliance and satisfaction questionnaire for patients after initiating treatment, and the retrospective study design.

## Conclusion

The fixed combination of brinzolamide 1% and brimonidine 0.2% provides effective IOP reduction in patients with POAG, PEG, and OHT who need to use multiple antiglaucoma agents. In most patients in our study, BBFC was well tolerated as a part of maximum medical therapy, increased treatment adherence by decreasing the number of drug containers used, and caused no adverse events other than the known ocular side effects of the component drugs.

### Ethics

**Ethics Committee Approval:** Ankara University Faculty of Medicine Clinical Research Ethics Committee, date: 23.10.2020, decision no: İ8-549-20.

**Informed Consent:** Obtained.

**Peer-review:** Externally and internally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: O.T., Concept: O.T., H.C.K., Design: O.T., H.C.K., Data Collection or Processing: H.C.K., Analysis or Interpretation: H.C.K., Literature Search: H.C.K., Writing: H.C.K.,

**Conflict of Interest:** No conflict of interest was declared by the authors.

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