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EFFECT OF TOPICAL DORZOLAMIDE/ TIMOLOL AS COMPARED TO BRINZOLAMIDE / BRIMONIDINE COMBINATION IN THE TREATMENT OF PRIMARY OPEN ANGLE GLAUCOMA

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Abstract

Background: *Glaucoma is a major cause of blindness worldwide, and managing it effectively is crucial to prevent vision loss. Eye drops play a vital role in controlling the pressure inside the eye, and using combinations of medications has become a popular approach. Our study looked at two commonly used eye drop combinations, dorzolamide/timolol (DTFC) and brinzolamide/brimonidine (BBFC), to see how well they work and how safe they are for patients with primary open-angle glaucoma (POAG).*

Study Design: *Cross Sectional Prospective Study.*

Study Setting: *This study was conducted at the Department of Ophthalmology, University Medical and Dental College, Faisalabad.*

Study Duration: *Five Months (December '24, to May '25).*

Methodology: *This cross sectional prospective study was conducted in 68 eyes of patients with POAG. Participants received either DTFC or BBFC combination eye drops twice daily for 12 weeks. Intraocular pressure IOP was measured at baseline, 1 and 3 months. Adverse events and ocular discomfort were also assessed.*

Results: *Both combinations significantly reduced intraocular pressure from baseline. However, DTFC showed a greater mean IOP reduction (-7.1 ± 2.4 mmHg) compared to BBFC (-5.2 ± 1.4 mmHg) at 12 weeks ($p < 0.05$). The incidence of ocular discomfort and blurred vision was higher with BBFC (41% vs. 11%, $p < 0.05$).*

Conclusion: *DTFC decreased intraocular pressure better than BBFC in POAG patients. These findings suggest that DTFC may be a superior choice for patients requiring combination therapy.*

INTRODUCTION

Glaucoma, a silent thief of sight, stealthily robs millions of their vision worldwide, leaving an indelible mark on individuals and communities alike. As the most common form of this debilitating disease, primary open-angle glaucoma (POAG) demands effective management to halt its relentless progression and preserve the precious gift of vision.[1]

The most common form POAG requires effective management to prevent progressive damage to the optic nerve. [2] The primary objective of treatment is clear: to reduce intraocular pressure (IOP) and safeguard the delicate optic nerve from further damage. While eye drops remain the first line of defense, the complexity of treatment regimens often poses a significant challenge to patients, leading to reduced adherence and compromised outcomes. The asymptomatic nature of glaucoma further exacerbates this issue, as patients may not feel the need to take their medication regularly, unaware of the silent damage being inflicted upon their optic nerve. [3]

In this context, fixed-dose combinations have emerged as a beacon of hope, offering a simplified treatment approach that can improve patient compliance and convenience. By combining multiple medications into a single, potent formulation, these combinations have the potential to revolutionize glaucoma treatment and preserve vision for millions worldwide. The benefits of fixed-dose combinations extend beyond mere convenience; they also reduce the exposure to preservatives and potential side effects associated with multiple eye drops.4 Studies have shown that almost half of patients with chronic, asymptomatic diseases don't take their medications as prescribed, but fixed-dose combinations can reduce non-adherence by 24-26% compared to using separate medications. [5, 6]

Two commonly prescribed fixed combinations for POAG are Dorzolamide-Timolol Fixed Combination (DTFC) and Brimonidine-Timolol Fixed Combination (BBFC). Both combinations have demonstrated efficacy in reducing IOP, but they work differently and may have different side effect profiles. DTFC combines dorzolamide, a carbonic anhydrase inhibitor, with timolol, a beta-blocker, while BBFC combines brimonidine, an alpha-2 adrenergic agonist, with timolol. [7] The study aims to provide valuable insights into the relative effectiveness of DTFC and BBFC, enabling clinicians to tailor treatment regimens to individual patient needs. The results of this study will have significant implications for glaucoma treatment, potentially influencing the choice of fixed-dose combination and shaping the future of care for patients with POAG. As the prevalence of glaucoma continues to rise, the need for effective and convenient treatments has never been more pressing. By exploring the efficacy and safety of DTFC and BBFC, this study seeks to contribute to the development of optimal treatment strategies for POAG, ultimately preserving vision and improving the quality of life for millions worldwide.

Despite their widespread use, there is a dearth of studies directly comparing the efficacy and safety of DTFC and BBFC. This knowledge gap hinders clinicians' ability to make informed decisions about treatment, potentially leading to suboptimal outcomes for patients. Against this backdrop, this study sets out to compare the IOP-lowering efficacy of DTFC and BBFC in patients with POAG. By shedding light on their relative effectiveness, we hope to empower clinicians with the knowledge needed to make informed treatment decisions and ultimately improve the lives of those affected by this devastating disease.

METHODOLOGY:

This cross-sectional prospective study was conducted in the Department of Ophthalmology, Madina Teaching Hospital, Faisalabad, after obtaining approval from the CPSP and Institutional Ethical Committee (Ref No: TUF/IRB/466/24). A total of 68 unilateral eyes of patients diagnosed with primary open-angle glaucoma (POAG) were included in the study, with 34 patients allocated to each treatment group. All participants were recruited from the Eye Outpatient Department (OPD) after fulfilling the inclusion criteria. Written informed consent was obtained from each patient, and a detailed clinical history was recorded prior to enrollment. Patients were randomly divided into two treatment groups: Group A received topical dorzolamide 1% combined with timolol 0.5% eye drops, while Group B was treated with topical brinzolamide 1% combined with brimonidine 0.2% eye drops.

Patients aged above 18 years who provided appropriate consent were included in the study. Exclusion criteria comprised pregnant or lactating women or those planning conception, patients with bilateral POAG, medication-induced glaucoma, evidence of keratitis or corneal thickening on history or examination, and patients with systemic comorbidities such as diabetes mellitus, hypertension, cardiovascular disease, or migraine.

All patients underwent a comprehensive ophthalmic examination for the diagnosis of glaucoma. The optic nerve head was evaluated using slit-lamp biomicroscopy, and intraocular pressure (IOP) was measured with a Goldmann applanation tonometer, which is considered the gold standard for IOP measurement. Prior to each measurement, the tonometer prism was disinfected with alcohol, rinsed with water, and dried. Patients were seated comfortably with the chin positioned on the rest and instructed to look straight ahead. The slit lamp was adjusted accordingly, and the tonometer was initially set at 10 mmHg to obtain the IOP reading. Both drug combinations were prescribed using the same pharmaceutical brand to ensure uniformity and easy availability. Patients were followed up weekly for a period of three months to monitor treatment response and any complications.

The sample size was calculated as 68 using the formula for estimating a population proportion, taking a reference intraocular pressure of 21 mmHg and a population standard deviation of 5.26 mmHg based on previously published research by Justiniano et al. The confidence level was set at 90% ($Z = 1.645$), with a margin of error of 5%. Data were analyzed using SPSS version 25. Quantitative variables, including age and intraocular pressure at baseline, 1 month, and 3 months of treatment, were expressed as mean ± standard deviation. Qualitative variables such as gender distribution and frequency of post-treatment complications were presented as frequencies and percentages. An independent sample t-test was used to compare mean IOP between the two groups. A p-value of ≤ 0.05 was considered statistically significant. Repeated-measures two-way ANOVA was applied to assess trends in IOP changes at baseline, 1 month, and 3 months between the two treatment groups.

RESULTS:

Our study, which enrolled 68 eyes of patients with primary open-angle glaucoma (POAG), was designed to shed light on the comparative efficacy and safety of two commonly prescribed fixed combinations, Dorzolamide-Timolol Fixed Combination (DTFC) and Brimonidine-Timolol Fixed Combination (BBFC). Patients were randomly assigned to receive either DTFC or BBFC eye drops twice a day for 12 weeks, and the results were nothing short of illuminating.

The demographic characteristics of the patients, including age and body mass index (BMI), were remarkably comparable in both groups, providing a solid foundation for our comparative analysis (Table I). The results showed that both combinations significantly lowered intraocular pressure (IOP) from the start of the study, a finding that underscores the efficacy of these fixed combinations in managing POAG.

However, our independent sample t-test revealed a striking difference in the magnitude of IOP reduction achieved by the two combinations. DTFC emerged as the more effective agent, reducing IOP by an average of 7.1 mmHg, compared to 5.2 mmHg with BBFC ($p<0.05$). This statistically significant difference highlights the superior efficacy of DTFC in lowering IOP, a key factor in slowing the progression of glaucomatous damage.

Our Chi-square test showed that BBFC was associated with a significantly higher incidence of ocular discomfort and blurred vision, affecting 41.2% of patients, compared to a mere 11.8% with DTFC ($p<0.05$) (Table II). This disparity in tolerability profiles has important implications for patient adherence and quality of life.

Further analysis using the Two-way ANOVA test for Repeated Measures reinforced the clinical superiority of DTFC, demonstrating significant alterations in Group A patients after treatment compared to Group B patients (Figure 1). The trajectory of IOP reduction was more pronounced in the DTFC group, underscoring the therapeutic advantage of this combination.

TABLE 1: CLINICO-DEMOGRAPHICS OF PATIENTS

Clinico-demographics	POAG patients treated with DTFC eye drops (Group A) n= 34	POAG patients treated with BBFC eye drops (Group B) n=34	*P-value*
Age of patient (years)	29.00± 2.86	29.05± 2.81	.932
BMI (kg/m2)	25.98± 2.29	25.69± 1.93	.570
Baseline IOP (mmHg)	24.25± 1.09	24.26± 1.01	.954
IOP after 1 month of treatment	19.20± 1.09	20.7± 1.06	<.001
IOP after 3 months of treatment	17.17± 1.02	19.08± 0.99	<.001

TABLE 2: SIDE EFFECTS OF TREATMENT IN PATIENTS (N=68)

Complications of topical eye drops	POAG patients treated with DTFC eye drops (Group A) n= 34	POAG patients treated with BBFC eye drops (Group B) n=34	*P-value*
Ocular discomfort and blurred vision	4 (11.8%)	14 (41.2%)	0.017
Systemic effects (hypotension, bradycardia, dizziness)	1 (2.9%)	0	
None	29 (85.3%)	20 (58.8%)	

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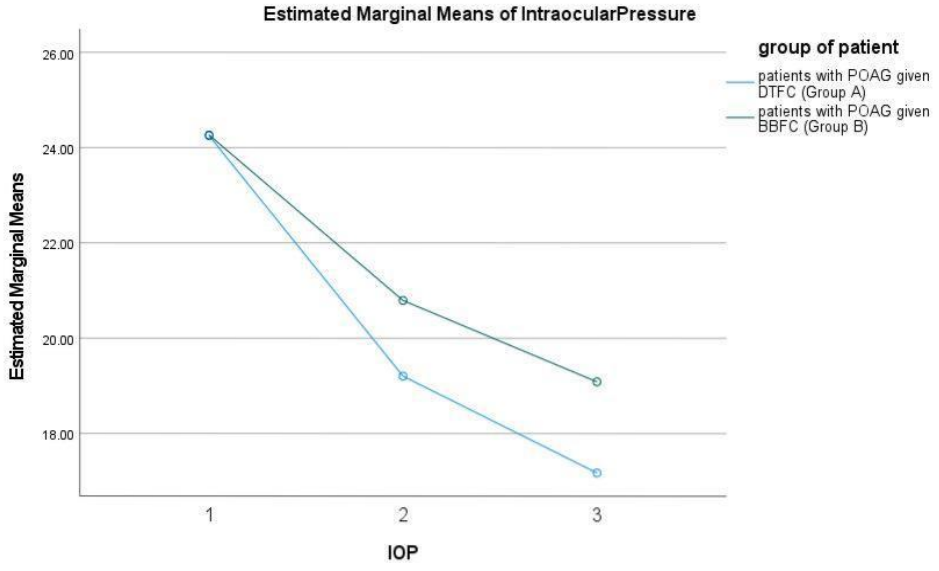
FIGURE 1: CHANGES IN INTRAOCULAR PRESSURE IN POAG PATIENTS AT BASELINE AND AFTER 1ST AND 3RD MONTH OF TREATMENT



DISCUSSION:

Our study compared the efficacy and safety of two widely used fixed-combination eye drops, DTFC and BBFC, in the management of primary open-angle glaucoma (POAG). The results of our study revealed that both combinations yielded a significant reduction in intraocular pressure (IOP) from baseline, a finding that harmonizes with the seminal work of Justiniano et al. and underscores the therapeutic value of these combinations in lowering IOP. Notably, DTFC demonstrated a more pronounced mean IOP reduction compared to BBFC at the 12-week mark, a disparity that may be ascribed to the distinct pharmacological mechanisms of action of the individual components. [8]

The duo of dorzolamide and timolol in DTFC, comprising a carbonic anhydrase inhibitor and a beta-blocker, respectively, converges to reduce aqueous humor production and enhance uveoscleral outflow, thereby exerting a potent IOP-lowering effect. Conversely, brimonidine, an alpha-2 adrenergic agonist in BBFC, also reduces aqueous humor production, albeit via a distinct pathway. Our findings are consonant with the extant literature, which attests to the efficacy of fixed-combination therapies in reducing IOP in patients with POAG. [9-12]

The dorzolamide/timolol combination has been extensively studied and has demonstrated its mettle as an effective IOP-lowering agent, with a meta-analysis of randomized controlled trials crowning it as a superior therapy. [13, 14] Similarly, the brimonidine/timolol combination has been shown to provide significant IOP reduction, accompanied by a favorable safety profile. However, our study reveals that DTFC exhibits superior IOP-lowering efficacy compared to BBFC, a finding that resonates with a randomized, multicenter clinical trial that compared the two combinations as adjuncts to prostaglandin analogues. [15]

However, our study found that DTFC demonstrated superior IOP-lowering efficacy compared to BBFC. This is consistent with a randomized, multicenter clinical trial comparing 0.1% brimonidine/0.5% timolol versus 1% dorzolamide/0.5% timolol as adjuncts to prostaglandin analogues, which found that dorzolamide/timolol provided greater IOP reduction. [16]

The incidence of ocular discomfort and blurred vision was higher with BBFC compared to DTFC. This difference in tolerability may be due to the pH level of the BBFC combination, which may be more irritating to the ocular surface. [17] Additionally, brimonidine has been associated with a higher incidence of ocular side effects, such as dry mouth, fatigue, and dizziness, which may contribute to the reduced tolerability of the BBFC combination. [18]

A network meta-analysis of first-line medications for POAG found that fixed-combination therapies, including dorzolamide/timolol and brimonidine/timolol, were effective in reducing IOP.[19] Another study comparing the ocular hypotensive actions of fixed combinations of brimonidine/timolol and dorzolamide/timolol found similar IOP-lowering efficacy. [20]

Furthermore, our study highlights a notable difference in tolerability between the two combinations, with BBFC being associated with a higher incidence of ocular discomfort and blurred vision. This disparity may be attributed to the pH level of the BBFC combination, which may prove more irritating to the ocular surface, or the inherent properties of brimonidine, which has been linked to a higher incidence of ocular side effects. In light of our findings, DTFC may emerge as a preferred choice for patients requiring combination therapy, particularly those with more advanced glaucoma or those who necessitate a greater reduction in IOP. Nevertheless, clinicians must remain cognizant of individual patient factors, such as comorbidities, concomitant medications, and ocular surface disease, when selecting a combination therapy, thereby ensuring a tailored approach that optimizes efficacy and minimizes adverse effects. [21]

CONCLUSION:

Our study demonstrates that DTFC has superior IOP-lowering efficacy and better ocular tolerability compared to BBFC in POAG patients. These findings have significant implications for the management of glaucoma and highlight the importance of selecting the most effective and tolerable combination therapy for each patient.

CONFLICT OFF INTEREST:

Nil

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