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ORIGINAL ARTICLE

Dorzolamide / timolol and brinzolamide / brimonidine fixed combination topical drug therapy tn the management of intraocular pressure in primary open angle glaucoma.

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ABSTRACT… Objective: To compare the mean change in intraocular pressure (IOP) achieved with dorzolamide/timolol versus brinzolamide/brimonidine fixed combination topical therapy in patients diagnosed with primary open-angle glaucoma (POAG). **Study Design:** Randomized Control Trial. **Setting:** Department of Ophthalmology, Mayo Hospital, Lahore. **Period:** May'2024 to October'2024. **Methods:** A total of 60 cases aged 40–70 years with primary open-angle glaucoma were included and randomly assigned to receive either dorzolamide/timolol (Group X) or brinzolamide/brimonidine (Group Y). IOP was measured weekly for four weeks using Goldman tonometry, with the primary outcome being mean IOP reduction at week four. **Results:** The mean baseline IOP was comparable in both groups (p=0.947). After 4 weeks, IOP reduction was significantly greater in Group Y (6.84 ± 2.34 mmHg) than Group X (5.37 ± 2.16 mmHg) (p=0.014). Stratified analysis showed a significant IOP reduction in older patients (56–70 years) and in females treated with brinzolamide/brimonidine (p=0.006 and p=0.049, respectively). **Conclusion:** Brinzolamide/brimonidine fixed combination therapy was more effective in reducing IOP than dorzolamide/timolol, especially in older patients and females, suggesting a potential demographic influence on drug response.

Key words: Primary Open-angle Glaucoma, Intraocular Pressure, Dorzolamide/timolol, Brinzolamide/brimonidine.

INTRODUCTION

Chronic primary open-angle glaucoma (POAG) causes optic nerve degeneration, increased intraocular pressure (IOP), and peripheral vision loss. Primary open-angle glaucoma is a major cause of blindness in Pakistan.[1] Age, family history of glaucoma, race, and systemic diseases including diabetes and hypertension can increase POAG risk. Regular eye exams and screenings are necessary for early detection and treatment of POAG, which is typically asymptomatic.[2-3]

The timing of initiating treatment for open-angle glaucoma remains a subject of debate. Certain practitioners treat elevated IOP once it surpasses 21 mmHg, while others delay intervention until there is clear evidence of optic nerve damage or a high likelihood of progression.[4] Treatment is warranted when structural damage from glaucoma is observed or when elevated IOP poses a threat to optic nerve health.[5] To evaluate both response and adverse effects, some physicians opt for a monocular trial, prescribing medication to one eye initially. The target IOP should be individually determined based on disease status, initial pressure readings, patient age, race, family history, and corneal biomechanical characteristics.[6-7]

Glaucoma causes most irreversible blindness worldwide. Medication, incisional surgery, or laser trabeculoplasty (LTP) can lower (IOP), the sole modifiable risk factor. Early acute IOP increase after LTP is prevalent. Temporary IOP rises can damage the optic nerve, exacerbate glaucoma, and cause permanent vision loss.

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Acetazolamide, apraclonidine, brimonidine, dipivefrin, pilocarpine, and timolol are indicated for postoperative IOP spikes and pain. Others have found that early postoperative IOP rise occurs regardless of perioperative glaucoma medicines.[8]

A separate study found that the fixed-dose combination of brinzolamide and brimonidine is a safe and effective alternative to beta-blocker-based therapy, particularly in patients with coexisting medical conditions, owing to its antihypertensive effects. After a 4-week follow-up, the mean reduction in morning IOP was 4.3 ± 2.3 mm Hg in the DT group and 7.0 ± 2.2 mm Hg in the BB group.[9] Depression frequently affects individuals diagnosed with or suspected of having glaucoma. Incorporating mental health screening and affordable treatment options into glaucoma-screening initiatives could enhance overall patient care.[10-11]

The rationale of this study is that no local data is available regarding this topic. So I have designed this study to determine the efficacy of dorzolamide/timolol and brinzolamide/brimonidine fixed combination topical drug therapy in the management of primary open-angle glaucoma. The drugs with better outcome and improved efficacy will be recommended for routine use. This will help in improving the time of recovery and decreasing morbidity associated with this disease, thus improving quality of life.

METHODS

This randomized controlled trial was conducted at the Department of Ophthalmology, Mayo Hospital, Lahore, over a period of six months (May'2024 to October'2024), following the approval of the research synopsis by the institutional review board (Reference No: EYE-III/147/MH, Dated: 09-05-2025). The study aimed to compare the mean change in IOP achieved with dorzolamide/timolol versus brinzolamide/brimonidine fixed combination topical therapy in patients diagnosed with primary open-angle glaucoma (POAG).

A total of 60 patients were enrolled in the study, with 30 patients allocated to each treatment group. The sample size was calculated using the WHO sample size calculator, based on expected mean IOP reductions of 4.8 ± 2.3 mmHg in the dorzolamide/timolol group and 7.0 ± 2.2 mmHg in the brinzolamide/brimonidine group, with a 95% confidence level and 90% power. Patients were recruited through non-probability consecutive sampling.

Patients aged 40 to 70 years of either gender who fulfilled the diagnostic criteria for primary open-angle glaucoma were included. Diagnosis was confirmed by an unbiased consultant ophthalmologist based on open angles seen on gonioscopy, cup-to-disc ratio greater than 0.5, IOP above 21 mmHg, characteristic visual field defects on perimetry, and otherwise healthy ocular status. Patients were excluded if they had undergone previous ocular surgeries, had other types of glaucoma, presented with IOP exceeding 36 mmHg, were pregnant, had Schaffer angle grade <2, a cup-to-disc ratio >0.8, severe central visual field loss, a history of chronic or recurrent inflammatory eye disease, ocular trauma, retinal disease, or any systemic condition affecting compliance. Patients with contraindications to beta-blockers were also excluded from the dorzolamide/timolol group. After obtaining informed consent, patients were randomly allocated to one of the two treatment arms. Group X received dorzolamide/timolol fixed combination topical therapy, while Group Y was treated with brinzolamide/brimonidine fixed combination drops. All participants underwent a complete ophthalmic examination before starting treatment. Intraocular pressure was measured using Goldmann applanation tonometry at baseline and then weekly for four consecutive weeks. The primary outcome was the mean reduction in IOP between the baseline and the fourth week. Data were analyzed using SPSS version 23. Quantitative variables such as age, baseline IOP, and change in IOP were presented as mean ± standard deviation. Qualitative variables such as gender were summarized using frequencies and percentages. The mean IOP reduction between the two groups was compared using an independent samples t-test. Stratification was performed for effect modifiers

such as age and gender, and post-stratification t-tests were applied to assess their influence on the outcome.

RESULTS

This table summarizes the demographic profile of the 60 patients enrolled in the study. Age distribution was nearly even, with 48.3% (n=29) of participants aged between 40 and 55 years, and 51.7% (n=31) aged between 56 and 70 years. The overall mean age was 55.57 ± 8.89 years. Regarding gender, there were slightly more males (55.0%, n=33) than females (45.0%, n=27) in the study population.

This table compares the mean IOP values at baseline and after four weeks between the two treatment groups: Group X (dorzolamide/timolol) and Group Y (brinzolamide/brimonidine). At baseline, the mean IOP was similar in both groups (25.99 ± 2.28 mmHg in Group X vs. 26.03 ± 2.26 mmHg in Group Y, p = 0.947). After four weeks, IOP decreased in both groups, with Group Y showing a slightly greater reduction (mean Week 4 IOP: 19.18 ± 2.98 mmHg) compared to Group X (20.62 ± 3.30 mmHg), (p = 0.083). However, the IOP reduction was significantly greater in Group Y (6.84 ± 2.34 mmHg) than in Group X (5.37 ± 2.16 mmHg), with a p-value of 0.014.

This table presents a subgroup analysis of IOP outcomes according to age. Among patients aged 40–55 years, baseline IOP and Week 4 IOP were slightly higher in the brinzolamide/brimonidine group. IOP reduction was slightly greater in Group Y (6.96 ± 2.81 mmHg) compared to Group X (6.05 ± 2.42 mmHg) (p = 0.359). In contrast, among patients aged 56–70 years, there was a statistically significant difference in both Week 4 IOP and IOP reduction. Group Y had a significantly lower Week 4 IOP (18.25 ± 2.62 mmHg) compared to Group X (21.57 ± 3.00 mmHg), with a p-value of 0.003. Additionally, Group Y achieved a significantly higher IOP reduction (6.72 ± 1.86 mmHg) compared to Group X (4.78 ± 1.78 mmHg), with a p-value of 0.006.

This table compares IOP changes between the two treatment groups stratified by gender. Among male patients, baseline and Week 4 IOP values were similar between groups. Although Group Y had a slightly higher IOP reduction (6.83 ± 2.26 mmHg) than Group X (5.66 ± 2.42 mmHg), (p = 0.162). Among female patients, however, a significant difference was observed in IOP reduction. Group Y females had a significantly greater reduction in IOP (6.86 ± 2.56 mmHg) compared to Group X females (5.08 ± 1.91 mmHg), with a p-value of 0.049, suggesting that brinzolamide/brimonidine may be more effective among female patients.

Variable	Group	Count	Percent
Age	40–55	29	48.3%
	56–70	31	51.7%
	Mean ± SD	55.57 ± 8.89	
Gender	Male	33	55.0%
	Female	27	45.0%

Table-I. Demographics of the (N=60) Table-I. Demographics of the (N=60)

Group		N	Mean	Std. Deviation	P-Value
Baseline IOP	X	30	25.99	2.28	0.947
	Y	30	26.03	2.26	
Week 4 IOP	X	30	20.62	3.30	0.083
	Y	30	19.18	2.98	
IOP Reduction	X	30	5.37	2.16	0.014
	Y	30	6.84	2.34	

Table-II. Comparison of mean change in IOP achieved in both groups (N=60)

DISCUSSION

The present study compared the efficacy of two fixed drug combinations—dorzolamide/timolol (Group X) and brinzolamide/brimonidine (Group Y)—in reducing IOP among patients with primary open-angle glaucoma (POAG). Overall findings demonstrated that both combinations significantly reduced IOP over a four-week period; however, the brinzolamide/brimonidine group showed a statistically greater mean reduction in IOP, particularly among females and in the older age group (56–70 years). These findings are largely consistent with prior studies, while also adding nuanced insights regarding demographic subgroups.

Age			N	Mean	Std. Deviation	P-Value
40-55	Baseline IOP	X	14	25.57	1.95	0.059
		Y	15	27.07	2.14	
	Week 4 IOP	X	14	19.53	3.41	0.629
		Y	15	20.12	3.10	
	IOP Reduction	X	14	6.05	2.42	0.359
		Y	15	6.96	2.81	
56-70	Baseline IOP	X	16	26.35	2.54	0.102
		Y	15	24.98	1.92	
	Week 4 IOP	X	16	21.57	3.00	0.003
		Y	15	18.25	2.62	
	IOP Reduction	X	16	4.78	1.78	0.006
		Y	15	6.72	1.86	

Table-III. Comparison of mean change in IOP achieved in both groups according to age (N=60)

Gender			N	Mean	Std. Deviation	P-Value
Male	Baseline IOP	X	15	26.14	2.34	0.789
		Y	18	25.90	2.56	
	Week 4 IOP	X	15	20.48	3.62	0.207
		Y	18	19.08	2.62	
	IOP Reduction	X	15	5.66	2.42	0.162
		Y	18	6.83	2.26	
Female	Baseline IOP	X	15	25.84	2.28	0.651
		Y	12	26.21	1.82	
	Week 4 IOP	X	15	20.75	3.08	0.281
		Y	12	19.34	3.57	
	IOP Reduction	X	15	5.08	1.91	0.049
		Y	12	6.86	2.56	

Table-IV. Comparison of mean change in IOP achieved in both groups according to gender (N=60)

A notable finding in the current study is the significantly greater IOP reduction in Group Y (6.84 ± 2.34 mmHg) compared to Group X (5.37 ± 2.16 mmHg, p = 0.014), supporting the superior efficacy of the brinzolamide/brimonidine combination. This aligns with a study by Davawala et al. (2024)[12], which found a significantly greater IOP reduction with brimonidine-timolol fixed combination (BT FDC) versus timolol monotherapy over ten weeks. Similarly, Padala et al (2020)[13] compared brinzolamide/timolol with brinzolamide/brimonidine and found both combinations effective (p = 0.7100), suggesting potential variability based on population characteristics. Interestingly, our findings differ from the meta-analysis by Cheng et al (2012)[14], which concluded that dorzolamide/timolol achieved a 29.9% mean diurnal IOP reduction compared to 28.1% with brimonidine/timolol, indicating slightly higher efficacy of the former. This discrepancy might be attributed to differences in study populations, duration, and drug combinations used. Notably, Cheng's[14] analysis did not include brinzolamide/brimonidine, limiting direct comparisons.

Subgroup analysis by age revealed that patients aged 56–70 years showed significantly greater IOP reduction in the brinzolamide/brimonidine group (6.72 ± 1.86 mmHg) compared to dorzolamide/timolol (4.78 ± 1.78 mmHg, p = 0.006), and also had significantly lower Week 4 IOP (p = 0.003). These findings are consistent with the study by Konstas et al[15] which demonstrated sustained 24-hour IOP-lowering efficacy with brimonidine-containing combinations in older adults. The enhanced performance of Group Y in older patients could reflect the synergistic action of α2-agonist and carbonic anhydrase inhibition, offering better control during nocturnal hours when aqueous production is naturally reduced. Gender-based analysis showed that females in Group Y experienced significantly greater IOP reduction than those in Group X (6.86 ± 2.56 mmHg vs. 5.08 ± 1.91 mmHg, p = 0.049). While no prior study has explicitly explored gender differences in response to fixed combinations, this observation may merit further investigation. Potential explanations could include hormonal variations influencing ocular physiology or differential pharmacodynamic responses between sexes. Our results also correspond with the findings of Galose et al[16] who reported that brinzolamide/timolol and dorzolamide/timolol both produce substantial IOP reductions, though tolerability profiles may differ, with brinzolamide combinations often being better accepted due to reduced ocular discomfort. Likewise, the Turkish study on brinzolamide/brimonidine noted strong efficacy and good patient compliance, especially in maximum medical therapy settings.

From a clinical standpoint, these results reinforce the utility of brinzolamide/brimonidine fixed combinations as an effective option for patients requiring dual-agent therapy, particularly those who may not tolerate beta-blockers well or in whom maximal pressure reduction is desired. The higher IOP-lowering potential observed in older adults and females further supports tailored treatment approaches based on patient demographics. However, some limitations should be acknowledged. The follow-up period was limited to four weeks, precluding assessment of long-term efficacy or adherence. Furthermore, the sample size, though adequate for primary analysis, was modest for subgroup evaluations, which may limit generalizability. Future studies should include longer follow-up and larger populations to validate demographic-specific differences and assess safety profiles.

CONCLUSION

Our findings suggest that brinzolamide/brimonidine fixed combination provides significantly greater IOP reduction compared to dorzolamide/timolol, particularly in older and female patients. These results add to the growing body of evidence supporting its role as a potent alternative in the management of POAG.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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1	**Fauzan Ayub:** Data collection, analysis and paper writing.
2	**Sidrah Latif:** Discussion writing, review of manuscript.
3	**Hafsa Latif:** Data collection, paper writing.
4	**Sidra Ahsan Shah:** Review of manuscript.
5	**Saman Ali:** Literature review, data entry.
6	**Muhammad Qasim Yazar:** Data analysis, review of manuscript.