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Original Research Article

A Comparative Observational Study on the Safety and Efficacy of Brimonidine Tartarate Versus Timolol Maleate in Glaucoma Patients

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Conflict of interest: Nil

Abstract

Aim: To compare the therapeutic effectiveness and safety profile of Brimonidine versus Timolol in glaucoma patients attending the ophthalmology outpatient department.

Objectives:

1. To evaluate and compare the efficacy of brimonidine tartrate and timolol maleate in glaucoma patients by assessing reduction in intraocular pressure using Goldmann Applanation Tonometry (GAT) and changes in visual field parameters including Mean Deviation (MD), Pattern Standard Deviation (PSD), Visual Field Index (VFI), and Glaucoma Hemifield Test (GHT).
2. To assess and compare the safety and tolerability of brimonidine and timolol using Conjunctival Hyperaemia Grading (CHG) Scale, and Ocular Symptoms Score (OSS).
3. To evaluate structural optic nerve damage and disease progression by measuring the Cup–Disc Ratio (CDR).
4. To assess patient adherence to antiglaucoma therapy using the Medication Adherence Rating Scale (MARS-10).

Methodology: It is a prospective comparative observational study. A total of 150 patients diagnosed with glaucoma attending the Ophthalmology Outpatient Department at Government General Hospital, Guntur were included in the study. Patients were divided into two groups: Brimonidine (n=75) and Timolol (n=75). Data were collected using a structured data collection form, including demographic details, clinical parameters, intraocular pressure measurements, visual field analysis, and adverse drug reactions.

Results: A total of 150 patients were included in the study, with 75 patients in each group. Both Brimonidine and Timolol showed significant reduction in intraocular pressure (IOP) within groups. However, when compared between groups, Brimonidine demonstrated a statistically significant greater reduction in IOP than Timolol, particularly in post-treatment values and percentage IOP reduction. Structural assessment using cup–disc ratio also showed significantly better optic nerve preservation in the Brimonidine group. Visual field parameters were largely comparable between the two groups, with only selective parameters showing significant differences. Medication adherence was similar in both groups with no statistically significant difference. Ocular symptoms and conjunctival hyperemia were more frequently observed in the Brimonidine group, although most were mild to moderate in severity.

Conclusion: Both Brimonidine and Timolol are effective in reducing intraocular pressure in patients with glaucoma. However, Brimonidine demonstrated significantly greater efficacy in lowering IOP and showed better outcomes in optic nerve head preservation compared to Timolol. Despite a higher incidence of mild ocular side effects, Brimonidine may be considered a more effective therapeutic option for achieving stronger disease control. The choice of treatment should be individualized based on patient tolerance, safety profile, and clinical condition, with careful consideration of the balance between efficacy and tolerability.

Keywords: Glaucoma, Intraocular Pressure Reduction, Brimonidine Tartrate, Timolol Maleate, Optic Nerve Protection, Visual Field Analysis, Ocular Tolerability, Adverse Drug Reactions.

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Introduction

Glaucoma is a chronic, progressive optic neuropathy characterized by degeneration of retinal ganglion cells and damage to the optic nerve head, leading to irreversible visual field loss. It is one of the leading causes of irreversible blindness worldwide and poses a major public health challenge due to its asymptomatic nature in early stages.[1,2,3,4]

The most commonly prescribed two anti-Glaucoma drugs are:

Brimonidine (Alpha-2 Adrenergic Agonists): It is also a neuroprotective and generally well-tolerated, though side effects such as ocular allergy and dryness can occur.

Dose: Brimonidine tartrate 0.2% ophthalmic solution — 1 drop in the affected eye(s) three times daily, about every ~8 hours.

Drug Class: Alpha-2 Adrenergic Agonist ciliary body of the eye. This leads to Reduction in aqueous humour production and Increase in uveoscleral outflow

Indications: Primary open-angle glaucoma, Ocular hypertension, Adjunctive therapy in patients inadequately controlled with other antiglaucoma medications [11,12,14]

Timolol (Beta-Blockers): It is highly effective but may cause systemic adverse effects like bradycardia, hypotension, bronchospasm—especially in susceptible patients.

Dose: Timolol maleate 0.5% ophthalmic solution — 1 drop in the affected eye(s) twice daily.

Drug Class: Non-selective Beta-Adrenergic Blocker

Mechanism of Action: Timolol blocks beta-1 and beta-2 adrenergic receptors in the ciliary epithelium, leading to Decreased aqueous humour production and no significant effect on aqueous outflow. This results in a sustained reduction in intraocular pressure.

Indications: Primary open-angle glaucoma, Ocular hypertension, Secondary glaucoma. [6,7,13]

Materials and Methods

Study Design: Prospective Comparative Observational Study.

Study Duration: 5 months (November2025 - March 2026).

Study Site: Department of Ophthalmology, Government General Hospital, Guntur.

Sample Size: Approximately 150 patients (75 in each group).

Study Methodology: A total of 150 patients diagnosed with glaucoma or ocular hypertension and fulfilling the inclusion criteria were enrolled during the study period.

Patients were divided into two equal groups based on the antiglaucoma medication prescribed by the treating ophthalmologist:

Group A (Brimonidine group): 75 patients
Group B (Timolol group): 75 patients

This allocation reflected real-world prescribing practices and no randomization or intervention was done by the investigators.

Inclusion Criteria

- Diagnosed cases of primary open-angle or angle-closure glaucoma.
- Patients aged ≥18 years.
- Patients on monotherapy with either brimonidine or timolol for at least 4 weeks.
- Patients willing to give informed consent and comply with follow-up.

Exclusion Criteria

- Patients on combination therapy or using any other antiglaucoma medications.
- History of ocular surgery within the past 3 months.
- Known allergy to brimonidine or timolol.
- Pregnant or breastfeeding women.
- Patients unwilling to participate.
- Patients with severe systemic illness (e.g., COPD, heart block—contraindicated for timolol).

Scales and Assessment Tools Used in the Study: This study utilized a combination of objective clinical measurements and validated assessment scales to comprehensively evaluate the efficacy, safety, tolerability, and compliance of Brimonidine tartrate and Timolol maleate in glaucoma patients.

1. Intraocular Pressure (IOP)

- IOP is the pressure inside the eye caused by the balance between: Aqueous humor production and Aqueous humor outflow
- Its Normal Range is:10–21 mmHg
- IOP was measured using Goldmann Applanation Tonometry (GAT), the gold-standard method for IOP assessment. Baseline IOP and follow-up IOP values were recorded to determine treatment efficacy.
- A reduction in IOP from baseline was considered the primary marker of therapeutic success. [1,2]

2. CUP–DISC Ratio (CDR)

- The Cup-to-Disc Ratio (CDR) is the proportion of the optic cup diameter to the optic disc diameter, assessed during fundus examination.
- The cup–disc ratio was used as a structural indicator of optic nerve damage. Normal CDR values were ≤0.3, while values ≥0.7 suggested glaucomatous damage.
- Progression was suspected when an increase in CDR or asymmetry >0.2 between eyes was observed. [8]

3. Visual Field Assessment

- Visual field evaluation was performed using the Humphrey Visual Field Analyzer (24-2) to assess functional vision loss.
- **Glaucoma Hemifield Test (GHT)** - categorize results as within normal limits, borderline, or outside normal limits. (Detects asymmetry between superior and inferior visual field hemifields)
- **Mean Deviation (MD) –** it represents the overall average difference between the patient's visual field sensitivity and age-matched normal values. it reflects the overall severity of visual field loss.
- **Pattern Standard Deviation (PSD) -** identifies localized visual field defects. [Low PSD → Normal or advanced uniform field loss, High PSD → Localized defects (glaucoma characteristic)]
- **Visual Field Index (VFI)** - express the functional vision as a percentage, with decreasing values indicating disease progression.
- These parameters together provided an assessment of disease severity and stability during treatment. [5,9]

4. Conjunctival Hyperaemia Grading Scale

- Ocular surface redness was assessed using a clinician-graded conjunctival hyperaemia scale (0–3). Higher grades indicated poorer ocular tolerability and were used as a safety outcome for topical therapy.
- It helps to compare ocular tolerability between brimonidine and timolol

5. Ocular Symptoms Score: Patients self-reported common ocular symptoms such as burning, dryness, itching, watering, foreign body sensation, and redness. Each symptom was graded from 0 (absent) to 3 (severe), with a total score ranging from 0 to 18. Higher scores reflected greater ocular discomfort and reduced tolerability.

6. WHO–UMC Causality Assessment Scale

- The World Health Organization–Uppsala Monitoring Centre (WHO–UMC) Causality Assessment Scale was used to systematically evaluate the relationship between the study drugs (brimonidine and timolol) and any observed adverse drug reactions (ADRs) during the study period.
- This scale strengthens the safety analysis by providing a standardized and internationallyaccepted method for ADR assessment.

7. Medication Adherence Rating Scale (MARS-10)

- Patient compliance was assessed using the Medication Adherence Rating Scale (MARS), a self-reported questionnaire.
- Higher scores indicated better adherence to prescribed antiglaucoma therapy, which is essential for long-term disease control.

Drug Therapy Details: Details of current treatment with Brimonidine or Timolol were documented, including dosage, frequency, duration of use, adherence, and any reported side effects.

Baseline IOP and Follow-up IOP

- Intraocular pressure (IOP) was collected from case files at baseline and reassessed using standard clinical methods to compare treatment response between the two drug groups.
- Formula: IOP Reduction (%) = (Baseline IOP − Follow-up IOP) / Baseline IOP × 100

Observation and Results

Demographic Distribution of Study Population

1. Distribution Based on Age Group

Table 1: Distribution based on age group

Age Group (years)	Brimonidine (n=75)	Timolol (n=75)	Total (n=150)	Percentage (%)
18-30	5	4	9	6%
31-40	8	7	15	10%
41-50	18	17	35	23.3%
51-60	22	23	45	30%
61-70	15	16	31	20.7%
71-80	7	8	15	10%
Total	75	75	150	100%

Interpretation: Majority of patients belonged to the 51–60 years age group, indicating higher prevalence of glaucoma in middle-aged and elderly population. Both Brimonidine and Timolol groups showed similar distribution across age categories.

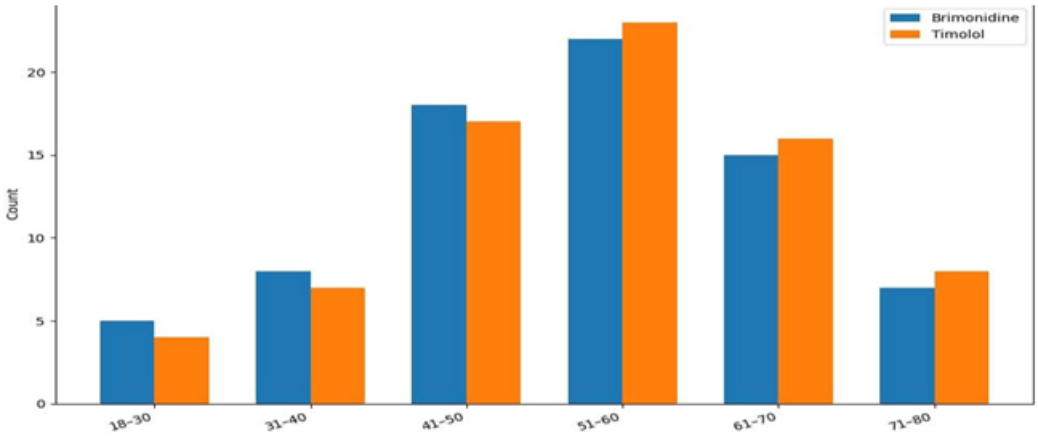

Figure 1: Distribution based on age group

2. Distribution Based on Gender

Table 2: Distribution based on gender

Gender	Brimonidine(n=75)	Timolol (n=75)	Total(n=150)	Percentage (%)
Male	43	44	87	58%
Female	32	31	63	42%
Total	75	75	150	100%

Interpretation: Male patients were more prevalent than females in both groups. The gender distribution was comparable between Brimonidine and Timolol groups.

Figure 2: Distribution based on gender

3. Distribution Based on Type of Glaucoma

Table 3: Distribution based on type of glaucoma

Type of Glaucoma	Brimonidine (n=75)	Timolol (n=75)	Total (n=150)	Percentage (%)
Primary Open Angle Glaucoma	50	48	98	65.3%
Angle Closure Glaucoma	16	18	34	22.7%
Secondary Glaucoma	9	9	18	12%
Total	75	75	150	100%

Interpretation: Primary Open-Angle Glaucoma (POAG) was the most common type in both groups. The distribution of glaucoma types was comparable between the two treatment groups.

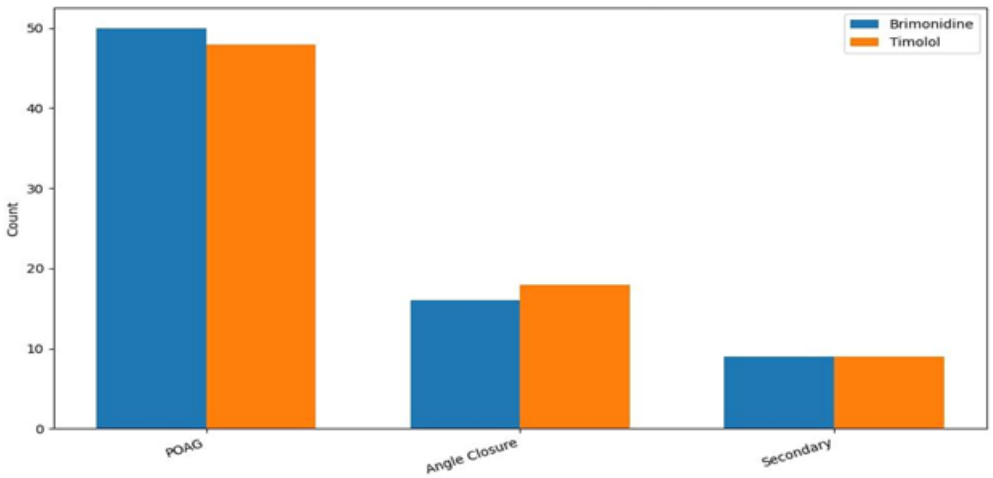

Figure 3: Distribution based on type of glaucoma

Clinical Outcomes

1a) IOP Reduction – Goldmann Applanation Tonometry (GAT)

Table 4: Baseline and Post-Treatment GAT Values (mmHg)

Parameter	Brimonidine (Right eye)	Timolol (Right eye)	Brimonidine (Left eye)	Timolol (Left eye)
Baseline	17.75	18.42	17.67	18.27
After Treatment	13.36	15.64	13.20	15.48

Table 5: Percentage Reduction in NCT

Parameter	Brimonidine (%)	Timolol (%)
Right Eye	24.65	15.03
Left Eye	25.21	15.25

1b) IOP Reduction – Non-Contact Tonometry (NCT)

Table 6: Baseline and Post-Treatment NCT Values (mmHg)

Parameter	Brimonidine (RE)	Timolol (RE)	Brimonidine (LE)	Timolol (LE)
Baseline	22.20	20.96	20.56	20.58
After Treatment	16.57	17.76	15.33	17.67

Table 7: Percentage Reduction in NCT

Parameter	Brimonidine (%)	Timolol (%)
Right Eye	25.91	15
Left Eye	25.44	14.14

2. Cup–Disc Ratio (CDR)

Table 8: Comparative Effectiveness of Cup–Disc Ratio

Parameter	Brimonidine	Timolol
Right Eye	0.70	0.75
Left Eye	0.69	0.75

3a) Glaucoma Hemifield Test (GHT)

Table 9: Evaluation of Visual Field Preservation Using GHT

GHT Category	Brimonidine n (%)	Timolol n (%)
Within Normal Limits	24 (32%)	18 (24%)
Borderline	19 (25.3%)	16(21.3%)
Outside Normal Limits	32 (42.7%)	41(54.7%)

3b) Mean Deviation (MD)

Table 10: Mean Deviation (MD)

Parameter	Brimonidine	Timolol
Right Eye	4.11	3.92
Left Eye	3.82	3.73

3c) Pattern Standard Deviation (PSD)

Table 11: Pattern Standard Deviation (PSD)

Parameter	Brimonidine	Timolol
Right Eye	3.42	3.43
Left Eye	3.31	3.01

3d) Visual Field Index (VFI)

Table 12: Comparative Effectiveness of VFI

Parameter	Brimonidine	Timolol
Right Eye	93.19	94.92
Left Eye	93.73	94.91

4. Conjunctival Hyperemia Grading Scale

Table 13: Comparison of Conjunctival Hyperemia Severity Between Treatment Groups

Grade of Hyperemia	Brimonidine (%)	Brimonidine (n)	Timolol (%)	Timolol (n)
No redness	58.9%	88	71.41%	107
Trace/ Very slight	25.5%	39	22.4%	34
Mild	11.8%	18	6.1%	9
Moderate	3%	5	0%	0
Total	100%	150	100%	150

5. Ocular Symptoms Score

Table 14: Comparative Distribution of Ocular Symptoms Between Brimonidine and Timolol Groups

Symptom	Timolol (%)	Timolol (n)	Brimonidine (%)	Brimonidine (n)
Burning sensation	~0%	0	~16.7%	25
Foreign body sensation	~6.7%	10	~0%	0
Dryness	~16.7%	25	~6.7%	10
Itching	~0%	0	~26.7%	40
Watering	~16.7%	25	~3.3%	5
Redness	~0%	0	~20%	30

6. WHO-UMC Scale

Causality Assessment of Adverse Drug Reactions

Table 15: Drug-wise Distribution of ADR Causality

Drug	Possible(n)	Probable/Likely (n)	Unlikely(n)	Total(n)
Brimonidine	4	3	2	9
Timolol	5	4	4	13
Total	9	7	6	22

7. Medication Adherence Rating Scale (MARS-10)

Table 16: Comparison of Medication Adherence (MARS-10) Between Brimonidine and Timolol Groups

Outcome	Brimonidine (n=75)	Timolol (n=75)
Adherent	57 (76%)	60 (80%)
Non-Adherent	18 (24%)	15 (20%)
Total	75	75

Discussion

A total of 150 patients were included in the study, with equal distribution between the two treatment groups. The outcomes were assessed using a comprehensive set of parameters, including IOP reduction, visual field indices, optic nerve head changes, ocular tolerability, adverse drug reactions, and medication adherence. This multifaceted approach allowed for a holistic evaluation of both therapeutic effectiveness and patient-centered outcomes.

Efficacy: Intraocular Pressure Reduction: Reduction in IOP is the primary goal in glaucoma management, as it directly correlates with slowing disease progression. [2,4] In the present study, Brimonidine demonstrated a significantly greater reduction in IOP compared to Timolol, as measured by both Goldmann Applanation Tonometry (GAT) and Non-Contact Tonometry (NCT). The percentage reduction in IOP with Brimonidine was approximately 24–26%, whereas Timolol achieved a reduction of around 14–15%. The enhanced efficacy of Brimonidine may be attributed to its dual mechanism of action, which includes both reduction of aqueous humor production and increased uveoscleral outflow. In contrast, Timolol, a non-selective beta-adrenergic blocker, primarily reduces aqueous humor production without influencing outflow pathways.The higher proportion of patients achieving clinically significant IOP reduction (≥20%) in the Brimonidine group (56.0%) compared to the Timolol group (46.7%) further supports its superior therapeutic efficacy. [11,12,14]

Structural Outcomes: Optic Nerve Head (Cup–Disc Ratio): Structural changes in the optic nerve head are critical indicators of glaucoma progression. In this study, the cup–disc ratio (CDR) was used as a marker of optic nerve damage. The Brimonidine group demonstrated better preservation of optic nerve structure, with lower mean CDR values compared to the Timolol group. [8]

Functional Outcomes: Visual Field Parameters: Visual field assessment is essential for evaluating the functional impact of glaucoma. In the present study, parameters such as Mean Deviation (MD), Pattern Standard Deviation (PSD), Visual Field Index (VFI), and Glaucoma Hemifield Test (GHT) were analyzed. The results showed that MD, PSD, and VFI were comparable between the two treatment groups, indicating that both Brimonidine and Timolol are similarly effective in maintaining visual function over the study period. However, GHT values showed better outcomes in the Brimonidine group, suggesting improved visual field symmetry and possibly earlier stabilization of glaucomatous damage. [5,9,10]

Safety and Tolerability: Safety and tolerability are important considerations in long-term glaucoma therapy, as adverse effects can impact patient compliance and overall treatment success. In this study, ocular tolerability was assessed using conjunctival hyperemia grading and ocular symptom scores. Timolol demonstrated a better tolerability profile, with a higher proportion of patients reporting no redness and lower incidence of symptoms such as burning, itching, and redness. In contrast, Brimonidine was associated with higher rates of ocular symptoms, particularly itching and redness, which may be attributed to its known side effect profile. Despite these differences, most adverse effects in both groups were mild to moderate in severity and did not necessitate discontinuation of therapy in the majority of patients.[13.14]

Adverse Drug Reactions and Causality Assessment: Adverse drug reactions (ADRs) were evaluated using the WHO–UMC causality assessment scale. The distribution of ADRs across categories such as possible, probable, and unlikely was similar between the two groups, indicating comparable safety profiles.

Medication Adherence: Medication adherence plays a crucial role in the successful management of glaucoma, as poor compliance can lead to inadequate IOP control and disease progression. In this study, adherence was assessed using the MARS-10 scale.

Timolol showed slightly higher adherence rates (80%) compared to Brimonidine (76%), which may be attributed to its better tolerability and lower incidence of ocular discomfort. The ease of use and patient familiarity with beta-blockers may also contribute to improved compliance.[1,2,10]

Conclusion

The findings of this study indicate that both Brimonidine and Timolol are effective in the management of glaucoma, with each drug demonstrating distinct advantages. Brimonidine showed superior efficacy in terms of IOP reduction, optic nerve preservation, and treatment response, while Timolol demonstrated better tolerability and slightly higher adherence.[2,4,10] From a clinical perspective, the choice of therapy should be individualized based on patient characteristics, severity of disease, and tolerance to medication. For patients requiring greater IOP reduction and structural protection, Brimonidine may be the preferred option. Conversely, Timolol may be more suitable for patients who prioritize tolerability and ease of use.

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