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Original Article

Comparison of Bimatoprost and Timolol for Treatment of Chronic Angle Closure Glaucoma

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ABSTRACT

Angle-closure glaucoma occurs when the normal drainage of fluid within the eye, specifically the aqueous humor, is obstructed or restricted. **Objective:** To assess and compare bimatoprost 0.03% administered once daily versus timolol 0.5% administered twice daily in patients diagnosed with chronic angle closure glaucoma (CACG). **Methods:** This randomized controlled study was performed at the Department of Ophthalmology, Bahawalpur Victoria Hospital, Bahawalpur, Pakistan, from August 2023 to January 2024. Patients of either gender, aged 18 years or older, and diagnosed with unilateral or bilateral CACG were included. Patients were randomly allocated to either Bimatoprost 0.03% (once daily at night) or Timolol malete 0.5% (two times morning and night daily) adopting a lottery method. Patients were asked to visit after one and 3 months (final outcome) and intraocular pressure (IOP) measurements were taken between 8 to 10 am using an applanation tonometer. **Results:** A total of 110 patients of which 64 (58.2%) were female. The mean age was 58.9 ± 10.5 years. At baseline, the mean intraocular pressure was calculated to be 24.2 ± 5.7 mmHg. After 1-month (18.7 ± 4.2 mmHg vs. 20.5 ± 4.7 mmHg, p=0.0418) and 3-months of treatment (16.8±4.6 mmHg vs. 19.6 ± 4.3 mmHg, p=0.0030), the mean IOP were significantly less in Bimatoprost group when compared to Timolol group. The commonest adverse events were conjunctival hyperaemia, and pruritus reported by 19 (17.3%), and 9 (8.2%) patients respectively. **Conclusions:** Bimatoprost exhibited a significantly better reduction in IOP compared to timolol in chronic angle closure glaucoma. Both drugs showed relatively good safety and tolerability profiles.

INTRODUCTION

The prevalence of angle closure glaucoma is an important ocular disorder with an estimated prevalence of 0.6% in the general population [1]. Data from Asia shows the prevalence of angle-closure glaucoma ranging between 0.6 to 1.9% [2-4]. Angle-closure glaucoma occurs when the normal drainage of fluid within the eye, specifically the aqueous humor, is obstructed or restricted. This blockage can damage the trabecular meshwork, a crucial part of the eye's drainage system, causing an increase in intraocular pressure (IOP) [5]. This elevated pressure can result in damage to the optic nerve, a condition known as glaucomatous optic neuropathy. The contact between the iris and the trabecular meshwork can gradually close off the drainage angle, often leading to the formation of adhesions between the iris and the trabecular meshwork, known as peripheral anterior synechiae [6]. This closure can further impede the outflow of aqueous humor, exacerbating the rise in intraocular pressure. When angle-closure glaucoma progresses to cause damage to the optic nerve, it is termed chronic angle-closure glaucoma (CACG). CACG can lead to permanent vision loss if not treated, making early detection and appropriate management crucial in preserving vision and preventing further damage to the optic nerve [7]. CACG is primarily treated with laser

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iridotomy at present, which alleviates pupillary blockage and hinders synechial closure [8]. Presently, the primary CACG treatment involves laser iridotomy to alleviate pupillary blockage and hinder synechial closure, along with pharmaceutical measures that lower IOP [9]. Combining laser with drug therapy does not consistently achieve success in treating CACG among Asian patients, with a majority eventually requiring additional surgery to alleviate the condition [10]. Literature shows latanoprost (a prostaglandin analog) to have a lesser incidence of systemic adverse events and greater efficacy in CACG patients to lower IOP compared to timolol alone or in combination with dorzolamide [11]. Bimatoprost (synthetic prostamide analog) enhances the aqueous humor drainage through the trabecular meshwork and uveoscleral route. The effectiveness and tolerance of bimatoprost has been evident in the past [12]. There is a dearth of information regarding the most suitable interventions for treating CACG, especially in Pakistan. The current study consisted of patients diagnosed with CACG and spanned over a treatment and evaluation period of three months.

The study aimed to assess and compare bimatoprost 0.03% administered once daily versus timolol 0.5% administered twice daily in patients diagnosed with chronic angle closure glaucoma.

METHODS

This randomized controlled study was carried out at the Department of Ophthalmology, Bahawalpur Victoria Hospital, Bahawalpur, Pakistan from August 2023 to January 2024, with prior approval from the "Institutional Ethical Committee" (2351/DME/QAMC Bahawalpur). The inclusion criteria was patients of either gender, aged 18 years or older, exhibiting good overall health, and diagnosed with unilateral or bilateral CACG confirmed via indentation gonioscopy. Additionally, patients requiring iridotomy or iridectomy performed in the last 3 months were excluded. The exclusion criteria was patients with other uncontrolled systemic or ocular diseases, substantial ocular discomfort, confirmed sensitivities to research medications or ingredients in formulations, expected alterations to current therapies affecting IOP, or chronic use of non-study ocular medications. Those with corneal abnormalities hindering accurate IOP measurement or recent ocular surgeries or procedures within the prior three months were not included. Patients with specific heart rate or blood pressure concerns based on age or for whom beta-blockers were contraindicated, pregnant or lactating female, or women of reproductive age using unreliable birth control methods were also not included. Open-EPI was used to calculate the sample size and prior informed consent was taken, CACG was diagnosed as damage to the optic nerve indicating glaucoma, along with visual field issues or reduced vision, and at least 180° of synechial angle closure observed during dynamic gonioscopy [13]. At the time of enrollment, gender, age, and residential area were noted in all patients. Patients were randomly allocated (55 patients in each group) to either Bimatoprost 0.03% (once daily at night) or Timolol maleate 0.5% (two times [morning and night] daily) adopting the lottery method. Patients underwent a suitable washout period before initiating treatment at the baseline visit. For topical beta-blockers or prostaglandins, the washout period was 4-weeks; for alpha-agonists or sympathomimetics, it was 2-weeks; and for carbonic anhydrase inhibitors or parasympathomimetics, it was 4-days. The administration of study medications involved the self-instillation of one drop for every eye between 7-9 am and 7-9 pm (in cases using Timolol). During subsequent study visits, the study medications were administered in the morning by investigators immediately following the measurement of IOP and the examination of the patient's eyes. Throughout the study, data from the eye exhibiting the most severe condition was utilized. Patients were asked to visit after one and 3 months (final outcome) and IOP measurements were taken between 8 to 10 am using an applanation tonometer. Treatment-related adverse events were also noted during the course of the study. Patients missing follow-up visits were left out of the subsequent analysis plans. Data analysis was done utilizing "IBM-SPSS Statistics" version 26.0. The qualitative data were shown as frequency and percentages and a chi-square test was used for the comparisons. Means and standard deviation were calculated to demonstrate the quantitative variables, while comparisons were made employing an independent sample t-test. A $p < 0.05$ was considered standard for significance.

RESULTS

In a total of 110 patients, 64 (58.2%) were female. The mean age was 58.9 ± 10.5 years, ranging between 35 to 85 years. Residential status was rural in 72 (65.5%) patients. Diabetes mellitus was noted in 25 (22.7%) patients. At baseline, the mean IOP was calculated to be 24.2 ± 5.7 mmHg (Table 1).

Table 1: Comparison of Baseline Characteristics (n=110)

Characteristics		Groups		p-Value
		Bimatoprost (n=55)	Timolol (n=55)	
Gender	Male	24 (43.6%)	22 (40.0%)	0.699
	Female	31 (56.4%)	33 (60.0%)	
Age in Years, (Mean ± SD)		58.4 ± 11.4	59.6 ± 9.2	0.545
Residence	Rural	35 (63.6%)	37 (67.3%)	0.688
	Urban	20 (36.4%)	18 (32.7%)	
Diabetes Mellitus		11 (20.0%)	14 (25.5%)	0.495
Intraocular Pressure		23.8 ± 6.2	24.6 ± 5.5	0.475

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At the 1-month follow-up, 2 patients in the Bimatoprost group and 4 patients in Timolol group did not appear for follow-up evaluation. After 3 months of treatment, 7 patients in Timolol group and 9 patients in Bimatoprost group left the final evaluation so these patients were excluded from the final analysis. After 1-month (18.7 ± 4.2 mmHg vs. 20.5 ± 4.7 mmHg, p = 0.0418) and 3-months treatment (16.8 ± 4.6 mmHg vs. 19.6 ± 4.3 mmHg, p = 0.0030), the mean IOP were significantly less in Bimatoprost group when compared to Timolol group (Table 2).

Table 2: Comparison of Mean IOP (mmHg) at Different Study Intervals in Both Study Groups

Group	IOP (mmHg) at Different Study Intervals		
	Baseline (n=110)	After 1-Month (n=104)	After 3-Months (n=94)
Bimatoprost (Mean ± SD)	23.8 ± 6.2	18.7 ± 4.2	16.8 ± 4.6
Timolol (Mean ± SD)	24.6 ± 5.5	20.5 ± 4.7	19.6 ± 4.3
p-Value	0.4756	0.0418	0.0030

The commonest adverse events were conjunctival hyperaemia, and pruritus reported by 19 (17.3%), and 9 (8.2%) patients respectively. Pruritus was significantly more common among Bimatoprost group patients (14.5% vs. 1.8%, p=0.0149). Comparison of most common adverse events during the course of study among patients of both study groups (Table 3).

Table 3: Frequency of Adverse Events among study participants

Adverse Events	Bimatoprost	Timolol	p-Value
Conjunctival Hyperaemia	12 (21.8%)	7 (12.7%)	0.2073
Pruritus	8 (14.5%)	1 (1.8%)	0.0149
Conjunctival Congestion	4 (7.3%)	-	0.0416
Eye Irritation	3 (5.5%)	3 (5.5%)	1
Eyelash Growth	3 (5.5%)	-	0.0791
Punctate Keratitis	-	3 (5.5%)	0.0791
Headache	2 (3.6%)	1 (1.8%)	0.5583

DISCUSSION

This study unveiled novel insights into bimatoprost effectiveness, safety, and tolerability among CACG patients. Bimatoprost was well-tolerated and showcased superior efficacy compared to timolol in reducing IOP and ensuring diurnal IOP control. Our findings stand aligned with Pongpun PR *et al* from Thailand where the researcher noted that the bimatoprost group showed a significantly higher mean reduction in IOP in comparison to timolol after 2 weeks (31% vs 19%; p < 0.05), 6-weeks (30% vs. 19%; p < 0.001), and 12-weeks (28% vs 18%, p < 0.001) [14]. Till now, the majority of research on bimatoprost's efficacy and tolerability has primarily involved open-angle glaucoma patients [15, 16]. A study by Agarwal *et al.*, analyzing CACG patients from India revealed that bimatoprost was demonstrated to reduce IOP by 31% in those patients who were previously taking timolol [17]. Chen *et al.*, reported both Bimatoprost and Timolol to impart significant reduction among CACG patients following iridotomy [15]. Chew *et al.*, reported similar findings to us when they documented one daily Bimatoprost to reduce IOP significantly greater than twice a day Timolol [18]. Higginbotham from UK noted Bimatoprost taken once a day offered a continuous reduction in IOP that surpassed the effects of both timolol and bimatoprost taken twice a day. Additionally, Bimatoprost helped more patients achieve the desired low IOP targets [19]. Collectively, these findings emphasize the excellent efficacy of synthetic prostaglandins Bimatoprost over timolol in reducing IOP among CACG patients. While these results reflect mean responses from patient groups and not the individual range of responses, the consistent and significantly greater reductions in IOP observed throughout the day with bimatoprost are noteworthy. The outcomes of this study offer reassurance to clinicians regarding the effectiveness of bimatoprost as a viable therapy for CACG, positioning it as a credible alternative to timolol. Bimatoprost's distinct mechanisms in reducing IOP make it a promising option for individuals who might not respond favorably to other synthetic prostaglandin analogues. These results also echo similar conclusions drawn from trials predominantly involving Caucasian patients with open-angle glaucoma [11]. The positive safety and tolerability records noted in Asian patients with CACG using both bimatoprost and timolol align with earlier research findings, and support bimatoprost's efficacy in diverse populations [14, 17]. This study showed that both bimatoprost and timolol had good tolerability, with reports of minimal systemic side effects, the majority being mild. There have been reports of withdrawal from the timolol treatment due to symptoms like breathlessness and bronchospasm and these observations underscore the possibility of respiratory side effects linked to timolol use, especially among patients with undetected respiratory conditions but this needs further research [14]. This emphasizes the importance of assessing respiratory function in patients, especially the elderly, undergoing topical timolol treatment [20]. In our study, localized adverse effects were slightly more frequent among patients on bimatoprost than in timolol-receiving patients. Despite the higher occurrence of local adverse effects with bimatoprost, the benefits of achieving a reduction in IOP to a greater extent may outweigh most of these local adverse events that may arise.

CONCLUSIONS

Bimatoprost exhibited a significantly better reduction in IOP compared to timolol in chronic angle closure glaucoma. Both drugs showed relatively good safety and tolerability profiles.

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Authors Contribution

Conceptualization: ZA, SF, MK
Methodology: ZA, NN, SAM, MJK
Formal analysis: ZA, NN, MK, SAM, MJK
Writing-review and editing: SF, MK, SAM, MJK

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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