

Prostaglandin Analogues Versus Topical Beta-Blockers in the Initial Pharmacological Management of Primary Open-Angle Glaucoma: Clinical Effectiveness and the Role of Medication Adherence

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Abstract

Primary open-angle glaucoma is a progressive optic neuropathy requiring sustained intraocular pressure control to prevent irreversible visual loss. Prostaglandin analogues and topical beta-blockers are widely used pharmacological therapies, although their clinical effectiveness is influenced by efficacy, safety, dosing convenience, and patient adherence. This narrative review compared the clinical effectiveness of both drug classes and examined the role of adherence in long-term treatment outcomes. Literature published primarily between 2021 and 2026 was identified from PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar. Prostaglandin analogues generally provide greater and more sustained intraocular pressure reduction than topical beta-blockers, with once-daily administration offering an additional practical advantage. However, local ocular and periocular adverse effects may reduce treatment acceptance. Topical beta-blockers remain effective alternatives for selected patients, although cardiovascular and respiratory adverse effects require careful consideration. The clinical benefits of both therapies may be reduced by missed doses, incorrect eye-drop administration, adverse effects, treatment cost, and limited medication access. Therefore, prostaglandin analogues are generally preferred as initial pharmacological therapy, whereas topical beta-blockers remain appropriate for selected patients based on tolerability, comorbidities, accessibility, and the likelihood of sustained adherence.

Keywords: Primary Open-Angle Glaucoma; Prostaglandin Analogues; Topical Beta-Blockers; Intraocular Pressure; Treatment Persistence.

INTRODUCTION

Primary open-angle glaucoma (POAG) is a chronic and progressive optic neuropathy characterized by the degeneration of retinal ganglion cells and their axons, leading to irreversible optic nerve damage, visual field loss, and blindness. Its pathogenesis is multifactorial and involves impaired aqueous humor drainage, elevated intraocular pressure (IOP), vascular dysregulation, oxidative stress, chronic inflammation, and genetic

susceptibility. Immune-related pathways, including Toll-like receptor 4 signaling, have also been proposed as contributors to trabecular meshwork dysfunction and glaucomatous neurodegeneration, although their clinical significance requires further investigation (Maidenko, 2022; Wagner et al., 2022). Glaucoma affects approximately 3.5% of the global population aged 40–80 years, and population aging is expected to increase the absolute number of affected individuals despite a decline in the age-standardized prevalence of glaucoma-related blindness (Reis et al., 2022).

Elevated IOP remains the most important modifiable risk factor for the development and progression of POAG. Persistent pressure elevation can induce mechanical strain within the lamina cribrosa, disrupt axonal transport, and contribute to retinal ganglion cell dysfunction. Clinical evidence demonstrates that lowering IOP reduces the risk of glaucoma progression, although the relationship between IOP and optic nerve damage varies according to individual susceptibility, ocular biomechanics, vascular conditions, and genetic factors (Asrani et al., 2024; Jayaram et al., 2023). Long-term IOP fluctuation may also increase the risk of visual field deterioration, indicating that glaucoma management should aim not only to achieve a target IOP but also to maintain stable pressure control over time (Lee et al., 2022).

Early detection and sustained treatment of POAG remain challenging because the disease commonly progresses without noticeable symptoms. Initial visual field defects frequently occur in the peripheral field and may remain unrecognized until substantial optic nerve damage has developed (Joshi et al., 2022). Because existing retinal ganglion cell loss and visual field defects cannot be reversed, POAG generally requires lifelong monitoring and treatment to prevent further deterioration (Kang & Tanna, 2021). Although IOP reduction remains the principal evidence-based strategy for slowing disease progression, some patients continue to experience structural or functional deterioration despite substantial pressure reduction, suggesting that pressure-independent mechanisms may also contribute to glaucomatous damage (Moghimani et al., 2025; Shalaby et al., 2022).

Topical antiglaucoma medications remain an important component of POAG management because they lower IOP through mechanisms that reduce aqueous humor production or increase aqueous humor outflow. Prostaglandin analogues, including latanoprost, travoprost, tafluprost, and bimatoprost, primarily increase uveoscleral aqueous humor outflow, whereas topical beta-blockers such as timolol and betaxolol reduce aqueous humor production by inhibiting beta-adrenergic receptors in the ciliary body (Aihara, 2021; Mincione et al., 2021). Prostaglandin analogues are commonly preferred as initial pharmacological therapy because they provide strong and sustained IOP reduction with once-daily administration. In contrast, topical beta-blockers remain useful alternatives or adjunctive agents in selected patients, particularly when prostaglandin analogues are unsuitable, poorly tolerated, or inaccessible (Cordeiro et al., 2024; Subbulakshmi et al., 2023).

The clinical value of both drug classes is influenced by their tolerability and the patient's ability to maintain treatment. Prostaglandin analogues may cause conjunctival hyperemia, iris pigmentation, eyelash growth, and periocular changes, whereas topical beta-blockers may produce ocular discomfort and systemic cardiovascular or respiratory effects.

These adverse effects, together with dosing frequency, medication cost, drug availability, limited disease knowledge, forgetfulness, and difficulty administering eye drops, can reduce adherence and treatment persistence (Cvenkel & Kolko, 2023; Gatwood et al., 2022; Moore et al., 2023). Poor adherence can prevent patients from achieving the expected IOP reduction and has been associated with higher IOP, faster visual field deterioration, and progressive retinal nerve fiber layer loss (Almidani et al., 2026; Oltramari et al., 2024; Shu et al., 2021).

Previous reviews have primarily compared prostaglandin analogues and topical beta-blockers based on their mechanisms of action, intraocular pressure-lowering efficacy, and adverse-effect profiles, whereas adherence studies have generally evaluated topical glaucoma medications as a broad therapeutic category. Consequently, the extent to which differences in dosing frequency, local and systemic tolerability, contraindications, cost, and treatment persistence influence the comparative clinical effectiveness of these two drug classes remains insufficiently integrated. This gap is clinically relevant because superior pharmacological efficacy may not translate into sustained intraocular pressure control when medication adherence is poor. Therefore, this narrative review aims to compare the clinical effectiveness of prostaglandin analogues and topical beta-blockers within the first-line pharmacological management of primary open-angle glaucoma, with particular emphasis on patient adherence and treatment persistence. By integrating intraocular pressure-lowering efficacy with treatment-related and patient-related factors, this review provides a patient-centered framework for selecting appropriate long-term topical therapy.

THODS

This article used a narrative literature review approach to compare the clinical effectiveness of prostaglandin analogues and topical beta-blockers in the initial pharmacological management of primary open-angle glaucoma, with particular emphasis on patient adherence. Literature was collected from PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar using keywords such as “primary open-angle glaucoma,” “prostaglandin analogues,” “topical beta-blockers,” “intraocular pressure,” “clinical effectiveness,” “medication adherence,” and “treatment persistence.” The review primarily included English-language clinical studies, systematic reviews, meta-analyses, and clinical guidelines published between 2021 and 2026, while earlier studies were considered when they provided fundamental evidence related to glaucoma pharmacotherapy.

The selected literature was reviewed descriptively by focusing on the pharmacological characteristics, intraocular pressure-lowering effectiveness, safety, tolerability, adherence, and treatment persistence of prostaglandin analogues and topical beta-blockers. The findings were synthesized to identify the comparative advantages and limitations of both drug classes and to examine how patient adherence influences their long-term clinical effectiveness in primary open-angle glaucoma.

DISCUSSION

3.1 Pharmacological Characteristics of Prostaglandin Analogues and Topical Beta-Blockers

Prostaglandin analogues lower intraocular pressure primarily by increasing aqueous humor outflow through the uveoscleral pathway. These agents activate prostanoid receptors and promote extracellular matrix remodeling within the ciliary muscle and sclera through changes in matrix metalloproteinase activity. The resulting reduction in extracellular matrix resistance creates additional spaces for aqueous humor drainage and supports sustained intraocular pressure reduction. Although the uveoscleral pathway is the principal route affected by conventional prostaglandin analogues, some agents may also enhance outflow through the trabecular meshwork. This distinction is particularly relevant for newer prostanoid receptor agonists, which may act through both conventional and unconventional aqueous humor outflow pathways (Aihara, 2021; Sharif et al., 2023; Shen et al., 2023).

Latanoprost, travoprost, bimatoprost, and tafluprost are the most widely used prostaglandin-based medications for reducing intraocular pressure in primary open-angle glaucoma. Latanoprost, travoprost, and tafluprost primarily act as prostaglandin FP receptor agonists after ocular conversion to their pharmacologically active forms, whereas bimatoprost has distinct structural and pharmacological characteristics despite being clinically grouped with prostaglandin analogues. Comparative evidence indicates that all four agents provide clinically meaningful intraocular pressure reduction, although treatment response varies among patients. A meta-analysis found no significant difference in overall responsiveness among these medications, but bimatoprost produced a greater mean pressure reduction than latanoprost in some comparisons (Cai et al., 2021). Long-term observational evidence has also shown broadly comparable effectiveness and safety among latanoprost, travoprost, and tafluprost, suggesting that treatment selection should consider individual response and tolerability in addition to average efficacy (Kim et al., 2021; Zhou et al., 2022).

Topical beta-blockers reduce intraocular pressure through a different pharmacological mechanism. By inhibiting beta-adrenergic receptors in the nonpigmented ciliary epithelium, these agents decrease intracellular cyclic adenosine monophosphate signaling and suppress aqueous humor production. Timolol is a widely used nonselective beta-blocker that inhibits both beta-1 and beta-2 receptors, whereas betaxolol is relatively selective for beta-1 receptors. Other nonselective topical beta-blockers include carteolol, levobunolol, and metipranolol. Beta-1 selectivity may offer an advantage for some patients at risk of beta-2 receptor-mediated respiratory effects, although betaxolol is not entirely free from systemic adverse effects. Experimental evidence also suggests that beta-adrenergic agents may influence ocular fluid clearance pathways; however, reduced aqueous humor production in the ciliary body remains their principal clinically recognized mechanism for lowering intraocular pressure (Hanna et al., 2021; Patton & Lee, 2024).

The differences in mechanism of action, dosing frequency, duration of effect, and systemic absorption influence the clinical use of prostaglandin analogues and topical beta-blockers. Prostaglandin analogues generally provide potent and prolonged intraocular pressure reduction with once-daily administration, contributing to their current position as the

preferred initial pharmacological therapy for many patients with primary open-angle glaucoma. Topical beta-blockers remain effective aqueous-suppressant agents but may require once- or twice-daily administration depending on the active substance and formulation. Their clinical use must also account for systemic beta-adrenergic blockade, particularly in patients with cardiovascular or respiratory comorbidities. Consequently, the therapeutic value of both drug classes cannot be determined solely by their pharmacological mechanisms. Dosing convenience, duration of pressure control, individual response, contraindications, and the ability of patients to maintain treatment should also be considered when comparing their long-term clinical effectiveness (Cai et al., 2021; Subbulakshmi et al., 2023; Zhou et al., 2022).

3.2 Comparative Effectiveness in Intraocular Pressure Reduction

Prostaglandin analogues generally produce greater intraocular pressure reduction than topical beta-blockers when used as monotherapy. A component network meta-analysis of 166 randomized controlled trials involving 36,494 participants reported a mean intraocular pressure reduction of 4.75 mmHg with prostaglandin analogues, compared with 3.29 mmHg with beta-blockers. Both estimates were supported by high-certainty evidence, indicating an average difference of approximately 1.46 mmHg in favor of prostaglandin analogues (Hsia et al., 2025). This greater pressure-lowering effect, together with favorable dosing characteristics, has contributed to the transition from traditional beta-blockers toward prostaglandin analogues as the preferred initial pharmacological treatment for many patients with primary open-angle glaucoma. Nevertheless, topical beta-blockers remain clinically effective, and the difference in average efficacy does not imply that every patient will respond more strongly to a prostaglandin analogue (Subbulakshmi et al., 2023).

Prostaglandin analogues also provide sustained intraocular pressure control with once-daily administration. Latanoprost, travoprost, bimatoprost, and tafluprost have sufficiently prolonged ocular activity to maintain a clinically relevant hypotensive effect throughout the dosing interval, with latanoprost showing effective 24-hour pressure control in clinical use (Benitez et al., 2024; Zhou et al., 2022). Once-daily administration reduces treatment complexity and may facilitate consistent long-term use compared with beta-blocker formulations that require once- or twice-daily administration. Topical beta-blockers effectively reduce intraocular pressure by suppressing aqueous humor production, but their pressure-lowering effect may vary across the daily cycle. However, the available evidence more clearly supports the overall and diurnal advantages of prostaglandin analogues than a definitive difference in nocturnal control. Therefore, the assertion that beta-blockers consistently provide inferior nocturnal pressure control should be interpreted cautiously until supported by additional direct 24-hour comparative studies (Subbulakshmi et al., 2023).

Clinical response to prostaglandin analogues and topical beta-blockers varies considerably among patients. Baseline intraocular pressure is one of the most consistent predictors of treatment response because patients with higher pretreatment pressure generally experience greater absolute reductions. Reitingger et al. (2025) found that responders to both latanoprost and timolol had significantly higher baseline intraocular pressure than nonresponders. The study also demonstrated that lower baseline uveoscleral outflow was associated with a greater response to latanoprost, suggesting that individual

aqueous humor dynamics influence the effectiveness of prostaglandin-based treatment. The relationship between baseline pressure and treatment response was similarly demonstrated in the LiGHT trial, in which pharmacological treatment produced greater absolute reductions among eyes with higher pretreatment pressure (Fahy et al., 2024). Genetic variants involving prostaglandin, beta-adrenergic, and drug-metabolizing pathways may also contribute to interindividual variability, although pharmacogenetic testing is not yet sufficiently established for routine treatment selection (Labay-Tejado et al., 2025). Evidence directly linking glaucoma severity to the relative response of these two drug classes remains less conclusive.

Long-term clinical effectiveness should not be determined solely by the average intraocular pressure reduction reported in short-term trials. Evaluation should also consider whether an individualized target pressure is achieved and maintained, whether the initial response decreases over time, and whether additional medication, laser treatment, or surgery becomes necessary. Although prostaglandin analogues demonstrate greater efficacy at the population level, their advantage in an individual patient depends on treatment tolerability, correct administration, adherence, and the stability of pressure control during follow-up. A beta-blocker that is used consistently may provide greater practical benefit than a more potent prostaglandin analogue that is frequently missed or discontinued. Comparative effectiveness should therefore integrate mean pressure reduction with target achievement, duration of control, treatment failure, need for therapeutic escalation, and the patient's ability to sustain treatment. This broader assessment distinguishes pharmacological efficacy under controlled conditions from long-term effectiveness in routine clinical practice (Hsia et al., 2025; Reitingner et al., 2025).

3.3 Comparative Safety and Tolerability

Prostaglandin analogues are generally well tolerated systemically, but they are frequently associated with local ocular and periocular adverse effects. Conjunctival hyperemia, increased iris and eyelid pigmentation, eyelash growth, ocular irritation, and hypertrichosis are among the most commonly reported reactions. The incidence and severity of these effects vary according to the specific agent and duration of treatment, with latanoprost generally producing less conjunctival hyperemia than bimatoprost or travoprost in comparative studies. Long-term therapy may also produce prostaglandin-associated periorbitopathy, which includes deepening of the upper eyelid sulcus, periorbital fat atrophy, enophthalmos, and eyelid changes. Although these reactions are not usually life-threatening, visible cosmetic alterations and persistent ocular discomfort may reduce treatment acceptance, particularly during long-term or unilateral therapy (Cordeiro et al., 2024; Sakata et al., 2022; Wu et al., 2024).

Topical beta-blockers have a different safety profile because ocular administration does not prevent systemic absorption. Medication reaching the nasolacrimal system may enter the systemic circulation and produce beta-adrenergic blockade outside the eye. A pharmacovigilance analysis of 8,793 adverse-event reports involving topical glaucoma beta-blockers identified safety signals for bradycardia, complete atrioventricular block, and bronchospasm (Aftab et al., 2024). Topical beta-blockers may also be associated with ocular irritation, reduced tear-film stability, and dry-eye symptoms, although these effects can partly

reflect preservatives rather than the active beta-blocker itself. A systematic review found limited and low-certainty evidence regarding differences in ocular-surface symptoms between preserved and preservative-free beta-blocker formulations, indicating that the contribution of preservatives should be considered when evaluating tolerability (Skov et al., 2022).

The possibility of systemic beta-blockade requires careful evaluation of respiratory and cardiovascular comorbidities before topical beta-blockers are prescribed. Nonselective agents such as timolol may inhibit pulmonary beta-2 receptors and reduce respiratory function in susceptible patients. A recent systematic review and meta-analysis found that topical beta-blocker exposure was associated with a reduction in forced expiratory volume in one second among patients with asthma, supporting the preferential selection of less risky alternatives when available (Marko & Pawliczak, 2025). However, observational evidence is not entirely consistent. A large claims-based cohort study did not find a statistically significant increase in asthma attacks among topical beta-blocker users with previous or current asthma treatment (Kido et al., 2022). Topical beta-blockers should therefore be used cautiously rather than assumed to produce identical risks in all patients, particularly in those with active asthma, severe obstructive respiratory disease, clinically significant bradycardia, or cardiac conduction abnormalities. Direct topical-specific evidence in chronic obstructive pulmonary disease remains less extensive than the evidence available for asthma and cardiovascular effects.

Local and systemic adverse effects can influence treatment tolerability, persistence, and clinical effectiveness, but discontinuation should not be attributed to adverse reactions alone. A meta-analysis involving approximately 961,000 patients showed that persistence with prostaglandin analogues declined from 75% at six months to 31% at three years, demonstrating that even once-daily and generally well-tolerated therapy is affected by substantial long-term discontinuation (Baudouin et al., 2025). Population-based evidence nevertheless indicates longer treatment duration with prostaglandin analogues than with beta-blockers among patients who continue first-line monotherapy (Purola et al., 2025). These differences likely reflect an interaction among adverse effects, dosing frequency, contraindications, perceived treatment benefits, cost, and patient preferences. Selection of long-term topical therapy should therefore balance the predominantly local and cosmetic adverse effects of prostaglandin analogues against the greater potential for systemic cardiovascular and respiratory effects with topical beta-blockers.

3.4 Comparative Factors Influencing Adherence to Prostaglandin Analogues and Topical Beta-Blockers

The once-daily administration of prostaglandin analogues may provide greater treatment convenience than topical beta-blockers that require once- or twice-daily administration, depending on the drug and formulation. A simpler dosing schedule can facilitate integration of eye-drop use into patients' daily routines and reduce opportunities for missed doses. The combination of prolonged intraocular pressure-lowering activity and once-daily administration contributed to the adoption of prostaglandin analogues as preferred initial pharmacological therapy for many patients with primary open-angle glaucoma (Cordeiro et al., 2024; Subbulakshmi et al., 2023). However, evidence directly quantifying differences in

adherence between once-daily prostaglandin analogues and topical beta-blockers remains limited. Therefore, the adherence advantage of prostaglandin analogues should be regarded as pharmacologically and behaviorally plausible rather than universally demonstrated in direct comparative studies.

The potential convenience of prostaglandin analogues may be offset by local ocular and cosmetic adverse effects. Conjunctival hyperemia, ocular irritation, iris or eyelid pigmentation, increased eyelash growth, and periocular tissue changes may create physical discomfort or dissatisfaction with appearance. Prostaglandin-associated periorbitopathy is particularly relevant during long-term or unilateral treatment because visible facial asymmetry and changes such as deepening of the upper eyelid sulcus may negatively affect treatment acceptance and confidence (Cordeiro et al., 2024; Sakata et al., 2022). Nevertheless, these adverse effects should not be regarded as the sole cause of nonadherence. A meta-analysis involving approximately 961,000 patients treated with prostaglandin analogues found that mean adherence was 44% at one year, while persistence decreased from 75% at six months to 31% at three years. These findings demonstrate substantial long-term treatment challenges but do not isolate cosmetic adverse effects from other influences such as forgetfulness, cost, treatment beliefs, and access to medication (Baudouin et al., 2025).

Topical beta-blockers present different adherence concerns because their ocular administration can produce both local and systemic effects. Cardiovascular or respiratory reactions may reduce treatment acceptability, particularly among patients who already have multiple chronic conditions or concerns about systemic safety. Systemic comorbidity itself is associated with poorer long-term glaucoma medication adherence, possibly because patients must manage several treatments simultaneously and may give lower priority to an asymptomatic eye disease. Patients with four or more comorbidities demonstrated an adherence reduction of approximately 11.8 percentage points by the fifth year after glaucoma onset compared with patients without comorbidity (Hou & Pu, 2024). However, this evidence concerns glaucoma therapy broadly and does not establish that beta-blocker adverse effects specifically caused the observed nonadherence. Evidence regarding respiratory risk is also not uniform; one large cohort did not identify a statistically significant increase in asthma attacks among topical beta-blocker users, although careful patient selection and counselling remain necessary (Kido et al., 2022). The relationship between beta-blocker safety and adherence should therefore be interpreted as clinically plausible but not yet fully quantified in direct drug-class comparisons.

Adherence to both prostaglandin analogues and topical beta-blockers is ultimately influenced by interacting treatment-related, patient-related, and healthcare-system factors. Higher medication cost, limited knowledge of glaucoma, low confidence in eye-drop administration, adverse-effect concerns, physical limitations, and treatment burden have been associated with poorer medication use (Moore et al., 2023). Forgetfulness, difficulty instilling drops, and difficulty following the prescribed schedule also represent important barriers, while patient education and dosing self-efficacy can facilitate adherence (Cvenkel & Kolko, 2023; Gatwood et al., 2022). Medication availability may further affect persistence, particularly in healthcare systems where patients experience interruptions in supply or must personally finance long-term therapy. Consequently, adherence differences between

prostaglandin analogues and topical beta-blockers cannot be attributed solely to dosing frequency or pharmacological class. Their real-world use reflects the combined effects of convenience, tolerability, comorbidity, cost, availability, instillation ability, and patient preferences.

3.5 Role of Adherence in the Comparative Clinical Effectiveness of Prostaglandin Analogues and Topical Beta-Blockers

The intrinsic intraocular pressure-lowering efficacy of prostaglandin analogues is determined by their pharmacological properties, whereas the translation of this efficacy into clinical effectiveness depends on regular and correct medication use. Although prostaglandin analogues are among the most effective topical monotherapies for glaucoma, their expected pressure-lowering benefit may not be sustained when doses are frequently missed, administered incorrectly, or discontinued (Subbulakshmi et al., 2023). A systematic review and meta-analysis of 47 studies involving approximately 961,000 patients found that 44% of prostaglandin analogue users were classified as adherent at one year, while treatment persistence declined from approximately 75% at six months to 31% at three years (Baudouin et al., 2025). However, adherence definitions and measurement methods varied across the included studies, and these findings do not directly quantify the effect of individual missed doses on intraocular pressure control.

The once-daily dosing schedule of prostaglandin analogues may facilitate adherence by reducing regimen complexity and making treatment easier to incorporate into daily routines. This practical advantage, together with prolonged intraocular pressure reduction, has contributed to their preferential use as initial pharmacological therapy for many patients with primary open-angle glaucoma (Cordeiro et al., 2024; Subbulakshmi et al., 2023). Nevertheless, simplified dosing alone does not ensure consistent medication use. Forgetfulness, incorrect eye-drop instillation, treatment cost, medication availability, treatment beliefs, and local ocular or cosmetic adverse effects may counterbalance the benefits of once-daily administration (Baudouin et al., 2025). Therefore, the adherence advantage of prostaglandin analogues should be interpreted as a potential benefit rather than a guarantee of superior long-term clinical effectiveness.

The clinical effectiveness of topical beta-blockers may similarly decline when doses are missed or treatment is discontinued because of ocular discomfort, systemic adverse effects, or concerns regarding cardiovascular and respiratory safety. Although direct evidence linking beta-blocker-specific discontinuation with deterioration in intraocular pressure control remains limited, broader evidence demonstrates that adherence to topical glaucoma medication is associated with long-term clinical outcomes. In a retrospective study of 6,343 patients followed for an average of 5.8 years, each 10-percentage-point increase in adherence was associated with a 0.006-dB-per-year reduction in the rate of visual field deterioration. The estimated time to reach a 3-dB decline in mean deviation was 8.3 years at 20% adherence and 9.3 years at 80% adherence (Shu et al., 2021). Because these findings concerned topical glaucoma therapy collectively rather than beta-blockers specifically, they support the general importance of adherence but do not establish a class-specific effect.

Comparative assessment of prostaglandin analogues and topical beta-blockers should therefore integrate pharmacological efficacy, dosing convenience, tolerability,

adherence, and treatment persistence. Prostaglandin analogues provide greater mean intraocular pressure reduction than beta-blockers at the population level, but this pharmacological advantage does not automatically establish superior effectiveness for every patient (Hsia et al., 2025). A consistently administered and well-tolerated beta-blocker may provide more reliable pressure control than a prostaglandin analogue that is frequently missed or discontinued. Nevertheless, direct class-specific evidence comparing adherence and persistence between these treatments remains limited, and several conclusions are derived from prostaglandin-specific persistence studies or broader studies of topical glaucoma therapy. The comparative clinical value of both drug classes should consequently be evaluated according to their ability to provide safe, acceptable, and sustained intraocular pressure control under real-world conditions. The principal clinical and adherence-related differences between prostaglandin analogues and topical beta-blockers are summarized in Table 1.

Tabel 1. Comparative clinical and adherence-related profiles of prostaglandin analogues and topical beta-blockers in primary open-angle glaucoma

Clinical domain	Prostaglandin analogues	Topical beta-blockers	References
Mechanism of action	Primarily increase aqueous humor outflow through the uveoscleral pathway.	Reduce aqueous humor production through beta-adrenergic receptor blockade in the ciliary body.	(Aihara, 2021; Hanna et al., 2021; Patton & Lee, 2024)
IOP-lowering effectiveness	Greater mean class-level IOP reduction, approximately 4.75 mmHg.	Clinically effective, with a mean class-level reduction of approximately 3.29 mmHg.	(Hsia et al., 2025)
Dosing characteristics	Generally administered once daily and provides prolonged pressure-lowering activity.	Administered once or twice daily, depending on the agent and formulation.	(Subbulakshmi et al., 2023; Zhou et al., 2022)
Principal safety concerns	Predominantly local ocular and periocular effects, including hyperemia, pigmentation, eyelash growth, and periorbital changes.	Greater potential for systemic cardiovascular and respiratory effects, including bradycardia, conduction abnormalities, and bronchospasm.	(Aftab et al., 2024; Cordeiro et al., 2024; Marko & Pawliczak, 2025)
Adherence and persistence considerations	Once-daily dosing may reduce regimen complexity, but local adverse effects, cost, incorrect instillation, and forgetfulness may limit	Dosing frequency, systemic safety concerns, comorbidities, and ocular discomfort may reduce treatment acceptance and	(Baudouin et al., 2025; Hou & Pu, 2024; Moore et al., 2023)

Clinical domain	Prostaglandin analogues	Topical beta-blockers	References
	sustained use.	persistence.	
Clinical position	Often preferred as initial pharmacological therapy when substantial and sustained IOP reduction is required.	Remain appropriate alternatives for selected patients when prostaglandin analogues are contraindicated, poorly tolerated, or inaccessible.	(Jóhannesson et al., 2024; Subbulakshmi et al., 2023)

Note. IOP = intraocular pressure. IOP reductions represent average class-level estimates. Direct comparative evidence on adherence and persistence between the two drug classes remains limited.

As summarized in Table 1, prostaglandin analogues offer a population-level advantage in intraocular pressure reduction and dosing simplicity, whereas topical beta-blockers remain clinically effective but require greater consideration of cardiovascular and respiratory safety. However, the stronger pharmacological efficacy of prostaglandin analogues does not necessarily translate into superior long-term effectiveness in every patient because treatment outcomes are also influenced by tolerability, comorbidities, medication accessibility, correct eye-drop administration, adherence, and persistence. Furthermore, evidence supporting differences in intraocular pressure reduction is more direct than evidence comparing adherence between the two drug classes. Treatment selection should therefore integrate class-level efficacy with individual clinical characteristics and the likelihood of sustained medication use. The pathway through which drug-class characteristics and patient- and healthcare-related factors influence medication adherence and real-world treatment outcomes is illustrated in Figure 1.



Figure 1. Conceptual relationship between drug-class characteristics, medication adherence, and real-world clinical effectiveness

Note. IOP = intraocular pressure. The framework represents a conceptual synthesis of the available evidence.

As illustrated in Figure 1, the comparative clinical effectiveness of prostaglandin analogues and topical beta-blockers is influenced by more than their intrinsic intraocular pressure-lowering efficacy. Dosing characteristics and safety profiles interact with comorbidities, treatment tolerability, medication accessibility, health literacy, eye-drop technique, and patient preferences. These factors may influence adherence and persistence, thereby affecting whether the expected pharmacological benefit is translated into sustained intraocular pressure control and preservation of visual function. The framework therefore emphasizes that treatment selection should integrate class-level efficacy with the feasibility of long-term medication use. However, because direct class-specific evidence comparing adherence between the two drug classes remains limited, the proposed relationships should be interpreted as an evidence-based conceptual synthesis rather than a quantified causal model.

3.6 Clinical Implications and Future Research Directions

Prostaglandin analogues are generally appropriate as initial pharmacological therapy for patients requiring substantial intraocular pressure reduction and a simple once-daily regimen. Their strong pressure-lowering effect, prolonged activity, and limited systemic adverse effects provide practical advantages for long-term treatment. Nevertheless, population-level superiority does not ensure optimal outcomes in every patient. Topical beta-blockers may remain appropriate when prostaglandin analogues are unavailable, unaffordable, contraindicated, or poorly tolerated. Their use requires careful assessment in patients with asthma, severe obstructive pulmonary disease, bradycardia, or cardiac conduction abnormalities. Conversely, conjunctival hyperemia, pigmentation changes, ocular-surface discomfort, and prostaglandin-associated periorbitopathy may limit the acceptability of prostaglandin analogues. The preferred treatment should therefore achieve an individualized target intraocular pressure while remaining safe, tolerable, and sustainable for long-term use (Hsia et al., 2025; Jóhannesson et al., 2024).

Treatment selection should incorporate comorbidities, concurrent medications, adverse-effect susceptibility, dosing convenience, medication cost, drug availability, eye-drop administration ability, and patient preferences. These considerations are important because a pharmacologically effective medication may provide limited clinical benefit when patients cannot obtain, tolerate, or administer it consistently. Shared decision-making should include patient education, assessment of eye-drop technique, discussion of anticipated adverse effects, and regular evaluation of adherence and persistence. When the prescribed medication fails to achieve target pressure or creates barriers to sustained use, switching therapy may be more appropriate than simply increasing regimen complexity. This patient-centered approach recognizes that long-term clinical effectiveness depends on the interaction between pharmacological efficacy, tolerability, accessibility, and consistent medication use (Baudouin et al., 2025; Moore et al., 2023; Quaranta et al., 2023).

Future head-to-head studies should evaluate prostaglandin analogues and topical beta-blockers under routine clinical conditions rather than focusing exclusively on short-term intraocular pressure reduction. Relevant outcomes should include target pressure achievement, pressure stability, objectively measured adherence, treatment persistence, adverse-effect-related discontinuation, visual-field progression, retinal nerve fiber layer changes, quality of life, and cost-effectiveness. Research in Indonesian populations is particularly needed because healthcare access, medication availability, out-of-pocket costs, health literacy, and eye-drop technique may influence treatment outcomes differently from those reported in high-income settings. Existing Indonesian studies indicate that education and family knowledge may support glaucoma medication adherence, but direct comparisons between prostaglandin analogues and topical beta-blockers remain limited (Wahyuni et al., 2023; Winarni et al., 2022). Multicenter prospective studies would therefore help determine which treatment strategies provide the most sustainable clinical benefits within the Indonesian healthcare context.

CONCLUSION

Prostaglandin analogues offer greater intraocular pressure reduction, longer action, and simpler once-daily dosing than topical beta-blockers, supporting their use as initial therapy for primary open-angle glaucoma. Beta-blockers remain valuable when prostaglandin analogues are contraindicated, poorly tolerated, inaccessible, or unaffordable. Selection should weigh not only pressure-lowering efficacy but also safety, comorbidities, cost, availability, and patient preference. Because adherence strongly shapes real-world outcomes, pharmacological superiority may not yield sustained control if dosing is irregular, whereas a consistently used beta-blocker can deliver lasting benefit. Patient education, correct instillation technique, and adherence monitoring are essential. Prospective Indonesian studies should compare both classes using standardized outcome measures.

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