

RESEARCH ARTICLE

Prescribing pattern and adverse events of drugs used in patients with primary open-angle glaucoma (POAG) attending a tertiary care hospital: Retrospective study

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ABSTRACT

Background: Primary open-angle glaucoma (POAG) is the most prevalent type of glaucoma leading to progressive loss of visual function in adults. **Aims and Objectives:** This study was conducted to determine the prescribing pattern and to assess the associated adverse reactions of drugs used in the treatment of POAG in a tertiary care teaching hospital. **Materials and Methods:** This was a retrospective, case-record-based study conducted on patients attending the department of ophthalmology for treatment of POAG at Srinivas Hospital, Mukka, from October 2014 to December 2015. The study was initiated after obtaining approval from the Institutional Ethics Committee. Data were analyzed using statistical package for social sciences version 17 and presented as percentages and frequency. **Results:** Out of 74 prescriptions analyzed, 48 (64.86%) patients were treated with monotherapy and 26 patients with combination therapy of drugs. The majority of patients were on timolol as monotherapy with prescription rate of 29.16% followed by bimatoprost 20.83%. Combination therapy was prescribed to 35.14% of the patients; the commonly used regimen was timolol + brimonidine (30.76% patients). 16 patients reported adverse effects such as blurred vision, ocular irritation, and foreign body sensation; however, the most of the patients tolerated the prescribed drugs well. **Conclusion:** The present study results help to know the different treatment strategies employed in the management of POAG, and reasons for the preference of prescribed drugs. Most of the patients tolerated the antiglaucoma medications well and had a few side effects which did not warrant discontinuation of treatment.

KEY WORDS: Antiglaucoma Drugs; Drug Prescribing Pattern; Primary Open-angle Glaucoma

INTRODUCTION

Glaucoma is a chronic, degenerative optic neuropathy, in which neuroretinal rim of the optic nerve becomes thinner

leading to enlargement of optic-nerve cup, degeneration of retinal ganglion cells, and their axons; it causes progressive visual field damage leading to irreversible loss of vision.^[1,2] Glaucoma is the second leading cause of blindness worldwide if left undiagnosed and or untreated leads to irreversible blindness.^[3,4] The prevalence of glaucoma increases significantly with age; primary open-angle glaucoma (POAG) is the most prevalent type of glaucoma in adult.^[5] POAG is characterized by unobstructed iridocorneal angle but diminished outflow of aqueous humor^[1] leading to raise in intraocular pressure (IOP) >21 mm Hg.^[6] Previous studies reported that about one-third of patients with glaucoma

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without elevated IOP are affected with normal-tension glaucoma.^[7] About 12% of all cases of blindness worldwide are due to POAG.^[3,4] It is predicted that incidence of patients with glaucoma may increase up to 79.6 million by 2020; of which, 74% may be affected with open-angle glaucoma.^[3] Randomized controlled trials have shown that reduction in IOP can delay glaucomatous nerve and field damage.^[7] IOP is the only modifiable risk factor in glaucoma.^[8] The treatment for POAG is mainly focused on controlling the IOP by medications to prevent disease progression and the need for surgical interventions. The commonly used drugs for the treatment of glaucoma include β -blockers, prostaglandin analogs, and carbonic anhydrase inhibitors.^[9] Newer antiglaucoma drugs have been introduced into the Indian market with increased efficacy and lesser adverse effects.^[10] When a monotherapy is not sufficient to achieve adequate IOP reduction, fixed dose combinations (FDCs) of drugs have been used to improve the compliance and quality of life.^[11]

Prescribing behavior of clinicians depends on sources such as academic literature, commercial publicities, government regulations, and professional colleagues.^[12] However, in a developing country like India, national drug policy is required to rationalize drug usage in this context. There is a paucity of studies on the prescription pattern of antiglaucoma drugs,^[13] hence in the present study, we have made an effort to evaluate the prescription pattern of drugs used in treatment of POAG, the preference pattern of drugs if any and adverse effects related to them in a tertiary care teaching hospital.

MATERIALS AND METHODS

A retrospective, case-record-based study was conducted from October 2014 to December 2015 at a tertiary care teaching Hospital (Srinivas Hospital, Mukka, Mangalore). The Institutional Ethics Committee approval was obtained before the commencement of the study.

Selection Criteria

Inclusion criteria

Patients of either sex; age > 40 years.

Patients diagnosed and treated for POAG in Srinivas Hospital, Mukka, Mangalore.

Patients with a minimum duration of therapy of 3 months.

Exclusion criteria

Patients diagnosed to have angle closure glaucoma and secondary glaucoma.

Patients diagnosed to have other ophthalmological disorders (ocular inflammation, corneal abnormality, and cataract)

that pose difficulty in applanation tonometry, visual field, or fundus evaluation.

All prescriptions of patients treated for POAG in the Department of Ophthalmology at Srinivas Hospital, during the aforementioned duration of the study; satisfying the inclusion criteria were included. With the help of a proforma, patients detailed demographics data (age, gender, and medical history) and drug data (generic/brand name, dosage form, route of administration, frequency of instillation, and duration of treatment) were recorded. Adverse effects that occurred due to antiglaucoma drugs were recorded, and the WHO causality assessment scale was used to assess suspected adverse drug reaction (ADR).^[14]

Statistical Analysis

Data analysis was carried out using statistical package for social sciences program version 17. The results obtained were expressed as frequency and percentage.

RESULTS

A total of 74 case records of patients diagnosed with POAG fulfilling the criteria for inclusion were analyzed; among them, 44 (59.45%) were male and 30 were (40.54%) female. The age distribution of patients with POAG is shown in (Table 1), peak incidence of POAG was observed in patients of age group 51-60 years (31 patients, 41.89%) followed by 61-70 years age group (22 patients, 29.72%).

Among 74 patients with POAG, monotherapy was prescribed to 48 patients (64.86%) and 26 patients (35.14%) received combinations. All the drugs in case of monotherapy were prescribed through topical route (eye drops). The different groups of drugs prescribed were β -blockers (41.66%), prostaglandin analogs (33.33%), α_2 adrenergic receptor agonist (16.66%), and carbonic anhydrase inhibitors (8.33%) (Figure 1). β -blockers followed by prostaglandin analogs were the most frequently prescribed group of drugs. Most commonly prescribed topical medication was timolol 0.5% solution (29.16%) followed by bimatoprost 0.03% solution (20.83%).

Concurrent and FDCs were prescribed to 26 patients who received combination therapy. Timolol + brimonidine (30.76%) was the most frequently prescribed FDC followed by topical timolol + oral acetazolamide (26.92%) combination.

Table 1: Age distribution of study group

Age (years)	Number of patients (%)
41-50	5 (6.75)
51-60	31 (41.89)
61-70	22 (29.72)
>71	16 (21.62)

The triple drug combination prescribed was timolol + brimonidine + acetazolamide (3.84%); the prescription rate of combination therapy is shown in Figure 2.

Out of 74 patients, mild ocular or periocular ADRs were reported in 16 patients, of which blurred vision was reported

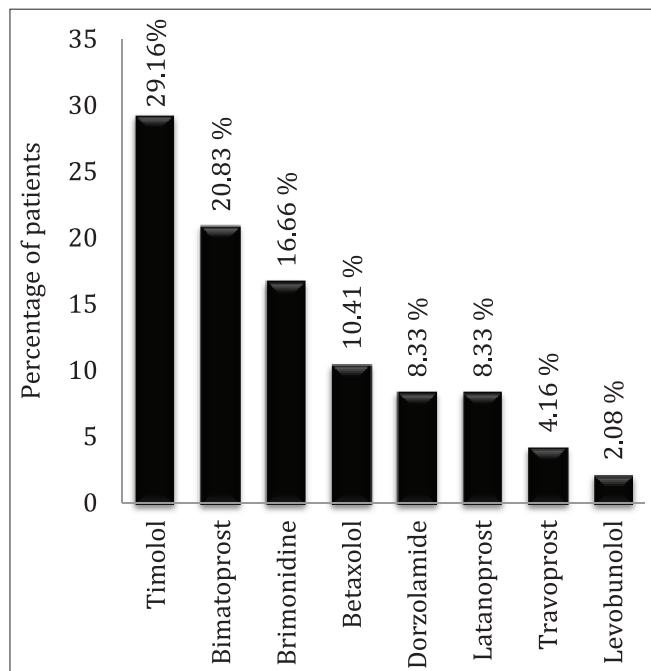


Figure 1: Prescribing pattern of drugs (monotherapy) for glaucoma

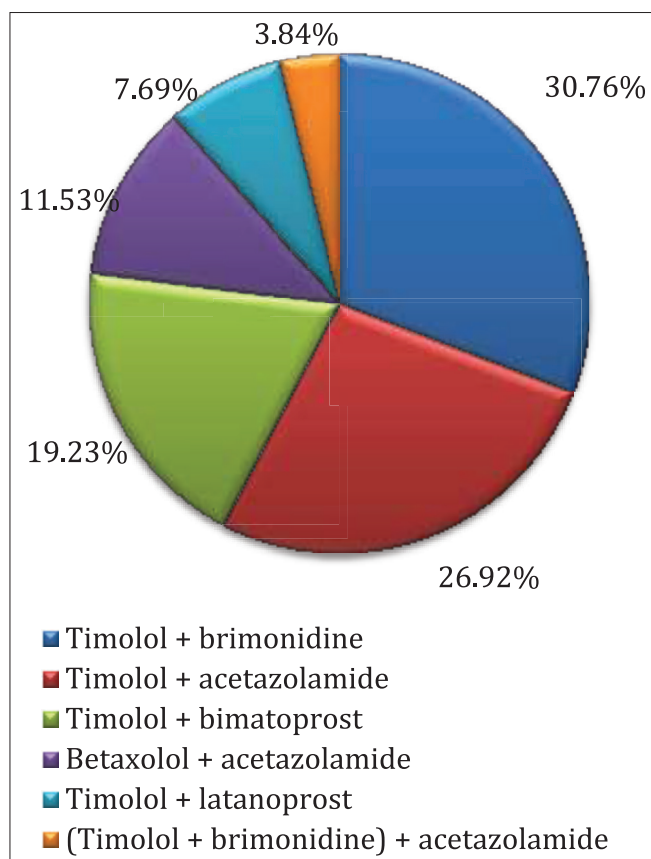


Figure 2: Prescription rate of different drugs used for combination therapies

by 3 patients (4.05%) who received timolol and 1 (1.35%) patient on timolol + latanoprost. Foreign body sensation was observed among 2 (2.70%) patients who were on timolol + brimonidine and 1 (1.35%) on latanoprost. Ocular irritation was reported by 1 (1.35%) patient on timolol + bimatoprost, 1 (1.35%) on timolol + acetazolamide, 2 (2.70%) on betaxolol, and 1 (1.35%) patient on bimatoprost had reported ocular stinging. Thickening and lengthening of eyelashes were reported by patients who were on prostaglandin analogs 1 (1.35%) on timolol + bimatoprost, 2 (2.70%) on latanoprost, and 1 (1.35%) on travoprost. Most of the drugs were well tolerated; none of the adverse effects were serious or required discontinuation of suspected drug. All ADRs were classified as “probable” according to the WHO causality term assessment criteria of suspected adverse drug reactions.

DISCUSSION

In this study, we evaluated the drug prescribing pattern of 74 patients with POAG; among them, 44 (59.45%) were males and 30 (40.54%) females. There was no significant gender predominance in our study group (M:F = 1.46:1). The peak incidence of POAG was observed in 31 (41.89%) patients of age group 51-60 years. These findings corroborated with the other similar studies carried out in India, revealing that there is no gender predilection in the prevalence of POAG but the risk increases along with advancing age.^[15,4] However, slight female predominance was observed in POAG studies reported in India.^[16,17]

The most common mode of therapy was topical, i.e., as eye drops, the only oral drug prescribed was acetazolamide; this result is similar to other studies reported from India.^[10,16] Rationale of preference of topical over oral therapy is to minimize systemic side effects.^[18]

In our analysis, 64.86% patients used topical monotherapy, with a β -blocker (41.66%), timolol 0.5% being the most common drug in the same group (29.16%). This pattern was consistent with similar studies carried out in India^[10,16] and New-Zealand^[19] but in contrast to previous studies reported from Australia,^[19] Japan,^[20] Canada,^[21] and North America,^[22] where the preferred first-line therapeutic agent for glaucoma was prostaglandin analogs. Economic constraints may be the reason for this difference among various countries as reported by a study conducted in New-Zealand, government restrictions and level of awareness were the factors favoring the prescription of β -blockers among the antiglaucoma drugs.^[19] In our study, other β -blockers used in monotherapy to treat POAG were betaxolol (10.41%) and levobunolol (2.08%); betaxolol was prescribed less frequently because it being a selective β_1 -blocker is less effective and levobunolol though comparable to timolol is expensive.^[10,16]

Prostaglandin analogs (33.33%) were the second most frequently prescribed group of drugs. Bimatoprost 0.03% solution was the commonly prescribed drug in this group

(20.83%). Other drugs such as latanoprost (8.33%) and travoprost (4.16%) were prescribed less frequently probably because among prostaglandin analogs bimatoprost is economical and needs single instillation at bedtime and latanoprost requires refrigeration.^[23,24] Prostaglandin analogs compared to β -blockers have greater efficacy in lowering diurnal and nocturnal IOP with lesser systemic adverse effects,^[25,26] justifying the changing trend in glaucoma prescription favoring prostaglandin analogs though expensive as compared to β -blockers. However, these findings were contrary to similar studies conducted in India where brimonidine, α_2 adrenergic receptor agonist, was the second most commonly prescribed drug in the treatment of POAG.^[16,18] In our study, only 16.66% of prescriptions include brimonidine as monotherapy which was much less as compared to other studies from India,^[10,16] probably less preferred because of the frequency of instillation required being higher (3 times a day).

In our study, topical carbonic anhydrase inhibitor dorzolamide was prescribed in (8.33%) patients, which was not the trend seen in other studies from India where dorzolamide was prescribed less frequently as monotherapy instead oral acetazolamide was prescribed;^[10] the reasons for less number of prescriptions for dorzolamide monotherapy probably are because of higher frequency of instillation being necessary 3 times a day as compared to prostaglandin analogs and higher cost as compared to β -blockers. Both these factors are important in considering the compliance in patients with POAG which plays an important role in control and prevention of progression of the disease.

As per studies, combination therapy yields better result than monotherapy; it tends to achieve a higher reduction in IOP.^[27] However, combination therapy is given only when the patient requires more than one antiglaucoma medications. Combination therapy can be with fixed drug combinations or concurrent use of more than one antiglaucoma medications. FDC therapy leads to improved compliance and enhances patient convenience as compared to concurrent use of medications separately, thereby simplifying the dosing regimen and also it becomes cost-effective.^[28,29] 26 of our patients (35.14%) received combination therapy in the form of FDC and concurrent therapy. Of these, FDC was used in 53.83% patients and 46.14% patients on concurrent therapy, this was in concordance with the similar study conducted in India where FDC was prescribed in 26.66% of prescriptions.^[16] The prescription rate of concurrent therapy being justified considering the inconvenience of using separate bottles adjusting the timing of medication and cost factor of two drugs to the patients.

In our study, timolol + brimonidine (30.76%) was the most frequently prescribed FDC followed by timolol + acetazolamide (26.92%). These findings are different from most of the earlier reported studies where timolol + acetazolamide was found to be most commonly prescribed combination.^[16,10] Here, it shows increasing trend toward prescribing topical medications over oral acetazolamide which has higher systemic side effects such as paresthesia,

metabolic acidosis, tinnitus, and bone marrow depression (26,28). In our hospital, acetazolamide was prescribed in cases of acute rise in IOP or IOP >30 mmHg for a short duration, along with topical drugs, then discontinued and the patient was continued on topical drugs thereby explaining the lesser use of acetazolamide. The triple drug combination prescribed was timolol + brimonidine + acetazolamide in 3.84% patients; most of the studies have not commented about use of triple drug combination. However, one of the earlier studies states that this combination is more effective in decreasing IOP and has neuroprotective effect.^[30]

Out of 74 patients, adverse effects were reported by 16 patients which include blurred vision, foreign body sensation, ocular irritation, ocular stinging, thickening, and lengthening of eyelashes. These ADRs were similar to those reported in previous studies.^[31,32] Some of the earlier studies have shown that higher frequency of instillation of drugs and the preservatives used in ophthalmic solutions are responsible for these symptoms.^[33-36] In our study, the reported adverse effects were not severe, and none of the patients had to discontinue the treatment. With respect to side effects, however, there is a need for further studies to elucidate the adverse event profile and long-term implications of the drugs used in the treatment of POAG.

There are some limitations in our study; results of this study cannot be generalized as it was conducted with limited sample size in a single center which may not be adequate to reflect the exact picture of the prescribing pattern. Since there is always under-reporting of side effects, the same study done prospectively would have been more useful. Hence, there is a need to conduct multicentric studies regarding the different therapeutic strategies used in treatment of POAG and probably formulate the guideline for ideal prescription pattern for POAG to improve the quality of patient care.

CONCLUSION

The present study results provide an insight into the different treatment strategies employed in the management of POAG. There is an increasing trend toward prescribing topical medication over systemic drugs; and FDC over concurrent use of topical drops. Timolol remains the first choice of treatment probably due to patients from the low socio-economic group in our study. Timolol + brimonidine is the most commonly prescribed combination. Our study provides a framework of adverse reactions to the drugs prescribed in treatment of POAG.

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