

Drug Prescribing Pattern & Adverse Drug Effects Of Anti Glaucoma Medication for Primary Glaucoma at Tertiary Care Hospital

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Abstract

Objective: The study aims to analyse the Drug prescribing pattern and Adverse drug effects of Antiglaucoma medication for Primary Glaucoma in a Tertiary care teaching hospital.

Methods: It is an Observational Study done on 100 patients of Primary Glaucoma presenting in Out patients department of Glaucoma unit at Sarojini Devi Eye Hospital. The study was carried for a period of 6 months. Details regarding patients demographic data, drugs prescribed and any adverse effects to Antiglaucoma medication were noted.

Results: Over a period of 6 months it was found that out of 100 cases of Primary Glaucoma 50 were males and 50 were females. There were more than 50% of PACG cases reported than POAG. Out of 100 cases Combination therapy was prescribed in 87 patients and Monotherapy in 13 patients. Among these combination therapy, 72 patients were on Concomitant therapy and remaining were on FDC. Dorzolamide & Timolol FDC were commonly prescribed followed by Brimonidine & Timolol and Timolol+Travoprost. Among monotherapy Beta blockers were commonly prescribed followed by Prostaglandin analogues & Carbonic Anhydrase Inhibitors.

In total of 100 cases 32 patients reported ADRs. Itching was the most common ADR. Most of ADRs were due to Dorzolamide + Timolol eye drops followed by Prostaglandin analogues.

Conclusion: From the present study it is concluded that there are various treatment strategies in the management of Primary Glaucoma. ADRs to Ocular hypotensive agent is not uncommon and have major impact on Glaucoma treatment. Ideal combination that can lower IOP with minimal adverse effect is preferable.

Keywords: ADR, FDC- Fixed drug combination, PACG, POAG.

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I. Introduction

The glaucomas are a group of diseases with characteristic optic disc changes correlating with the visual field changes where there is a progressive ganglion cell loss, intraocular pressure being a modifiable risk factor.

Glaucoma affecting 60 million people all over the world and it will be 80 million till 2020. There are approximately 11.2 million persons aged 40 years and older with glaucoma in India.^[1] Glaucoma is the second leading cause of vision loss worldwide after cataracts.^[2-3]

Primary open angle glaucoma (POAG) is the most common type of glaucoma accounting for three-quarters (74%) of all glaucoma cases. A recent review estimated the global number of POAG cases in 2013 at 44 million, rising to 53 million by 2020 due to population ageing. Review also showed that the greatest increase of POAG cases is estimated to be in lower income countries, particularly Asia, due to more rapid ageing compared with countries of European ancestry. This will have considerable impact on the total number of cases, as Asia has 60% of the world's adult and aged population.^[4]

The highest prevalence rates of PACG were reported in Japan (1.19%) and China (1.10%), followed by Middle East (0.97%), South East Asia (0.66%), and India (0.46%). A recent systematic review found that the prevalence of PACG in those 40 years or more in European derived populations is 0.4%. Therefore, the

prevalence of PACG in Asians, especially in East Asians and South East Asians, is higher than those in Europeans.^[5]

1.1 Types Of Glaucoma:-

There are several types of glaucoma of which primary open angle and angle-closure glaucoma are common.

Other variants of Open angle and Angle closure glaucoma are less common & they are Secondary glaucoma, Congenital glaucoma, Pigmentary glaucoma, Pseudoexfoliative glaucoma, Traumatic glaucoma, Neovascular glaucoma, Irido Corneal Endothelial Syndrome .

Secondary glaucoma can result from trauma, certain medications such as corticosteroids, inflammation, tumor, or conditions such as pigment dispersion or pseudo-exfoliation.

1.2 Classification of Antiglaucoma agents:^[6]

Depending on their route of administration Antiglaucoma agents may be classified as:-

Topical drugs: Cholinergic agents (eg. pilocarpine, carbachol, demecarium bromide and echothiophate iodide). Adrenergic agonists (e.g. epinephrine, dipivefrine, brimonidine and apraclonidine), Beta blockers (e.g. timolol, carteolol, betaxolol, levobunolol and metoprolol), Prostaglandin analogs (e.g. PGF2α , latanoprost, unoprostone and PHXA-85), Carbonic anhydrase inhibitors (e.g. dorzolamide and brinzolamide).

Systemic drugs:

1. Carbonic anhydrase inhibitors e.g. acetazolamide and methazolamide.
2. Osmotic agents e.g. glycerine, mannitol and urea.

Miscellaneous drugs include forskolin, ethacrynic acid, steroid antagonists, cannabinoids, angiotensin converting enzyme inhibitors, atrial natriuretic peptide and neuroprotective agents.

1.3 Mechanisms of action of Antiglaucoma agents:-

The antiglaucoma agents act on the aqueous humor dynamics to reduce the intraocular pressure mainly by three mechanisms.

- Decrease aqueous production in the ciliary body
- Increase aqueous humor outflow through the trabecular meshwork and
- Increase aqueous humor outflow via the uveoscleral pathway

1.3 Table:- Local and systemic adverse events associated with glaucoma medications^[7]

Glaucoma medication	Local part of the eye	Systemic adverse events
Parasympathomimetic drugs	+	++
Sympathomimetic drugs	+	+
Beta-blockers	+	++
Carbonate dehydrate inhibitors	+	-
Prostaglandin analogs	++	-
Alpha-1 blockers	+	-
Alpha-2 adrenergic agonist	+	+

Notes: ++ innumerable; + many; few

Preservatives are contained in most ophthalmic preparations and prolong the shelf life of many by preventing biodegradation and maintaining potency. ^[8] Benzalkoniumchloride (BAK), which has surfactant, bactericidal, and bacteriostatic properties, is the most commonly used preservative in ophthalmic preparations. ^[9] Other Compound used as preservative in topical medication are PQ (polyquaternium-1), BAK, Sofzia.^[10]

Studies have shown that chronic topical glaucoma therapy can lead to alterations in both tear film and fluoresceine staining of the corneal surface, and an increase in inflammatory cytokines among other deleterious effects.^[11-14] These ocular surface changes have typically been blamed on the preservative commonly used in multidose bottles of topical medication, BAK ²

Due to adverse reactions, some patients' medication compliance may decrease because of bothersome cosmetic adverse reactions (eg, conjunctival hyperaemia, eyelid pigmentation); some patients may choose to discontinue glaucoma medications on their own. Therefore, adverse reactions should be thoroughly explained to patients before beginning a new glaucoma eye drop and their presence should be checked at every clinic

evaluation . In the present study we have made an effort to evaluate the prescription pattern and Adverse drug effects of Antiglaucoma medications for Primary glaucoma.

II. Materials And Methods

An Observational ,prospective open labelled study conducted at Sarojini Devi Eye Hospital which included 100 patients with Primary Glaucoma ,over a peroid of 6 months after approval from the Institutional Ethics Committee and informed consent from the patients.

2.1 Selection Criteria:

Inclusion Criteria:

Patients > 40 years of age diagnosed as Primary glaucoma and on medication.

Newly diagnosed patients with primary glaucoma

Patients of either sex.

Exclusion Criteria:

- Glaucoma due to secondary causes.

- Patients with diagnosis of any corneal pathology.

- Patients of ocular trauma

- Patients with a diagnosis of ocular inflammation e.g. uveitis

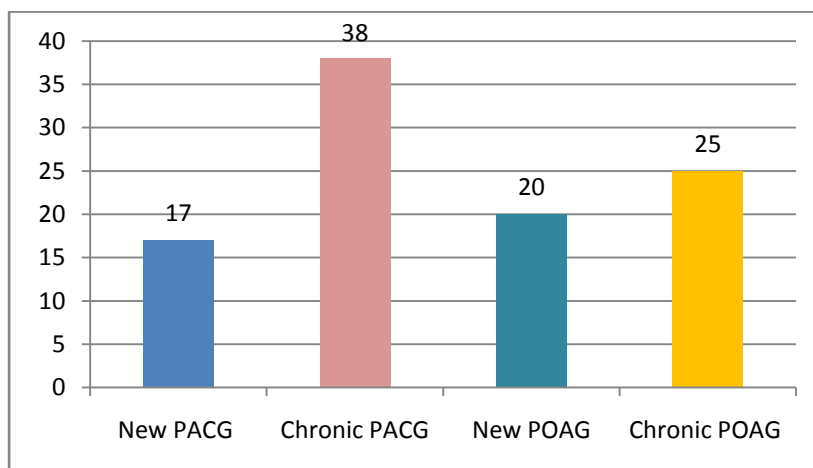
-Pregnant or lactating female

With the help of a proforma, patients demographic data and drug data were recorded (generic name, dosage form, route of administration, frequency of instillation, and duration of treatment). All prescriptions of patients treated for Primary glaucoma and the adverse effects of antiglaucoma medications during 6 months period at Sarojini Devi Eye Hospital were recorded.

2.2 Statistical analysis: Microsoft Excel, SPSS

III. Results

In 6 months duration of of study,out of 100 cases of primary glaucoma, 50 were males and 50 were females. Peak incidence was seen in age group 40 -60 yrs .Out of 100 cases of primary glaucoma there were 20 newly diagnosed cases of POAG,17 newly diagnosed cases of PACG,25 cases of chronic POAG, 38 cases of chronic PACG reported.

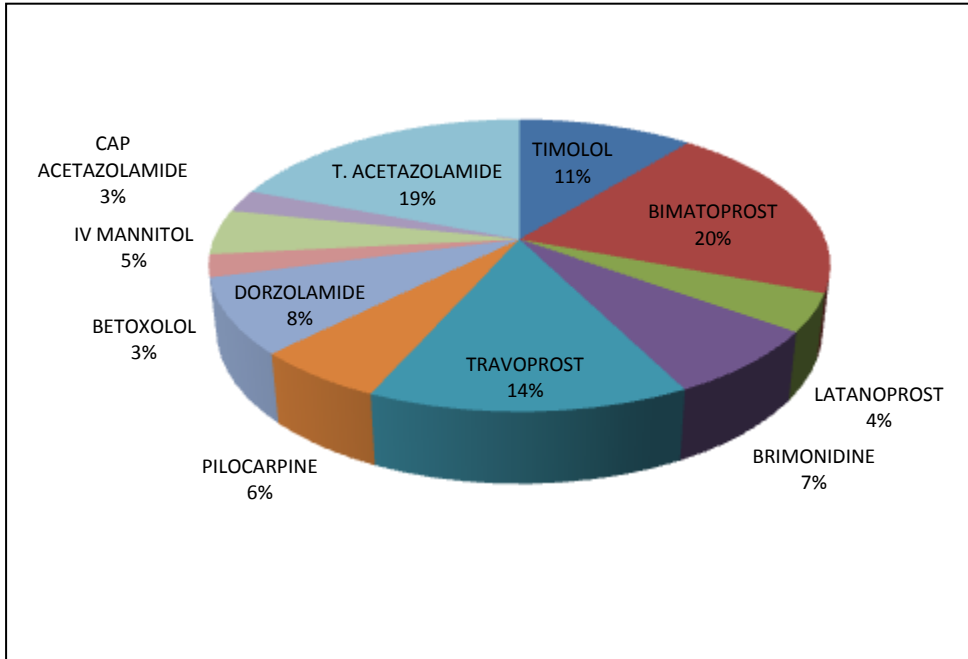


Different drugs were prescribed through different routes of administration(topical route,oral and parenteral).It was found that maximum numbers of drugs were prescribed through topical route followed by oral and parenteral route.

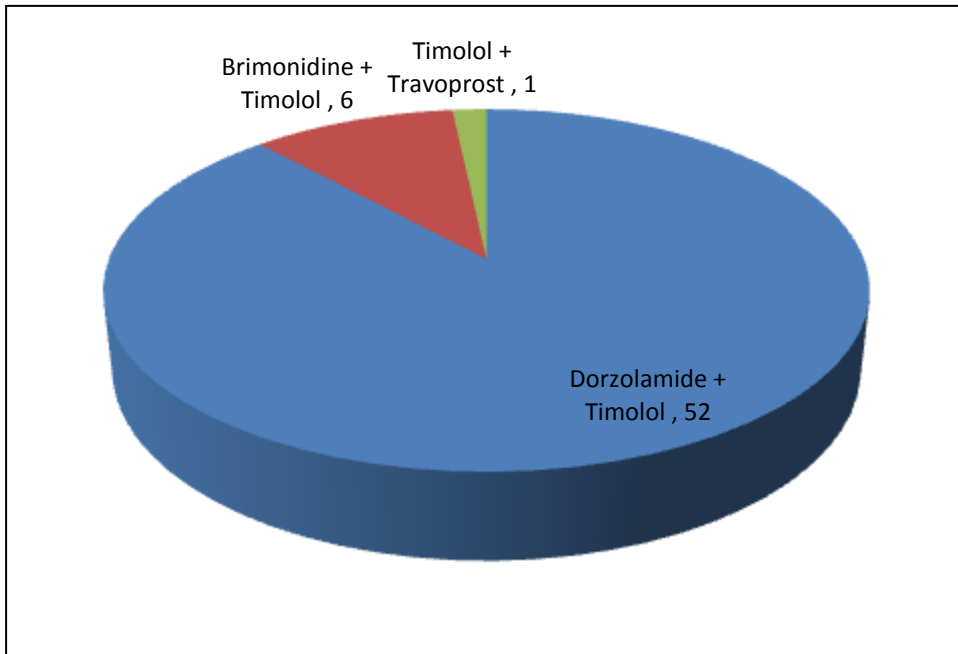
Combination therapy (which includes FDC & concomitant therapy) were prescribed in 87 patients and monotherapy in 13 patients. Of these FDC was prescribed in 15 patients (dorzolamide + timolol in 13 patients,brimonidine + timolol in 1 patient,timolol + travoprost in 1 patient) and the remaining 72 patients were on concomitant therapy. Among monotherapy, betablockers were commonly prescribed followed by prostaglandin analogues ,carbonic anhydrase inhibitors. Acetazolamide (carbonic anhydrase inhibitor) was the orally prescribed drug (tablet form and capsule form). Mannitol (osmotic diuretic) was the parenterally (I.V) prescribed drug.

In our study dorzolamide + timolol was the most commonly prescribed fixed drug combination followed by Brimonidine + timolol, Timolol+ travoprost.

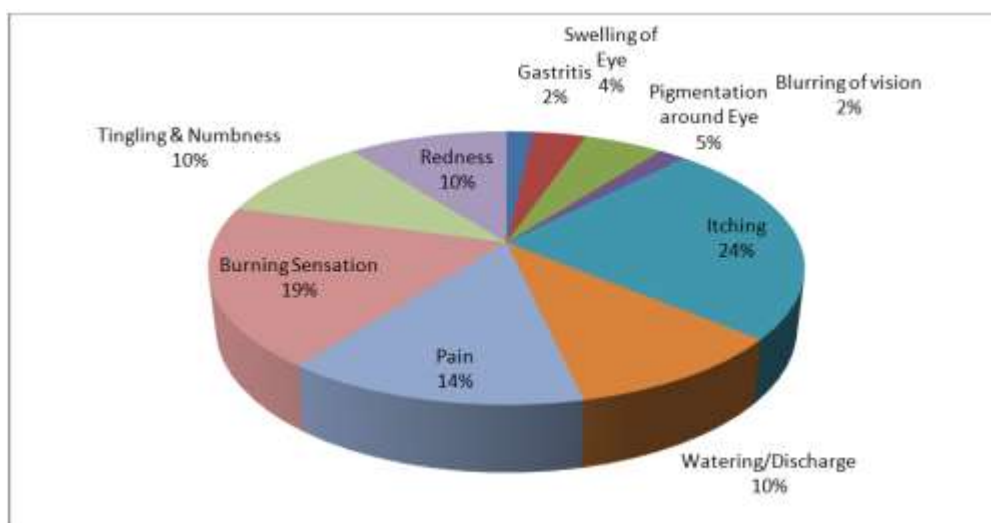
PRESCRIPTION PATTERN OF ANTIGLAUCOMA MEDICATION



FIXED DRUG COMBINATIONS



32 patients out of 100 reported adverse drug effects. Itching(24%) was the most common ADR followed by burning sensation of the eyes(19%), pain(14%), watering/discharge(10%), redness(10%),tingling and numbness(10%).



IV. Discussion

Glaucoma still continues to be the major cause of irreversible visual disability all over the world. In this study, we evaluated the drug prescribing pattern and adverse effects of antiglaucoma medication of 100 patients with Primary glaucoma. The peak incidence of Primary Glaucoma was observed in 40-60 years. There is no sex predilection. Out of 100 patients with primary glaucoma, chronic PACG cases were most commonly reported. These findings are similar to previously reported studies. Patients were treated with various drugs in different dosage forms & ongoing medical treatment was modified according to the response.

Beta blockers (timolol) are the most common class of monotherapeutic agents prescribed followed by prostaglandin analogues. Carbonic anhydrase inhibitors (acetazolamide, dorzolamide) were the next class of drugs prescribed. Acetazolamide was prescribed both in tablet and capsule form. Oral acetazolamide was prescribed in 5 patients who are newly diagnosed cases of POAG, 8 patients who are newly diagnosed cases of PACG, in 2 patients of chronic POAG, 8 chronic cases of PACG. Cholinergic drugs (Pilocarpine) were the next class of drug prescribed. Adrenergic agonists were the other class. Among them alpha 2 agonist brimonidine was prescribed. Osmotic diuretic (Mannitol) was the parenteral drug prescribed. 2 patients with chronic primary angle closure glaucoma required I.V Mannitol. The most common fixed drug combination prescribed for primary glaucoma was dorzolamide + timolol, through topical route. Other fixed drug combinations were Brimonidine+timolol, Timolol+travoprost.

4.1 Adverse Drug Effects:- 6 patients reported adverse effects with use of prostaglandin analogues. Among them 2 patients using bimatoprost eye drops reported periocular pigmentation, 2 patients reported redness and itching of eyes. 1 patient using travoprost eye drops reported pain, itching and watering of eyes, 1 patient reported ocular pain. 1 patient using bimatoprost reported pain, redness, itching of eyes for two consecutive days. 4 patients reported tingling sensation in feet, face and hands with oral acetazolamide. Dorzolamide was given topically and 3 patients reported ADRs which included ocular pain, blurred vision, watering, itching of eyes. 4 patients reported burning sensation in eyes after instillation of eye drops (pilocarpine) lasting for initial 5 -10 mins and later subsided.

2 patients reported ADRs with use of alpha 2 agonist brimonidine which included pain, itching, watering, burning sensation in the eyes.

2 patients reported tingling sensation in feet, hands with intravenous Mannitol

7 patients using Dorzolamide+timolol eye drops reported adverse effects which included ocular pain, burning sensation of eyes, watering and itching of eyes

Few patients discontinued the prescribed medication due to adverse effects. Among them 1 patient (brimonidine eye drops), 2 patients (dorzolamide eye drops), 1 patient (bimatoprost eye drops), 1 patient using FDC of brimonidine & timolol eye drops, 2 patients who were prescribed oral acetazolamide discontinued the medication due to intolerable adverse effects.

V. CONCLUSION

In our study PACG accounted for more than 50% of the glaucoma cases.

From the present study, it is concluded that there are various treatment strategies in the management of Primary glaucoma (both closed angle and open angle). There is an increasing trend of using topical fixed drug combination over systemic drugs. More than 30-40% glaucoma patients require two or more drugs to achieve the target intraocular pressure (IOP).

FDC therapy leads to improved compliance and enhances patient convenience as compared to concomitant therapy, thereby simplifying the dosing regimen and also it is cost effective^[15,16]

In our study ADRs occurred most frequently with use of topical FDC dorzolamide & timolol followed by prostaglandin analogues. This study has identified those patients who presented subjectively with signs & symptoms. Under-reporting of ADRs is common and it is possible that several patients with local and systemic ADRs may be missed. These undesirable effects may reduce the tolerability of drugs and discontinuation of the drug. Use of preservative-free medication improves the compliance.

Treatment of glaucoma has a long course of duration and hence adherence to the treatment regimen is desirable. In a country like India where financial resources are limited, it becomes necessary to provide treatment of glaucoma in a cost-effective manner. Ideal combination therapy that can lower IOP with minimal adverse effects is preferable. Our study provides a framework of prescribing pattern & adverse effects to the drugs prescribed in the treatment of primary glaucoma (open angle & angle closure) at Sarojini Devi Eye Hospital. This pattern of drug prescription in an Apex institution in Telangana may not reflect the drug prescribing pattern of the whole community because this hospital renders services to many patients who are below the poverty line. Keeping this in mind, the physician prescribed dorzolamide and timolol FDC as a choice rather than going for prostaglandin analogues.

Extensive research in this field will lead us forward into a promising era of glaucoma therapy.

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