Naturalistic Evaluation of Prescription Pattern in Glaucoma Clinic of a Tertiary Care Hospital: A Developing Country’s Perspective

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Background: Glaucoma is a chronic, gradual and progressive eye disorder characterized by visual loss and involving the typical changes in optic nerves and associated structures. Currently, the mainstay treatment lies in the reduction of intraocular pressure (IOP) involving the usage of two or three medications concurrently. However, prescription pattern of antiglaucoma drugs remains largely unstudied so far. Therefore, there is a dire need of drug utilization studies to ensure rational prescribing for better treatment outcomes. Aim: This study was conducted to assess the prescription pattern in glaucoma patients to encourage rational use of drugs. Materials and Methods: The pertinent data of confirmed glaucoma patients were entered in a predesigned case record form (CRF) including patient demographic details, type of glaucoma, number of drug prescribed, drug dosage and dosage formulation with prior patient consent, and finally, the data were analyzed using Microsoft Excel. Results: A total of 247 glaucoma patients were recorded in the study. The mean SD number of drugs per prescription was 2.18 (1.68). Monotherapy was prescribed to 72 (29.15%) patients, and the most common monotherapy prescribed was timolol, whereas in fixed-dose combinations (FDCs), brimonidine and timolol FDCs were most commonly encountered. Furthermore, prescriptions consisting of generic drugs only and prescribed as per the National List of Essential Medicines (NLEM) were 48 (19.43%) and 41 (16.59%), respectively. Conclusion: This study showed the judicious use of medications in tune with principles of rational drug use in our center, and the rationale practices can be extended to the peripheral centers of the country for better drug utilization.

Keywords: Drug utilization study, glaucoma, prescription, rational drug use, tertiary care center

INTRODUCTION

Drug utilization research as defined by the World Health Organization (WHO) as evaluation of the “marketing, distribution, prescription, and use of drugs in a society with special emphasis on resulting medical, social and economic consequences.”[1] Drug utilization studies are powerful exploratory tools to ascertain the role of drugs because the periodic monitoring of prescribing pattern helps in the advancement of rational use of drugs.[2] The principle aim of drug utilization research is to encourage the rational use of drugs by analyzing the drug use pattern, generating early signs of irrational drug use, and suggesting intervention to improved drug usage.[3]

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Glaucoma is the second most common cause of blindness worldwide,\[^4\] and the third most cause of blindness in India.\[^5\] In India, around 12 million people are affected, which account for 12.8% of the country's blindness.\[^6\] Several antiglaucoma drugs are available, and newer drugs are being marketed. Various classes of drugs commonly used for glaucoma include beta adrenergic blocker (timolol), carbonic anhydrase inhibitors (acetazolamide, brinzolamide, and dorzolamide), prostaglandin analogues (bimatoprost, latanoprost, and travoprost), and α adrenergic agonist (brimonidine).\[^7\]-\[^11\] Various combinations of drugs, used in treating the glaucoma disorder, might lead to irrational prescription.

Critical appraisal of drug utilization studies in glaucoma is not investigated so far. Nevertheless, the importance of such studies cannot be ignored. There is no denying that nonadherence of specialists to the regulatory guidelines can lead toward irrational use of drugs.\[^12\] Therefore, this study was carried out to determine the prescription pattern in glaucoma clinic to promote rationale use of drugs, which may help in improving the patient compliance, and hence, the effectiveness of the treatment.

**Materials and Methods**

**Site of study**

This observational study was conducted in Glaucoma Clinic, Advanced Eye Center, Postgraduate Institute of Medical Sciences and Research (PGIMER), Chandigarh, India, a tertiary care government hospital in India, with prior approval from Institutional Ethics Committee (vide letter no. INT/IEC/2016/875).

**Inclusion and exclusion criteria**

The study included the participants of either sex with confirmed glaucoma disorder. Patients diagnosed with any ophthalmic disorder, other than glaucoma, were excluded in the study.

**Data collection**

A total of 247 diagnosed patients of glaucoma attending Glaucoma Clinic outpatient department (OPD) between February and November 2016, were included in the study. All pertinent data including demographic details, drugs prescribed, dose, route of administration, dosage formulation, frequency, and duration of treatment were recorded in a predesigned case record form (CRF). Diagnosis was made on the basis of intraocular pressure (IOP), fundus evaluation, gonioscopy examination, or some relevant family history of patient by using advanced technique such as optical coherence tomography. Heidelberg retinal tomography was performed wherever required, under the supervision of consultant or professor of glaucoma clinic. The prescription data were obtained and recorded in CRF after obtaining consent from the patient.

**Study outcome**

The study outcomes include the number of drugs per prescription, most commonly prescribed class of drugs in primary open-angle glaucoma (POAG) and primary angle-closure glaucoma (PCAG); percentage of prescriptions prescribed as monotherapy, polytherapy, or fixed-dose combinations (FDCs); percentage of patients prescribed as generics, branded or both; and number of prescriptions consisting medicines as per National List of Essential Medicines (NLEM-2015).

**Statistical Analysis**

Data were presented as mean (standard deviation [SD]) or percentage (%) and were analyzed by using the Microsoft Office Excel 2013 (version 15.0). Data were presented in both text and tabular form.

**Results**

A total of 247 prescriptions were evaluated. The characteristics of patients are detailed in Table 1. Mean (SD) of drugs per prescription was 2.18 (1.68), and specifically, in case of POAG, it was 2.47 (1.46), whereas in 145 encounters of referral cases, mean (SD) of drugs per prescription was 5.04 (1.52). Among referred 145 patients, 37 were receiving steroids either in topical or inhalant form, and importantly, four of them were diagnosed as steroid-induced glaucoma. All these four patients were receiving inhalational steroids for bronchial asthma.

Although carbonic anhydrase inhibitor appears to be most prescribed class 69 (27.35%) but, only as an adjuvant drug, not as a monotherapy. Prostaglandin analogues and pilocarpine were prescribed, either as monotherapy or in combination with other agents in 60 (24.29%) and 10 (4.05%) encounters, respectively. Nearly, 41% (101) patients were prescribed with FDCs. In addition, timolol and brimonidine (52 of 101) are the most prescribed FDCs, followed by dorzolamide and timolol (48 of 101) [Table 2].

POAG was seen in 157 (63.56%) patients, and hence, it is the most encountered type of glaucoma in our study. The prescription pattern in POAG patients is same as of the overall glaucoma prescription pattern. Timolol (26 of 157) is the most prescribed monotherapy in POAG patients followed by travoprost (20 of 157) and brimonidine (17 of 157) [Table 2].
Among 247 cases of glaucoma, 72 patients were prescribed monotherapy with timolol as the most prescribed agent (28 of 72), followed by travoprost (25 of 72), brimonidine (18 of 72), and levobunolol (1 of 72). On remaining 175 encounters, patients were either prescribed polytherapy or were advised for surgery or both, depending on the IOP after topical or oral medications [Table 3].

A total of 19.43% (48 of 247) prescriptions were prescribed with generic drugs only, and 16.6% (41 of 247) were prescribed as per the NLEM only (NLEM-2015). The most commonly used dosage formulation is either eye drops alone 69.23% (171 of 247) or in combination with oral medications 29.55% (73 of 247) [Table 4].

**DISCUSSION**

Pharmacoepidemiology is a branch of science that focuses on the analysis of prescriptions and depicts the unbiased use of prescribing pattern among other things. There is a paucity of drug pattern monitoring studies for glaucoma, especially in middle- and low-income countries. The principal aim of prescription pattern and monitoring studies was to promote rational use of drugs and to minimize drug misuse. In a systematic review of SEARO (Southeast Asia Regional Office) region of WHO, it was concluded that drug utilization studies need to be promoted for the rational use. Therefore, this type of study paves path for rational and better drug usage.

This study predominantly recorded cases of open-angle glaucoma (157) followed by angle-closure glaucoma (67). Besides, 23 cases of secondary glaucoma were recorded, and they were found to be attributed to the usage of steroid drugs or some traumatic injury to the eye. At the time of presentation in Advance Eye Centre of this institute, 37 patients of total 145 referred cases from other clinics and hospitals received either steroids alone or in FDCs, which eventually lead to steroid-induced glaucoma in four patients. Secondary type of glaucoma is a well-known adverse effect of steroids.

In this study, steroids were promptly discontinued in many patients at our center, which if allowed to continue, could amount to more cases of glaucoma, and hence, it depicts that steroid-induced glaucoma is totally preventable if irrational use of steroids can be minimized.

Average number of drugs per prescription is an important indicator of prescribing pattern and helps in the assessment of rational prescription. It is worth noting that an average of two drugs was used in our center, whereas an average of five drugs was used by prescribers from other hospitals. In addition, increased number of glaucoma medications also predisposes the patients at increased risk of ocular surface disorder and preservative toxicity, and hence, likely to be another reason to keep the prescription limited to 2–3 antiglaucoma medications. Furthermore, polypharmacy not only increases the risk of adverse drug reactions, but also affects adherence and cost of therapy. This study showed that practice in our center was in tune with recommendations for the management of glaucoma. Therefore, discontinuation of unnecessary drugs can be practiced at other clinics as well to reduce the cost burden.

The current guideline of WHO recommends that drug should be preferentially prescribed by their generic name. In this study, 48 (19.43) patients were prescribed with generic drugs only, and the findings are almost similar to the results of other studies. Prescription by brand name is common in India, but cannot be considered as an idealistic pattern because of more probable chance in prescribing error. Importantly, most of glaucoma medications are now off patent and

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**Table 1: Characteristics of patients and patterns of drug prescriptions in glaucoma clinic**

| Characteristics                                      | Number (SD)/% |
|------------------------------------------------------|---------------|
| Age: Mean (SD)                                       | 47.14 (16.90) |
| Sex: Male/female                                     | 142 (57.49)/105 (42.51) |
| Total number of prescriptions/patients               | 247           |
| POAG                                                  | 157 (63.56)   |
| PACG                                                  | 67 (27.12)    |
| Secondary glaucoma (traumatic and steroid-induced glaucoma) | 23 (9.31)   |
| Drugs per prescription/range                         | 2.18 (1.68)/1–6 |
| Referred patients/drugs per prescription             | 145 (58.70%)/5.04 (1.52) |
| Number of referred patients taking steroids/inhalational/topical | 37/5/32 |
| Steroid-induced glaucoma                             | 4 (1.61) |
| Patients receiving FDCs for glaucoma                 | 101 (40.89) |

SD = standard deviation, % = percentage, POAG = primary open-angle glaucoma, PCAG = primary angle-closure glaucoma, FDCs = fixed-dose combinations
hence, prescribing generics would be a good practice to sustain health-care system. Moreover, generic drugs are comparatively lower in cost and equally effective as their branded counterparts. However, in India, there are several issues with the use of generics such as government directives should be followed for use of generics but absence of regulatory control does not always ensure that directives are being followed. In addition, quality control is always a concern for generic drugs; therefore, a better quality control is an important consideration for generics to build a confidence among prescribers. Furthermore, there are numbers of patients prescribed with FDCs, which are currently not available as generics.

| Different classes of antiglaucoma drug | Number of prescriptions of all glaucoma patients containing respective drug (%) (N = 247) | Number of prescriptions of POAG patients containing respective drug (%) (N = 157) |
|----------------------------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------------------------|
| Beta adrenergic blocker                | 29 (11.74)                                                                      | 26 (16.56)                                                                      |
| Timolol                               | 28 (11.33)                                                                      | 26 (16.56)                                                                      |
| Levobunolol                           | 1 (0.40)                                                                        | Nil                                                                             |
| Carbonic anhydrase inhibitor          | 69 (27.94)                                                                      | 59 (37.57)                                                                      |
| Acetazolamide                         | 63 (25.50)                                                                      | 53 (33.76)                                                                      |
| Brinzolamide                          | 4 (1.62)                                                                        | 4 (2.55)                                                                        |
| Dorzolamide                           | 2 (0.81)                                                                        | 2 (1.27)                                                                        |
| Prostaglandin analogues               | 60 (24.29)                                                                      | 53 (33.76)                                                                      |
| Traboprost                            | 25 (10.12)                                                                      | 20 (12.74)                                                                      |
| Bimatoprost                           | 18 (7.29)                                                                       | 18 (11.46)                                                                      |
| Latanoprost                           | 17 (6.88)                                                                       | 15 (9.55)                                                                       |
| α adrenergic agonist                  | 18 (7.28)                                                                       | 17 (10.83)                                                                      |
| Brimonidine                           | 18 (7.28)                                                                       | 17 (10.83)                                                                      |
| Miotics                               | 10 (4.04)                                                                       | 9 (5.73)                                                                        |
| Pilocarpine                           | 10 (4.04)                                                                       | 9 (5.73)                                                                        |
| Fixed-dose combinations               | 101 (40.89)                                                                     | 87 (55.41)                                                                      |
| Brimonidine + timolol                 | 52 (21.05)                                                                      | 46 (29.3)                                                                       |
| Dorzolamide + timolol                 | 48 (19.43)                                                                      | 40 (25.48)                                                                      |
| Bimatoprost + timolol                 | 1 (0.40)                                                                        | 1 (0.64)                                                                        |

SD = standard deviation, % = percentage, POAG = primary open-angle glaucoma

## Table 3: Summary of various classes of antiglaucoma drugs used in the glaucoma clinic

| Different classes of antiglaucoma drug | Number of prescriptions of all glaucoma patients containing respective drug (%) (N = 247) | Number of prescriptions of POAG patients containing respective drug (%) (N = 157) |
|----------------------------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------------------------|
| Total (N)                              | 72                                                                              | 63                                                                              |
| Timolol                                | 28 (38.89)                                                                      | 26 (41.26)                                                                      |
| Levobunolol                            | 1 (1.39)                                                                        | Nil                                                                             |
| Traboprost                             | 25 (34.72)                                                                      | 20 (31.74)                                                                      |
| Brimonidine                            | 18 (25)                                                                         | 17 (26.98)                                                                      |

% = percentage, POAG = primary open-angle glaucoma

## Table 4: Details of generic and branded drugs and various formulations of drug used in glaucoma clinic

| Prescriptions containing:              | Number of prescriptions (%) |
|----------------------------------------|-----------------------------|
| Generic drug only                      | 48 (19.43)                  |
| Branded drug only                      | 161 (65.18)                 |
| Branded and generic drugs both         | 38 (15.38)                  |
| Eye drops only                         | 171 (69.23)                 |
| Eye drops and oral tablets both        | 73 (29.55)                  |
| Injections                             | 3 (1.21)                    |
| Medicines from NLEM only               | 41 (16.60)                  |

% = percentage, NLEM = National List of Essential Medicines

In addition, quality control is always a concern for generic drugs; therefore, a better quality control is an important consideration for generics to build a confidence among prescribers. Furthermore, there are numbers of patients prescribed with FDCs, which are currently not available as generics.
The most commonly used medications for glaucoma in our clinic was timolol. Timolol was also used in this study as FDC with brimonidine, which is a strong inhibitor of aqueous humor production. Besides, brimonidine is also a neuroprotective agent, and it considerably lowers the IOP, and therefore, is considered as the emerging first-line therapy for POAG cases. Efficacy of brimonidine is comparable to timolol, but unlike timolol, it has cardiopulmonary adverse side effects, if used alone.

Nearly, one-sixth of prescriptions (41 of 247) was prescribed as per the NLEM-2015. However, brimonidine was very frequently prescribed in spite of not enlisted in NLEM.

In this study, eye drops were the most commonly prescribed dosage form, either alone or in combination with oral tablets, which can be attributed to the well-known fact that local administration will have least systemic adverse drug reactions.

**CONCLUSION**

A plethora of drug utilization studies is the need of the hour for judicious selection of the drugs. This study emphasized on the rationale drug usage to avoid the use of unnecessary medications. Indeed, the practice of generic drugs should be promoted to reduce the treatment cost burden, and eventually, to lead to better compliance. This study center seems to be in accordance with the rationale drug prescribing, and their practice patterns need to be implemented at other centers also. This study is not without its limitations and may be considered as underreporting in some referred cases because of the nonavailability of previous treatment history from patient’s end. The further studies can be planned with more sample size and by monitoring the follow-up schedules for better findings.

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**Conflicts of interest**

There are no conflicts of interest.

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