Original Article

Factors Responsible for Non-Compliance of Glaucoma Patients to Topical Medications in Our Setup

Hina Khan, Yousaf Jamal Mahsood, Nazli Gul, Omer Ilyas, Sanaullah Jan

Pak J Ophthalmol 2018, Vol. 34, No. 4

See end of article for authors affiliations

Correspondence to:
Yousaf Jamal Mahsood,
Assistant Professor Glaucoma,
Department of Ophthalmology,
Hayatabad Medical Complex,
Peshawar.
E-mail:yousaf82@hotmail.com

Purpose: To identify the factors affecting the compliance of glaucoma patients to topical medical treatment in our setup.

Study Design: Cross sectional study.

Place and Duration of Study: This study was carried out at department of clinical ophthalmology, KIOMS, Hayatabad Medical Complex, Peshawar from 1st February 2016 till 31st July 2016.

Material and Methods: Patients meeting our inclusion criteria were recruited in this study on consecutive non-probability sampling technique. All the patients were interviewed and the causes of non-compliance to topical medical therapy were recorded. Stratification of non-compliance was also analyzed with respect to age groups and gender. Sample size was calculated using open epi software with confidence level of 95% and power of 80.

Results: Total of 179 subjects participated in this study that had been advised topical anti-glaucoma medication. Mean age of our subjects were 51.9 ± 13.2 years with most (49.2%) of patients in age group between 50.01 – 65.00 years. Non-compliance was observed in 76.5% of patients with high cost of the medicines being on top of the list (54%). Male gender and older age group were found statistically significant to be more non-compliant.

Conclusion: High cost of topical anti-glaucoma medications is the leading cause of non-compliance in our setup.

Keywords: Glaucoma, Non-compliance, Non-adherence.

Glaucoma is the second leading cause of bilateral blindness worldwide[1]. Chronic open angle glaucoma is reported as leading cause of bilateral blindness in African Americans[1]. It affects 2% of the population above 40years and up to 10% above 80years of age globally[2]. It is estimated that about 2.47 million are affected by chronic open angle glaucoma in USA, of whom 5.3% are blind bilaterally[1]. The blindness caused by glaucoma can be prevented, if appropriate treatment with ocular hypotensive medicines is initiated on time. Consistent IOP lowering by these medications is associated with reduced risk of optic nerve damage and preventing its progression[1]. However this requires early diagnosis of the disease as well as compliance with appropriate ocular hypotensive medications and access to proper eye care[1,3]. The term compliance has been replaced by more specific terms i.e. adherence and persistence. "Adherence is a measure of degree to which patient follows prescribed instruction during a defined period of time". "Persistence is defined as the criterion that evaluates the time until the patient first discontinues use of medication"[1]. Chronic and initially asymptomatic diseases like glaucoma are subject to patients' poor adherence and persistence and have a higher rate of visual loss in affected individuals[4,5].

The risk factors for non compliance with antiglaucoma medications remain poorly understood and defined[6]. Many studies have been carried out in west to determine the factors responsible for noncompliance to topical glaucoma therapy. There are three different techniques which are used for data collection regarding poor adherence and persistence to anti glaucoma medications. These are Patient self report, Pharmacy refill data, and electronic monitoring[1,4].

The factors presumed to be responsible for non adherence include cost, tolerability, difficulty in administering drops, denial, lack of education[7], travel issues, old age, forgetfulness, careless attitude, patient physical disability, adverse effects of the drug, inconvenient frequency[8] and lack of symptoms without treatment[1,4]. According to one study, 44% patients were compliant and 35% were non compliant[4] and the remaining were lost to follow up. According to another study 84%, patients were non compliant, and factors responsible were living alone, lacking an escort and transport issues. According to another study, the most prevalent barriers were belief that there was no problem with one's eyes (44.4%) and lack of escort (19.7%)[7].

As far as cost is concerned, 41% had difficulty paying for their medications and 11.5% who had paid fully for the medications themselves stated that the expenses of medications on occasions prevented them from filling their prescription and that 76% of patients had an income of less than 30,000 USD/year[6].

Recent observational studies showed that those with poor health literacy were 75% more likely to miss eye drops at least two times a month[6].

Lack of accessibility for a patient living in a remote area is an another major factor, a recent study showed that those who had no car were 2.08 times more likely to be noncompliant then who had a transport[1].

A study showed a variable influence of age on compliance, out of 273 patients, 189(69.3%) were compliant (mean age 58.1+/-1.4) and 84(30.7%) were noncompliant (mean age 53.7+/- 1.8)[1].

The rationale behind this study is that most of the studies or data reported are from developed countries and no data exists regarding factors responsible for noncompliance to glaucoma medications in Pakistan. It is obvious that there are a lot of social differences including literacy rate, economical, cultural and environmental differences between developed countries and our region. Keeping these differences in our mind, we expect that the factors affecting compliance to anti glaucoma medication may be different in our community than the developed countries. We also presume that some of factors mainly involved in anti glaucoma compliance in our country may be responsible with different magnitude and frequency compared to developed countries. Therefore, we designed this study to identify the factors responsible for noncompliance of topical anti glaucoma medications in our community. The results will be discussed with public health individuals and health care providers to minimize the problems related to noncompliance and to reduce the burden of glaucoma blindness.

MATERIAL AND METHODS

This study was carried out at department of clinical ophthalmology, KIOMS, Hayatabad Medical Complex, Peshawar from 1st February 2016 till 31st July 2016. It was a cross sectional study using consecutive, convenient sampling. There were 179 patients included in the study.

Inclusion criteria were: patients with established diagnosis of open angle glaucoma, primary open angle glaucoma (POAG) and pseudoexfoliation (PXE) glaucoma patients above 40 years only, all cases who had been prescribed anti glaucoma medications. both out-patients and in-patients and post trab patients of atleast 3 months duration who has been advised and were using topical anti glaucoma medications.

Exclusion criteria were: any other type of glaucoma not fulfilling the inclusion criteria---Steroid induced glaucoma, Primary angle closure glaucoma, secondary angle closure glaucoma, neovascular glaucoma, lens induced glaucoma, congenital glaucoma, juvenile glaucoma, traumatic glaucoma, increase IOP secondary to any major ocular surgery, patients having psychiatric disorders.

All patients were diagnosed and reviewed on the basis of history clinical examination (fundoscopy, gonioscopy and IOP measurements) and relevant investigations by consultants of our department. Approval was obtained from hospital research and ethical committee before initiating the study. Informed verbal consent was taken after explaining to the patients the purpose and benefits of the study and with the permission that the study was only for data review and publication followed by a thorough interview by me. All the information taken from the

patient was recorded on a pre designed proforma on the spot.

Non Compliance was defined as Interruption of antiglaucoma eye drops use for at least 5 consecutive days or missing at least 10 doses at various occasions in 30 days or no use of the medications at all since prescribed.

Common factors of non-compliance which were studied included; **High Cost or non-affordability:** Patients were asked regarding financial burden due to the cost of the anti-glaucoma medications and if the patient considered it costly they will be taken as a financial burden. **Poor health literacy:** patients who did not know that glaucoma can lead to permanent blindness. **Lack of Accessibility:** patients living in a remote area where their residence is at a distance of more than 10 km from a specialist health care facility (teaching hospital, DHQ, THQ), making availability of drugs and doctors difficult. The patients were interviewed directly and their current place of residence was taken as a reference. Their responses to the above mentioned factors of non-compliance were recorded on a designed performa.

Data was analyzed by SPSS version 23. Presentation of results was done by charts and tables. Categorical variable like high cost, poor health literacy, old age and lack of accessibility were presented as frequencies whereas numerical variable like age was presented as mean SD. Noncompliance and leading factors was stratified among age and gender to see the effect modifiers.

RESULTS

The study comprised a total of 179 patients diagnosed with glaucoma who had been advised topical anti glaucoma medications for treatment. The mean age of the patients of the whole study population was 51.9 ± 13.2 years. The patients were distributed with regards to different ages into four groups; 20 to 35 years, 36 to 50 years, 51 to 65 years and 66 years and above. It was observed that there were 11.2% patients in the first age group, 29.6% in second, 49.2% in the third and 10.1% in the fourth age group respectively (Table 1).

With regards to gender, we had 48.6% males and 51.4% females. As per operational definitions, we observed that non-compliance to topical anti glaucoma medication was observed in 76.5% of patients.

The most common factor leading to non-compliance in our study was found to be high cost in 54.0% of non compliant patients followed by poor health literacy in 44.5% and lack of accessibility to drugs in 19% of patients (Table 2).

Table 1: Age Wise Distribution (n = 179).

Mean Age	**51.98±12.35 years**	
Age Group	**Frequency (n)**	**Percentage (%)**
20 – 35 years	20	11.2
36 – 50 years	53	29.6
51 – 65 years	88	49.2
>65 years	18	10.1

Table 2: Common Factors Leading to Non Compliance (n = 179).

	Frequency	**Percentage**
High Cost[a]		
Yes	74	54
No	63	46
Total	137	100
Poor Health Literacy[a]		
Yes	61	44.5
No	76	55.5
Total	137	100
Lack of Accessibility to Drugs[a]		
Yes	26	19
No	111	81
Total	137	100

a. Non Compliance to Antiglaucoma Drugs = Yes

On stratifying the non compliance with regards to gender a statistically significant difference was found between males & females. Males tend to be more non compliant than females p value 0.001 (Table3).

On stratifying the non-compliance with regards to different age groups a statistically significant difference was found among various age groups. Older age tends to be more non compliant p value 0.049 (Table 4).

We also stratified individual factors leading to non-compliance with regards to gender. While applying chi square we didn't find any significant difference with regards to gender for each high cost (p value 0.39), Poor health literacy (p value 0.525) and Lack of accessibility to drug (p 0.533).

We also stratified individual factors leading to non compliance with regards to different age groups. While applying chi square we didn't find any

Table 3: Gender Wise Comparison of Non Compliance (n = 179).

Gender of Patient	Non Compliance to Antiglaucoma Drugs				
			Non Compliance to Antiglaucoma Drugs		Total
			Yes	No	
Gender of Patient	Male	Count	76	11	87
		% within Gender of Patient	87.4%	12.6%	100.0%
	Female	Count	61	31	92
		% within Gender of Patient	66.3%	33.7%	100.0%
Total		Count	137	42	179
		% within Gender of Patient	76.5%	23.5%	100.0%

Chi square applied, p = 0.001

Table 4: Age Groups Wise Comparison of Non Compliance (n = 179).

	Non Compliance to Anti-glaucoma Drugs		Total
	Yes	No	
Age Groups	20 to 35 years	16	4	20
	36 to 50 years	36	17	53
	51 to 65 years	67	21	88
	66.years & above	18	0	18
	Total	137	42	179

Chi square applied, p = 0.049

significant difference with regards to different age groups for each high cost (p value 0.33), Poor health literacy (p value 0.163) and Lack of accessibility to drug (p 0.638).

DISCUSSION

Glaucoma continues to be a challenging disease in some patients, as the diseases continues to progress in spite of a controlled IOP. Vascular phenomenon and its role in glaucoma has been significantly discussed[8], as significant data has been presented to support its role in the development of optic neuropathy. In the light of these descriptions, stress should be made on establishing the hemodynamic profile of glaucoma treatments, as well as their role in IOP.

In order to have a significant effect on ocular blood flow, any topical glaucoma drug should not only have the ability to penetrate the anterior surface of the eye, it should also attain the critical levels to attain the required physiological effects on local hemodynamics. All of the glaucoma therapies have the inherent potential to effect the vascular smooth muscle[9].

To preserve vision, glaucoma patients need to have a long term treatment plan and carefully planned follow-up care. Though glaucoma is considered a preventable cause of blindness, multiple studies, in both developed and underdeveloped parts of the world, have shown that still there are multiple causes of failure to prevent blindness from glaucoma; the commonest being inadequate access to eye care resources and failure to adhere to the treatment.

Identification of partial compliance or non compliance to the prescribed medications is determined by following the difference between the patient's dosing history and the prescribed dosing regimen. However, with the advent of electronic monitoring method, first used in 1977, the identification of partial and non-compliance has become somewhat simple[10]. Before this, other methods of determining compliance like counts of returned, untaken doses; questionnaires; histories; diaries; assays of drug concentration in plasma[11]; and audits of prescription refills — were not very accurate as they only gave an idea of dosing history that indicated only dosing omissions but gave no information about the number of doses that were omitted[12].

However, there are studies that show varying results where providers estimate can be poorly related to the adherence[13] and the self-reporting of the patient can be better related to the measure of adherence[14].

Our study showed that 76.5% of the total patients were noncompliant to their glaucoma drugs in contrast to another study of 2004 whereby only 60% of the patients were found to be noncompliant[15].Such a high rate of noncompliance is attributed to multiplicity of drugs as such patients are more likely to have problems in remembering their drugs, increased incidence of side effects compelling the patients to restrict their medications and inconvenience of timings to dosing. So to avoid these problems, stress should be laid upon simplifying the regimen as much as possible. This principle of simplifying the regimen has worked very well in other diseases in terms of improving the adherence[16]. Our study shows levels of non compliance to glaucoma medication that are both higher[17] and lower[13] than the previous reports. This may be partly attributed to the differences in study populations.

The adherence rate for patients who are taking drugs for various chronic diseases varies from 43-78%[12]. So far, no standard criteria for adherence rates in clinical trials has been defined, however, an adherence rate of more than 80% is considered acceptable.

The findings of our study are generally consistent with the literature. In comparison to several other studies[18,19], health literacy appeared to be associated with compliance in our sample. However, this may be attributed to the fact that we didn't include frequency of dosing as a measure which would have been a more sensitive measure.

Recently, behavioral and lifestyle issues have been identified as factors with significant impact on adherence to glaucoma drugs[20]. Many of these factors may be modifiable and a thorough understanding of these issues may help us in a better understanding of the long-term management of glaucoma medication adherence[7]. Similarly, co-existing chronic health issues may also have a significant effect on medication adherence[21].

Different studies have measured adherence differently. They have either used the direct evaluation or the indirect evaluation[13]. Direct evaluation involves direct observation of the patient by the observer while taking the dose or assessing the level of the drug or its metabolite in the blood, urine or stool. Indirect evaluation is assessment of the adherence by indirect indicators like pharmacy information, clinical response to the regimen, patients diary etc. still there is no consensus as to the better method of assessment as different studies have shown different results; most studies showing that the observers are poor predictors of the patients compliance and patients consistently over-represent their degree of adherence[12,22].

The adherence to ophthalmic drugs should be considered a different entity and similarly the dynamics of ophthalmic drugs administration are different from that of the oral drugs. In a study by Vrijens and coworkers[23], the dynamics of ophthalmic drug administration have been staged as the acceptance of the therapy, persistency in administering the drugs, and the ability to "execute" or correctly administer the drops. As compared to the administration of ophthalmic drugs, the administration of oral drugs is a somewhat straight forward phenomenon unless the patient is having a psychomotor deficit and can be executed without any observation. In contrast to the oral medications that can be easily taken, the self-administration of ophthalmic drugs is somewhat cumbersome and challenging and depends upon the optimum coordination between the psychomotor components of the human body. The addition of another drug to an ophthalmic regimen can make the process more difficult to execute[24]. Poor adherence is compounded if the drop is not appropriately placed in the eye. The issue can be made worse if the patient is an elderly person with multiple comorbidities like diabetes mellitus, hypertension, cardiac issues and osteoporosis.

However, those patients who were aware of the nature and course of the disease and the potential complications were found to be more compliant. Various psychological diseases like depression may also have an impact on compliance[13]. Increasing the complexity of doses may have a negative impact on compliance[24]. However, various studies failed to establish an association between adherence and side effects of the drugs[13, 4].

The role of the prescribing doctor should never be under-rated in increasing the compliance to the medications as efficient counselling keeping all the impacting factors in to consideration can have a major impact on the level of compliance[12,13,22].

Currently there is a paucity of research examining intervention strategies to enhance glaucoma medication adherence. While doctor-patient communication strategies and increased patient education have been emphasized and shown to be

effective[13], examinations of health promotion-based efforts are also other strategies worthy of investigation in this area given the link between medication adherence and health behaviors.

However, certain studies have shown that input in preventive and promotional medicine whereby patients are educated about the nature, course and potential complications of the disease have shown promising results in terms of long term adherence especially in people with chronic health conditions[25]. So more efforts should be put into designing such preventive and health education programs to address the issue of non-adherence to anti glaucoma medications. But these efforts should be based on a more comprehensive understanding of the factors that lead to non-compliance to anti-glaucoma medications.

CONCLUSION

We found that more than 2/3rd of glaucoma patients are non-compliant to topical treatment and the leading cause is non-affordability in our setup.

Author's affiliation

Dr. Hina Khan
MBBS, FCPS, Trainee Registrar
Department of ophthalmology, Hayatabad Medical Complex, Peshawar.

Dr. Yousaf Jamal Mahsood
MBBS, FICO (UK), FRCS (Glasg), FCPS
Assistant Professor Glaucoma,
Department of ophthalmology, Khyber Medical Girls college, Hayatabad Medical Complex, Peshawar.

Dr. Nazli Gul
MBBS, FCPS
Department of ophthalmology,
Kyber Teaching Hospital, Peshawar.

Dr. Omer Ilyas
MBBS, FICO, FCPS, FRCS (Glasg), Trainee Medical Officer (Vitreoretina)
Department of ophthalmology, Hayatabad Medical Complex, Peshawar.

Dr. Sanaullah Jan
MBBS, FRCS (Glasg), FRCS (Edin), FCPS, Professor of vitreoretina
Department of ophthalmology, Khyber Girls Medical college, Hayatabad Medical Complex, Peshawar.

Role of Authors

Dr. Hina Khan
Concept and Design, Data Collection, Writing of manuscript.
Dr. Yousaf Jamal Mahsood
Literature Review, Critical review, Data analysis.

Dr. Nazli Gul
Data Collection, Writing of manuscript.

Dr. Omer Ilyas
Writing of Manuscript, Critical Review.

Dr. Sanaullah Jan
Critical review, Concept and Design.

REFERENCES

1. **Gwira J, Vistamehr S, Shelsta H, Bashford K, Forster S, Palmisano P, et al.** Factors associated with failure to follow up after glaucoma screening. Am Acad Ophthalmol. 2006; 113: 1315-1319.
2. **Kanski JJ, Bowling B (eds).** Glaucoma: Chapter 10. In: Clinical ophthalmology, 7th ed, Elsevier, London, 2011: 311-99.3.
3. **Quigley H, Friedman D, Hahn S.** Evaluation of practice patterns for the care of open angle glaucoma compared with claims data .Am Acad Ophthalmol. 2007; 114: 1599_1606.
4. **Schwartz G, Quigley H.** Adherence and persistence with glaucoma therapy. Surv Ophthalmol. 2008; 53: S57_S68.
5. **Muir K, Santiago_turla C, Stirnett S, Herndon L, Allingham R, Challa P, et al.** Health literacy and adherence to glaucoma therapy. Am J Ophthalmol. 2006; 142: 223-226.
6. **Tsai J.** A comprehensive perspective on patient adherence to topical glaucoma therapy. Am Acadophthalmol. 2009; 116: S30_S36.
7. **Lee B, Sathyan P, John R, Singh K, Robin A.** Predictors of and barriers associated with poor follow up in patients with glaucoma in south India. Arch Ophthalmol. 2008; 126 (10): 1448-1454.
8. **Weinreb RN, Harris A, eds.** Ocular Blood Flow in Glaucoma: The 6th Consensus Report of the World Glaucoma Association. Amsterdam: Kugler Publications; 2009: 1-159. 11.
9. **Costa VP, Harris A, Stefánsson E.** The effects of antiglaucoma and systemic medications on ocular blood flow. Prog Retin Eye Res. 2003; 22: 769-805.
10. **Kass MA, Meltzer DW, Gordon M.** A miniature compliance monitor for eye drop medication. Arch. Ophthalmol. 1984; 102: 1550–54.
11. **Podsadecki TJ, Vrijens BC, Tousset EP, Rode RA, Hanna GJ**. "White coat compliance" limits the reliability of therapeutic drug monitoring in HIV-1-infected patients. HIV Clin. Trials, 2008; 9: 238–46.

12. **Osterberg L, Blaschke T.** Adherence to medication. N. Engl. J. Med. 2005; 353: 487–97.
13. **Okeke CO, Quigley, Jampel HD.** Adherence with topical glaucoma medication monitored electronically. The travatan dosing aid study, Ophthalmology, 2009; 116 (2): 191–199.
14. **Sleath B, Blalock SJ, Stone JL.** Validation of a short version of the glaucoma medication self-efficacy questionnaire, British Journal of Ophthalmology, 2012; 96 (2): 258–262.
15. **Sleath B, Robin AL, Covert D, Byrd JE, Tudor G, Svarstad B.** Patient-reported behavior and problems in using glaucoma medications," Ophthalmology, 2006; 113 (3): 431–436.
16. **Roter DL, Hall JA, Merisca R, Nordstrom B, Cretin D, Svarstad B.** Effectiveness of interventions to improve patient compliance a meta-analysis. Medical Care, 1998; 36 (8): 1138–1161.
17. **Robin AL, Novack GD, Covert DW, Crockett RS, Marcic TS.** Adherence in glaucoma: objective measurements of once-daily and adjunctive medication use. Am J Ophthal, 2007; 144 (4): 533–540.
18. **Pappa C, Hypthantis T, Pappa S, et al.** Psychiatric manifestations and personality traits associated with compliance with glaucoma treatment. Journal of Psychosomatic Research, 2006; 61: 609–617.
19. **MacKean JM, Elkington AR.** Compliance with treatment of patients with chronic open-angle Glaucoma. Br J Ophthalmol. 1983; 67: 46–49.
20. **Friedman D, Okeke CO, Jampel H, et al.** Risk factors for poor adherence to eye drops in electronically monitored patients with glaucoma. Ophthalmology, 2009; 116: 1097–1105.
21. **Heisler M, Faul J, Hayward R, Langa K, Blaum C, Weir D.** Mechanisms for racial and ethnic disparities in glycemic control in middle-aged and older Americans in the health and retirement study. Archives of Internal Medicine, 2007; 167: 1853–1860.
22. **Friedman DS, Quigley HA, Gelb L, Tan J, Margolis J, Shah SN, et al.** Using Pharmacy Claims Data to Study Adherence to Glaucoma Medications: Methodology and Findings of the Glaucoma Adherence and Persistency Study (GAPS) Invest Ophthalmol Vis Sci. 2007; 48: 5052–7.
23. **Vrijens BB, Vincze G, Kristanto P, Urquhart J Burnier M.** Adherence to Prescribed Anti-Hypertensive Drug Treatments: Longitudinal study of electronically compiled dosing histories. Br Med J. 2008; 336: 1114–7.
24. **Robin AL, Covert D.** Does Adjunctive Glaucoma Therapy Affect Adherence to the Initial Primary Therapy? Ophthalmology, 2005; 112: 863–8.
25. **Berkley-Patton J, Goggin K, Liston R, Bradley-Edwin A.** Adapting effective narrative-based HIV prevention interventions to increase minorities' engagement in HIV/AIDS services. Health Communication, 2009; 24: 199–209.