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Assessment of Topical Glaucoma Side Effects and Adherence to the Glaucoma Medications in Eye Care Centres at Palakkad- a Prospective Study

			
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ABSTRACT

Objective: To determine the side effects of topical antiglaucoma drugs and adherence to the glaucoma medications in 239 patients at different eye care centers Palakkad. **Methodology:** A prospective study was conducted in 239 glaucoma patients at two eye care centers Palakkad, for a period of 6 months duration (November 2016- April 2017). Glaucoma patients with age > 40 were selected. Comparison of ophthalmic medication for tolerability (COMPTOL) and Morisky medication Adhesion Score-MMAS-8 were used to assess the intensity of side effects and adherence to the anti-glaucoma medications. Statistical analysis was carried out by graphpad prism software. **Results:** The study showed that there was statistically significant difference in the intensity of side effects of brimonidine (P value 0.0008) compared to the drug travoprost (P= 0.5099) and timolol (P= 0.0811). Out of 116 patients using prostaglandin derivatives, 81% of patients were satisfied with their eye drop and 63.38% of patients were unsatisfied (n=71) with brimonidine eye drop. Out of 239 patients, 141 patients (58.99%) were adherent to the glaucoma eye drops, and 98 (41.5%) were non adherent (with a Morisky scale of less than 6 points). **Conclusion:** Using Comparison of ophthalmic medication for tolerability (COMPTOL) and Morisky medication Adhesion Score-MMAS-8, fewer side effects such as itching, watering were reported for brimonidine (18.82%) and adherence to antiglaucoma medication was found in 58.9% patients.

INTRODUCTION

Glaucoma is an acquired disease of the optic nerve (neuropathy) characterized by specific structural changes with associated visual field defects. More than 60 million people have glaucoma, the second most common cause of blindness worldwide⁵. Side effects of glaucoma medication are frequently documented in case reports in a small series of patients without any comparison to other drugs. A useful method to study the side effects of glaucoma medication would be to combine clinical observations or measurements of side effects with more subjective measurements, such as assessing the patients' perspective with respect to side effects with a "patient reported outcome" (PRO) instrument. In the present study, COMPTOL (comparison of ophthalmic medication for tolerability) questionnaire was used to assess the frequency and bother of side effects of different drugs and patient satisfaction with their medication.

The major ocular side effects shown by glaucoma medications were burning, stinging, conjunctival hyperaemia, itching, ocular secretion, ocular pain, tearing, brow ache, dryness, foreign body sensation, eyelid redness, eyelid edema, blurred vision, visual acuity loss, accommodation difficulties, and night vision problems¹.

A major determinant of success in medical therapy is the adherence of patients to their medication. Adherence is defined as the extent to which a patient's behavior in taking medication corresponds with agreed recommendations from a doctor⁶. In contrast to the term "compliance," adherence requires the patient's agreement to the recommendation. Nonadherence is one of the major problems in glaucoma treatment. The reason is that there are no obvious symptoms in the earlier course for glaucoma patients¹⁰. Furthermore, glaucoma medication may have negative side effects. Finally, the glaucoma patient usually requires a lifelong treatment but often does not realize any direct benefits from the therapy. However, nonadherence behavior has long term impacts on the visual function of the patient³. Without hypotensive eyedrops, an elevated IOP may lead to progressive optic nerve degeneration and deterioration of the visual field^(7,8). It is estimated that approximately 10% of visual field defects are caused by nonadherence⁷. Additionally, nonadherence is associated with improper use of prescribed medication, which may lead to a further burden on our health-economic system⁹. In the present study, Morisky scale was used to assess the adherence among glaucoma patients. The Morisky Accession scale is one of the most

validated questionnaires used to assess the adherence to medication that has been used not only in ophthalmology but mainly in glaucoma².

MATERIALS AND METHODS

A prospective study was conducted at two eye care centers Palakkad, for a period of 6 months duration (November 2016- April 2017). After getting approval from the ethics committee of the hospital, subjects were selected based on inclusion and exclusion criteria.

Inclusion criteria

- Glaucoma subjects with age >40 years
- Subjects with and without Comorbid conditions

Exclusion criteria

- Subjects with other eye problems
- Patients who are not willing to participate in the study

Signed informed consent was obtained from all participants prior to the study. Questionnaire survey COMPTOL (Comparison of ophthalmic medication for tolerability) and (Morisky Medication Adhesion Score-MMAS-8) was conducted to assess the side effects and noncompliance among glaucoma patients. Other relevant information on the disease, associated symptoms, diagnosis, and treatment plan were collected on a data entry form.

STUDY PROCEDURE

To identify the side effects and non-compliance of glaucoma medications, 239 patients were asked to fill the questionnaires (Comparison of ophthalmic medication for tolerability) and (Morisky Medication Adhesion Score-MMAS-8). For each side effect, the frequency of the symptoms and the severity of bothering to the patient were documented. The questions concerning the frequency of the effects were graded from 'Did not experience', 'One day', 'several days', 'about half of days', 'Almost every day' and 'Everyday'. The questions concerning the intensity of bother were graded from 'Not at all bothered', 'A little bothered', 'Quite bothered', 'Much bothered' and 'Extremely bothered'. In addition, questions were asked concerning patient satisfaction with their medication. The patients were asked to

indicate their level of satisfaction on a 7-point scale: ‘Very unsatisfied’, ‘Unsatisfied’, ‘A little unsatisfied’, ‘Not unsatisfied nor satisfied’, ‘A little satisfied’, ‘Satisfied’ and ‘Very satisfied’.

ANALYSIS

For the analysis of side effects, the items concerning the frequency of side effects were scored on a scale from 0 to 5. On this scale, 0 represented ‘Did not experience’ and 5 represented ‘Every day’. Likewise, the items concerning the severity of bother were scored on a scale from 0 (‘Not at all bothered’) to 4 (‘extremely bothered’). Both scores were multiplied to determine the final score per item on ocular side effects. Next, these final scores per type of side effect were summed over all types of side effects. This sum was used to assess the median value. The next step was to calculate per glaucoma drug the percentage of patients with a lower or higher score than this median value.

For adherence, 8 questions were asked to the patients regarding the adhesion to eye drops. Each negative response was worth 1 point (questions 1 to 4), question 5 is reversed, so if the answer was affirmative it would be worth 1 point, and questions 6 and 7 would be like the first four. The last question would be worth 1.0 to zero, being the count every 0.25. If the person scored between 0 and 5.75, they were considered non-adherent, if scored from 6 to 8 they would be classified as adherent. One way ANOVA was used to find the statistical difference between the intensity of the side effects of drugs and chi-square test was applied to analyze significant differences between adherence & non-adherence.

RESULTS

Table 1: Prescription pattern of antiglaucoma drugs

Therapy	Frequency	Percentage (%)
Mono therapy	113	46
Fixed drug	73	29
Dual therapy	63	25

In the present study Table, 1 shows that 46% of patients underwent monotherapy with Travoprost followed by 29% fixed dose combination of timolol + brimonidine and 25% showed dual therapy with travoprost.

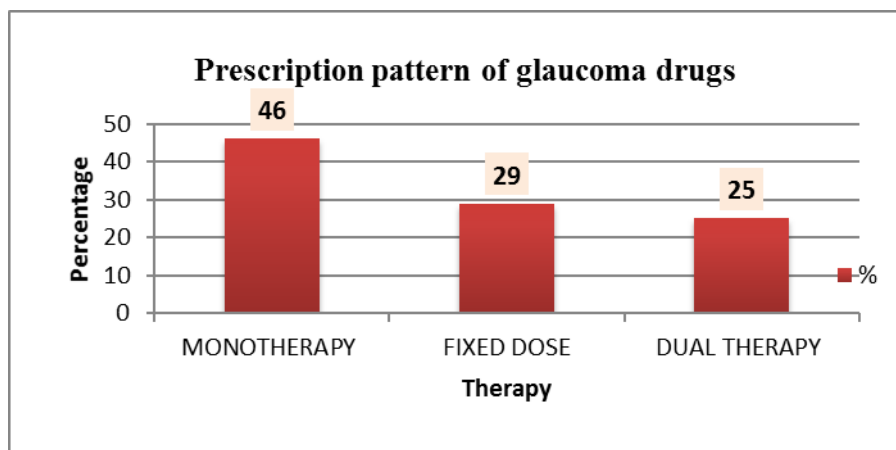


Figure: 1: Prescription pattern of glaucoma drugs

Commonly prescribed antiglaucoma drugs

By analyzing the prescription pattern of glaucoma patients, the most commonly prescribed class of drugs were prostaglandin derivatives 48.53% (n= 116) followed by combination drugs (Prostaglandin derivatives + Beta Blocker, + Carbonic anhydrase inhibitors + Beta Blocker) 39.33% (n=94), alpha agonist 29.7% (n=71) , carbonic anhydrase 21.3% (n=51) and beta blocker 13.8% (n=33) respectively.

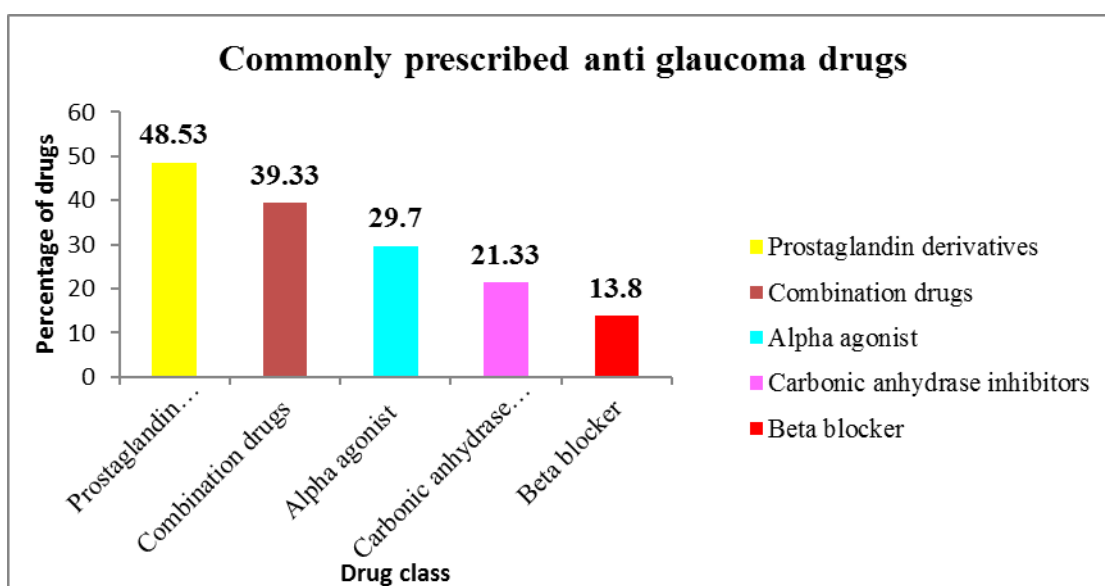


Figure: 2: Commonly prescribed anti glaucoma drugs

Table: 2 Side effects of antiglaucoma drugs

DRUGS	SIDE EFFECTS	NO. OF PATIENTS	PERCENTAGE	P-VALUE
BRIMONIDINE	Itching	20	44.44	0.0008
	watering	16	35.55	
	itching + watering	9	20	
TRAVOPROST	Redness	6	66.66	0.5099
	long eye lashes	3	33.33	
TIMOLOL	Itching	6	66.66	0.0811
	Burning	3	33.33	

In the present study, only a small percentage of patients showed side effects to glaucoma drugs. Out of 239 patients, 18.82 % of patients exhibited side effects such as itching, watering to Brimonidine, followed by 3.76 % of patients shown side effects such as redness, long eyelashes to travoprost & itching, burning to the drug timolol. 73.64 % of patients did not experience any side effects of antiglaucoma medications.

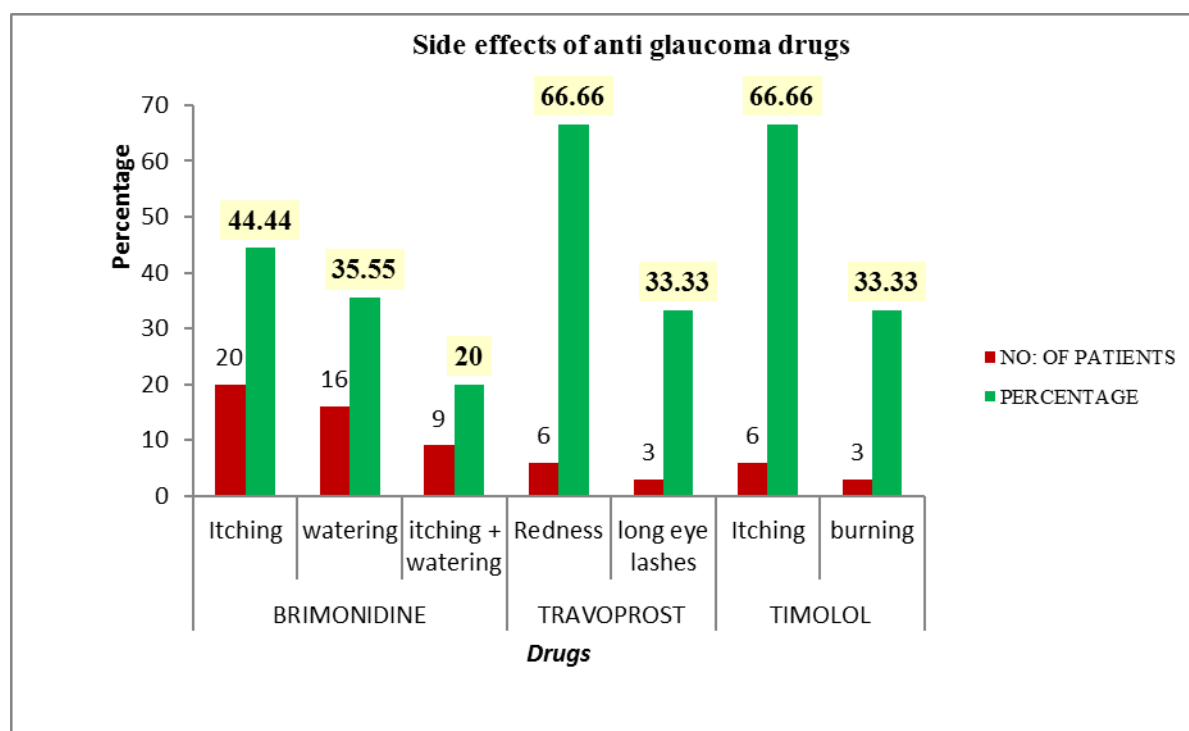


Figure: 3: Side effects of antiglaucoma drugs

Table: 3 level of patient satisfaction with glaucoma medications

DRUGS	NO:OF PATIENTS n=239	SATISFIED (%)	LITTLE SATISFIED (%)	UN SATISFIED (%)
BRIMONIDINE	71	25.3	11.26	63.38
PROSTAGLANDIN DERIVATIVES	116	81	11.2	97.75
TIMOLOL	33	72.7	0	27.27
COMBINATION DRUGS	94	76.59	51	14.89
CARBONIC ANHYDRASE INHIBITORS	15	66.66	33.33	0

Table 4 shows that out of 116 patients using prostaglandin derivatives 81% of patients were satisfied with their eye drop. And 63.38% of patients were unsatisfied (n=71) with their brimonidine eye drop.

Table 4: Adherence to glaucoma drugs based on Morisky scale

		HUMAN ADHERENT (%) n=141	NON ADHERENT (%) n= 98	P-VALUE
SEX	MALE	77.3	78.57	0.8632
	FEMALE	22.69	21.42	
EDUCATION	INTERMEDIATE	8.5	31.63	<0.0001
	MATRIC	24.82	56.12	
	GRADUATION	53.9	12.24	
NO: OF EYE DROPS	POST GRADUATION	12.76	0	0.0011
	1	90.78	74.48	
	2	9.21	25.51	

Out of 239 patients, 141 patients (58.99%) were adherent to the glaucoma eye drops, and 98 (41.5%) were non-adherent (with a Morisky scale of less than 6 points). Of all the patients, 186 were males (78%) and 53 (22%) were females. The table shows that education ($P=0.0001$) and number of eye drops ($P=0.001$) had significant influence on the adherence of patients with their medications.

DISCUSSION

In the present study regarding the side effects of glaucoma eye drops, there was statistically significant difference in the intensity of side effects of brimonidine (P -value 0.0008) compared to the drug travoprost ($P= 0.5099$) and timolol ($P= 0.0811$). From the study it was clear that out of 239 patients, only a small percentage of patients 18.82 % of patients exhibited side effects such as itching, watering to Brimonidine, followed by 3.76% of patients shown side effects such as redness, long eyelashes to travoprost & itching, burning to the drug timolol. 73.64% of patients did not experience any side effects to antiglaucoma medications. A similar study conducted by Henny J M. Beckers et al, fewer side effects were observed for timolol gellans.

Considering the level of patient satisfaction to the glaucoma medication out of 116 patients using prostaglandin derivatives 81% of patients were satisfied with their eye drop. Followed by 63.38% of patients were unsatisfied ($n=71$) with brimonidine, timolol ($n=33$) 72.6% were satisfied 14.8% were unsatisfied, combination drugs (Prostaglandin derivatives + Beta Blocker, + Carbonic anhydrase inhibitors +Beta Blocker) 76.5% were satisfied and 14.89 were unsatisfied, and for carbonic anhydrase inhibitors majority patients were satisfied ($n=15$) 66.6% were satisfied and little satisfied 33.1% with their eye drop.

Out of 239 patients, 141 patients (58.99%) were adherent to the glaucoma eye drops, and 98 (41.5%) were non-adherent (with a Morisky scale of less than 6 points). Of all the patients, 186 were males (78%) and 53 (22%) were females. From the study it was clear that patient education ($P=<0.0001$) and a number of eye drops ($P =0.0011$) they were using had a significant influence on patient's adherence behavior to the medication, is highly qualified patients were well aware that inappropriate use of eye drops lead to bad control of intraocular pressure and thus to optic neuropathy leading to vision loss. Similar study conducted by Marina Viegas Moura Rezende Ribeiro et al. number of eye drops ($p =0.03$) had a significant influence on adherence to glaucoma medication. It was also observed that in the group

adherent more patients used only one eye drop (32.28%) compared to 20.56% of non-adherent. It is believed that a better adhesion occurs in patients who only use eyedrops because it would be easier to remember using less medication².

The main reasons for non-adherence in (41.5%) patients who were non-adherent, the majority reported that forgetfulness as the main cause, some of them reported difficulty with time, busy life and cost affordability.

CONCLUSION

The present study concluded that there was statistically significant difference in intensity of side effects of brimonidine (compared to travoprost and timolol. Considering the level of patient satisfaction to the glaucoma medication, Out of 116 patients using prostaglandin derivatives 81% of patients were satisfied with their eye drop and 63.38% of patients were unsatisfied (n=71 with brimonidine eye drop. From the study, it was also clear that (58.99%) patients were adherent to the glaucoma eye drops, and (41.5%) were non-adherent. Forgetfulness, difficulty with time, busy life and cost affordability were the reported causes for non-adherence. The ophthalmologist may guide their patients to best use of their medications to reduce visual loss in glaucoma that can be caused by non-adhesion of patients to their medication.

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