

Compliance of Glaucoma Patients to Their Medical Treatment in Jeddah

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ABSTRACT

Introduction: Glaucoma is an asymptomatic chronic eye disease in which timely treatment is important to prevent the potential irreversible blindness. Patient's compliance with treatment is crucial for effective management.

Objectives: To estimate patient's compliance with glaucoma treatment (CGT) and follow-up visits (CGF) for the patients in Jeddah, Saudi Arabia. We aimed also to identify the predictors associated with noncompliance to both factors.

Methods: 575 patients were interviewed and were asked to answer an electronically adapted questionnaire where their clinical data, perception and attitude about glaucoma and its treatment, CGT, CGF, and their relationship with the physicians could be collected.

Results: The overall CGT was 72.2% and CGF was 73%. The significant predictors of noncompliance to treatment were: difficulty in self-administration ($p < 0.001$), and lack of knowledge about importance of eye drops ($p < 0.001$), disease symptoms ($p < 0.001$) and seriousness ($p < 0.001$). Drug-related predictors included long-term treatment (more than 5 years, $p < 0.001$), high cost ($p < 0.048$), taking medications more than 4 times per day ($p < 0.021$), and prescribing more than 2 drugs ($p < 0.001$). Failure to adequately explain drug benefits ($p < 0.001$), methods and frequencies of administrations

($p < 0.009$ and $p < 0.004$ respectively), and inability to properly educate patients ($p < 0.001$) were the most significant physician-centered predictors of noncompliance.

Conclusion: Our patients showed satisfactory compliance rates with glaucoma treatment and appointment schedules. If possible, once-daily dosing, convenient drug administration, and providing sufficient knowledge and education to the patient are suggested to improve the clinical outcomes and patients' compliance to treatment.

Keywords: Compliance, Glaucoma Management, Adherence, Glaucoma, Ocular Hypertension.

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INTRODUCTION

Glaucoma is a progressive optic neuropathy affecting more than 70 million patients worldwide with about 10% bilaterally blind.¹ Glaucoma can remain without symptoms until it reaches an advanced stage, a fact which increases the likelihood that the number of unidentified patients is much higher than those who are known to have it.² The exact pathogenic pattern of the disease can vary from some imperceptible changes to irreversible blindness. In Saudi Arabia, the prevalence of low vision and blindness were of considerable rates (7.8% and 1.5% respectively)³ and this was supported by other blindness estimates from the neighboring nations such as Qatar⁴ and Oman⁵ with 1.28% and 1.1% respectively. Another evidence⁶ showed that the glaucoma prevalence reached up to 10% and this would be expected to continue increasing in the following years.

The failure to perform adequate screening of glaucoma risk factors may be due to inability to have acceptable tests of high specificity and sensitivity.⁷ Therefore, glaucoma timely treatment is considered an important objective particularly in terms of prevention of progressive vision loss and subsequent disability. The first-line globally-accepted managerial approach for glaucoma is the use of topical intraocular pressure-lowering agents. In addition, medical therapy for treatment of open-angle glaucoma would cause a marked reduction of the risk of vision impairment in patients with ocular hypertension.⁸

A common feature of the successful therapies for chronic diseases is the patient's compliance with treatment. It can be obviously concluded that failure to treatment compliance frequently leads to failure of treatment and disease deterioration.

Furthermore, noncompliance to treatment would basically yield unneeded societal costs in the form of higher drug costs, need of advanced interventions, and loss of productivity. For example, glaucoma and other visual disorders led to a major economic burden for the national economy of the United States especially when those diseases affected patients older than 40 years and more.⁹ In addition, there has been a four-fold increase in the economic burden in Europe due to the direct medical costs of glaucoma management in patients with mild to severe forms.¹⁰ On the other hand, appropriate management of glaucoma by improving compliance to treatment would inevitably lead to a significant delay in disease progression and subsequently reduce the economic burden. Several factors such as forgetfulness, lack of proper understanding of the disease, and misbeliefs about the effects of glaucoma drugs, may contribute to the lack of compliance to treatment. In this context, we investigated patient's compliance to glaucoma treatment and the risk factors that could lead to poor adherence to it. Additionally, we evaluated the major aspects of poor treatment compliance in order to conduct efficient educational programs accordingly.

METHODS

This cross-sectional study was carried out among adult patient following for glaucoma at the Ophthalmology clinic in King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia. The study included patients with a confirmed glaucoma diagnosis in one or two eyes more than 30 days before the start of the study, and diagnosis confirmation should be done by an ophthalmologist using Goldmann applanation tonometry and gonioscopy. Patients should be receiving eye drops for glaucoma, prescribed at least 30 days before the start of the study. Patients aged <18 years and mentally-disabled patients were excluded. The study protocol was approved by the institutional review board of KAUH.

Sample size (N=289) was calculated to detect 25% of poor or noncompliance¹¹, with 95% confidence interval, 80% statistical power and 5% margin error. Estimating a dropout rate of 40%, the sample size was increased accordingly and rounded to 500. A convenience sampling method was used to include all patients attending the Ophthalmology clinic until reaching the target sample size.

A semi-structured questionnaire was used to collect the following data:

- 1) Sociodemographic data including gender, age at diagnosis, educational level, marital status;
- 2) Clinical data including personal medical history (comorbidities), treatment duration, number of prescribed drugs, number of prescribed anti-glaucoma eye drops, frequency of anti-glaucoma eye drops per day, number of oral tablets;
- 3) Knowledge and perception about glaucoma, including the following questions: is acute ocular pain the only symptom of glaucoma? Can a person easily be aware that he/she has glaucoma by its symptoms? Was are the medical tests used to diagnose glaucoma?;
- 4) Attitude regarding glaucoma and glaucoma treatment including agreement level (strongly agree, do not agree, strongly disagree, do not know) about the following statements: glaucoma is a serious blinding disease, eye drops advised for my glaucoma are important, treatment side effects and complications may lead to noncompliance, I have difficulty in self-medication, glaucoma

medications engender high costs, and eventual barriers to treatment compliance;

5) Compliance with glaucoma follow up (CGF) (Are you going to eye doctor on time for follow up?) and compliance with glaucoma treatment (CGT) (Do you take medications on time?), compliance-related behaviors such as history of anti-glaucoma medication taking without prescription, use of herbal and alternative medicine for glaucoma, and whether the participant stopped medication without medical advice;

6) Patient-doctor relationship including whether the physician explained administration method, frequency, and benefit and side effects of eye drops, and whether the patient feels having received enough education about his/her disease and treatment. The questionnaire was adapted in an electronic form and administered by trained medical students using a digital tablet.

Statistical Analysis

Statistical analysis was performed with the Statistical Package for Social Sciences version 21.0 for Windows (SPSS Inc., Chicago, IL, USA). The study primary outcome variable was CGF and CGT, defined as the answer "yes" to the respective questions. Chi-square test was used to analyze the correlation of demographic and clinical factors as well as knowledge and attitude with CGF and CGT, separately. Results are presented as frequency (percentage). Binary logistic regression was carried out to analyze predictors of noncompliance (separately to follow-up visits and glaucoma treatment) using the significant factors as the independent variables. Results are presented as odds-ratio (OR) with 95% confidence interval (CI). A p value of <0.05 was considered to reject the null hypothesis.

RESULTS

Demographic and Clinical Criteria

Table 1 shows the frequencies and percentages of the demographic and clinical characteristics of the participants. In general, the study included a total of 575 patients (57.6% males, 52.2% aged 40-59 years, 75.3% married) who satisfied inclusion criteria and accepted to participate. Regarding the patient's or guardian's educational level, it has been found that 78 patients (13.6%) were illiterate, whereas 192 patients (33.4%) had university+ education.

Nearly half of the participants were receiving two eye drop medications per patient (46%) with a frequency of 2 drops per day for 45.7% of the patients while most of them were not receiving oral glaucoma treatment (79.1%). A considerable number of patients had one comorbid condition with glaucoma (40.3%) with more frequencies of the associated diabetes (43.7%) and hypertension (43.0%).

Patients' Knowledge and Attitude about Glaucoma and Its Treatment

Approximately half of the respondents (53%) thought that the patient could not know that he/she is experiencing glaucoma from the symptoms and nearly the same percentage (55.1%) correctly perceived that the physician would perform the tests of eye pressure, visual field, and optic nerve examination in order to reach a definite diagnosis (Table 2). About two-thirds of the respondents opted for the laser approach (62.4%). Most of the participants had a perception of the seriousness of glaucoma as a cause of blindness (77%) and that the prescribed eye drops are important for the disease (87.5%). The most notable reason for

noncompliance to glaucoma treatment was the high cost of medications (53.7%), while there was no clear consensus about

the effects of drug complications and the difficulties of self-administration on noncompliance to glaucoma treatment.

Table 1: Participants' demographic and clinical characteristics (N=575)

PARAMETER	CATEGORY	Frequency	Percentage
Gender	Male	331	57.6
	Female	244	42.4
Age at diagnosis (years)	Neonate (0 – 1)	18	3.1
	1 – 15	31	5.4
	16-40	45	7.8
	40-49	139	24.2
	50-59	161	28.0
	60-70	106	18.4
	70+	70	12.2
Patient's or guardian's educational Level	Illiterate	78	13.6
	Writes and reads	48	8.3
	Primary	62	10.8
	Middle school	71	12.3
	Secondary	124	21.6
	University+	192	33.4
Marital status	Married	433	75.3
	Bachelor	57	9.9
	Divorced	17	3.0
	Widowed	68	11.8
Treatment duration	Newly diagnosed	77	13.4
	<5 years	128	22.3
	5-10 years	181	31.5
	>10 years	189	32.9
No. of prescribed drugs	1	181	31.5
	2	231	40.2
	3	103	17.9
	4+	60	10.4
No. of prescribed anti-glaucoma eye drops	One	149	25.9
	Two	266	46.3
	3+	160	27.8
Frequency of drops administration per day	2	263	45.7
	3	121	21.0
	4-5	38	6.6
	>5	14	2.4
Oral treatment for glaucoma	No	455	79.1
	Yes	86	15.0
Comorbidity	Diabetes	251	43.7
	Hypertension	247	43.0
	Dyslipidemia	144	25.0
	Other	71	12.3
Number of comorbidities	0	133	23.1
	1	232	40.3
	2	149	25.9
	3+	61	10.6

Because of missing data, all frequencies do not sum up to the total

Table 2: Knowledge and attitude about glaucoma and glaucoma treatment (N=575)

PARAMETER / ITEM	ANSWER	Frequency	Percentage
KNOWLEDGE			
If a person is suffering from glaucoma, will he/she be able to know it by symptoms?	Yes	143	24.9
	No	305	53.0
	I don't know	127	22.1
Acute pain in the eye is the only symptom of glaucoma	Yes	176	30.6
	No	228	39.7
	I don't know	171	29.7
How a doctor can diagnose glaucoma?	Eye pressure	116	20.2
	Visual field	2	0.3
	Optic nerve examination	12	2.1
	All the previous	317	55.1
	Do not know	122	21.2
	Others	6	1.0

ATTITUDE			
Would you opt for laser surgery to treat glaucoma?	Yes	359	62.4
	No	216	37.6
Reasons for laser surgery refusal	Fear of surgery	28	4.9
	Fear of postop blindness	11	1.9
	Fear of complications	47	8.2
	Option not offered by doctor	110	19.1
	Other reason	12	2.1
Glaucoma is a serious blinding disease	Strongly agree	443	77.0
	Disagree	34	5.9
	Strongly disagree	6	1.0
	Do not know	92	16.0
Eye drops advised for my glaucoma treatment are important	Strongly agree	503	87.5
	Disagree	20	3.5
	Strongly disagree	10	1.7
	Do not know	42	7.3
Noncompliance is due to complications of medicines used	Strongly agree	189	32.9
	Disagree	213	37.0
	Strongly disagree	62	10.8
	Do not know	111	19.3
Difficulty in self medication	Strongly agree	222	38.6
	Disagree	200	34.8
	Strongly disagree	136	23.7
	Do not know	17	3.0
High cost of medicine	Strongly agree	309	53.7
	Disagree	161	28.0
	Strongly disagree	87	15.1
	Do not know	18	3.1
What are the barriers to treatment adherence?	Forgetfulness	155	27.0
	Other Priorities	83	14.4
	Lack Of Information	16	2.8
	Disability/Disease (Dementia, Tremor, Etc.)	4	.7
	Other	113	19.7
	More Than One Barrier	159	27.7
	None	45	7.8

Because of missing data, all frequencies do not sum up to the total; Freq. frequency; % percentage;

Table 3: Practice in and adherence to glaucoma treatment and physician's support (N=575)

PARAMETER	CATEGORY	Frequency	Percentage
Interval between two eye drops	Immediately	206	35.8
	1-5 minutes	132	23.0
	5-10 minutes	73	12.7
	10-15 minutes	62	10.8
	>15 minutes	102	17.7
	No	546	95.0
Compliance with follow-up visits	Yes always	420	73.0
	Sometimes	113	19.7
	No	42	7.3
Compliance with medication taking on time	Yes always	415	72.2
	Sometimes	146	25.4
	No	14	2.4
Use of glaucoma treatment without prescription	Yes	29	5.0
	No	546	95.0
Ever stopped glaucoma treatment	Yes	206	35.8
	Sometimes	44	7.7
	Never	325	56.5
Use of herbals and alternative medicine for glaucoma	Rose water + Chinese herbs	3	0.5
	Chinese herbs	2	0.3
	Yes, other	26	4.5
	No	544	94.6
Did physician explain how to administer the eye drops?	Yes	519	90.3
	No	56	9.7
Did physician explain frequency of eye drops?	Yes	559	97.2
	No	16	2.8
Did physician explain benefits and side effects?	Yes	319	55.5
	No	256	44.5
Did you receive enough education about glaucoma and its treatment?	Yes	329	57.2
	No	234	40.7

Table 4: Demographic and clinical factors of compliance to glaucoma treatment (N=575)

PARAMETER	CATEGORY	COMPLIANCE RATE			
		Follow-up visit		Treatment taking on time	
		%	p-value	%	p-value
Gender	Male	72.5	.736	74.9	.086
	Female	73.8		68.4	
Age at diagnosis (years)	Neonate (0 – 1)	88.9	<.001*	77.8	<.001*
	1 – 15	87.1		87.1	
	16-40	95.6		86.7	
	40-49	62.6		67.6	
	50-59	61.5		61.5	
	60-70	74.5		72.6	
	70+	94.3		88.6	
Patient's or guardian's educational Level	Illiterate	66.7	<.001*	74.4	<.001*
	Writes and reads	62.5		58.3	
	Primary	59.7		59.7	
	Middle school	56.3		59.2	
	Secondary	73.4		67.7	
Marital status	University+	88.5	<.001*	86.5	<.001*
	Married	76.7		76.0	
	Bachelor	86.0		75.4	
	Divorced	58.8		47.1	
Treatment duration	Widowed	42.6	<.001*	51.5	<.001*
	Newly diagnosed	92.2		87.0	
	<5 years	81.3		76.6	
	5-10 years	74.0		68.5	
No. of prescribed drugs	>10 years	58.7	<.001*	66.7	.003*
	1	80.7		77.9	
	2	62.3		62.3	
	3	73.8		71.8	
No. of prescribed anti-glaucoma eye drops	4+	90.0	.001*	93.3	.575
	One	72.5		72.5	
	Two	66.9		70.3	
Frequency of drops administration per day	3+	83.8	.067	75.0	.011*
	2	70.7		70.7	
	3	74.4		74.4	
	4-5	89.5		89.5	
Oral treatment for glaucoma	>5	85.7	.054	100.0	.005*
	No	74.1		74.3	
Herbal use for glaucoma	Yes	64.0	.789	59.3	.328
	No	73.2		72.6	
Diabetes	Yes	71.0	.114	64.6	.997
	No	75.6		72.2	
Hypertension	Yes	69.7	<.001*	72.1	.120
	No	79.6		74.7	
Dyslipidemia	Yes	64.4	.859	68.8	.510
	No	72.9		71.5	
Other	Yes	73.6	.001*	74.3	.436
	No	70.6		71.6	
Number of comorbidities	Yes	90.1	.001*	76.1	.073
	0	78.9		76.7	
	1	75.4		70.7	
	2	61.1		66.4	
	3+	80.3		82.0	

Because of missing data, all frequencies do not sum up to the total

Practice in and Compliance to Glaucoma Treatment and Physician's Support

Most of the participants showed a high compliance to taking their medications on time (72.2%) and also the compliance with their regular follow-up (73%, Table 3). Five percent of the respondents declared ever using glaucoma medications without prescriptions and 5.3% declared using herbal alternatives while 35.8% stated that they had ever stopped the glaucoma treatment. Regarding physician's role, most of the respondents perceived that the physician provided a good explanation of the frequency (97.2%)

and the method of administration (90.3%) of eye drops. Importantly, less than half of the participants (40.7%) believed that they did not receive adequate education about glaucoma and its treatment.

Demographic and Clinical Factors of CGF and CGT

Participants older than 70 years and those having a university+ educational level had significant increases in their CGF ($p<.001$) and CGT ($p<.001$) if compared to their counterparts (Table 4). The CGF and CGT were significantly higher in newly diagnosed cases ($p<.001$ and $.003$ respectively), and decreased gradually with the

duration of the disease. Additionally, CGF was increased if the number of eye drops was more than 3 ($p=0.001$), whereas CGT significantly increased with higher frequency of drops administration ($p=.011$) and decreased when the patient was taking oral medication for glaucoma treatment ($p=.005$).

Patients' Knowledge, Attitude and Practice as Factors for CGT and CGF

The correlation between CGT and CGF and knowledge, attitude and practice factors is depicted in Table 5. Both CGT and CGF were significantly higher among the participants who believed that the symptoms may be indicative of glaucoma ($p<.001$ and $p<.001$ respectively). Despite some inconsistent findings, CGF and CGT

were generally higher among participants who perceived glaucoma as a blinding disease and those who believed eye drops are important, and were lower among those who agreed the treatment costs are high. Additionally, behaviors including stopping treatment, taking treatment without prescription were significantly associated with less compliance. Regarding physician-patient relationship, explaining how to administer the eye drops was associated with higher CGT ($p=.008$) but did not impact CGF ($p=.774$); whereas the other parameters including explaining the frequency of eye drop administration, explaining benefits and side effects and patient-perceived good education were associated with significant increase in both CGF and CGT.

Table 5: Knowledge, attitude and practice factors of compliance to glaucoma treatment

PARAMETER	CATEGORY	COMPLIANCE RATE			
		Follow-up visit		Treatment timing	
		%	p-value	%	p-value
A person may be able to know glaucoma by symptoms?	Yes	86.0		89.5	
	No	73.1	<.001*	65.9	<.001*
	I don't know	58.3		67.7	
Acute pain in the eye is the only symptom of glaucoma	Yes	75.6		76.1	
	No	77.6	.008*	70.2	.368
	I don't know	64.3		70.8	
Knowledge about diagnostic criteria	Incorrect	81.4		77.9	
	Correct	66.2	<.001*	67.5	.006*
Glaucoma is a serious blinding disease	Strongly agree	79.7		77.0	
	Disagree	41.2		41.2	
	Strongly disagree	100.0	<.001*	100.0	<.001*
	Do not know	51.1		58.7	
Eye drops advised for my glaucoma treatment are important	Strongly agree	77.9		77.5	
	Disagree	50.0		20.0	
	Strongly disagree	60.0	<.001*	40.0	<.001*
	Do not know	28.6		40.5	
Noncompliance is due to complications of medicines used	Strongly agree	76.2		75.1	
	Disagree	71.8		69.0	
	Strongly disagree	90.3	<.001*	74.2	.571
	Do not know	60.4		72.1	
Difficulty in self medication	Strongly agree	58.6		59.0	
	Disagree	78.5		77.5	
	Strongly disagree	87.5	<.001*	86.0	<.001*
	Do not know	82.4		70.6	
High cost of medicine	Strongly agree	69.6		67.0	
	Disagree	72.0		80.7	
	Strongly disagree	88.5	.005*	78.2	.003*
	Do not know	66.7		55.6	
What are the barriers to treatment adherence?	Forgetfulness	71.0		63.2	
	Other priorities	55.4		63.9	
	Lack of information	50.0		50.0	
	Disability	100.0	<.001*	100.0	.005*
	Other	78.8		81.4	
	>1 barrier	79.9		72.3	
Ever stopped glaucoma treatment	Yes	50.0		52.9	
	No	84.6	<.001*	84.3	<.001*
	Somewhat	95.5		72.7	
Glaucoma treatment without prescription	Yes	34.5		34.5	
	No	75.1	<.001*	74.2	<.001*
Did physician explain how to administer the eye drops?	Yes	73.2		73.8	
	No	71.4	.774	57.1	.008*
Did physician explain frequency of eye drops?	Yes	74.1		73.2	
	No	37.5	.001*	37.5	.002*
Did physician explain benefits and side effects?	Yes	84.5		81.5	
	No	58.6	<.001*	60.5	<.001*
Did you receive enough education about glaucoma and its treatment?	Yes	86.0		86.3	
	No	54.3	<.001*	52.6	<.001*

Because of missing data, all frequencies do not sum up to the total.

Table 6: Demographic and clinical predictors of noncompliance to glaucoma follow-up visits and treatment timing

PARAMETER	CATEGORY	Noncompliance to follow-up			Noncompliance to treatment timing				
		O.R	95%CI	p-value	O.R	95%CI	p-value		
Age at diagnosis (years)	Neonate (0 – 1)	Ref	-	-	Ref	-	-		
	1 – 15	1.19	0.19	7.22	.854	0.52	2.39	.400	
	16-40	0.37	0.05	2.87	.343	0.54	0.13	2.19	.388
	40-49	4.78	1.06	21.64	.042*	1.68	0.52	5.38	.386
	50-59	5.01	1.11	22.54	.026*	2.19	0.69	6.96	.183
	60-70	2.73	0.59	12.67	.199	1.32	0.40	4.33	.649
	70+	0.48	0.08	2.88	.426	0.45	0.12	1.71	.242
Patient's or guardian's educational Level	Illiterate	Ref	-	-	Ref	-	-		
	Writes and reads	1.20	0.57	2.54	.634	2.07	0.96	4.46	.063
	Primary	1.35	0.68	2.70	.394	1.96	0.96	4.02	.066
	Middle school	1.55	0.80	3.01	.196	2.00	1.00	4.01	.050
	Secondary	0.73	0.39	1.34	.307	1.38	0.73	2.60	.317
	University+	0.26	0.14	0.49	<.001*	0.45	0.24	0.87	.018*
Treatment duration	Newly diagnosed	Ref	-	-	Ref	-	-		
	<5 years	2.73	1.06	7.02	.037*	2.05	0.94	4.48	.071
	5-10 years	4.15	1.69	10.18	.002*	3.08	1.48	6.42	.003*
	>10 years	8.32	3.44	20.09	<.001*	3.35	1.61	6.95	.001*
No. of prescribed drugs	1	Ref	-	-	Ref	-	-		
	2	2.52	1.60	3.97	<.001*	2.13	1.37	3.31	.001*
	3	1.48	0.84	2.63	.179	1.38	0.79	2.41	.254
	4+	0.46	0.18	1.16	.102	0.25	0.09	0.74	.012*
No. of prescribed anti-glaucoma eye drops	One	Ref	-	-	Ref	-	-		
	Two	1.30	0.84	2.02	.240	1.11	0.71	1.74	.638
	3+	0.51	0.29	0.89	.017*	0.88	0.53	1.46	.615
Frequency of drops administration per day	2	Ref	-	-	Ref	-	-		
	3	0.83	0.51	1.35	.459	0.83	0.51	1.35	.459
	4-5	0.28	0.10	0.83	.021*	0.28	0.10	0.83	.021*
	>5	0.40	0.09	1.84	.241	NC	NC	NC	.998
Oral treatment for glaucoma	No	Ref	-	-	Ref	-	-		
	Yes	1.61	0.99	2.62	.056	1.98	1.23	3.20	.005*

Table 7: Attitudes and knowledge as predictors for noncompliance to glaucoma follow-up visits and treatment timing

PARAMETER	CATEGORY	Noncompliance to follow-up			Noncompliance to treatment timing				
		O.R	95%CI	p-value	O.R	95%CI	p-value		
A person may be able to know glaucoma by symptoms?	Yes	Ref	-	-	Ref	-	-		
	No	2.26	1.32	3.87	.003*	4.42	2.46	7.93	<.001*
	I don't know	4.40	2.44	7.94	<.001*	4.07	2.12	7.81	<.001*
Acute pain in the eye is the only symptom of glaucoma	Yes	Ref	-	-	Ref	-	-		
	No	0.89	0.56	1.42	.627	1.36	0.87	2.12	.183
	I don't know	1.72	1.08	2.73	.023*	1.32	0.82	2.13	.257
Diagnostic criteria by physician	Incorrect	0.45	0.30	0.66	<.001*	0.59	0.40	0.86	.006*
	Correct	Ref	-	-	Ref	-	-		
Glaucoma is a serious blinding disease ‡	Disagree	5.60	2.72	11.52	<.001*	4.78	2.33	9.79	<.001*
	Strongly disagree	NC	NCc	NC	.999	NC	NC	NC	.999
	Do not know	2.76	2.35	6.01	<.001*	2.35	1.47	3.77	<.001*
Eye drops advised for my glaucoma are important ‡	Disagree	3.53	1.43	8.70	.006*	13.01	4.53	42.12	<.001*
	Strongly disagree	2.35	0.65	8.49	.191	5.18	1.44	18.66	.012*
	Do not know	8.83	4.38	17.81	<.001*	5.08	2.65	9.73	<.001*
Noncompliance is due to complications of medicines used ‡	Disagree	1.25	0.80	1.97	.321	1.36	0.87	2.11	.174
	Strongly disagree	0.34	0.14	0.85	.021*	1.05	0.54	2.03	.882
	Do not know	2.10	1.27	3.49	.004*	1.17	0.69	1.99	.560
Difficulty in self-medication ‡	Disagree	0.39	0.25	0.60	<.001*	0.42	0.27	0.64	<.001*
	Strongly disagree	0.20	0.11	0.39	<.001*	0.23	0.13	0.41	<.001*
	Do not know	0.30	0.85	1.08	.066	0.60	0.20	1.76	.352
High cost of treatments ‡	Disagree	0.89	0.58	1.35	.578	0.48	0.31	0.77	.002*
	Strongly disagree	0.30	0.15	0.60	.001*	0.57	0.32	0.99	.048*
	Do not know	1.14	0.42	3.14	.794	1.62	0.62	4.24	.322
Ever stopped glaucoma treatment	Yes	Ref	-	-	Ref	-	-		
	No	0.18	0.12	0.27	<.001*	0.21	0.14	0.31	<.001*
	Somewhat	0.48	0.11	0.20	<.001*	0.42	0.21	0.86	.018*
Glaucoma treatment without prescription	Yes	5.73	2.60	12.62	<.001*	5.46	2.48	12.02	<.001*
Administration explained	No	1.09	0.59	2.02	.774	2.11	1.20	3.71	.009*
Frequency explained	No	4.76	1.70	13.32	.003*	4.54	1.62	12.72	.004*
Benefits and SE explained	No	3.89	2.63	5.77	<.001*	2.87	1.97	4.19	<.001*
Enough educated	No	5.18	3.46	7.76	<.001*	5.70	3.80	8.55	<.001*

OR: Odds ratio; CI: confidence interval; ref: reference category; NC: not calculable; ‡ reference category=strongly agree;

Predictors to Non-Compliance to Follow-Up Visits (N-CGF) and Treatment (N-CGT)

Demographic and clinical predictors of N-CGF and N-CGT are demonstrated in Table 6. Significant demographic and clinical predictors of N-CGF included: middle-aged patients (between 40 and 59 years old), university+ education, long treatment duration, taking two prescribed drugs, and taking three eye drop medications with a frequency of 4-5 drops per day. Significant demographic and clinical predictors of N-CGT administration time included: university+ education, long treatment duration, taking 2-4 prescribed drugs, using eye drops at a frequency of 4-5 drops per day.

Table 7 shows patients' attitudes and knowledge as well as the physician-patient relationship as important predictors for N-CGF and N-CGT. Patients' attitudes and knowledge as predictors of N-CGF included: lack of knowledge about glaucoma symptoms and its seriousness, patients' beliefs that the eye drops are not important, lack of knowledge about treatment complications, stopping treatment or taking it without prescription, and when the medications are of high costs. Regarding physician-patient relationship, the significant predictors for N-CGF were: lack of knowledge about glaucoma diagnostic criteria by the physician, failure to adequately explain drug benefits and frequency and inability to get enough education about glaucoma.

The predictors for N-CGT which are related to patients' attitude and knowledge were as follow: lack of knowledge about glaucoma symptoms and its seriousness and lack of perception about the importance of the prescribed eye drops. Drug-related factors included drug complications, difficulty in self-administration, high costs, stopping treatment or taking the medications without prescriptions. Finally, the significant predictors for N-CGT which are related to the relationship between the physician and the patient were: lack of knowledge about glaucoma diagnostic criteria by the physician, failure to adequately explain drug benefits, methods of administrations, and frequency and inability to get enough education about glaucoma.

DISCUSSION

Glaucoma is classified into primary open-angle or angle-closure glaucoma according to the etiology and angle status. Secondary forms can also occur following several ocular or systemic diseases. Conventional glaucoma therapy entails using topical β -blocker or a topical prostaglandin analog. In cases of acute rises of intraocular pressure, the administration of systemic carbonic anhydrase inhibitors may be valuable. Several environmental, medication regimen-related, physician, and patient factors are attributable to be barriers to compliance with glaucoma treatment. Our study showed that the overall noncompliance rate (either partial or total) to glaucoma treatment was 27.8%. This may be considered relatively lower than the average estimate (40%) of other reports.¹²⁻¹⁴ In Asia, up to our knowledge, all studies have shown marked increases in the noncompliance rates which exceeded half of the studied populations: 63.4% in Hong Kong¹⁵, 75.8% in Taiwan¹⁶, 65.5% in Pakistan¹⁷ and 49% in a recent study in India.¹⁸ The difference between our findings and those of other reports may be due to the effects of the specifically-designed programs aimed at raising the overall knowledge of adherence to treatment among glaucoma patients. In addition, noncompliance to follow-up visits in our patients was 27% indicating improved

patients' knowledge and supported by the role of the physicians in providing optimal healthcare services. Only one study conducted at a Saudi institution demonstrated a noncompliance rate at 19.4% (lower than ours), a matter which could be related to the effective awareness programs established there.¹⁹

Indeed, factors related to CGT are also remarkably applicable to CGF. This can be clearly found in the similarity between both outcomes in relation to the most of other factors. Both CGT and CGF were high among patients who perceived the seriousness of glaucoma as a blinding disease. Another supportive finding stated that the patients with a poor understanding of glaucoma are less likely to be compliant with follow-up schedules and treatment.²⁰ Conversely, a clinic-based study showed that even the well-perceived patients were noncompliant with follow-up visits because of the costly examinations, lack of knowledge about the timing of schedules, and discounting their asymptomatic disease.²¹ Similarly, both CGT and CGF are higher among patients who believed that the eye drops are important for treatment. Such finding may be ascribed to obtaining adequate health-related knowledge, ability to read medicine labels and inserts and other healthcare information, understanding the oral and written instructions by their physician, nurses, and pharmacists, and finally to adequately respond to the given directions and procedures related to their treatment and/or follow-up visits.²² On the other hand, patients with poor health literacy usually miss their scheduled appointments and also are more likely to be nonadherent to their eye drop medications at least two times per month.²³ In Oman, a cross-sectional descriptive study demonstrated that noncompliance with glaucoma treatment was high (up to 75.2%), and the major impactful risk factors were the lack of knowledge and awareness to glaucoma and the importance of ocular pressure hypotensives.⁵ Other consequences of such lack of health knowledge include stopping treatment or taking it without prescription, and this observation occurred also in our study as demonstrated in the predictors of noncompliance to glaucoma treatment and follow-up visits.

Medication-related factors can commonly affect CGT. One of the major problems in our study which hinders patients' compliance is the increased drug cost. Actually, this observation is frequently expected in all studies although it is difficult to assess because many of the patients who don't comply with treatment never discuss this issue with their physician. Patients without prescription drug insurance and those who paid more money for their treatment showed more difficulty to get the medications.²⁴ Ophthalmologists and other healthcare providers should be aware of the costs of the prescribed medications, particularly for chronic illnesses, and the amount of copay required for each one, including those acting systemically. Such attitude would ultimately help the physician to expect a high degree of compliance with the treatment for long periods. In addition, each eye care provider should discuss with the patients the amount of money paid monthly for their drugs and adjust the whole regimen according to the patient's economic status, considering those with low-income to receive low-costly or even free drugs.

Difficulties in drug administration and its side effects have been reported as predictors of both N-CGT and N-CGF. This is consistent with the findings of another survey, where difficulties in eye drop self-administration led to poor compliance in 44% of patients, while 16% discontinued their drugs due to the reported

complications.²⁴ Several patients reported inconvenience, inability to squeeze the bottle, difficulty to read the printed text on it and difficulty in removing the seal.^{11,23} These findings may be more frequently observed in elderly patients who would potentially use a mirror for self-administration or relying on other family members to take the drops.²⁵ Therefore, physicians should discuss these issues with the patient as well as his/her family members.

Overall, providing accurate discussion to the patient is important for multiple reasons. Patient's compliance with treatment and appointments is essentially dependent on the explanation of methods of administration, frequency, benefits, and side effects of the eye drop as per results of this study. It is imperative to create a convenient condition for the patients in order to discuss their adherence problems. A friendly approach may be required to adjust patients' behavior and encourage them to talk about their noncompliance factors. About 69% of the patients in a study of Winfield et al reported lack of discussions with their providers in terms of adherence problems and difficulties.²⁶ It is worthy to note that the doctor-patient relationship or communication is physician-oriented rather than related to the patient.²⁷ Physicians should educate the patients about how to administer their drugs, such as how to lean back their head, and the interval between administering 2 different types of eye drops, and providing useful other tips. The method of drug administration is the sole variable which was significantly associated with patients' adherence in a recent study²⁸, yet other educational aspects about the side effects and purpose of the medications did not affect patients' compliance during the first 2 months post visits.

Finally, an effective patient-centered communication should include 4-step adherence assessment²⁹ starting with discussing whether the patient understand the medical regimen, then asking if taking medication is difficult or it is common to miss or forget one dose, and the patient should perceive that the medication target a specific disease state and is dependent on how the patient has been taking the medication. The fourth factor while assessing patient's adherence is asking directly about the adherence.

In conclusion, compliance with glaucoma treatment is a real challenge for eye care providers as the potential barriers to treatment adherence are numerous. The findings of this study revealed relatively lower levels of noncompliance to both treatment and appointments if compared to other studies. The observed factors of noncompliance were as follow: drug-related factors (high costs, methods of administration, side effects, and complexity of the regimen), and patient-centered factors, such as the difficulties in self-medication and health literacy regarding the disease and treatment. Physicians have the responsibility of providing enough education about the disease and its treatment and discussing noncompliance issues considering all of the mentioned factors.

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