

Compliance and knowledge about glaucoma in patients at tertiary glaucoma units

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Abstract To document the rate of self-reported compliance and glaucoma-related knowledge in Swiss patients and to identify risk factors for their poor compliance. This was an observational study, including a total of 200 consecutive patients already under glaucoma medication in two Swiss tertiary glaucoma clinics (Geneva and Bern). Personal characteristics, presence of systemic disease, compliance with glaucoma medication, attitude to the ophthalmologist, and glaucoma-related attitudes were ascertained by means of a predetermined questionnaire with 40 questions. Patients were subsequently assessed for the ability to correctly instil placebo eye drops. Non-compliance with glaucoma medication was defined as omitting more than two doses a week as reported by the patient. Logistic regression was used to evaluate how patient characteristics and knowledge about the disease were related to compliance. Overall, 81% ($n = 162$) of patients reported to be compliant. Forgetfulness was the most frequently cited reason for non-compliance with dosing regimen (63%). Although 90.5% ($n = 181$) of patients believed glaucoma medication

to be efficient, only 28% ($n = 56$) could correctly define glaucoma. Factors positively associated with compliance were ‘knowledge of glaucoma’ [adjusted odds ratio (OR) 4.77 (95% CI 1.36–16.70)] and ‘getting help for administration of drops’ [OR 2.95 (1.25–6.94)]. These findings indicate that despite the comparatively high compliance rate among glaucoma patients, knowledge of glaucoma remains poor in long-term glaucoma sufferers. Improving knowledge about the disease is important since it is positively associated with compliance in our study.

Keywords Glaucoma · Compliance · Knowledge · Switzerland · Vascular dysregulation

Introduction

Compliance with a medication regimen is generally defined as the extent to which patients take medication as prescribed by their physician. It is established that compliance with a prescribed drug regimen is often inadequate particularly among patients on long-term medication for chronic disease, including ophthalmic diseases [1–3]. Among these, glaucoma patients constitute the most important group as it is the second leading cause of blindness worldwide [4]. At present, the only treatable risk factor for glaucoma progression is elevated intraocular pressure (IOP). The fact, however, that glaucoma treatment is considered palliative rather than curative as well as the general

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absence of symptoms in glaucoma patients increases their risk of non-compliance. Analysis of the Collaborative Initial Glaucoma Treatment Study identified an important role of compliance for IOP control during treatment [5]. In the light of these findings, high rates of non-compliance with glaucoma treatment in different populations constitute a significant public health concern.

There is no standardised methodology for measurement of compliance, and there is generally a lack of agreement in compliance findings between measurement methodologies [6]. Progression of glaucoma despite medical therapy is generally dealt with by adding more potent compounds or resorting to surgery. This could potentially be inappropriate as patient's non-compliance with the prescribed regimen rather than drug inefficacy may be the underlying factor. Therefore, specific information on the risk factors for non-compliance is important in formulating practical policies for glaucoma care. We report here the findings of a study to ascertain the extent of patients' non-compliance and knowledge about their disease in a Swiss hospital setting and their contributing risk factors.

Materials and methods

This was a cross-sectional, observational cohort study. We enrolled 200 consecutive patients receiving ocular hypotensive treatment for primary open-angle glaucoma (POAG) in two linguistically distinct Swiss tertiary glaucoma clinics (University Department of Ophthalmology Geneva, glaucoma sector, henceforth referred to as 'centre 1', and University Department of Ophthalmology Bern, glaucoma sector, 'centre 2'). Each centre recruited 100 patients. The participants were diagnosed in the past with POAG and had been taking one or more hypotensive drugs for at least 6 months. The diagnosis of POAG required typical glaucomatous optic nerve damage and visual field abnormalities with or without a history of high IOPs. Institutional Review Board approval was obtained and all patients signed an informed consent. We developed a structured questionnaire based upon the existing literature. A pilot study on 10 patients was performed and their suggestions were used to develop a final version. The questionnaire consisted of 40 questions. The first part dealt with the practice of glaucoma

treatment and knowledge about glaucoma. The second part included general personal characteristics. On average, it took patients 15 min to complete the questionnaire.

After enrolment in the study and signing an informed consent, patients were handed the questionnaire and were given sufficient time to complete it before leaving the clinic. All patients were informed that the questionnaire would remain anonymous and no negative consequence for the follow-up would arise from their participation and responses. In accordance with the published literature, clinically significant non-compliance was defined as omitting more than two doses of glaucoma medication during any given week [7]. Knowledge of glaucoma was defined as being able to give a simple, correct explanation of the disease. The acceptability of the answers was assessed by two investigators whose agreement was required. In case of disagreement, a third investigator adjudicated. To evaluate unintentional non-compliance (dyscompliance), patients were asked to demonstrate the instillation of placebo eye drops. A drug bottle containing sodium chloride 5.0% was used for this purpose. Patients were categorised as 'successful' if they were able to instil the drop correctly, kept the eye closed afterwards for a minimum of 1 min and/or exercised pressure on the punctum for at least 1 min, 'moderately successful' if they had to try more than once to instil their drop, and 'unsuccessful' if they touched the eye or missed the eye more than 50% of the time. Patients who did not apply their own drops were asked to describe exactly how the drop instillation was performed at home.

Statistical analysis

Sample size calculation was based on a 25% compliance rate as the reference value. For each centre to reach a power of $1 - \beta = 0.90$, given $\alpha = 0.05$ with an acceptable error of 10%, 70 patients were needed. We increased this sample to 100 to account for incomplete answering. Descriptive statistics were calculated for 19 independent variables (e.g., number of drops, duration of glaucoma treatment, family history of glaucoma, age, gender, systemic disease, family status, and education) and for dependent variables (compliance and glaucoma knowledge). Next, bivariate analysis was used to examine variables associated with compliance and knowledge.

Associations with a P value of <0.2 or those that could logically or intuitively be considered to be related to patient compliance or knowledge were retained for further analysis. Multiple logistic regression analysis was then used to examine how the preselected variables were associated with compliance and knowledge. We also tested the effect of centre as a categorical variable. The model was then refined by using a standard stepwise backward elimination procedure. After each regression run, we eliminated the independent variable showing the least significant relationship to the outcome of interest. The process was continued until only variables with P values <0.05 were left. Statistical analysis was performed with the Stata 9.0 software package.

Results

Two hundred patients were included from the two centres (100 each). We obtained 160 complete and 40

incomplete records. All records were included in the analysis. In all, 52.5% of patients were on a single topical glaucoma medication, 36% on two medications, 11% on three medications, and 0.5% on four medications. Table 1 presents the complete demographic characteristics of the patients. Table 2 provides an overview of the type of medication used by participants.

Glaucoma had been discovered during a routine ophthalmic examination by their ophthalmologist in 93 patients (46.5%), at a tertiary referral centre ($n = 49$, 24.5%), based on suspicion by an optician ($n = 9$, 4.5%), general practitioner ($n = 6$, 3.0%), due to personal awareness secondary to media coverage ($n = 7$, 3.5%) or affected family members ($n = 5$, 2.5%). Duration of glaucoma was less than a year in 25 patients (12.5%), between 1 and 3 years in 51 (25.5%), between 4 and 5 years in 36 (18.0%), between 6 and 10 years in 34 (17.0%), and >10 years in 42 patients (21.0%). The rest of the patients could not give an answer. Fifty-nine (29.5%) patients reported a positive family history of glaucoma.

Table 1 Patient demographics ($n = 200$)

	Geneva ($n = 100$)	Bern ($n = 100$)	Both centres ($n = 200$)	P
Age (mean, SD)	64.4 (± 14.1)	68.3 (± 12.9)	66.3 (± 13.6)	0.05
Gender				
Male	41% (41)	49% (49)	45.5% (91)	NS
Female	59% (59)	51% (51)	54.5% (109)	NS
Income				
<5000 CHF	21% (21)	33% (33)	27.0% (54)	NS
5001–8000 CHF	10% (10)	13% (13)	11.5% (23)	NS
>8000 CHF	14% (14)	6% (6)	5.0% (20)	<0.05
No answer	55% (55)	48% (48)	51.5% (103)	NS
Education				
Primary	60% (60)	79% (79)	69.5% (139)	<0.05
Secondary	10% (10)	9% (9)	9.5% (19)	NS
Tertiary	14% (14)	7% (7)	10.5% (21)	<0.05
Social status				
Married	45% (45)	58% (58)	51.5% (103)	NS
Divorced	12% (12)	12% (12)	12.0% (24)	NS
Widower	20% (20)	22% (22)	21.0% (42)	NS
Bachelor	20% (20)	7% (7)	13.5% (27)	<0.05
No. of glaucoma medications				
1	62% (62)	43% (43)	52.5% (105)	<0.05
2	33% (33)	39% (39)	36.0% (72)	NS
3	5% (5)	17% (17)	11.0% (22)	<0.05
4	0	1% (1)	0.5% (1)	NS

NS statistically not significant, CHF Swiss Franc

Table 2 Type of medication used in the Swiss Compliance Trial (including multiple therapy)

Medication	Patients, no. (%)
Prostaglandin analogue	104 (52)
Carbonic anhydrase inhibitors/ β -adrenergic antagonist combination	50 (25)
β -Adrenergic antagonist	32 (16)
α -Agonist	31 (15.5)
Carbonic anhydrase inhibitors	28 (14)
Prostaglandin analogue/ β -adrenergic antagonist combination	15 (7.5)
α -Agonist/ β -adrenergic antagonist combination	11 (5.5)

Inability to administer eye drops correctly (termed as dyscompliance) was found in 7%, acceptable method of instillation in 28% and good mode of instillation in 64%. Presence of self-reported arthritis (RR 2.05; 95% CI 1.30–2.88) was significantly associated with dyscompliance. Age over 60 years (RR 1.76; 95% CI 1.07–1.91) and lower educational level (RR 1.16; 95% CI 1.02–1.33) were significantly associated with the practice of waiting less than 3 min between different glaucoma drops.

One hundred and thirteen patients (56.5%) stated that they never forgot a single drop, 36 (18.0%) that they forgot one drop a week, 13 (6.5%) that they forgot two drops a week, and nine patients (4.5%) forgot more than two drops in a week. The remainder could not give an answer. Therefore, according to our definition, the rate of compliance was 81.0% ($n = 162$; 95% CI 75.6–86.4). Compliance was significantly higher in patients from Bern compared to those from Geneva (87 vs. 75%, $P = 0.031$). This difference was chiefly due to a higher number of participants who did not give an answer at centre 1 and were therefore categorised as non-compliant. The main reasons for defaulting were (in descending order): forgetfulness (63%), being away from home/travel (16%), inconvenience during work (7%), difficulty to instil the drops (4%), eye irritation (3.5%), disbelief in efficiency of drops (3.5%), and other reasons (3%).

The most frequent method to remember therapy was daily application at the same time ($n = 150$, 75.0%), followed by reminding through family members or partners ($n = 8$, 4.0%), and use of an alarm-clock/device ($n = 6$, 3.0%). No side-effects of

medical glaucoma therapy were felt by 60.5% of patients, while 14% experienced moderate to severe side-effects, the most frequent being severe burning of the eye (5.0%). We did not find any effect of age on the reporting of side-effects. Of those patients who suffered from side-effects, only 5% had stopped the treatment before consulting their physician. No relationship between reporting of side-effects and compliance was found. Ninety percent of respondents felt their glaucoma treatment to be useful, out of which 53% believed it to be very useful, while the rest believed it had little or no effect at all. Sixty-eight percent claimed to always study the package information of new glaucoma medication. A total of 79.6% administered their own drops, while 4.8% required occasional assistance, and 14.2% required frequent assistance. Concerning the goal of therapy, 136 patients (68.0%) believed it to be maintaining current vision, 32 (16.0%) believed it to be improving vision and 7 patients (3.5%) believed in other reasons.

Knowledge about glaucoma (Odds ratio (OR) 4.77; 95% CI 1.36–16.70), and assistance by others to administer the glaucoma drops (OR 2.94; 95% CI 1.25–6.94) were positively associated while recruitment at Geneva was negatively associated (OR 0.35; 95% CI 0.15–0.80) with compliance in a multiple regression model. No association could be found between compliance with the glaucoma treatment and the total number of glaucoma drops (OR 0.91; 95% CI 0.33–2.50), positive family history of glaucoma (OR 4.32; 95% CI 0.85–21.89), gender (crude OR 0.74; 95% CI 0.40–1.35), tobacco smoking (OR 0.21; 95% CI 0.02–2.21), use of optical correction (OR 0.51; 95% CI 0.16–1.61), or previous eye surgery (crude OR 1.05; 95% CI 0.58–1.96). Table 3 shows a complete list of compliance-related factors as crude OR and after multiple logistic regression analysis.

Knowledge about glaucoma

Patients were asked to describe the term ‘glaucoma’ in simple words. Only 56 (28%) could give a correct answer, 43 (21.5%) gave an incorrect or insufficient description, and the remaining 50.5% gave no answer at all. Ninety (45.0%) patients knew the value of their highest measured IOP and 74 (37%) also knew their highest IOP before the start of medical therapy. On multivariate analysis, level of education was positively associated with knowledge about glaucoma (OR

Table 3 Patient-reported compliance and its examined predictors

Independent variables	Crude OR			Adjusted OR			Last retained variables		
	Point estimate	95% CI	<i>P</i> value	Point estimate	95% CI	<i>P</i> value	Point estimate	95% CI	<i>P</i> value
Age above 60 years	1.04	0.54–2.00	0.91						
Gender: female	0.74	0.40–1.35	0.31						
Years of education	1.41	0.60–3.32	0.42						
Work: active	2.60	0.96–7.07	0.04	1.35	0.34–5.24	0.66			
No. of glaucoma medications	0.99	0.56–1.76	0.98	0.91	0.33–2.50	0.86			
Duration of glaucoma: ≥ 5 years	1.20	0.65–2.22	0.56						
Family history of glaucoma: positive	1.57	0.77–3.22	0.20	4.32	0.85–21.89	0.07			
Knowledge of glaucoma	4.54	1.45–14.16	0.002	3.03	0.59–15.32	0.17	4.77	1.36–16.70	0.01
No desire for information	0.66	0.36–1.20	0.17	0.97	0.33–2.85	0.96			
Living as a couple	0.79	0.43–1.44	0.44						
Help with drop administration	2.41	1.33–4.38	0.004	4.28	1.43–12.84	0.009	2.94	1.25–6.94	0.01
Use of optical correction	0.61	0.33–1.12	0.12	0.51	0.16–1.61	0.25			
Previous eye surgery	1.04	0.58–1.96	0.84						
Vascular dysregulation	0.99	0.48–2.05	0.98						
Migraine	1.16	0.52–2.60	0.72						
Diabetes	2.18	1.01–4.70	0.05	1.83	0.54–6.20	0.33			
Arthritis	1.66	0.88–3.14	0.12	0.79	0.24–2.62	0.70			
Smoking	0.37	0.09–1.47	0.12	0.21	0.02–2.21	0.19			
Centre: Geneva	0.52	0.28–0.96	0.03	0.33	0.11–0.98	0.04	0.35	0.15–0.80	0.01

CI confidence interval

2.00; 95% CI 0.98–4.09, $P < 0.05$), while the lack of interest for additional glaucoma information was negatively associated with knowledge (OR 0.26; 95% CI 0.11–0.59, $P < 0.01$) (Table 4). Only 43.5% of participants reported their income level and therefore this variable was excluded from the model. All other factors did not show any significant association with better knowledge. Seventeen patients (8.5%) were not sure whether they suffered from glaucoma and two patients (1%) thought that they did not.

Discussion

This is the first study investigating the rate of compliance and glaucoma-related knowledge in Swiss patients. With 81% reporting to omit no more than two glaucoma doses per week, self-reported compliance in

this Swiss cohort was substantially higher than that reported in other studies [6–11]. Using the same definition, Konstas et al. [12] distributed questionnaires to 100 Greek patients and showed 29% non-compliance, while 56% claimed to never miss a single dose. This rate is almost identical to our cohort (56.5%). Similarly, a Canadian multicentre study reported an overall proportion of non-compliance of 27.9% [11]. Rigal et al. [13], using the questionnaire developed for the present study, reported a 90% compliance rate in 100 Austrian patients of a specialised glaucoma practice. That study, however, was carried out in a smaller setting which can explain the exceptionally high compliance rate. Sleath et al. [8] reported that the rate of non-compliance (defined as less than 100% adherence in the previous week) was 14% in four different private practices. The clinical relevance of such a definition, however, can be

Table 4 Knowledge and its examined predictors

Independent variables	Crude OR			Adjusted OR			Last retained variables		
	Point estimate	95% CI	<i>P</i> value	Point estimate	95% CI	<i>P</i> value	Point estimate	95% CI	<i>P</i> value
Age above 60 years	0.87	0.69–1.08	0.17	1.87	0.60–5.79	0.27			
Gender: female	0.95	0.80–1.14	0.59	1.10	0.51–2.38	0.79			
Years of education	1.29	1.00–1.65	0.02	1.45	0.63–3.35	0.37	2.00	0.98–4.09	0.05
Work: active	1.59	1.19–2.11	<0.01	3.85	1.36–10.90	0.01			
Duration of glaucoma: ≥ 5 years	1.24	1.01–1.52	0.02	1.90	0.88–4.10	0.10			
Family history of glaucoma: positive	1.17	0.94–1.44	0.12	1.13	0.51–2.52	0.75			
No desire for information	0.69	0.58–0.82	<0.01	0.25	0.10–0.64	<0.01	0.26	0.11–0.59	<0.01
Living as a couple	1.05	0.88–1.25	0.62						
Use of optical correction	0.94	0.77–1.14	0.54						
Previous eye surgery	1.03	0.86–1.24	0.72						
Vascular dysregulation	0.85	0.68–1.06	0.12						
Migraine	1.07	0.85–1.34	0.60						
Diabetes	1.40	1.21–1.62	0.01	5.52	0.67–4.56	0.11			
Smoking	0.88	0.66–1.18	0.35						
Centre: Geneva	1.03	0.86–1.22	0.75						

CI confidence interval

contested as it is generally assumed that patient compliance may increase shortly before the scheduled medical appointment [14]. Higher rates of non-compliance have been reported in a number of publications. Spooner et al. [15] while addressing discontinuation found non-compliance in 38% of glaucoma patients. Khandekar et al. [7] used a different approach based on questions related to compliance and calculated an overall score in an Omani population. They showed ‘excellent’ overall compliance in 24.8% but some type of non-compliance was noted in 75.2% of the respondents. The wide variety in compliance rates reported in the literature has several explanations, the main ones being varying definitions of compliance and different appraisal methods.

There is no consensual standard for what constitutes clinically adequate compliance. Cut-off levels for non-compliance have varied according to studies from missing more than one dose per month to not having taken any prescription over a period of 12 months. We applied the definition most used in recent publications, which is up to two missed doses per week. This limit is in itself imperfect since two missed doses per week might not have the same clinical

implication depending on overall number of drops and glaucoma severity. When we used a stricter definition of compliance (less than two missed doses per week), 74.5% were still compliant with their medication. One reason for the high compliance in our sample could be the fact that financial considerations of medical therapy do not play a major role since all our patients were insured and got 90% of the treatment costs reimbursed.

It has been reported that compliance would be improved by a simpler drug regimen [16]. To our surprise, no such correlation could be found in the present cohort. This finding is in accordance with Okeke et al. [17, 18] who showed that adherence with once-daily prostaglandin was not substantially higher than previously reported compliance rates with beta-blockers twice-daily or pilocarpine 4 times daily. In another study, 58 Hungarian patients treated with a once-daily prostaglandin failed to show such an association [19]. In contrast, Sleath et al. [8] found that patients taking more glaucoma medications were more likely to have poor compliance and more problems taking their eye drops. At the current state of knowledge, the evidence for improved

compliance—the main advantage of combination drugs—with fewer doses remains contested. Furthermore, we found that patients reporting side-effects had equal compliance rates to those not reporting them. This counterintuitive finding was also reported by Friedman et al. [20] in a recent study on 196 patients from two specialised glaucoma clinics monitored using the Travatan® Dosing Aid.

We found that 79.6% of patients always administered their own drops while 14.2% often or always relied on assistance. This rate is comparable to Sleath et al. [8] who reported a 13% dependency rate. These patients were likely to be older than 60 years, suffer from arthritis and using multiple glaucoma therapy. In multivariate regression analysis, getting help with administration emerged as the second most important predictor of good compliance.

With 28% correctly defining glaucoma, the level of knowledge about glaucoma in our cohort was low. This might have been influenced by asking the patient to actively define glaucoma rather than offering him/her the choice between multiple choice answers. A telephone survey of normal households in Switzerland showed similar findings with only 24.7% of interviewees being able to describe glaucoma as an eye disease [21]. We therefore believe that the true rate of knowledge in our cohort may be higher but that a significant number may not feel confident enough to expose their knowledge in the chosen study format. Low levels of knowledge should be a matter of concern. Most studies have suggested that patient education can enhance compliance in glaucoma patients based on observation [6, 13, 17, 22]. Particularly worrying in our study was the finding that positive family history (almost 30% of patients) did not improve the level of knowledge in this cohort (OR 1.13; 95% CI 0.51–2.52).

Limitations

The present study has several inherent limitations. First, our study was conducted in two university-based glaucoma clinics in two linguistically different Swiss cantons. Therefore, it could be affected by selection bias and not reflect glaucoma patients in the community. The second limitation is that self-reporting has inherent weaknesses, the main one being a tendency of a patient to give favourable answers to please the physician. Hollo et al. [23] measured the influence of psychological characteristics on compliance with

glaucoma medication. They found that social desirability was significantly increased in a cohort of glaucoma patients as compared with normal subjects. Not surprisingly, studies that use medication monitors or completed prescription data as a surrogate for patient compliance consistently show higher rates of non-compliance [6, 11, 20]. High rates of compliance, however, are not uniquely observed in questionnaire-based studies. A mean coverage of 97% was found in an electronic monitoring study [16]. Furthermore, de Klerk et al. [24] have shown that questionnaires can have a similarly good predictive value compared to the electronic medication monitoring. In our questionnaire we tried to normalise patients' behaviour by asking in a non-judgemental way that "Glaucoma is a chronic disease and it is often difficult to put ones' eye drops regularly. Does it happen to you to omit a dose?" Later in the questionnaire, we included a control question ("Do you always take your eye drops?"). We found almost perfect agreement (89%) between the answers to both questions. We further tried to reduce this bias by guaranteeing anonymity and having non-medical personnel act as intermediaries. Another limitation was our method for assessing the level of knowledge, which was based on subjective evaluation by the investigators. Two investigators had to agree whether the provided definition of glaucoma was acceptable. This might have introduced some inconsistencies; however, the rationale behind this approach was to provide flexibility instead of a creating arbitrary definition criterion in the absence of a uniform case definition for glaucoma. A strength of our study is that we asked about other disease states that could impact a patient's ability to use his/her eye drops. We found a significant association between dyscompliance and self-reported arthritis (crude OR 1.62; 95% CI 1.03–2.69), which goes hand-in-hand with the strong association between getting help for drop administration and better compliance (OR 2.94; 95% CI 1.25–6.94). Another strength of the present paper is that contrary to most studies that did not track those patients who declined to participate in the survey, we had a high response rate with only four patients refusing participation.

Conclusions

The present study provides new information about the extent of glaucoma-related knowledge and risk factors

for non-compliance. We were able to show that despite high rates of compliance in Swiss patients most seem to lack an adequate knowledge about their disease. With knowledge of glaucoma being the strongest predictor of adherence in our cohort, ophthalmologists should put more emphasis on information.

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