

Compliance and viewpoint of glaucoma patients in Greece

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Abstract

Purpose To document the prevalence of non-compliance and to investigate patients' perceptions concerning glaucoma in a Greek cohort.

Methods We investigated 100 consecutive patients referred to our glaucoma clinic and already treated for chronic glaucoma. Compliance and patients' insight were ascertained by two independent observers by means of a predetermined questionnaire. All patients were subsequently assessed for their ability to instil their eyedrops accurately.

Results Fifty one per cent of our patients were not aware of the nature of glaucoma, but 80% were afraid it might lead to blindness.

Clinically significant non-compliance (more than two doses missed per week) was established in 44% of our patients. Men and those using eyedrops more than 4 times a day were more likely to default. Non-compliant patients exhibited higher mean intraocular pressure (22.9 vs 18.5 mmHg; $p > 0.001$) and worse visual field loss (10.8 vs 7.0 dB; $p = 0.008$) compared with compliant patients. Involuntary non-compliance was also common in our group, with only 53% instilling their eye drops accurately.

Conclusion Non-compliance is a significant limiting factor in glaucoma therapy in Greece.

Key words Compliance, Exfoliation glaucoma, Glaucoma therapy, POAG

Non-compliance can be regarded as deliberate or involuntary failure to comply with a doctor's directions in the administration of topical or systemic medications.¹ The disease of glaucoma predisposes to non-compliance due to its insidious asymptomatic nature, the need for lifelong medication and the lack of subjective improvement following treatment.² Defaulting is a major problem in glaucoma therapy because it may compound, or be the principal cause of, progression of visual loss.¹⁻⁴ It has been estimated⁴ that at least 10% of glaucomatous visual loss is due to poor compliance.

The magnitude of the problem of non-compliance may still be unfamiliar to many clinicians⁵⁻⁷ since the ophthalmologist cannot

predict accurately the behaviour of the glaucoma patient and is often unable to distinguish between the compliant and non-compliant patient.⁸ Furthermore, the problem may be compounded if the ophthalmologist mistakes non-compliance for ineffectiveness of a given glaucoma medication and prescribes more potent medications.⁷ Overall, there is a growing awareness that there is a high prevalence of undiagnosed non-compliance in elderly patients with glaucoma, with significant repercussions for their management.⁹⁻¹¹ To explain the reasons why patients do not take their antiglaucoma medications as prescribed it is vital to consider their viewpoint of glaucoma.¹²

Glaucoma is a major contributor to blindness in Greece.^{13,14} The present study was established firstly to document the Greek patients' viewpoint of glaucoma and secondly to determine the extent and significance of non-compliance in a cohort of glaucoma patients.

Materials and methods

This prospective study was set up to provide data on the compliance and viewpoint of Greek glaucoma patients receiving topical treatment with eyedrops. The study recruited 100 consecutive patients with chronic open angle glaucoma referred to our glaucoma clinic and already receiving antiglaucoma medications. Our university hospital provides secondary and tertiary care for a population of approximately 1.5 million people. Between January 1996 and July 1997 100 consecutive patients with either primary open angle glaucoma ($n = 52$) or exfoliation glaucoma ($n = 48$) were enrolled into this study, which was conducted in the University Department of Ophthalmology, AHEPA Hospital, Thessaloniki, Greece. Exfoliation glaucoma and primary open angle glaucoma patients were chosen because they comprise the vast majority of glaucoma patients in Greece.¹³ Patients included in the present study were previously diagnosed and treated for glaucoma by state insurance or private ophthalmologists. However, the patients recruited to this study were not selected (i.e. were not 'problem patients') since the majority of glaucoma patients in our area are insured in

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the state insurance scheme (IKA) and are routinely co-managed with their ophthalmologist, who refers them for confirmation of the diagnosis and visual fields. Furthermore, many patients book an appointment in our glaucoma clinic to obtain a hospital prescription which allows them to obtain their antiglaucoma medications almost free of charge.

Excluded from this study were patients with other types of glaucoma such as congenital, closed angle, or other secondary glaucomas (pigmentary, etc.). Patients with other ophthalmic conditions, or those who underwent surgery (factors that might influence the management of glaucoma), were also excluded. All patients recruited demonstrated typical glaucomatous visual field loss and glaucomatous optic nerve head cupping with open, normal-appearing angles.

Patients were first interviewed by two observers (S.G. and C.S.) who at the time of the study were medical students. An open questionnaire strategy was used and all patients were informed that the interview was confidential. The questions to assess the patients' viewpoint of glaucoma included the following: How did you find out that you had glaucoma? Did your ophthalmologist provide adequate information concerning the disease? What do you know about glaucoma? What do you fear most about glaucoma? Can you name your eyedrops and how often in a day you have to take them? Patients were also asked whether they had any problems with their medications and if so whether these had influenced their administration. Compliance with antiglaucoma therapy was investigated in all patients during this interview by asking how often they miss a dose of their medication and the reason, if any, for missing doses. Emphasis was also placed on whether they had encountered side effects in the past and, if so, whether this influenced their use of eyedrops.

Following the interview all patients underwent a comprehensive evaluation of their glaucoma by two glaucoma specialists (A.G.P.K. and G.M.) who were masked to the questionnaire results. Glaucoma data from all patients were stored in a standard protocol. Information documented on all patients included: sex, age, systemic disorders, family history of glaucoma and glaucoma data from the time of diagnosis to the present. All concomitant systemic disorders (e.g. arthritis) that might adversely influence the use of drops were recorded. Patients were divided into three categories depending on the prescribed frequency of instillation of their eyedrops (up to twice a day, up to four times a day, and more than four times a day). Ocular evaluation included Snellen visual acuity, Goldmann appplanation tonometry, examination of the ocular adnexa, slit-lamp biomicroscopy, gonioscopy and stereoscopic evaluation of the fundus with the Volk 90 D lens. Glaucomatous visual field loss was determined by automated static threshold perimetry (Octopus 500 EZ; peridata 6.2c). To identify unintentional non-compliance (termed dyscompliance) all patients were tested for their manual dexterity in compressing the drug bottles and their ability to instil the drops accurately. Data from this

assessment were inserted in the patient protocols and were used to determine the rate of dyscompliance. Patients were divided into three categories: 'successful', if they were capable of targeting the drop accurately; 'moderately successful', if they had to try more than once and eventually managed to instil sufficient quantity of their medication, or if they relied on someone else to successfully instil their drops; and 'unsuccessful' (clinically significant problem), if they missed the eye more than 50% of the time due to poor manual dexterity and targeting.

Following this assessment, all patients were given detailed instruction on how to comply with their medication regimes. In many cases the same treatment regime obtained a significant reduction in intraocular pressure. Patients who could not, or were not able to, comply were offered another management option (laser treatment or surgery).

Statistical analyses were performed with the Excel 5.0 software package. Student's *t*-test, the chi-square analysis and Fisher's exact test were used where appropriate. The significance level was set at 5%.

Results

At the time of the interview the average age of the patients was 65.4 years (range 43–82 years). There were 47 men and 53 women. In our cohort only 9 patients (9%) had been diagnosed as a result of glaucoma screening (due to a positive family history and other risk factors). Some patients were diagnosed by a random eye check (39%) and others because of perceived visual disturbances (35%), or on account of ill-defined complaints (17%). In 42 patients the prescribed daily frequency of glaucoma medications was up to two times a day (beta-blockers or dorzolamide), in 20 patients up to four times a day (beta-blockers combined with dipivefrine or dorzolamide) and in 38 patients more than four times a day (beta-blockers with pilocarpine and other combinations).

To assess the viewpoint of our patients regarding the nature of glaucoma we defined as the 'correct' answer 'a disorder with increased pressure in the eye commensurate with optic nerve damage'. Although a definition of glaucoma that includes raised intraocular pressure may not be appropriate nowadays amongst glaucoma specialists, this simplification was felt necessary for our patients. This question elicited, in descending order, that 51% of our patients did not know what glaucoma is; that 27% knew only that glaucoma is a disease that leads to blindness; and finally, that only 22% had a relatively accurate idea about the nature of glaucoma (20 knew it was pressure elevation in the eye, and 2 knew it included nerve damage due to pressure). Sixty-five per cent of our patients claimed that at the time of diagnosis their ophthalmologist did not provide adequate information concerning their disease. The majority of our patients stated that what they fear most about having glaucoma is blindness (80%); 18 patients feared nothing and 2 feared they might need surgery.

During the interview 64 patients could not accurately identify the name of their medications and 14 could not remember the exact dosing regime. With regard to problems perceived by patients with the daily use of medications, these (in descending order) were: irritation/itching (56%), redness (5%), blurring of vision (5%). Thirty-four patients (34%) did not report any problem with their medications.

The assessment of drug compliance revealed that unsatisfactory compliance with medications was common: of the 100 patients interviewed only 56 stated categorically that they never miss a dose. Fifteen patients reported that they only missed a dose 1–3 times a month. A clinically significant problem with non-compliance (deemed as more than two doses missed per week) was identified in 29 patients who stated that they missed more than 2 doses every week (15%), or missed more than half their doses (11%). Finally 3 patients (3%) were not using their medications at all. Reasons quoted for defaulting were (in descending order) lack of visual symptoms without treatment and/or blurring of vision with medication (34%), forgetfulness (28%), medication unavailable (15%), inconvenient frequency (16%) and absence of someone to instil the drops (5%).

Of equal importance was the assessment of unintentional non-compliance (termed dyscompliance). Only 53 of the 100 patients tested were judged very capable of instilling their drops accurately. Thirty-two patients (32%) were moderately successful either by trying more than once and eventually instilling sufficient a quantity of their medication, or by relying on someone else to instil their eyedrops. Fifteen patients, however, had a clinically significant problem, missing the eye more than 50% of the time due to poor manual dexterity and targeting. Thirteen of these patients were responsible for administering their own eyedrops and 2 had a relative to assist them. Of these 15 unintentional non-compliers there were 4 elderly individuals (4%) for whom dyscompliance was due to physical inability to use their antiglaucoma bottles properly due to systemic conditions (arthritis, tremor). None of the other patients had a significant problem with systemic diseases or, if they did, their drops were instilled successfully by a relative. Therefore in the present study the rate of clinically significant non-compliance was 44% (29% voluntary and 15% involuntary non-compliance).

These 44 non-compliant patients showed higher mean intraocular pressure (22.9 ± 3.7 mmHg) compared with the compliant patients (18.6 ± 3.5 mmHg; $p > 0.001$). They also exhibited more disc cupping (0.69 ± 0.1 vs 0.62 ± 0.1 ; $p = 0.017$) and worse mean visual field loss (10.8 ± 5.8 vs 7.0 ± 5.4 dB; $p = 0.008$) compared with compliant patients. There was no difference in the mean visual acuity of the two groups (0.83 ± 0.2 vs 0.89 ± 0.1 ; $p = 0.195$).

When comparing the prescribed frequency of instillation with the reported compliance there was a significant difference between non-compliance in the glaucoma group using eyedrops up to two times a day (5 of 42 patients; 12%) compared with the glaucoma group

prescribed eyedrops more than four times a day (16 of 38 patients; 42%) ($p < 0.05$). Furthermore, in our glaucoma cohort non-compliance was found to be more prevalent in men (21 of 47; 45%) than women (8 of 53; 15%) ($p < 0.05$).

No relationship was found between non-compliance and type of glaucoma (exfoliation glaucoma or primary open angle glaucoma), age, frequency of side effects to medications (indeed side effects were reported most commonly amongst those who were compliant). We were unable to compare the effect of patients' knowledge about glaucoma with the frequency of non-compliance because the vast majority of our patients (78%) did not have an accurate viewpoint of the nature of glaucoma.

Discussion

This is the first study investigating the rate of non-compliance in a Greek glaucoma cohort. Our results support previous research^{6,10,11} which suggests that non-compliance is a major contributor to glaucoma blindness. Between 28% and 58% of glaucoma patients do not use their medications as prescribed.^{3,6,8,10,15} Even this may be a conservative estimate because the true extent of non-compliance remains unknown in many cohorts¹⁶ and our compliance data may be partially flawed. The latter point was illustrated by Novack *et al.*¹⁷ who found that the participation of glaucoma patients in a study investigating compliance may improve their compliance by up to 30%. Importantly, our study did not encompass the rate of a patient's participation in his or her health care (e.g. in keeping hospital appointments or seeking medical advice) and thus may underestimate non-compliance.

In our study the most common reason for non-compliance was the perceived lack of visual symptoms with glaucoma. Thus, in our cohort non-compliance was associated with lack of insight into the nature of glaucoma. First Riffenburgh¹⁸ has stated that glaucoma is the most important area where the patient's viewpoint can alter the results. Poor understanding of the disease and its treatment, as seen in our study cohort, may lead to a higher degree of non-compliance.¹⁹ Vincent²⁰ reported that compliant patients were more likely to know that glaucoma is associated with increased intraocular pressure. In another study,³ which like ours used the interview technique, non-compliant patients with glaucoma were inadequately aware of the association between glaucoma and blindness. In general medicine it has been shown that medication compliance can improve by up to 36% by intensive individual teaching of patients in the clinic and at home.²¹ In another randomised clinical trial employing a medication monitor, Norell²² found that education significantly improved compliance.

The results of our study demonstrate that in Greece there is a need for continuing patient education of glaucoma patients. It is well established in the literature that poor communication between patient and clinician leads to more defaulting.^{3,16,19} Parkin *et al.*¹⁹ found that

46 of the 66 non-compliant patients in their study did not have a clear understanding of their regimen. It is clear from the available literature^{1,6,7} that better doctor-patient communication may improve a patient's knowledge of glaucoma and facilitate better compliance.

Differing criteria for defining non-compliance make it difficult to compare the various studies. For instance Vincent²⁰ reported a rate of 58% for non-compliance by using the criterion of more than one missed dose of medication per month. Using that criterion most of our patients would have been classified as defaulters. We decided to arbitrarily define 'clinically significant non-compliance' as more than two doses missed per week, as we felt this figure would be more relevant to clinical practice. It is to be emphasised that this definition is not ideal since missing two doses would be of far greater significance to a patient who only uses a beta-blocker once a day than to a patient who uses eight drops a day.

There are limitations in studies such as ours which attempt to establish the rate of non-compliance using hospital interviews. Our cohort is a selected clinic-based population. There is often underreporting of missed doses by an interview⁵ and estimates of non-compliance based on reports by patients may be inaccurate.^{11,23} Electronic monitors may provide more accurate data, but as illustrated by Novack *et al.*¹⁷ patients participating in a study investigating compliance with monitors may show a better than 'real world' compliance by up to 30%. In a study that attempted to side-step direct information on compliance Rotchford and Murphy¹¹ calculated in 55 patients how much timolol was dispensed relative to their need based on their regimen. They found that 51% of their patients had insufficient drops dispensed to comply with treatment as prescribed, and calculated for non-compliant patients a mean period of 85 days per year without drops.

In the light of the results from the present study it is clear that a significant proportion of our patients unintentionally default from the prescribed treatment. Unintentional non-compliance, or dyscompliance, was an unexpected but clinically significant problem in our group which cannot be solved by the prescription of more medications and more frequent dosing. Increased vigilance is required to identify patients who cannot instil their drops properly. As in the study by Winfield *et al.*²⁴ our study has identified dyscompliance as a significant component of non-compliance. It is probably worthwhile for ophthalmologists to ask their patients to demonstrate how they instil their eyedrops and to emphasise proper application techniques. Further studies are necessary to assess the scale of dyscompliance amongst glaucoma patients since this component of non-compliance should be more amenable to therapeutic intervention (teaching, drops instilled by a relative).

Our study has found that non-compliant patients had higher mean treated intraocular pressure and worse visual field loss. Although these findings show a noteworthy association it is by no means possible to demonstrate a causal relationship from a study such as

ours. Further research is required to determine the impact of non-compliance in the rate of glaucomatous visual loss.

Non-compliance may be of greater importance in a high-pressure glaucoma such as exfoliation glaucoma (48% of our cohort) for which it is likely that the worse intraocular pressure characteristics account for the more rapid visual deterioration in comparison with primary open angle glaucoma.²⁵⁻³⁰ Furthermore, exfoliation glaucoma patients often require treatment with more antiglaucoma drops.^{13,25} It is therefore crucial to identify non-compliers with hypertensive glaucomas and to consider prompt surgical intervention.

The impressions of previous workers¹⁰ that non-compliance may be more common in patients receiving more medications is validated in the present study. We found a correlation between the rate of non-compliance and the frequency of administration of antiglaucoma medications. Currently, the availability of new, well-tolerated glaucoma medications (e.g. latanoprost, brimonidine, Cosopt) may offer a wider range of therapeutic choices and, most importantly, require less frequent administration. Keeping glaucoma regimens as simple as possible, using single-eyedrop regimens and longer-acting antiglaucoma eyedrops may diminish the rate of non-compliance.^{7,31} Further research is required to validate this. There is also much scope for further research in the success of patient education in reducing clinically significant non-compliance and thus glaucoma blindness. Such data are important to determine whether glaucoma patients' behaviour can be meaningfully influenced, since appropriate treatment strategies can be implemented either way (i.e. teaching or earlier surgery for non-compliers) to prevent visual loss.

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