

Compliance with Medical Management in Glaucoma

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Non-compliance with medical therapy has long been recognised as an important limiting factor in the medical management of many chronic diseases.^{1,2} Patients with glaucoma who have lower rates of compliance are presumed to be at greater risk of developing progressive visual loss³ and van Buskirk suggests that the problem of non-compliance is “a leading cause of glaucoma blindness”.⁴

Medical therapy is a cost-effective strategy that can reduce the need for surgery.⁵ However, poor compliance can adversely affect an individual’s response to therapy since erratic dosing intervals can diminish the effect of a drug or increase adverse effects.⁶ Rates of compliance with therapeutic regimens for chronic disease may be as low as 50% and non-compliance has been associated with an increase in hospital admissions, length of stay, and health care costs.⁷

Non-compliance may be minimised through an understanding of the reasons patients have for failing to adhere to therapy.⁸ Compliance may vary depending on the type of illness and treatment, or even on a daily basis for a single individual. Patients may misunderstand the instructions, become confused about medications, or simply make inadvertent errors when trying to follow the schedule. Complex treatment regimens are associated with non-compliance;⁵ since the risk of chronic disease often increases with

advancing age, compliance in older patients may be further complicated by additional therapies for concomitant illness.

Factors Affecting Compliance

In recent years, many studies, both in general medicine and ophthalmology, have been performed to assess the impact of non-compliance on disease progression. While non-compliance is recognised as being difficult to determine with any certainty, Weintraub estimates that 10% to 25% of patients take none of their prescribed medication, some of whom do not even fill their prescriptions.⁹ Approximately 25% to 35% of patients comply almost 100% with therapy, while a few people may even take more than the prescribed dose. The largest group are the partial compliers, who establish their own schedules.

Not surprisingly, the compliance rate is lower with suppressive or preventive

medication than with treatment for acute symptomatic illness.⁶ Compliance also seems to depend more on a given situation than on individual tendencies. The reasons most frequently given for non-compliance include feeling better, carelessness, insufficient money to fill the prescription, misunderstanding of directions, not feeling better, or side effects.

In addition, compliance studies have correlated non-compliance with psychiatric illness, complex therapeutic regimens, side effects, missed appointments, inappropriate health beliefs, increased waiting times in outpatient clinics, unfavourable impression of the doctor, and family instability.

Measurement of compliance is difficult and may not always be correct. For example, a patient history may not always be accurate, drug serum concentrations may suggest regular medication use when the drug is only taken shortly before the test, and pill counts show only the total pills taken but not the dosing interval.⁷ The Medication Event Monitoring System (MEMS; Apex Corp., Fremont, CA, USA) enables compliance studies to register accurately the pill-taking habits of individual patients in terms of the number of daily doses taken and how closely the prescribed schedule is followed.

Using MEMS containers, Cramer *et al.* were able to observe the compliance of 24 anti-epileptic drug users. 5599 of 7413 drug doses (76%) were taken as prescribed, with the compliance rate declining with



Non-compliance with Medication⁶

- Failure to take medication as prescribed — missed doses, inadequate doses, and premature discontinuation of therapy.
- Increased dosing with the aim of increasing the benefit of the medication.
- Improper timing of dosages — failure to comprehend the importance of spacing medications throughout the day, failure to integrate new medications into a complex treatment schedule, difficulty in correct timing of 6- or 8-hourly medications.
- Taking medication for incorrect reasons — confusion regarding the purpose of each drug when taking multiple medications.

Table 1. Overall compliance rate with anti-epileptic drug use by dosing regimen⁷

	Once daily (%)	Twice daily (%)	3 times daily (%)	4 times daily (%)
Compliance rate (range)	87 (73-99)	81 (44-100)	77 (52-90)	39 (3-68)

increasing dosing frequency (table 1).⁷ The average pill count was 92%, with a range of 59% to 108%, indicating that some patients took more doses on some days and fewer on others. Five patients had at least one seizure associated with missed doses. These researchers concluded that despite the "medically dangerous consequences", patients with epilepsy took only 76% of their medication as prescribed.

Compliance in Glaucoma

If left untreated, glaucoma may result in increasing damage to the optic nerve, causing a reduction in visual field and, eventually, blindness,⁵ yet a major barrier to the successful treatment of glaucoma is poor patient compliance with the treatment regimen.¹⁰ Since glaucoma produces few symptomatic signs, there is little desire for patients to continue treatment, particularly

when, prior to late complications such as visual field loss, the only symptoms may be the side effects of the medication.⁶ The aim of therapy for glaucoma is to preserve vision with minimal side effects and inconvenience.¹¹

A major determinant of compliance with glaucoma medication is a patient's awareness of having glaucoma and the potential for blindness — the more serious their visual loss, the more likely it is that patients will take medication as prescribed.⁶ In addition, patients who miss follow-up appointments are more likely to misuse their medication. Non-compliance is further hindered by the physical inability of patients to use eye drops adequately, with difficulty aiming the drop, expelling the drop, and blinking on insertion frequently being reported.¹² Technical difficulties are termed 'dyscompliance'.

Judgements about patient compliance,

and therefore alternative treatments, are often based on clinical assessments and measurements of intraocular pressure (IOP), pupillary diameter and reactivity to light, weight of eye drops used from a bottle, patients' reports, and the physician's subjective impression of the patient.³ However, IOP and pupillary diameter have a low correlation with compliance with glaucoma treatment and pupillary response to light has a modest correlation. Similarly, non-compliant patients are not identified reliably by daily treatment records, questionnaire, or measuring the weight of the eye drops used. In addition, there is only a modest correlation between the physician's predictions about patient's compliance and the results of monitoring. Since none of these measures accurately indicates patients' compliance, an eye drop monitor is required for identification of patients who default from therapy.

Using an unobtrusive eye drop monitor as an objective measure, Kass *et al.* found considerable over-reporting of compliance with glaucoma medication in an interview situation (table 2).¹³ Patients administered a mean of 76% of the prescribed dose, with 6% of patients taking less than one-quarter of their prescribed medication, and 15.2% taking less than half. However, when interviewed, the patients reported taking a mean of 97.1% of the prescribed dose (figure 1). This result suggests that patients are either unaware of their poor compliance or may fear a reprimand if they admit to taking medication incorrectly.

Granström identified 3 different deviations from the prescribed treatment in a study of 15 non-compliant patients using pilocarpine eyedrops 3 times daily:¹⁴

- inadequate spacing of doses during the day, with long intervals at night
- omitting the midday dose
- long interruptions in medication.

The number of missed doses reported by interview was inaccurately low when

Table 2. Summary of compliance by eye drop monitor and by patient report¹³

Percent of prescribed doses taken	Patient report		Eye drop monitor	
	Number	%	Number	%
0 - 24.9	0	0	11	6.0
25 - 49.9	0	0	17	9.2
50 - 74.9	2	1.1	35	19.0
75 - 100	182	98.9	121	65.8

Figure 1. Distribution of compliance with topical pilocarpine treatment as reported by the patients and recorded by the eyedrop monitor.

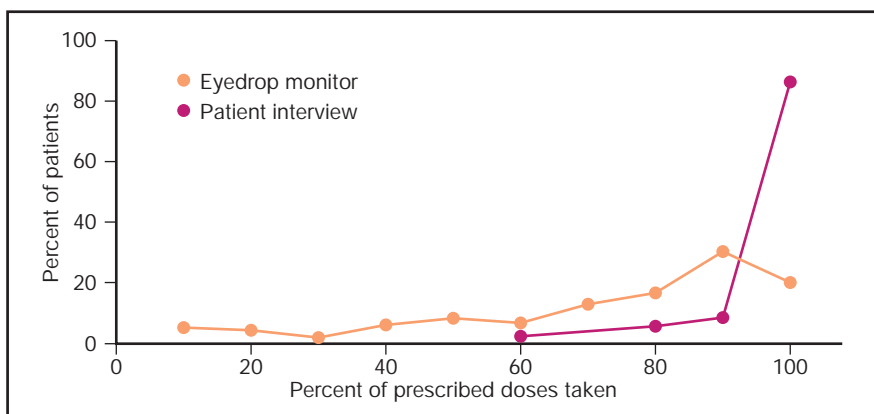


Table 3. Number of missed doses during 7 days according to interview and monitor data¹⁴

Patient number	Interview	Monitor
1	0	3
2	0	8
3	0	0
4	0	2
5	0	1
6	0	—*
7	—†	—*
8	0	8
9	0	8
10	0	3
11	0	3
12	0	8
13	4	15
14	0	6
15	0	0

* Lost to monitor records; † no interview obtained.

compared with the monitor reading (table 3), and 11 patients reported tailoring the doses to lifestyle events such as meal or sleep times. While the inaccuracy of the interview technique was highlighted, discussion with patients may be valuable in determining the most convenient times for medication. In this way, the ophthalmologist may be able to assist the patient to minimise lifestyle disruption, thereby facilitating compliance.

Rotchford and Murphy found that 24% of 86 patients admitted to omitting their glaucoma treatment either frequently or occasionally.¹⁵ Patients who always took their eye drops were significantly more likely to regard their drops as being 'vital' to their treatment as opposed to 'important'. The 13 patients registered as blind or partially sighted reported never missing a dose.

Physical inability to administer drops to the eye may have a role in visual loss that is additive to other aspects of non-compliance.¹⁶ Winfield *et al.* performed a study to elucidate the physical difficulties experienced by 200 patients during eye drop administration.¹² 57% of patients had some difficulty administering their drops with 21% always needing assistance. Fear of the dropper touching the eye resulted in patients holding the dropper too far away, making

Table 4. Problems encountered during self-administration of eyedrops¹²

Problem	Patients (%)
Directing the bottle	
miss frequently	36
miss occasionally	13
Shaky hand	8
Difficulty squeezing the bottle	20
Blinking	12
Poor visibility of dropper tip	13
Inadvertently inserting dropper tip into eye	9
Reading labels and identifying medication	14

the aim difficult and encouraging the blink reflex (table 4). Older patients, particularly those with arthritic conditions, had difficulty in physically administering eye drops. Interestingly, since patients were reluctant to discuss these difficulties with their doctors, the medical staff involved in their care were largely unaware of the problems associated with eye drop administration. Dyscompliance is even less recognised than non-compliance.

Complex regimens are suspected to be a cause of non-compliance in terms of both number of medications and number of daily doses. Since glaucoma patients are often prescribed multiple medications and may have concomitant therapy for other chronic diseases, they may be at high risk for non-compliance.

Strategies for Improving Compliance

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A major factor in the medical management of glaucoma is the extent to which patients comply with the treatment regimen.^{10,17} Progression of the disease often leads to more potent drugs being given, which may be inappropriate if the progression is due to non-compliance rather than to treatment failure.^{14,17} In addition, necessary glaucoma surgery may be postponed if non-compliant patients have a low IOP at clinic visits as a result of taking the medication only during the preceding hours.¹⁴

Strategies to improve compliance include educating patients about the disease and its treatment combined with tailoring the therapeutic regimen to the patient's lifestyle.¹⁷ Patient education measures may take the form of videos, booklets, drug schedule diaries, and nurse education, with review and reinforcement at clinic visits. It is also important to work with patients to ensure that eye drops are correctly administered.

The usefulness of a 6-minute videotape in educating 98 patients with glaucoma about their disease was evaluated by Rosenthal *et al.*¹⁸ A questionnaire, used to determine how much patients remembered from the video, showed that patients knowledge was significantly improved immediately after viewing ($p < 0.001$). After 6 months, patients with glaucoma retained more knowledge of the disease than did the controls who did not have glaucoma, although there was a significant drop in knowledge from immediately after viewing ($p < 0.001$). Patients responded positively to seeing the film and were grateful for the opportunity to view the tape. Provision of an accompanying brochure for the patient to take home may help to solve the problem of recall after time.

Streamlining a regimen to the patient's lifestyle is important to improve compliance, and once- or twice-daily medication interrupts patients' lifestyles far less than more frequent dosing.¹⁷ Tailoring a medication to lifestyle requires investigation of patients' routines such as sleeping and eating patterns and work routines, and selecting a medication that will work well with these regular habits.¹⁷

Studies comparing fixed combination dorzolamide and timolol with timolol plus pilocarpine given concomitantly found that patients preferred the combination by a ratio of 4 to 1 ($p < 0.001$).¹¹ One of the main reasons given was that the combination interfered significantly less with daily life in



terms of activity limitations and side effects. Compliance was also significantly better with the combination.

Similarly, Schenker *et al.* found that significantly more patients (71%) preferred timolol gel once daily to timolol solution twice daily ($p < 0.001$), with 92% giving the once-daily dosing regimen as the reason for their preference.¹⁹ Patients also reported significantly fewer missed doses while using timolol gel ($p = 0.005$), suggesting that, when appropriate, patients appreciate having their therapy simplified.

Latanoprost has a once-daily dosing schedule and has been shown to decrease IOP as much or greater than other glaucoma medications.²⁰ This agent, therefore, may be substituted for one or more glaucoma drugs to simplify the dosing schedule. Smith *et al.* found that 43 of 61 patients (70.4%) effectively simplified their daily medication without an adverse effect on IOP by switching to latanoprost (table 5).²¹ These researchers concluded that latanoprost may be used to simplify the regimen for glaucoma patients by reducing the number of doses per day while maintaining an appropriate IOP level.

Other measures to improve compliance include more complete labelling of medicines, increased supervision and counselling, medication calendars, and reduction of

medication-induced side effects.⁶ The use of different sizes or shapes of medications and their containers will help patients to discriminate between different treatments⁸ and obtaining help from a family member may improve compliance.¹⁷

In Conclusion

There are a number of reasons for poor compliance with glaucoma medications, including lack of understanding of the disease, no obvious symptoms, complicated or too frequent drug schedules, side effects, physical difficulty in administering eye drops, and cost. Simplification of the treatment regimen and interactive health education appear to be the most important factors for improving compliance.⁵ In addition, modifying the treatment regimen to fit with a patient's lifestyle may promote compliance by diminishing adverse effects while achieving maximal benefit.⁹

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Table 5. Number of patients and daily glaucoma medication doses before and after switching to latanoprost (n = 43)²¹

Number of daily medication doses	Number of patients	
	Baseline visit	After switching to latanoprost *
10	1	0
9	3	0
8	5	0
7	1	0
6	4	2
5	9	0
4	5	2
3	4	5
2	11	4
1	0	30

* $p < 0.001$ vs baseline

