Adherence with Topical Glaucoma Medication Monitored Electronically

The Travatan Dosing Aid Study

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Purpose: To assess patient adherence and behaviors with topical once-daily therapy for glaucoma.

Design: Prospective, observational cohort study.

Participants: One hundred ninety-six patients with glaucoma who were being treated with a prostaglandin analog in 1 or both eyes at the Scheie or Wilmer Eye Institutes between August 2006 and June 2007.

Methods: Detailed medical history was obtained from each patient. All subjects used the Travatan Dosing Aid (DA; Alcon, Fort Worth, TX) to administer travoprost as prescribed. Devices were collected at 3 months and the data of drop usage was downloaded using software provided with the dosing aid. Data were analyzed for the 8-week period starting 2 weeks after the enrollment visit and ending 2 weeks before the 3-month visit.

Main Outcome Measures: Assessment of adherence and patterns of drop usage as indicated by the DA.

Results: A total of 282 subjects consented to be in the study and 86 (30%) withdrew before study completion or had device errors, leaving 196 subjects (70%) with evaluable data at 3 months. The overall mean (±standard deviation) adherence rate was 0.71 (±0.24), ranging from 0.02 to 0.97. One hundred nine of these patients (55.6%) took greater than 75% of the expected doses. Those with adherence of less than 50% of expected doses showed substantially increased dose taking immediately after the office visit and just before the return visit at 3 months ($P = 0.03$). The mean adherence rate estimates of the physician and patient self-report were 0.77 and 0.95, respectively. The agreement between the physician assessment and DA-recorded adherence rate showed poor correlation for individual cases (intraclass correlation coefficient, 0.09; 95% confidence interval, 0.00–0.19).

Conclusions: Nearly 45% of patients using an electronic monitoring device who knew they were being monitored and were provided free medication used their drops less than 75% of the time. Patients reported far higher medication use than their actual behavior. The ability of the physician to identify which persons are poorly adherent from their self-report or from other subjective clues is poor.

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Controlled clinical trials have demonstrated that reduction of intraocular pressure (IOP) retards the occurrence and progression of glaucoma.[1–4] Although laser trabeculoplasty and incisional surgery each have been shown to have equal merit as initial approaches for lowering IOP,[5,6] the vast majority of glaucoma patients initially receive topical ocular hypotensives.[7] Recent reports indicate that more than 90% of patients with glaucoma fail to refill their ocular medications continuously during the first year of therapy and that less than 60% continue to refill eye drop prescriptions at 1 year.[8,9] Low adherence with topical ocular hypotensive agents is similar to adherence with use of oral medications for hypertension, hypercholesterolemia, and other chronic, asymptomatic conditions.[10,11]

With the exception of studies conducted nearly 25 years ago,[12–14] studies of patient adherence with glaucoma medications generally have relied on patient self-report or pharmacy refill data. Self-report is now known to overestimate actual use greatly.[15] Although claims database measures can be useful,[16] they also have the potential to differ somewhat compared with actual chart data.[8] A more accurate method of determining how patients use medications is electronic monitoring, an approach that has been widely used in other medical specialties.[17–19] Electronic monitoring of drop-taking has been performed rarely, in part because of the technological difficulties involved. A recent report[20] assessed adherence and patterns of use with a device that housed eyedrop bottles and recorded electronically the opening and closing of the container. There may be large differences between adherence measured by short-term electronic monitoring and adherence estimated from pharmacy refill data.[21]

The Travatan Dosing Aid (DA; Alcon, Fort Worth, TX) can provide data on use of travoprost only, because no other bottles for glaucoma medications fit within it. A bottle of travoprost is placed in the device and a lever is used to

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squeeze out a drop. A built-in memory chip records the time and date when the lever is depressed. These data are downloaded to a computer at a later date.

It has been suggested that medication adherence may be improved substantially by choosing a drug that needs to be taken less often.[12] Very few published studies have evaluated once-daily glaucoma medication with electronic monitoring. This article reports the dosing patterns of patients using the DA for 3 months.

Patients and Methods

Study Organization

The study protocol had 2 phases: phase 1 was a prospective, observational cohort study of patient adherence to travoprost therapy when using the DA to administer drops (described in this article); phase 2 was a randomized, controlled trial to improve adherence for those found to have low adherence in phase 1 (subject of a subsequent report). Patients were recruited from the Glaucoma Services of the Wilmer Eye Institute and the Scheie Eye Institute. Institutional review boards at both centers approved the study protocol, and written informed consent was obtained from all study subjects.

Eligibility Criteria

Patients were required to have one of the following diagnoses: open-angle glaucoma, angle-closure glaucoma, glaucoma suspect, or ocular hypertension. Some participants had undergone past laser or surgical glaucoma therapy, but not within the 3 months before study enrollment. Subjects requiring surgery during the study were censored at the time of surgery. Patients were excluded if they were unable to understand the study, if they did not instill their own drops, or if they were incapable of using the DA device after a brief demonstration.

All eligible patients had to be 18 years of age or older and currently taking a topical prostaglandin analog to lower IOP or being prescribed their first use of a prostaglandin analog. Patients also had to be willing to return for 3- and 6-month follow-up visits.

Patient Recruitment and Follow-up

Eligible subjects examined by a study physician (CO, HQ, HJ, DF) during a routine glaucoma care visit were offered participation. After watching a descriptive video presentation, consenting patients were prescribed travoprost and were instructed in using the DA by a trained study coordinator (RP). Consenting patients who were receiving latanoprost or bimatoprost were switched to travoprost during the study. Sufficient travoprost bottles for the study period were provided free of charge to participants.

Baseline demographic and medical information, including age; gender; self-reported ethnicity; presence of comorbid diseases; ocular medications and dosages; systemic medications and dosages; family history of glaucoma; baseline untreated IOP of each eye (if available); length of past glaucoma treatment and types of past ocular medication, including allergies and severe side effects; and current target IOP of each eye, were obtained from the patient's chart. Use of prostaglandin analog medication either unilaterally or bilaterally was recorded. In addition, all IOP measures of each eye and medications for the preceding 2 years were recorded along with visit dates for later comparison with IOP obtained during the study. Data for each eye from the most recent visual fields and most recent evaluation of the optic disc by clinical assessment, laser imaging, or photography also were recorded.

Consenting patients responded to a brief self-administered questionnaire on attitudes about administering eyedrops, self-report of adherence with topical ocular hypotensives, self-report of health,[22] and a brief survey for depression (the Center for Epidemiologic Studies Short Depression scale).[23] They also were asked about the impact of glaucoma on their vision as well as their attitudes about and understanding of glaucoma. The physician was asked to estimate, on a scale from 0 to 100, 2 features of each patient: their knowledge of glaucoma and their adherence with eyedrops. The knowledge of glaucoma was estimated based on whether the doctor believed that the patient understood the reason for taking their drops, how the drops worked to lower IOP, and how often they should use their drops. The adherence with drops was estimated based on the assessment of the physician regarding how well the patient actually took their medications.

The DA device records the time and date when the lever that releases a drop of travoprost is depressed. All patients were instructed on the method of placing a bottle of travoprost in the DA and in how to depress the lever arm to deliver a drop. Patients watched an instructional video and practiced using the device under supervision before starting the study. Subjects were told that the device records when the lever is depressed. All patients also were told that the DA was being assessed for its ability to aid the patient in delivering the eyedrops. Patients were enrolled only on days when the study coordinator was available in the clinic.

Patients were instructed to use the device to deliver their travoprost each night until the 3-month follow-up visit. A telephone call was made at 1 week to ask if the patient was having difficulty using the device. If there were problems, the patient was asked to return to the clinic to undergo repeat instruction in using the DA, and the 3-month follow-up period was restarted from that point. If the patient did not feel comfortable using the device after the repeat instruction, the patient was removed from the study.

Patients brought their DA device to the 3-month visit, the information was downloaded, the battery was changed, and a questionnaire was administered to estimate self-reported adherence and satisfaction with the device. At the 3-month visit, visual acuity and applanation IOP were measured. The downloaded data from the DA were used to identify patients taking less than 75% of the daily doses. Because there is no universal definition in the literature that defines adherence, this cutoff at 75% was chosen arbitrarily a priori to embody what 3 glaucoma specialists (CO, HQ, DF) believed was an adequate level of adherence. Because it is postulated that patient adherence is artificially higher just after and just before doctor visits,[13,24] the adherence rate was calculated from 2 weeks after the baseline visit until 2 weeks before the follow-up visit. A dose was considered taken if the lever of the DA was depressed and recorded within 4 hours of the routine dosing hour for the appropriate number of eyes. For example, if 8 PM was the patient median dosing hour and the prescribed medication was for unilateral use, then any 1 dose taken between 4 PM and 12 AM was considered to have been taken appropriately. Because the authors recognized from their previous study[22] that the device has the potential to make extra recordings when the lever is depressed erroneously, more than 1 dose taken per eye per day was not counted in the adherence rate calculation. When the lever was depressed outside the time window, it was assumed that a dose was not taken, and when the lever was depressed multiple times in the time window, only a single dose was assumed to have been delivered.

Masking

Technicians who obtained the IOP measurements were not masked to the patient's participation in the study, but were masked to the DA information retrieved. Data on treatment effects were not provided to the participating physicians or technicians during the course of the study.

Statistical Analysis

Baseline characteristics were compared between patients who completed 3 months of the study (completed visit) and those who did not (uncompleted visit). Comparisons for patient-level characteristics were made by the Fisher exact test for the comparison of proportions and by the Student *t* test for the comparison of means. Comparisons of ocular characteristics were made using generalized estimating equations to adjust for correlation between eyes when data from both eyes were included. Eyes with missing data were excluded from the analysis. When analyzing adherence rates over the 3 months between baseline and follow-up, a 1-way analysis of variance (ANOVA) was chosen as the statistical model because a categorical variable with 2 or more levels was being analyzed. An ANOVA performs a group comparison that determines whether a significant difference exists somewhere between the groups being studied. Scatterplots and intraclass correlations were used to assess the agreement of adherence estimates among the DA calculation, physician interview, and patient self-report.

Results

Study recruitment began in August 2006 and ended in June 2007. A total of 282 patients were identified between the 2 sites; 86 (30%) withdrew before 3 months, leaving 196 subjects (70%) with complete data on drop-taking behavior at 3 months. The reasons why 30% of patients did not complete the study included: side effects (n = 33/86 [38%]), use of travoprost without the DA device (n = 15/86 [17%]), lost to follow-up (n = 12/86 [14%]), patient report that DA device interferes with using drops (n = 6/86 [7%]), DA device malfunctioned (n = 5/86 [6%]), patients failed to follow instructions (n = 3/86 [3%]), and other reasons (n = 12/86 [14%]).

Baseline Characteristics

Study patients completing 3 months of treatment were 64.7±12.2 years of age (mean±standard deviation), ranging from 24 to 93 years, which did not differ significantly from those who did not complete the study before 3 months ($P = 0.33$; Table 1). Men comprised 58% of those completing the initial 3-month study (114/196). Most of the completed patients (91%) had at least a high school degree or higher. Approximately 85% reported good or excellent general health. Nearly half (43%) of the completed patients had a history of high blood pressure, and 15% had arthritis. Although only 5% (10/196) of the patients completing 3 months of follow-up reported a history of depression, their answers on a depression instrument (Center for Epidemiologic Studies Short Depression scale) indicated that 21% (42/196) were in the highest quartile for depression scores.

Those who completed the study did not differ from those who did not based on ocular characteristics (Table 2). Nearly 80% of eyes in completed study participants (302/392) had open-angle glaucoma. Most patients had bilateral disease and 75% had been receiving glaucoma medications for at least 1 year before entering the study. Most had mild to moderate disease severity as measured by visual field loss and optic nerve findings. Fifty percent (97/196) of completed patients were taking only travoprost, 34% (66/196) were taking a second agent, and 17% (33/196) were taking 3 agents or more. The adherence rates (standard errors) for each group were 0.68 (0.02), 0.73 (0.03), and 0.74 (0.04), respectively, which did not differ significantly from each other ($P = 0.34$).

Adherence to Therapy

The mean±standard deviation adherence rate was 0.71±0.24, and the median (Q1, Q3) adherence rate was 0.81 (0.58, 0.90). The range of adherence rate was from 0.02 to 0.97. One hundred nine (55.6%) subjects took 75% or more of their drops, and the overall mean adherence rate in this group was 0.88. Forty-nine subjects (25.0%) took from more than 50% to less than 75% of their drops and had an overall mean adherence rate of 0.65. Thirty-eight subjects (19.4%) took 50% or less of their doses with a mean adherence rate of 0.30.

For those taking 75% or more of the doses as prescribed, adherence rates were significantly different over the 3 months between baseline and follow-up ($P<0.0001$, for the comparison among 12 weeks based on ANOVA with 12 levels; Fig 1). The rate of adherence was significantly lower immediately after and just before office visits than during the remainder of the 3 months (overall adherence rate decreased to 0.83 from 0.90; $P<0.0001$, from 1-way ANOVA with 2 levels). For those with adherence of 50% of doses or less, the rate of adherence was significantly higher immediately after and just before (Fig 1; first week [f1w] and last week [1w]) office visits than during the remainder (middle 10 weeks) of the 3 months (overall adherence rate increased to 0.43 from 0.35; $P = 0.03$; Fig 1). For those with adherence of more than 50% to 75%, the difference in the rate of adherence was not significantly different between office visits ($P = 0.57$, for the comparison of the first and last week with the middle 10 weeks).

Adherence Rate Compared with Self-report and Physician Estimate

The mean (median) adherence rate from physicians' estimate was 0.77 (0.80), similar to the mean adherence rate estimated from the DA device (Table 3). However, the agreement between the physician estimate and DA recordings as shown by a scatterplot is poor (Fig 2), with intraclass correlation of 0.09 (95% confidence interval, 0.00–0.19).

By contrast, patients greatly overreported their adherence, with mean (median) adherence of 0.95 (1.00). Because many patients reported near perfect adherence, the scatterplot of these 2 variables was highly skewed and showed poor agreement (Fig 3), with intraclass correlation of 0.14 (95% confidence interval, 0.08–0.21).

Discussion

It has been hypothesized and reported that medication adherence would be improved by a simpler drug regimen.[25–29] By contrast, the authors found that once-daily prostaglandin adherence was not substantially better than previously reported drop taking with β-blockers twice daily or pilocarpine 4 times daily.[13,14] After 3 months of electronic monitoring with the DA, the mean adherence rate for travoprost was 71% in the current cohort of patients. Kass

Table 1. Summary of General Baseline Characteristics of Completed and Uncompleted Patients at the 3-Month Visit

Characteristic	Completed Visit (n = 196), n (%)	Uncompleted Visit (n = 86), n (%)	*P* Value
Age (yrs)			0.39*
<50	22 (11.2)	10 (11.6)	
50–59	49 (25.0)	15 (17.4)	
60–69	53 (27.0)	22 (25.6)	
70–79	52 (26.5)	24 (27.9)	
≥80	20 (10.2)	15 (17.4)	
Mean (SD)	64.7 (12.2)	66.5 (15.3)	0.33†
Gender			0.004*
Male	114 (58.2)	34 (39.5)	
Female	82 (41.8)	52 (60.5)	
Ethnicity			0.005*
Black	90 (45.9)	42 (48.8)	
White	100 (51.0)	33 (38.4)	
Other	6 (3.06)	11 (12.8)	
Education			0.28*
Less than high school	18 (9.28)	14 (16.5)	
High school	49 (25.3)	24 (28.2)	
College	77 (39.7)	29 (34.1)	
Graduate school	50 (25.8)	18 (21.2)	
General health			0.04*
Excellent	51 (26.0)	12 (14.0)	
Good	116 (59.2)	54 (62.8)	
Fair or poor	29 (14.8)	20 (23.3)	
Medical history			
Heart disease	19 (9.69)	7 (8.14)	0.82*
Hypertension	85 (43.4)	41 (47.7)	0.52*
Diabetes mellitus	44 (22.5)	19 (22.1)	1.00*
Elevated cholesterol	38 (19.4)	18 (20.9)	0.75*
Depression	10 (5.10)	3 (3.49)	0.76*
Arthritis	29 (14.8)	12 (14.0)	1.00*
Asthma	14 (7.14)	6 (6.98)	1.00*
Parkinson's	1 (0.51)	0 (0.00)	1.00*
Other	90 (45.9)	43 (50.0)	0.60*
None	35 (17.9)	13 (15.1)	0.61*
Depression score			0.04*
<0.1	72 (36.7)	24 (27.9)	
(0.1, 0.3)	44 (22.5)	14 (16.3)	
(0.3, 0.7)	38 (19.4)	30 (34.9)	
(0.7, 2.5)	42 (21.4)	18 (20.9)	
Mean (SD)	0.45 (0.54)	0.53 (0.54)	0.28†
Glaucoma family history			0.52*
None	118 (60.2)	54 (62.8)	
1	61 (31.1)	22 (25.6)	
≥2	17 (8.67)	10 (11.6)	

SD = standard deviation.
*Fisher exact test for the comparison of proportions between completed and uncompleted visit.
†*t* test for the comparison of means between completed and uncompleted visit.

et al[13,14] used an electronic monitoring device to monitor use of 4 times daily pilocarpine and twice daily timolol, measuring a mean adherence of 76% with pilocarpine and 83% with timolol. It is remarkable how similar these rates are to those in the current study 2 decades later and with once-daily prostaglandin. By contrast, a recent report by Robin et al[20] estimated higher adherence using an electronic medication event monitoring system cap container (which holds the eyedrop bottles and records when the lid is opened and closed). After 60 days, the mean coverage for once-daily use was 97% for persons using 1 drug and 86% for those using 2 different eyedrop types. Possible explanations for the much higher rates in the medication event monitoring system cap study include: a different patient population, failure of the DA devices to record all doses taken, differences in the impact of using the monitoring devices on patient behaviors, and different criteria for determining adherence.

The adherence rate in the current patients by electronic monitoring is consistent with the value for medication possession ratio found in research on patient adherence using large claims databases.[8] However, the 2 measures estimate

Table 2. Summary of Baseline Ocular Characteristics of Completed and Uncompleted Eyes of Patients at the 3-Month Visit

Ocular Characteristics	Completed Visit (n = 392 eyes), n (%)	Uncompleted Visit (n = 172 eyes), n (%)	*P* Value
Glaucoma type			0.59*
Open-angle glaucoma	302 (77.0)	132 (76.7)	
Angle-closure glaucoma	7 (1.79)	8 (4.65)	
Secondary	1 (0.26)	1 (0.58)	
Ocular hypertension	25 (6.38)	7 (4.07)	
Glaucoma suspect	23 (5.87)	7 (4.07)	
Other	22 (5.61)	14 (8.14)	
No glaucoma/unknown	12 (3.06)	3 (1.74)	
Duration of glaucoma medication treatment			0.84*
≤1 yr	87 (22.2)	43 (25.0)	
>1 yr	295 (75.3)	124 (72.1)	
Unknown	10 (2.55)	5 (2.91)	
Mean (SD)†	8.13 (8.72)	7.40 (8.89)	0.51*
Cup-to-disc ratio			0.09*
0 to 0.7	200 (51.0)	73 (42.4)	
>0.7 to ≤0.9	143 (36.5)	58 (33.7)	
>0.9	41 (10.5)	32 (18.6)	
Unknown	8 (2.04)	9 (5.23)	
Mean (SD)†	0.78 (0.98)	0.78 (0.69)	0.97*
Visual field (db)			0.17*
0 to 5	207 (52.8)	81 (47.1)	
>5, ≤15	93 (23.7)	33 (19.2)	
>15	73 (18.6)	41 (23.8)	
Unknown	19 (4.85)	17 (9.88)	
Mean (SD)†	7.81 (8.90)	9.24 (9.90)	0.20*
PSD			
Mean (SD)	5.25 (3.82)	5.47 (3.97)	0.61*
IOP (mmHg)			0.34*
7–15	194 (49.5)	84 (48.8)	
>15–≤17	73 (18.6)	22 (12.8)	
>17–≤20	64 (16.3)	29 (16.9)	
>20–≤36	60 (15.3)	35 (20.4)	
Unknown	1 (0.26)	2 (1.16)	
Mean (SD)†	16.2 (5.33)	16.4 (6.23)	0.81*
Use of other glaucoma medications	(n = 196 patients)	(n = 86 patients)	0.84‡
Only travoprost	97 (49.5)	41 (47.7)	
Second agent	66 (33.7)	28 (32.6)	
Three agents or more	33 (16.8)	17 (19.8)	
Glaucoma medicine type§			
Unilateral	49 (25.0)		
Bilateral	147 (75.0)		

IOP = intraocular pressure; PSD = pattern standard deviation; SD = standard deviation.
*From the generalized estimating equations with correlations from paired eyes of a patient adjusted.
†Unknowns were excluded from the comparison of means.
‡Fisher exact test for the comparison of proportions.
§For the glaucoma medicine type, this information is only for the completed patients because the data were unavailable for the uncompleted patients.

different aspects of eyedrop taking. Medication possession ratio gauges whether the patient has a drug on hand, but cannot determine if it is being taken, other than by the fact that prescriptions are being refilled. The DA device, which has been shown to record accurately up to 97% of drop usage in novice users,[30] estimates the likelihood that a patient who clearly has the drug in hand (provided at no cost in this study) attempted to put a drop in an eye at a time close to the daily interval prescribed.

Low adherence rates also have been reported by Rotchford and Murphy,[31] who, using pharmacy records, found 51% of timolol-treated patients to be nonadherent defined as insufficient drops dispensed to comply with treatment as prescribed. Patel and Spaeth[32] reported rates of patient-reported nonadherence with glaucoma medications as high as 59%. A metaanalysis found that nonadherence ranges from 5% to 80% for glaucoma patients, although definitions for adherence were not standardized.[33] Persistence (duration of continuous treatment with the initially prescribed medication) and adherence (the prevalence of use of the initial medication at various time points) is reported to be higher for prostaglandins than with other drug classes

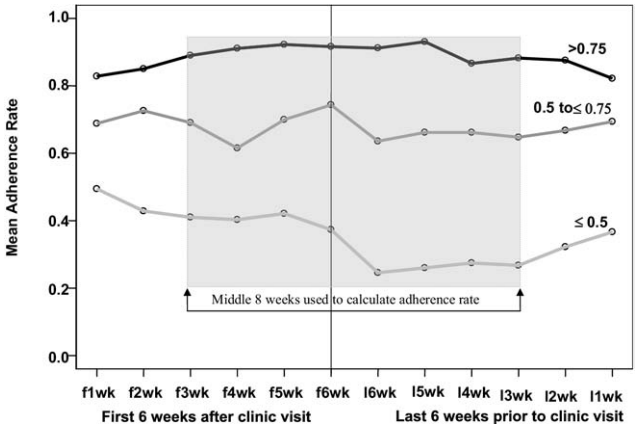

Figure 1. Graph showing weekly rates of adherence 6 weeks after and 6 weeks before the clinic visit (total, 12 weeks) for the completed patients at 3 months (n = 197). The completed patients were divided into 3 groups based on average adherence rate over the middle 8 weeks of monitoring, >0.75 (n = 109), >0.50 to 0.75 (n = 49), and ≤0.50 (n = 39). f = first; wk = week; 1 = last.

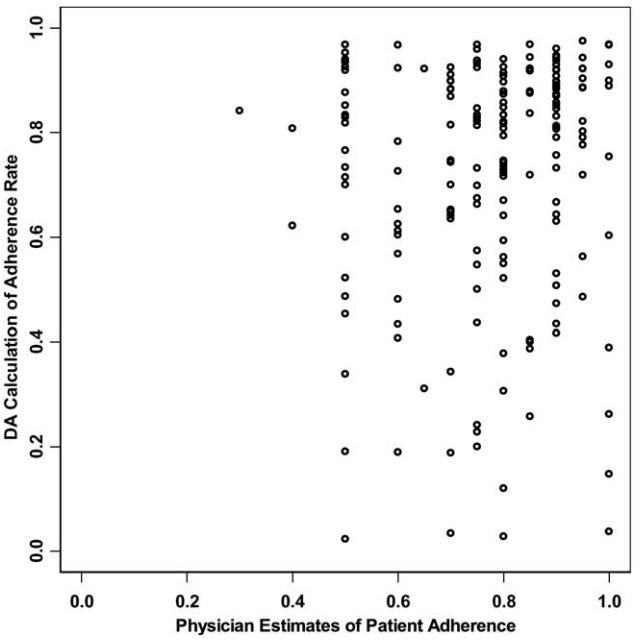

Figure 2. Scatterplot showing the adherence rate from dosing aid calculation (y-axis) versus the physician estimate of patient adherence (x-axis). The intraclass correlation coefficient was 0.09 (95% confidence interval, 0.00–0.19). DA = Dosing Aid.

based on pharmacy records, but there has been no direct comparison using electronic monitoring.[34] It will be of great interest to develop a method to compare adherence by electronic monitoring between the once-daily hypotensive agents and other glaucoma drugs that require more frequent dosage.

Although the behavior of patients in taking medication can be observed by indirect means (interviewing, weighing medication bottles before and after use, measuring serum drug levels, assessing pharmacy records), each of these has limitations. Electronic monitoring has several advantages and may be more accurate than any present alternative.[10,35] Electronic devices have been used widely in compliance research in other fields, but infrequently in ophthalmic research. In part, this is because of the greater difficulty of gauging eyedrop usage compared with gauging pill usage. Alteration of the eyedrop bottle itself is expensive and may require Food and Drug Administration reapproval of packaging for an agent if a monitor is involved.

Although electronic monitoring is considered to be the gold standard for compliance measurements, there are still limitations to the method, including the effect of patient knowledge of being monitored.[21] Persons who know they are monitored may change their behaviors simply because of being observed: the Hawthorne effect.[36] In an attempt to account partially for this effect, the adherence rate from 2 weeks after the baseline visit until 2 weeks before the follow-up visit was calculated. Although patients were aware for the entire study period that they were being monitored, many clinical trials have found poor adherence despite patients' knowledge of monitoring, and often any effects that may be attributed to monitoring reactivity are transitory.[37]

Some of the patients did not complete the study because of problems using the DA device. To minimize such difficulties, each participant viewed an instructional video about the device and its use and was observed self-administering a drop with the device. However, after using the device, some patients believed that the device interfered with drop delivery and discontinued its use before the 3-month time point. In an additional minority, the timing recording device malfunctioned, and the data were lost. Furthermore, some patients who had been using a different prostaglandin before study entry preferred their initial medication and subsequently dropped out of the study. There is no way to know if these patients were more or less likely to take their eye drops than those for whom 3-month data were available.

Table 3. The Agreement of Adherence Estimate between the Dosing Aid Calculation, Physician Estimate of Patient Behavior, and Patient Self-reported Adherence Rate

	Mean (Standard Deviation)	Median (First Quartile Third Quartile)	Intraclass Correlation (95% Confidence Interval)		
			Dosing Aid Calculation	*Physician Estimate*	*Patient Self-report*
Dosing Aid calculation	0.71 (0.24)	0.81 (0.58, 0.90)	1.0		
Physician estimate	0.77 (0.15)	0.80 (0.70, 0.90)	0.09 (0.00–0.19)	1.0	
Patient self-report	0.95 (0.14)	1.00 (0.97, 1.00)	0.15 (0.09–0.21)	0.11 (0.05–0.17)	1.0

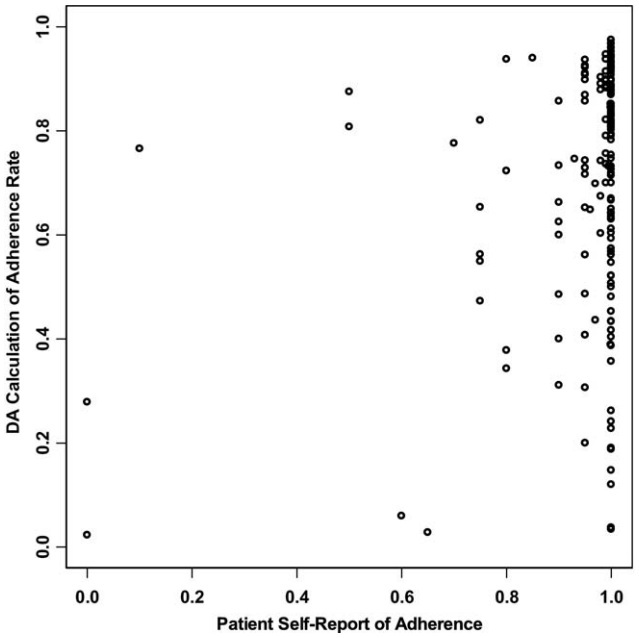

Figure 3. Scatterplot showing the dosing aid calculation (y-axis) versus patient self-reported adherence rate (x-axis). The intraclass correlation calculation was 0.15 (95%, confidence interval, 0.09–0.21). DA = Dosing Aid.

A substantial number of patients took less than 50% of doses. These same persons were more likely to become less adherent during the interval between visits, increasing drop taking during the 2 weeks before next office visit. Not only does this indicate that the IOP measurement obtained during the office visit is a poor surrogate for identifying their poor adherence, but it clearly represents a possible explanation for the phenomenon of progressive worsening of disc and field with IOP that is seemingly at or below the target IOP. This behavior of increased drug use near visit time has been reported before with the use of electronic monitoring for glaucoma, but not specifically among those who were less than 50% adherent. Kass et al[13] reported a significant increase in adherence within the 24-hour period before the office visit. Norell[12] previously had detected a decrease in pilocarpine adherence, monitored electronically, with increasing time since the last visit, as was found in the least adherent patients in this study.

The findings of Meltzer and Kass,[13] that patients report far higher medication use than their actual behavior, is confirmed with the current results. Several reasons have been suggested for this behavior, including patients wanting to please the doctor, patients not wanting to admit their error, or patients not feeling comfortable enough to admit their problems with the medication. Patients sometimes do admit their underusage of medications as prescribed. In the report by Rotchford and Murphy,[31] 24% of patients admitted missing eyedrops either occasionally or frequently. By contrast, the current study population claimed to be taking 95% of their medications. It is likely that the ability of the patient to admit the true level of nonadherence is affected by the atmosphere and method of questioning.

There was a weak correlation between physician estimation of patient adherence and the DA recordings of drop usage. Physicians in the present study were not able to distinguish patients who adhered to the travoprost regimen 20% of the time from those who used their drops 95% of the time. Kass et al[14,38] reported a very similar finding for pilocarpine and timolol use, detecting a wide variation between physician estimate and actual recorded eyedrop use. The present findings emphasize the inadequacies of the physician in identifying which persons are poorly adherent from their self-report, from the IOP measurement, or from other subjective clues. It also points to the need for better interactive communication skills, better electronic monitoring, or both if we are to identify the more nonadherent patients.

To the authors' knowledge, this is the largest study to measure objectively the usage patterns of once-daily ocular hypotensive medications in glaucoma patients with electronic monitoring. It is also the largest study comparing glaucoma patient self-report and physician estimates of medication use to recorded electronic monitoring data.

This study had some limitations. The study population, although coming from 2 different institutions and including a broad range of education and income levels, may not be representative of all glaucoma patients. Also, participants were informed that they were being monitored electronically. There is literature that indicates that this knowledge does not substantially alter patient behavior[39,37]; however, there is also literature that supports the Hawthorne effect,[36] as mentioned earlier. The authors chose not to use deception because when deception in a trial is revealed, either during the course of the trial or after, it has the potential to create a distrust of the investigator and all clinical research that can impact the community's relationship with the institution. Finally, free eye drops were provided to participants, removing the barriers of cost and the physical burden of drug acquisition. Again, this may have increased the adherence rates compared with what would happen in standard clinical practice. Because these findings found adherence to be far from perfect, these factors clearly did not impair the ability to study adherence problems.

The present report provides data that adherence with once-daily prostaglandin medication for glaucoma is imperfect and remarkably similar to that measured for other topical hypotensive agents by more indirect methods. Neither patient self-report nor physician estimation of adherence are accurate reflections of true behavior as measured by the DA. Fully 44% of study participants who knew they were being monitored and were provided free medications took less than 75% of intended doses. Poor adherence with therapy remains an important barrier to providing optimal care to glaucoma patients.

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