Original Article

Patients' Self-Reported Adherence to Cardiovascular Medication Using Electronic Monitors as Comparators

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The aim of this study was to evaluate self-reporting of adherence to cardiovascular medication using electronic pillboxes (medical event monitoring system [MEMS]) as the gold standard comparator. In total, 78 individuals (52% hypertensives, 21% diabetics, 27% with dyslipidemia) were recruited prospectively from an outpatient clinic setting in Switzerland. Participants completed two self-report measures (visual analogue scale [VAS] and a validated self-reporting questionnaire) at baseline and were asked to use MEMS as their pillbox for the subsequent 10 weeks. Patients expressed their medication adherence behaviour on a VAS (0 mm="I never take any tablets"; 100 mm="I take all tablets as prescribed") and entered one of six numbers (from 1: perfect adherence to 6: non-adherence) on the questionnaire. Medication compliance was monitored for 75 d on average. Mean (±SD, range) scores for MEMS with respect to timing adherence, correct dosing, and self-administration adherence were 79±25% (8–100%), 83±20% (24–100%), and 92±17% (54–118%), respectively. A majority of participants (78.8%) over-reported their adherence to the VAS (93±7 mm, 73–100), and VAS scores correlated poorly with MEMS recordings (Spearman's ρ for timing adherence, correct dosing, self-administration adherence 0.29 [$p=0.018$], 0.24 [$p=0.051$], 0.26 [$p=0.036$], respectively). Similarly, we found no correlation between adherence as expressed in the questionnaire and MEMS (regression coefficients <0.1). We conclude that a majority of patients over-report adherence to cardiovascular medication if asked to complete a visual analogue scale and a validated questionnaire. Therefore, using self-reporting as the sole means of assessing medication compliance is insufficiently accurate to detect poor adherence. (*Hypertens Res* 2008; 31: 2037–2043)

***Key Words*: hypertension, adherence, compliance, self-reporting**

Introduction

Poor adherence to medication treatment regimens remains a major public health problem (*1*). Generally, treatment discontinuation events steadily increase over time in the case of patients who have chronic conditions such as dyslipidemia, hypertension, or diabetes (*2–4*). Regular evaluation of adherence in clinical practice is therefore an essential but difficult task. A variety of direct and indirect measurement tools are available to assess adherence to medication. Methods include self-reporting, pill counts, prescription refills and measurement of drug levels in urine or serum. However, all of these instruments have disadvantages and are prone to error (*5*). Pillboxes that electronically record every opening event (*e.g.*, medical event monitoring system [MEMS]) are considered

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closest to a gold standard in measuring adherence (*6*). Because of their higher cost, however, they have been used primarily as a research tool.

Assessment of adherence to medication must be quick, cheap, and reliable. Self-reporting adherence questionnaires fulfil these criteria but have only been used with ethnic minorities (*7*, *8*); they have not been validated against the accepted gold standard (*9*–*11*) or were only tested in small study samples (*12*, *13*). Recently, an adherence self-report questionnaire suggested by Schroeder *et al*. (*14*) was validated in 239 patients with hypertension in a primary care setting using electronic pillboxes as the gold standard comparator (*15*). This tool showed good face validity, high patient acceptability, and considerable content validity.

Another readily available method for measuring adherence to medication is the visual analogue scale. Most experience in using this approach for gauging adherence comes from research in HIV/AIDS (*16*, *17*). A visual analogue scale has the advantage that it can be easily self-administered, that it places a lower response burden on the patient than a face-to-face interview, and that it can be quickly assessed by the presiding physician.

The aim of our study was to compare patients' self-estimation (self-reporting) of adherence to cardiovascular medication in a medical outpatient clinic between the use of self-reporting measures (questionnaire and visual analogue scale) and electronic monitors as the gold standard comparator.

Methods

Participants

Participants were recruited prospectively from the Medical Outpatient Department, University Hospital, Basel, Switzerland. The study was approved by the local ethical committee. Written informed consent was obtained from all subjects.

Between January and July 2006, patients with a clinical diagnosis of hypertension, diabetes, or dyslipidemia were screened for inclusion. The aim was to recruit as many patients as possible during this period of time. Patients with hypertension were eligible if 1) the diagnosis of arterial hypertension was documented in their medical records, and 2) the patient was being prescribed at least one medication for high blood pressure regardless of whether hypertension was controlled (<140 mmHg systolic and <90 mmHg diastolic) or uncontrolled (≥140 mmHg or ≥90 mmHg). Patients with type 2 diabetes were eligible if 1) the diagnosis of non–insulin-dependent diabetes was documented in their medical records and 2) the patient took at least one oral antidiabetic drug. Patients with dyslipidemia were eligible if 1) the diagnosis was documented in their medical records and 2) the patient was being prescribed an antilipidemic drug (statins or fibrates). Patients were excluded if one or more of the following were present: 1) age <18, 2) diagnosis of severe cognitive impairment (*e.g.*, severe dementia), 3) known secondary cause of hypertension (*e.g.*, endocrine, renal or pregnancy-related), 4) inability to provide informed consent or other reasons given by the treating physician (*e.g.*, terminal illness or recent bereavement), 5) use of a dose organizer ("dosette box") and 6) illiteracy.

Table 1. Baseline Characteristics of the Study Population

Characteristic	Description
Age, years	61.9±12.5
Male gender, *n* (%)	46 (58.9)
Body mass index, kg/m^2	28.9±5.4
Non-smokers, *n* (%)	60 (76.9)
Systolic blood pressure, mmHg	138±20
Diastolic blood pressure, mmHg	73±15
Glycosylated hemoglobin (HbA1c)	6.6±1.1
Lipid values	
Total cholesterol, mmol/L	4.7±1.0
LDL cholesterol, mmol/L	2.6±0.8
HDL cholesterol, mmol/L	1.4±0.4
Triglycerides, mmol/L	1.7±0.9
Number of drugs per day	4.1±2.3

Data are mean±SD or *n* (%). LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Measuring Adherence

Adherence was assessed using three different methods: 1) an Adherence Self-Report Questionnaire (*14*, *15*), 2) a Visual Analogue Scale (VAS) on which participants were asked to estimate their own medication-taking behaviour, and 3) electronic pillboxes (MEMS; AARDEX Ltd., Zug, Switzerland) that are considered the current "gold standard" in adherence measurement (*6*). These electronic monitors consist of a container similar to a traditional pillbox but with a larger lid, which contains a microchip and a pressure release system. This system is activated each time a pillbox is opened and closed. The system stores the exact time and date of each opening event, and summary data can be downloaded onto a personal computer. Data can be displayed graphically using the PowerView software. For reasons of cost and feasibility, MEMS was only used for one antihypertensive, antidiabetic or antilipidemic drug per person. If patients suffered from two or more of the three conditions assessed ($n=8$; 10.2%), the physician determined which class of drug was to be monitored using the electronic pillbox.

The Adherence Self-Report Questionnaire (ASRQ) uses six numbers to describe patients with different levels of adherence (ranging from 1: perfect adherence to 6: poor adherence). Participants were asked to indicate which of these descriptions best described their medication compliance.

The VAS consisted of a 100-mm–long horizontal line. Patients were asked to place a vertical mark on the line to indicate the regularity with which they self-administered their

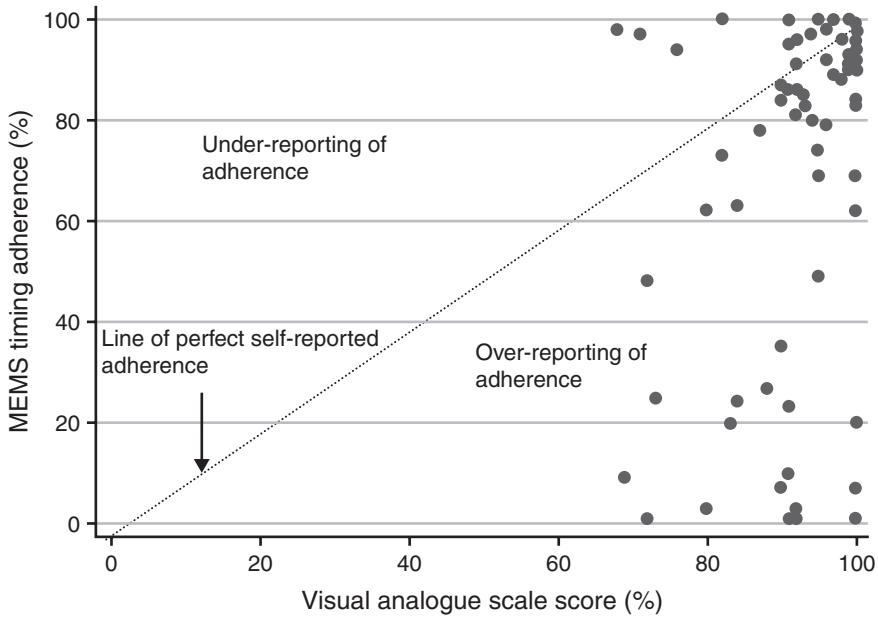

Fig. 1. *Scatter plot of the relationship between MEMS-measured timing adherence and patients' self-reported adherence assessed using a visual analogue scale.*

tablets. The question was: "How regularly are you able to take your tablets as prescribed by your doctor?" The line was anchored by the following word descriptors at each end: "I take hardly any tablets as prescribed" (0 mm, at the left end of the line), and "I take all of my tablets regularly as prescribed" (100 mm, at the right end of the line). The VAS score was determined by measuring from the left end of the line to the point marked by the participant (in mm).

Patients were approached at our facility during a routine consultation at the Medical Outpatient Department. Patients were asked by their physician whether they would be interested in participating in a clinical research study that aimed to discover whether medication compliance can be measured correctly using two different questionnaires. If a patient was interested, further information on the study schedule was provided by the principal investigator (A.Z.) or by his deputy (E.R.) on the same day. If patients consented to take part in the study, their baseline characteristics were recorded and participants completed the ASRQ and the VAS. The electronic pillbox was then issued to the patients. Participants were asked to install a 10-week supply of their drug into the monitor under investigator supervision. Patients were instructed to use the device as a drug dispenser for the subsequent 10 weeks.

Two thirds of the individuals received detailed information on the monitor and were informed that their adherence would be monitored during the study period. One third of subjects were given the monitors without further information regarding the fact that the MEMS would continuously assess their medication compliance. Patients were randomly allocated to the two groups using random number tables.

Outcome Measures

The principal outcome was adherence as measured by MEMS during the 10-week period. We compared this to the VAS score and patients' self-reported adherence as assessed by the ASRQ. MEMS adherence was defined in terms of "timing adherence," the strictest definition for self-administration of medications. The term refers to the number of doses taken at 24±6 h intervals (for a once-daily regimen) or at 12±3 h intervals (for a twice-daily regimen), divided by the total number of days and expressed as a percentage. Secondary outcomes were two less-strict measures of adherence. The first was "correct dosing," which denotes the percentage of days on which the correct number of doses were taken. The second was "self-administration adherence," defined as the percentage of the prescribed number of doses that were taken.

Statistical Analyses

Results are presented as descriptive statistics (*i.e.*, proportions, means, and SD). To assess the link between patients' self-estimation of adherence and adherence measured using MEMS (considered the gold standard), Spearman rank correlation coefficients were calculated for the VAS score and an ordered logistic regression was performed for the ASRQ. To evaluate potential differences in terms of adherence among the three study groups, a one-way analysis of variance (ANOVA) was performed. For inter-group comparisons,

Table 2. MEMS Measured Adherence Rates in the Hypertensive, Diabetic, and Dyslipidemic Subgroups

	Hypertension (n=27)	Diabetes (n=17)	Dyslipidemia (n=22)	p value
Timing adherence, %	71.5±34.2	61.5±34.8	67.1±36.7	0.66
Correct dosing, %	74.3±31.7	68.6±32.3	72.7±31.5	0.84
Self-administration adherence, %	81.6±33.2	85.1±30.2	79.2±32.5	0.85

Data are mean±SD. p values are derived from one-way analysis of variance (ANOVA). MEMS, medical event monitoring system.

Table 3. MEMS Measured Medication Compliance, Consistent with Whether Patients Received Detailed or No Information on the Purpose of the Electronic Pillbox

	Info MEMS "yes" (n=49)	Info MEMS "no" (n=17)	p value
Timing adherence, %	71.3±34.0	56.4±36.2	0.10
Correct dosing, %	76.9±29.8	58.9±32.8	0.035
Self-administration adherence, %	82.8±30.6	78.5±35.8	0.64

Data are mean±SD. p values correspond to the Mann–Whitney two-sample rank-sum test. MEMS, medical event monitoring system; info, information.

Mann–Whitney U statistics were applied. Two-sided p values below 0.05 were considered significant. To discriminate between sufficient and insufficient adherence, a commonly applied cut-off of 80% was used (*18*). All analyses were performed using STATA® (Stata Corp., College Station, USA).

Results

Over a 6-month period, 125 patients who had previously been diagnosed with arterial hypertension, diabetes mellitus type 2, or dyslipidemia were invited to take part and 78 consented to participate (recruitment rate 62.4%). Baseline characteristics of the studied population are given in Table 1. In total, 33 hypertensives (42.3%), 18 diabetics (23.1%), and 27 (34.6%) patients with dyslipidemia were included. Nearly half of the participants were retired (47.4%), 41% of the subjects were employed, and 11.6% were unemployed or claiming social/welfare benefits. The vast majority of patients were on a once-daily oral treatment regimen (84.6%). All patients with hypertension and all subjects with dyslipidemia were prescribed a once-daily medication. Angiotensin receptor blockers were the most frequently prescribed antihypertensive drug group (42.4%), followed by β-blockers (21.2%), angiotensin-converting enzyme inhibitors (18.1%), calcium channel blockers (15.2.%), and diuretics (3.1%). Two thirds of diabetic patients took metformin twice daily, one third took a sulfonylurea (mostly once daily), and all patients with dyslipidemia took hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitors (statins) in the evening.

We analyzed data from 66 (84.6%) electronic monitors. Seven participants failed to return the pillbox, the ASRQ and the VAS despite repeated reminders. Four subjects did not use the electronic monitor despite having consented to do so, and one patient died shortly after commencement of the study. The electronic monitors operated reliably and no failures occurred. Adherence was monitored on 75±27 (mean±SD) d and patients took a mean of 68±38 tablets out of the monitor.

Mean±SD of timing adherence across the whole study population was 67.5±34.8% (range 1–100). Correct dosing and self-administration adherence had means of 72.3±31.4 (range 1–100) and 81.7±31.8% (range 2–129), respectively. In reference to MEMS-measured timing adherence, only 58% of participants had good compliance, as defined by successfully taking their medication more than 80% of the time (63% of hypertensives, 47% of diabetics, and 59% of patients with dyslipidemia). Adherence rates in individual patients neither increased nor decreased considerably during the study. Patients with good adherence during the first month continued in that manner throughout the entire observation period. If a patient began with poor self-administration of the drug, the poor adherence persisted until the end of the study.

Figure 1 presents a scatter plot showing all patients with available MEMS-measured timing adherence against their self-reported adherence on the VAS (n=66). Overall, a majority of participants (78.8%) over-reported their adherence on the VAS compared with MEMS-measured adherence (Fig. 1). Fifty-nine patients (89.4%) self-reported their medication adherence as greater than or equal to 80 mm on the VAS. Of the remaining seven patients who stated that their medication compliance was below 80 mm on the VAS, three (4.5%) under-reported and four (6.1%) over-reported their adherence on the VAS. Detailed MEMS-measured adherence rates for the three studied subgroups are presented in Table 2. No relevant differences in adherence rates were identified among hypertensive, diabetic, and dyslipidemic patients (p>0.05).

The vast majority of participants chose ASRQ's description 1 (46.2%) or description 2 (47.4%), corresponding to perfect and nearly perfect adherence, respectively. Four subjects (5.1%) self-reported their medication compliance under

description 3, and one subject chose description 5 (1.3%). The VAS score across all individuals had a mean±SD of 91.3±9.0 mm (range 66–100). No significant differences between means of the VAS scores were found across the three study groups ($p=0.26$).

The Spearman rank correlation coefficients for the association between patients' self-reporting and MEMS-measured timing adherence, correct dosing, and self-administration adherence were 0.29 ($p=0.018$), 0.24 ($p=0.051$), and 0.26 ($p=0.036$), respectively. Patients clearly tended to over-report the extent to which they adhered to their medication regimen. Ordinate logistic regression to assess the relation between the description chosen in the questionnaire and MEMS-measured adherence also showed no association between patients' self-reporting and the gold standard comparator (regression coefficient for timing adherence was 0.05, $p=0.53$; for correct dosing and self-administration adherence 0.03, $p=0.74$, and 0.02, $p=0.95$, respectively). In patients who were prescribed only one drug per day ($n=10$; 12.8%) we also found no association between VAS and ASRQ-reported medication compliance and the MEMS-measured adherence (Spearman rank correlation coefficient <0.2).

Table 3 shows MEMS-measured medication compliance as a function of whether the patients received detailed or no prior information on the purpose of the electronic pillbox. Participants who were informed that they were being monitored by MEMS tended to have better adherence rates than subjects who were not informed. For MEMS-measured correct dosing events, the difference between the two groups of subjects was marginally significant ($p=0.035$).

Discussion

Addressing adherence to medication regimes in clinical practice is essential but challenging. In therapeutic trials, various strategies such as pill counting at return visits, verification of prescription filling, or electronic devices are often used. In primary care practice, such methods are not feasible due to financial and time constraints. Patients' self-reports on medication self-administration are often the only means available in routine practice settings. However, their accuracy and agreement with other data sources remain problematic. We designed a study to evaluate patients' self-reported adherence in taking cardiovascular medication in an outpatient setting using electronic monitors as the gold standard comparator. A majority of patients over-reported their adherence to antihypertensive, antidiabetic, or antilipidemic drug treatments.

The value of patients' self-reported adherence to medication remains a controversial subject. Our results are consistent with two studies that compared self-reported adherence to prescription refills (*19*, *20*). In one study that followed 200 hypertensive patients, adherence was assessed using a telephone survey (*19*). Patients substantially overstated their adherence and the agreement between self-reported adherence and refill rates was very poor. In another study, in which electronic monitors were used as the gold standard, patient self-reports of adherence to blood pressure–lowering therapy were considered imprecise (*21*). Also, physicians' ability to predict patient adherence to medication is limited, as recently shown by our group (*22*). In contrast, patients' self-reported drug use appears to be fairly reliable if pharmacy records (*23*, *24*), pill counts (*25*), or electronic monitors (*26*) are used as comparators.

Patients may over-report adherence for several reasons. First, information on how patients should take their medication might be inadequately communicated by the physician. As a consequence, patients may take lower doses, they may self-administer their medications less frequently than they should, or they may take tablets only when they feel symptoms—all while genuinely considering themselves to be adhering to their prescribed medication regimen. Second, the desire to please the researcher or physician by stating better adherence than is actually the case might contribute to over-reporting. Third, self-reporting of adherence requires a good memory, in particular when patients are asked to state their medication-taking retrospectively. To exclude recall bias, we chose a prospective approach.

It would help if patients were to accurately report non-adherence when questioned, but denial of non-adherence and over-reporting of adherence are both common phenomena (*27*). A cohort study that followed 286 individuals on a single-drug blood pressure lowering therapy explored possible risk factors for over-reporting of antihypertensive adherence. Dosing frequency, socioeconomic status, and health beliefs independently predicted over-reporting of adherence (*28*). Patients' beliefs and attitudes substantially influence how they take drugs (*29*). Patients' ideas might arise from feelings that are unrelated to the pharmacology of a particular treatment. Many patients are ambivalent about taking their medication, and they question the necessity of their medication weighed against potential adverse effects (*30*). Similarly, another study showed that patients seem to be concerned about the necessity of their prescribed medication and have a fairly negative view of drugs in general (*29*). Patients' decisions about whether to take antihypertensive drugs were analysed in patients who had been diagnosed with high blood pressure (*31*). About three in four individuals (76%) had reservations about taking antihypertensive agents and two thirds preferred to lower their blood pressure without taking drugs. Nearly 40% of patients were concerned about experiencing side effects in the near future or in the long term. Doctors may pay inadequate attention to patients' views or may make assumptions about those opinions. Determining patients' actual opinions about their medications might be a key factor in maintaining or achieving the best possible adherence.

To evaluate the potential presence of an intervention effect when electronic monitors were introduced to patients, one third of the participants in our study received no information on the purpose and function of the device. We found an obvious trend towards better adherence rates in the informed

group compared with patients from whom the relevant information had been withheld. This supports our opinion that there exists no ideal method to measure adherence. One key limitation of electronic monitors, which are considered "near" the gold standard (*6*), is the vulnerability of measurements to the Hawthorne effect. The Hawthorne effect is a change in patient behaviour as a result of being monitored in a study (*32*). To mitigate the potential adherence-enhancing effect of patients using a MEMS device, we decided to assess medication compliance over a 10-week period. This approach is justified by studies that report waning of the adherence-enhancing effect after around 5 weeks (*33*, *34*) and by other research that suggests electronic monitors present no such effect at all (*35*). In contrast, certain researchers also believe that this waning effect is more prolonged (up to 6 months) (*36*). Bearing their potential limitations in mind, electronic monitors still offer several advantages, which include indirect objective real-time assessment of adherence, information on dosing patterns such as day-to-day variability in self-administration of medication, or identification of intentional deviations in adherence such as an improvement in adherence in the days preceding a consultation. In clinical practice the use of MEMS devices seems to be helpful, because the monitors improve the management of patients with refractory hypertension (*37*). Such devices also have the potential to prevent unnecessary treatment escalations (*38*). However, there also exists evidence that the use of MEMS devices does not justify the increased costs compared with standard care practices in patients who suffer from poor adherence in any case (*39*). To obtain the best possible estimate of true dosing history, future studies may focus on the development of a composite adherence score using multiple adherence measurement techniques (*40*).

To summarise, our results suggest that a majority of patients over-report adherence to cardiovascular medication. Physicians should be aware of this fact when non- or maladherence is considered as a possible explanation for unsuccessful treatment profiles. Future work on the development of more accurate strategies is essential to make further advances in the challenging field of adherence measurement.

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