Original Article

Physicians' Ability to Predict Patients' Adherence to Antihypertensive Medication in Primary Care

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Addressing adherence to medication is essential and notoriously difficult. The purpose of this study was to determine physicians' ability to predict patients' adherence to antihypertensive therapy. Primary care physicians were asked to predict the adherence to medication of their hypertensive patients (n=42) by using a visual analogue scale (VAS) at the beginning of the study period. The patients were asked to report their adherence to medication using a VAS. The adherence was then monitored by using a Medical Event Monitoring System (MEMS) for 42±14 d. The means±SD (range) of MEMS measures for timing adherence, correct dosing, and adherence to medication were 82±27% (0 to 100%), 87±24% (4 to 100%), and 94±18% (4 to 108%), respectively. The physicians' prediction of their patients' adherence was 92±15%. The Spearman rank correlations between the physician's prediction and the MEMS measures of timing adherence, correct dosing, and adherence to medication was 0.42 (p=0.006), 0.47 (p=0.002), and −0.02 (p=0.888), respectively. The patients reported their own adherence to medication at 98±2% (range 83 to 100%). The Spearman correlations between the reported and actual behaviours were 0.27 (p=0.08) for timing adherence, 0.25 (p=0.12) for correct dosing, and 0.11 (p=0.51) for adherence to medication. The physicians' ability to predict patients' adherence to antihypertensive medication is limited and not accurate for identifying non-adherent patients in clinical practice. Even patients themselves are unable to give accurate reports of their own adherence to medication. (*Hypertens Res* 2008; 31: 1765–1771)

***Key Words*: hypertension, adherence, compliance, primary care, visual analogue scale**

Introduction

Numerous clinical trials have clearly demonstrated that correct antihypertensive drug treatment significantly reduces cardiovascular morbidity and mortality (*1*, *2*). To obtain the most benefit from blood pressure lowering drug treatments, patients' adherence to medication is crucial (*3*). If blood pressure targets are not achieved, many clinicians find it difficult to differentiate between non-response and non-adherence to drug treatment. To differentiate between the two possibilities, physicians would first assess patients' adherence to their prescribed medication. Regular assessment of compliance is an important issue in clinical practice, particularly in a mostly asymptomatic condition such as arterial hypertension. A variety of direct and indirect measurement tools such as pill counts, prescription refills, patients' clinical response, and bioassays of drug levels are available to assess patients' compliance. However, all of these instruments have disadvantages and are prone to error (*4*). In fact, no single method of measuring adherence is suitable for all settings or outcomes, and a commonly accepted standard does not exist (*5*, *6*). Pillboxes that electronically record every opening (*e.g.*, Medical Event Monitoring System, MEMS®) are considered to be the method that comes closest to a gold standard in measuring adherence. Because of the higher cost, however, they have

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been used mainly as a research tool.

In busy clinical practices, physicians must often make estimates of their patients' compliance without any external aids. Prior studies suggest that medical providers estimate their patients' adherence inaccurately (*7*, *8*). Most of the data on this issue, however, are derived from studies conducted among HIV-positive patients (*9*–*12*) or in patients with tuberculosis (*13*). To the best of our knowledge, data on the accuracy of physicians' estimates of adherence to medication in their patients with hypertension are currently lacking. We hypothesized that, for hypertensive patients, general practitioners (GPs) would have difficulty in estimating patients' adherence and in identifying non-adherent patients appropriately. Therefore, the aim of the present study was to evaluate how accurately physicians can predict adherence to antihypertensive medication in a primary care setting.

Methods

Participants

Three GPs and six hospital-based physicians took part in this study and estimated the adherence to medication of 42 of their patients. The study was approved by the local Ethical Committee. Written informed consent was obtained from all subjects. Consecutive patients were recruited from three general practices in the Basel area and from the Medical Outpatient Department, University Hospital Basel, Switzerland. Eligible patients were those above the age of 18 with an established clinical diagnosis of hypertension and taking at least one antihypertensive agent. Both patients with controlled ($<$140 mmHg systolic and $<$90 mmHg diastolic) and uncontrolled ($\geq$140 mmHg or $\geq$90 mmHg) hypertension were included. Exclusion criteria were a diagnosis of cognitive impairment (*e.g.*, severe dementia), use of a dose organizer (dosette box), known secondary cause of hypertension (*e.g.*, endocrine, renal, pregnancy related), illiteracy, inability to provide informed consent, or other reasons given by the treating physician (*e.g.*, terminal illness or recent bereavement). It was at the discretion of the treating physicians to select an eligible patient from their practice register. Every physician was asked to recruit at least five patients.

Assessment of Adherence

The GPs and hospital-based primary care physicians were asked to estimate their patients' adherence to antihypertensive medication by using a visual analogue scale (VAS). The VAS consisted of a horizontal line that was 100 mm long. On the day of recruitment, physicians placed a vertical mark on the line to indicate how they predicted their patients' adherence during the following 6-week period. The question accompanying the VAS was: "How regularly will the patient take his/her tablets—as prescribed by you—during the next 6 weeks?" The line was anchored by the following word descriptors at each end: "The patient takes hardly any tablet as prescribed" (0 mm at the left end of the line), and the "patient takes regularly all his/her tablets as prescribed" (100 mm at the right end of the line). The VAS score was determined by measuring in mm from the left-hand end of the line to the point that the physician marked. Furthermore, physicians were asked how confident they were of their estimates using a VAS (100 mm in length) anchored by the term "extremely poor prediction" at the left end and "perfect prediction" at the right end.

In addition, patients were asked to assess their own medication taking. The question was: "How regularly are you able to take your tablets as prescribed by your doctor?" The line was anchored by the word descriptors at each end: "I take hardly any of my 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).

On the day of recruitment, patients were given an electronic pillbox (MEMS®; AARDEX, Ltd., Zug, Switzerland) by the practice nurse and were asked to put a 6-week supply of one antihypertensive agent into the monitor. For cost and feasibility reasons, the MEMS was used for only one antihypertensive drug per person. The patients were asked to use the device as a drug dispenser for the next 6 weeks. The electronic pillbox consists of a container (similar to traditional drug bottles) and a larger lid, which holds a microchip and a pressure release system. This system is activated each time a monitor is opened and closed, and this is termed a "medication event." The monitor stores the exact time and date of each opening sequence, and the summary data can be downloaded onto a personal computer. The data can be displayed graphically using the PowerView® software (AARDEX, Ltd.). The patients were informed that their adherence would be monitored. While there was no assurance that patients actually consumed their medications, it is unlikely that they cheated, as they would have had to open and close the bottle at prescribed intervals on a daily basis in order to create a false pattern of adherence.

Outcome Measures

The principal outcome was "timing adherence" measured by MEMS during the 6-week period. "Timing adherence," the strictest definition of medication taking, is the number of doses taken in a 24 ± 6 h period for a once-daily regimen or in a 12 ± 3 h period for a twice daily regimen, divided by the total number of days and multiplied by 100%. Secondary outcomes were the two less strict measures of adherence ("correct dosing," which is the percentage of days on which the correct number of doses were taken, and "adherence to medication," defined as the percentage of prescribed number of doses taken). The main predictors were the physicians' prediction of adherence as determined by the VAS score and the patients' self-assessment of adherence to medication assessed by the VAS score.

Table 1. Baseline Characteristics of the Study Population (*n*=42)

Characteristic	Description
Mean age, years	66±11
Male gender, *n* (%)	26 (62)
Non-smokers, *n* (%)	28 (67)
Systolic blood pressure, mmHg	140.4±13.4
Diastolic blood pressure, mmHg	88.9±8.3
Blood pressure controlled*, *n* (%)	16 (38)
Pillboxes available for analyses, *n* (%)	42 (100)

Data are mean±SD or *n* (%). *Controlled blood pressure refers to systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg.

Table 2. Mean MEMS Measured Adherence (*n*=42)

	Adherence (range), %
Timing adherence	82±27 (0–100)
Correct dosing	87±24 (4–100)
Adherence to medication	94±18 (4–108)

Data are mean±SD. MEMS, Medical Event Monitoring System.

Statistical Analysis

The results are presented as descriptive statistics, *i.e.*, proportions, means, and standard deviations. To estimate the level of agreement between physicians' predictions on VAS and patients' adherence to medication measured with MEMS®, the Bland and Altman technique was used (*14*). Additionally, scatter plots were drawn, and Spearman rank correlations were calculated. The diagnostic "test characteristics" (sensitivity, specificity, negative and positive predictive values) of physicians' estimates for identifying non-adherence were calculated from cross tabulations. We used a commonly used definition for non-adherence of <80% (*15*). To evaluate differences in adherence between several groups, a one-way analysis of variance (ANOVA) was performed. For paired-group comparisons, Mann-Whitney *U*-statistics were calculated. Two-sided *p* values below 0.05 were considered significant. All analyses were performed using STATA® (Stata Statistical Software, 2005; Stata Corp., Collage Station, USA).

Results

The baseline characteristics of the study population ($n=42$) are given in Table 1. Two-thirds of the participants were retired, all were of Caucasian origin, and 34 (85%) of the subjects had had hypertension for more than 1 year, while 26 (65%) had had hypertension for more than 5 years. On average, the patients were prescribed 3.1 (range 1 to 6) drugs per day and nine of ten patients were on a once-daily regimen of antihypertensive agents. The angiotensin receptor blockers were the most frequently dispensed antihypertensive drug (33.3%), followed by β-blockers (16.7%), angiotensin-converting enzyme (ACE) inhibitors (14.2%), calcium channel blockers (11.9%), diuretics (2.3%) and others (21.6%). No significant difference in adherence was found between the various drug classes ($p=0.16$). The patients were monitored by MEMS for 42±14 d. The physicians had known patients for 6.4 years. The GPs were older compared with hospital-based physicians (48 *vs*. 34 years). The physicians were confident in their ability to predict adherence. On average, they placed the mark on the VAS at 82±12 mm (range 50 to 100); where 0 indicated extremely poor prediction and 100 indicated perfect ability to predict.

The MEMS based adherence measures are presented in Table 2. In 11 patients (26%), timing adherence (the strictest definition of adherence) was below 80%. No difference in baseline characteristics (*i.e.*, age, sex, smoking habits, blood pressure levels, controlled blood pressure levels) was found between the patients who were adherent (≥80%) and those who were not (<80%) ($p>0.05$). For instance, systolic blood pressure was similar in patients with adherence rates ≥80% and <80%, respectively (141±13 *vs*. 138±15 mmHg, $p=0.47$).

The adherence predicted by physicians on the VAS was 92±15% (range 30 to 100%). Figure 1 shows the scatter plots of the relation between timing adherence and adherence stated by physicians and patients, respectively. The Spearman rank correlations between physicians' prediction of adherence and timing adherence, correct dosing, and adherence to medication were 0.42 ($p=0.006$), 0.47 ($p=0.002$), and −0.02 ($p=0.888$), respectively. The correlations between the MEMS adherence measures and the VAS adherence predictions from each participating physician varied widely (the Spearman rank correlation range was 0.19 to 0.79).

Figure 2 shows a Bland and Altman plot (*14*) to measure the agreement between the VAS score for predicted adherence and the timing adherence. The mean difference between the two methods was 9.9±24.7% (95% confidence interval 2.2 to 17.9). The limits of agreement (mean difference±2 SD) were −39.5% to 59.3%. Thus, the VAS score may be 39.5% below or 59.3% above the timing adherence, which would make it not useful for clinical purposes. The sensitivity of detecting non-adherent patients by physicians was 27%, and the specificity was 94%, when adherence was defined as taking <80% of medication. The positive (PPV) and negative predictive values (NPV) were 60% and 78%, respectively. Patients assessed their adherence to medication at a value of 98±2% (range 83 to 100%). The Spearman correlations were 0.27 ($p=0.08$) for timing adherence, 0.25 ($p=0.12$) for correct dosing, and 0.11 ($p=0.51$) for adherence to medication (Fig. 1, lower). The patients with sufficient adherence as measured by MEMS (>80%) were more likely to correctly assess their adherence to medication on the VAS ($r=0.44$, $p=0.001$), whereas the self-assessment of adherence among

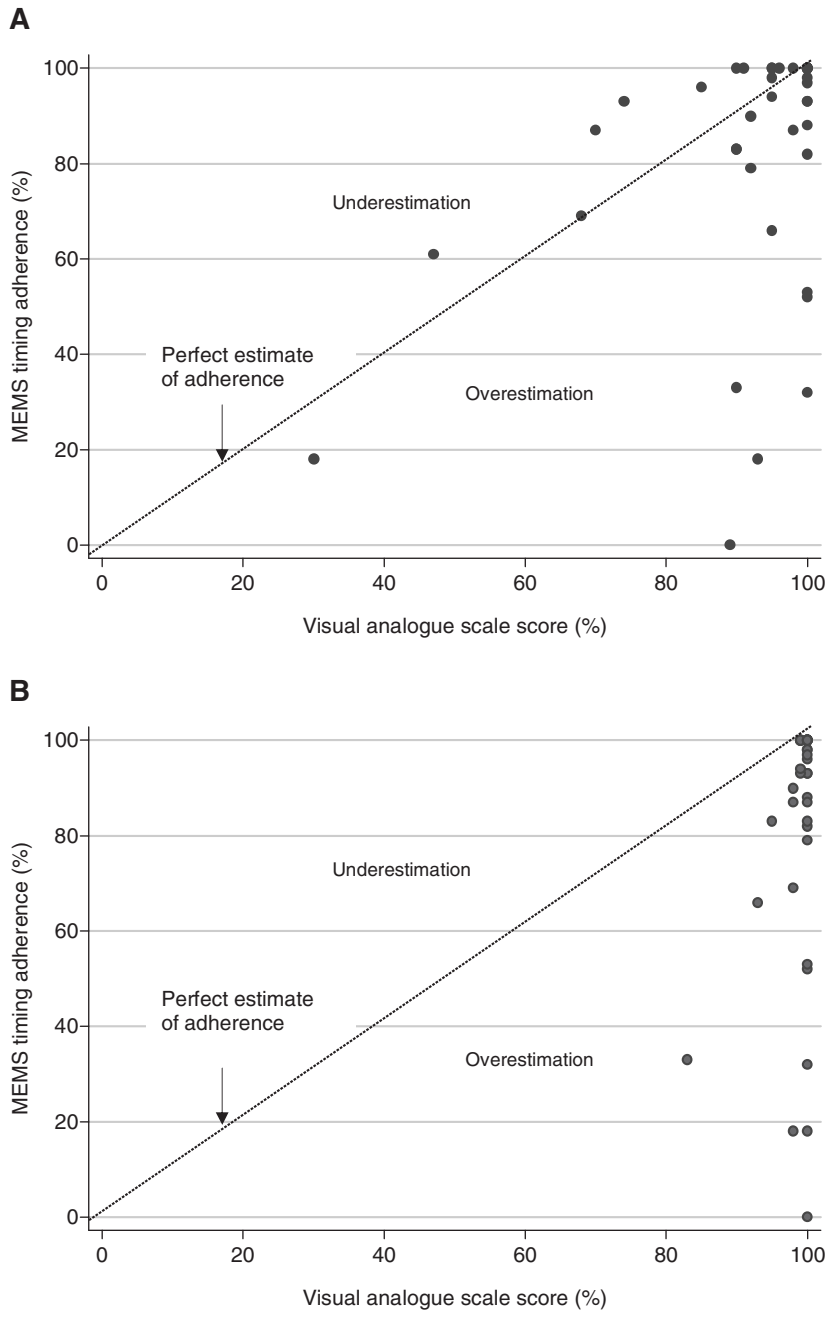

Fig. 1. *Scatter plots of the relationship between MEMS measured timing adherence and physicians' predictions (A) and patients' self-assessments (B) of adherence to medication. The Spearman rank correlation coefficients were 0.42 ($p=0.006$) and 0.27 ($p=0.08$), respectively.*

non-adherent patients was poor (correlation coefficient for the patients with adherence rates <80% was 0.01).

Discussion

Adherence to medication is crucial for effective therapy. For a chronic and mostly asymptomatic condition such as arterial hypertension, regularly taking tablets as prescribed is challenging for patients. If blood pressure targets are not achieved, it may be due to non-adherence or poor adherence. We conducted a study to evaluate physicians' ability to predict adherence to antihypertensive therapy in a primary care setting. We found that the physicians' prediction of their patients' adherence to medication was substantially inaccurate. However, physicians' estimates of adherence seem to be more reliable than patients' self-assessment of compliance.

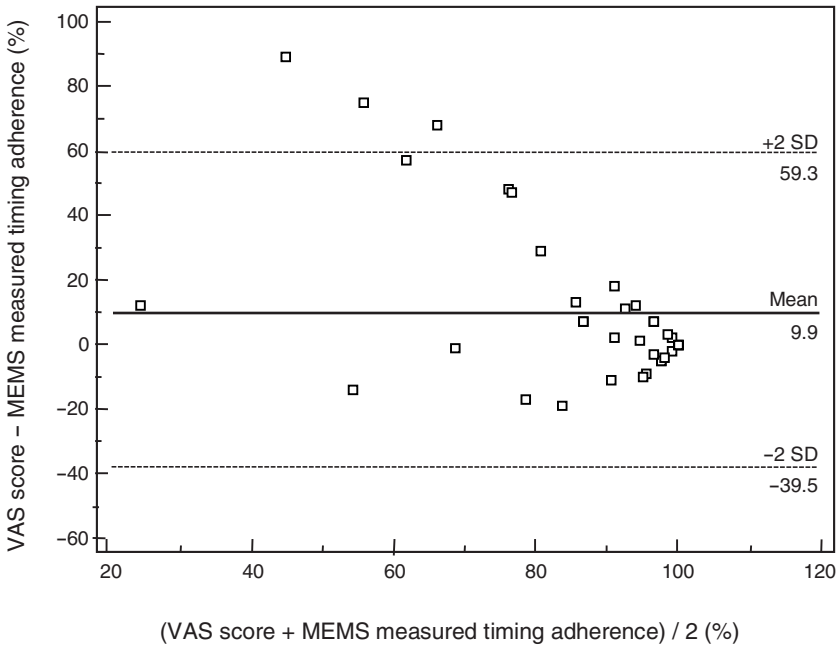

Fig. 2. *Agreement between VAS score and MEMS measured timing adherence, using the Bland and Altman technique (14).*

The assessment of adherence to blood pressure lowering therapy is a common task in a busy clinical practice. These assessments are often made by the GPs without using additional aids such as questionnaires or prescription refill rates. Only a few studies have evaluated physicians' ability to predict adherence to cardiovascular medications. In one study, physicians were asked to estimate adherence to digoxin treatment (*8*). The sensitivity of physicians' judgment of non-adherence was only 10%. The authors concluded that physicians were unable to predict adherence better than chance, even for patients they had known for 5 or more years. Also in the present study, GPs failed to accurately identify non-adherent patients (defined as MEMS measured adherence <80%). The low sensitivity (27%) and predictive values (PPV 60%, NPV 78%) indicate that physicians' predictions are not useful for clinical purposes. Most of the data on assessing medication adherence are from HIV-infected populations (*9–12*), in which very high adherence rates (>95%) are essential to avoid the development of multi-drug–resistant HIV strains and therapeutic failure (*16*). In all these studies, physicians' estimates of adherence were considered to be inadequate. Our results are in line with previous findings and suggest that, for patients who are prescribed antihypertensive agents, GPs' ability to predict adherence is also inadequate.

To improve the accuracy of GPs' assessments of adherence in clinical practice, several tools such as questionnaires have been developed. These questionnaires can be administered during a routine consultation and may aid in the assessment of patients' compliance. To date, three questionnaires have been validated with the electronic pillbox as the gold standard among patients with hypertension (*17–19*). Unfortunately, the diagnostic performance of the tools in terms of identifying non- or poorly adherent patients has been disappointing (sensitivity <50%), and they do not appear to be adequate for clinical purposes.

Another method of obtaining information on adherence to medication is to quantify how regularly patients fill their prescriptions. In a retrospective cohort study, adherence to antihypertensive medication was assessed in 1,395 patients using pharmacy repeat prescriptions (*20*). Patients belonged to the Medicaid managed–care program in the United States and had uncomplicated hypertension. Overall, the failure to refill prescriptions of antihypertensive medication occurred in 2,410 (33%) of 7,413 opportunities. The authors concluded that the non-redemption of prescriptions could identify non-adherent patients with a fair sensitivity and a high degree of specificity, as patients in the study population did not have alternative sources of medication. The advantage of pharmacy prescription profile-based methods is that patients are not aware of the fact that their adherence is being monitored. However, non-redemption of prescriptions gives only a crude estimate of adherence, and it varies with age, sex, exemption status (*21*), and class of the antihypertensive agent prescribed (*20*).

In a clinical setting, asking patients about their medication use is probably the most practical method to assess adherence, as it is time efficient and inexpensive. Obviously, it is very helpful when patients admit non-adherence, but patients' denial of non-adherence is common (*22*). In a study published about 20 years ago, interviewing patients about their degree of compliance was considered to be prone to error (*23*). In the present study, we observed that patients substantially overes-

timated their adherence when asked to self-assess it using a VAS. However, there is evidence that interviewing patients may still be a valuable source of information to assess adherence, if appropriate communication skills are applied. In a prospective observational study, employees from 14 different work-sites were screened for high blood pressure (*24*). Hypertensive workers were interviewed about their medication taking by trained nurses and physicians. Patients reporting strict adherence to prescribed therapy had lower systolic and diastolic blood pressure than those who admitted lapses in medication taking. The authors stressed the point that patients who are asked about adherence should not be embarrassed or "lose face" in front of the health care provider. Thus, it was recommended that questions addressing medication adherence be formulated in a non-judgmental and non-threatening manner (*e.g.*, "Many people have difficulty taking their tablets regularly. Do you ever miss or forget to take your medicine?") (*25*).

An overriding limitation in measuring adherence by electronic medication dispensers is the vulnerability of measurements to the "Hawthorne effect," or the change in patients' behaviour as a result of being monitored in a study (*26*). This is particularly true when patients know the methods being used to measure adherence or anticipate negative consequences resulting from non-adherence. Not informing patients that adherence is being measured can alleviate this problem, but this is problematic from an ethical perspective. A broad consensus supports the view that patients should be informed that their drug intake is being measured (*27*). We have no conclusive information if or by how much the monitoring process, or just taking part in a study, may have affected the study participants' medication taking behaviour. There is some evidence that adherence is no better in patients who were informed that their drug intake was being monitored than in those unaware of the monitoring (*28*, *29*). In contrast, Burnier *et al*. have suggested that the electronic pillbox may be a useful option in managing patients with refractory hypertension (*30*). For the time being, and even in the near future, the high cost and the limited availability of electronic medication measurement systems limit their widespread use in ambulatory settings. However, it is important to realise that electronic pillboxes probably are the most objective method available to estimate patients' adherence to medication.

We are aware of the fact that using VAS to assess adherence to antihypertensive medication has not been validated against electronic monitors as yet. However, data from studies of HIV-infected populations suggest that the use of VAS might be a useful method to evaluate adherence to medication in general (*31*, *32*).

In conclusion, our findings show that physicians' ability to predict patients' adherence to antihypertensive medication is limited and not accurate enough to identify non-adherent patients in clinical practice. Physicians tended to overestimate patients' adherence, and patients considerably over-reported their adherence to blood pressure lowering medication. Further investigations will be needed to develop feasible and effective strategies to identify those patients who have difficulties adhering to their antihypertensive medication.

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