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PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

Clinical evaluation of IDAS II, a new electronic device enabling drug adherence monitoring

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Abstract
Objective The goal of this study was to evaluate clinically the acceptability of the IDAS II (Intelligent Drug Administration System), a new electronic device that enables drug adherence monitoring.
Methods IDAS II was compared to another electronic monitor, the Medication Event Monitoring System (MEMS) in a randomised two-way cross-over study involving 24 hypertensive patients treated with irbesartan. Patients used each device for 2 months. The main parameter of evaluation was the patients' opinion on both devices. Rates of adherence and blood pressure were also assessed.
Results Most patients considered both devices to be reliable reminders (IDAS II: 75%;MEMS: 84%, p = ns). Ten patients (42%) preferred the MEMS, while 11 (46%) preferred the IDAS II; three (12%) expressed no preference. Patients found the MEMS device easier to use than the IDAS device ($p<0.001$) but appreciated the IDAS blister packs better than the MEMS bulk packaging ($p<0.01$). Over the 4-month period, the median "taking adherence" was excellent (99.2%) and comparable with both devices. However, the regularity of drug intake timing was higher with the IDAS II ($p<0.01$).
Conclusion IDAS II, a new electronic device enabling drug adherence monitoring without reconditioning of the drugs appears to be a well-accepted device. Overall, practicability and acceptability of the IDAS II and the MEMS device were similar. Thus, IDAS II could be a useful tool for the management of long-term therapies.

Keywords Acceptability · Clinical assessment · Electronic monitoring device · Hypertension · Patient adherence

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Introduction

Adherence to prescribed medications is a key factor in disease management. However, low adherence to chronic medications is frequent [1], and about one in four patients do not adhere well to prescribed drug therapy [7]. The World Health Organization (WHO) estimated that 50–70% of patients in a general hypertensive population do not take their antihypertensive medication as prescribed and described poor adherence as one of "the most important cause of uncontrolled blood pressure". The WHO recognises the importance of supporting chronic patients in increasing and maintaining long-term drug adherence [14].

The detection and assessment of poor adherence is a difficult and problematic task for healthcare professionals. In clinical settings, questions directly addressed to patients on their drug intake are the most practical means of ascertainment, but this method is prone to inaccuracy [10]. Patients usually tend to overestimate their adherence due to difficulties recalling the details of their medication taking or in attempts to please their physicians. Consequently, physicians must frequently rely on their own clinical judgement which, unfortunately, is often inaccurate in terms of identifying poor adherers [3, 9].

To date, the electronic monitoring system called MEMS (Medication Event Monitoring System; AARDEX, Zug, Switzerland) is the most reliable non-invasive method for assessing patient adherence, [2, 4] and, thereby, assisting healthcare professionals to make rational therapeutic decisions [4]. Indeed, the MEMS device provides an accurate, dynamic and "real time" follow-up of the patient's pill-taking behaviour [6, 13]. To our knowledge, very few other reliable electronic monitoring devices are available in clinical practice. However, the use of the MEMS device requires reconditioning of the drugs from their original packaging, a procedure which is time-consuming, costly and not accepted in some countries.

Given the clinical importance of the drug adherence issue, new, easy-to-use devices would be welcome. We report here the results of a randomised crossover study in which we evaluated the clinical acceptability of a new electronic device for monitoring patient's drug adherence – the IDAS II (Intelligent Drug Administration System; Bang and Olufsen Medicom, Denmark) and compared it to the MEMS device.

Methods

Study design

This 4-month randomised (1:1) open cross-over study was conducted at the Hypertension Outpatient Unit of the University Hospital (CHUV) and the Pharmacy of the University Outpatient Medical Clinic (PMU), Lausanne, Switzerland. One pharmacist (VS) and two physicians (GW and MB) were involved in the inclusion and follow-up of the patients. The study protocol was approved by the local ethics committee, and written informed consent was obtained from all participating patients.

Patients were invited to participate if they met the following inclusion criteria: (1) hypertensive patient currently treated with irbesartan 150 or 300 mg once a day, or (2) newly diagnosed patient with hypertension on the point of starting with irbesartan 150 or 300 mg daily and (3) an understanding of French and the aim of the protocol. Patients were prescribed irbesartan without any changes in their regimen during the whole study. Additional treatments were allowed during the study but were not monitored electronically.

Study protocol and assessments

After inclusion in the study by physicians, patients were referred to the pharmacist who dispensed, in a random sequence, irbesartan in the MEMS 6 SmartCap device (Table 1) or in the IDAS II device for a 2-month period. At the end of the first 2 months, patients received the alternative device for a second 2-month period. There was no washout period. Randomisation was performed using a computer-generated random-number table.

Patients were seen on three occasions: at a randomly chosen time and at the end of each 2-month period. At inclusion, patients were instructed on the correct use of the electronic monitoring device in a interview with the pharmacist who prepared and dispensed the devices. At

Table 1 Description of the IDAS II and MEMS devices

The IDAS I (Intelligent Drug Administration System, Bang and Olufsen Medicom, Denmark) is an electronic device that accommodates blister packs. An electric foil is fixed upon the tablet slots. Each time a pill is taken, the electric foil is ruptured which activates the recording of the date and hour at which the drug was removed from the blister. This device has two reminders: (1) one visual which indicates time elapsed since the last dose and the actual time and (2) one audible which sounds at chosen and fixed time for 1 min or until the patient opens the device. The audible reminder can be deactivated upon request.

The MEMS 6 SmartCap (Medication Event Monitoring System, AARDEX, Zug, Switzerland) consists of a usual bulk pill container fitted with a special cap, which contains a microelectronic system that automatically records the date and hour of each opening of the bottle and a LCD display on top of the bottle. The LCD display indicates the number of daily openings and the number of hours elapsed since the last opening.

the second visit, patients returned the device to the pharmacy and filled in a questionnaire (Questionnaire 1) assessing the acceptability and usefulness of the device. This questionnaire assessed six items: (1) handling (easiness), (2) LCD display information (understanding and helpfulness), (3) reminder functions (understanding and helpfulness), (4) subjective appreciation of impact on drug intake, (5) patient satisfaction with the device and (6) technical problems with the device. At the final visit, patients once again filled in Questionnaire1 and were asked in addition to fill in a second questionnaire. Questionnaire 2 assessed the following items: (1) overall patient's preferences as well as specific preferences in handling, cumbersome and packaging, (2) subjective appreciation of impact on drug intake. Answers to Questionnaires 1 and 2 were dichotomous (yes/no) or graduated on a four-point Likert scale "from a lot" to "not at all" (0–4). The questionnaires were developed specifically for this study, and understanding was tested by four patients, one pharmacist and two physicians before the study was initiated. At each visit, the pharmacist downloaded the data from the electronic monitor, printed out the adherence report (calendar and chronology plot) and reviewed it with the patient.

Five indices were used to quantify drug adherence [10]. First, the *percentage of doses taken* was calculated as the number of times the MEMS/IDAS II had been opened/activated divided by the number of times the device should have been opened/activated during the considered period. *Taking adherence* was defined as the percentage of days with correct dosing. *Timing adherence* was defined as the percentage of correct intervals between two doses (an interval was defined as being correct if it was located within ±25% of the prescribed interval). *Drug holidays* were defined as no medication intake during a time period longer than 24 h. The percentage of drug holidays is the number of drugs holidays (expressed in days) divided by the number of monitored days. In addition, we computed a *timing distribution index*. To calculate this index, we identified the hour at which the medication was taken most frequently (mode of hour distribution). We then calculated the sum of deviations from this mode, divided by the number of days at which drug was taken using the following formula: $DI = \frac{\sum_{i=1}^{n} |hi-h0|}{n}$ where h0 is the mode of distribution of the hour of drug intake, hi is the hour of drug intake on day I and n is the number of days at which drug was taken. Days when drugs are not taken or taken twice were not counted. For example, a patient took his/her medication 21 times at 7 a.m., 4 times at 6 a.m., 3 times at 8 a.m. and 2 times at 9 a.m. for 30 days. His mode is 7 a.m.. The timing distribution index is: $\{[(7-7) \times 21] + [(7-6) \times 4] + [(8-7) \times 3] + [(9-7) \times 2]\}/30$. A small distribution index means a regular timing of drug intake.

Statistical analysis

Baseline characteristics were summarised as means (±SD) or as percentages, as appropriate. Adherence indices were compared using the Wilcoxon rank sum test. The answers to Questionnaire 2 were compared using binomial probability test. Two-sided p values less than 0.05 were considered to be statistically significant. Statistical analysis was performed with STATA ver. 9.0 (STATA Corp, College Station, TX).

Results

The baseline characteristics of the patients are shown in Table 2. Three patients were newly treated with irbesartan. Twenty-five patients were included in the study, but only 24 completed it. One patient withdrew from the IDAS II period because he was unable to handle the device.

All patients were able to handle the MEMS device, and 98% of them were able to use the IDAS II device appropriately. More than one third of the patients (9/24; 38%) indicated that pressing down on the tablets to get them out of the special blister cards of the IDAS was difficult; however, replacing the blister card with a new one was easy for nearly all patients (23/24; 96%). One patient experienced difficulties in opening the IDAS II, in releasing the latches and in pressing down on the tablets to get them out of the blister card. One patient did not use the IDAS II correctly, and the device did not record the doses.

Table 2 Baseline characteristics of the patients (n=25)

Characteristics	
Sex (men/women)	12/13
Mean age, years (range)	58.0 (35–75)
Mean systolic BP, mmHg (SD)	144.0 (24.8)
Mean diastolic BP, mmHg (SD)	85.9 (12.1)
Mean body mass index, kg/m^2 (SD)	28 (5.4)
Monitored treatment	
Ibesartan 150 mg/d qd	20
Ibesartan 300 mg/d qd	5
Additional antihypertensive drugs prescribed	
Diuretics	11
Calcium antagonists	5
Beta-blockers	5
Number of antihypertensive therapies	
Monotherapy	12
Bitherapy	7
Tritherapy or more	6
Mean number of antihypertensive drugs (range)	1.9 (1–4)

BP, Blood pressure; SD, standard deviation; qd, once a day

Table 3 Results of Questionnaire 2: comparison of both devices

Questions	MEMS	IDAS II	*p* value[a]	None	Both	No answer
Which device was easier to use?	17 (71)	5 (21)	<0.001	0 (0)	2 (8)	0 (0)
Which device was less cumbersome?	11 (46)	10 (42)	ns	1 (4)	2 (8)	0 (0)
Which drug presentation did you prefer?[b]	8 (35)	15 (63)	<0.01	0 (0)	0 (0)	1 (4)
Which device supported your drug intake the most?	4 (17)	10 (42)	<0.05	9 (37)	1 (4)	0 (0)
Which device did you prefer?	10 (42)	11 (46)	ns	2 (8)	1 (4)	0 (0)

Values are numbers (percentages) of patients, unless stated otherwise
[a] MEMS vs. IDAS II (binomial probability test)
[b] MEMS, Bulk pill-container vs. IDAS II, blister pack

No patient expressed problems reading the information displayed on both devices. Most of the patients characterised the display information of the IDAS II (21/24; 88%) and the MEMS device (21/25; 84%) as "easy to understand". The answers differed in terms of the usefulness of the visual and audible reminders. The MEMS LCD display information indicating the number of doses taken during the present day and the number of hours elapsed since the last opening were considered to be useful by 64% (16/25) and 28% (7/25) of the patients, respectively. The IDAS II digital display indicating the time since last dose, the visual blinking reminder and the audible reminder were considered to be useful by 46% (11/24), 38% (9/24) and 42% (10/24) of patients, respectively. Four patients asked the pharmacist to deactivate the IDAS II audible reminder.

Patients reported two types of technical failures with the IDAS device. First, the IDAS II had a higher incidence of LCD display failures than the MEMS device (42 vs. 20%; $p=0.017$). Secondly, one patient encountered troubles with the IDAS audible reminder, which sometimes rang at the wrong time although the settings were correct and the pharmacist did not experience any technical problem in the preparation and setting of both electronic devices. On average, a total of 7 min (range 12–20 min) were required to prepare the IDAS II device and 17 min (range 5–10 min) to prepare the MEMS device ($p<0.001$). A total of 7 min (range 5–10 min) was necessary for the MEMS' initial instruction session and 18 min (range 10–40 min) for the IDAS II device ($p<0.001$).

In terms of drug intake, 14 patients with the MEMS (56%) and 12 patients (50%) with the IDAS II reported that the devices helped them maintain a more regular drug intake. The assessment of patient satisfaction revealed that the majority of the patients considered both electronic devices to be a reliable reminder (84% with the MEMS vs. 75% with the IDAS II). Only two patients felt that they were being "observed" too much with both devices. Two patients (8%) did not take any interest in the MEMS device, and three (12%) considered it to be useless. Eight patients (33%) did not take any interest in the IDAS II device, and eight (33%) considered it to be useless. Approximately half of the patients expressed a willingness to use both devices in the future.

Table 3 shows the comparison of both devices (Questionnaire 2). Patients' preference in terms of handling tended towards the MEMS device, but there was no difference of opinion on the cumbersomeness of both electronic devices. Patients preferred the blister pack (IDAS II) to the bulk pill-container (MEMS) because of better expected hygiene. More patients preferred the IDAS II as a supporting device over the MEMS. However, nine patients said that neither of the devices was of any help for the

Table 4 Electronically monitored drug adherence to irbesartan 150 mg or 300 mg once a day using the IDAS II vs. MEMS device

	2-month monitoring period		
	IDAS II (n=23)	MEMS (n=25)	*p-value*
Duration of monitoring (days)	62	63	–
Median (range)	(48.0, 70.0)	(47.0, 104.0)	
Percentage of doses taken	100.0	100.0	ns
Median (range)	(40.3, 100.0)	(50.0, 101.8)	
Taking adherence (%)	100.0	100.0	ns
Median (range)	(40.3, 100.0)	(50.0, 100.0)	
Timing adherence (%)	96.7	97.2	ns
Median (range)	(23.0, 100.0)	(21.8, 100.0)	
Distribution index (mean±SD)	0.60±0.55	1.03±0.68	<0.01

ns, Not significant; range is expressed as (minimum, maximum)

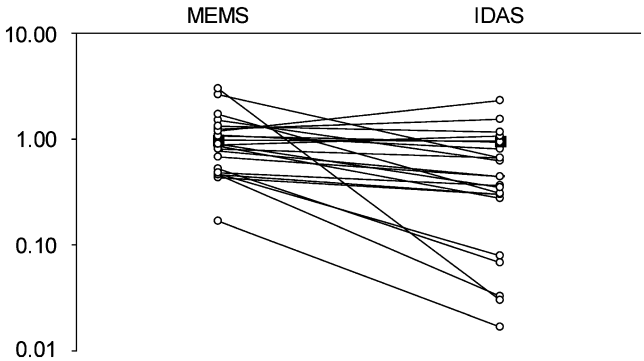

Fig. 1 Timing distribution index with each device calculated as indicated in the Methods section

simple reason that they already had a strong daily routine for drug intake (i.e. teeth-brushing, mealtimes, walking the dog and shaving). Patients did not show any significant preference for one device or the other one.

Over the 4-month study, the adherence was very high whatever the device, with a median taking adherence of 99.2% (range 62.7–100 %). During the first 2-month period, the median taking adherence was 100% (range 40.3–100%), with only two patients having a taking adherence <80%. During the last 2-month period, adherence was still excellent, with a median taking adherence of 98.4% (range 84.1–100%) (Table 4). The median distribution index was lower with the IDAS II device, indicating that the patients showed a stricter adherence to taking their drug at the same time, day after day with the IDAS II than with the MEMS device (Fig. 1).

Discussion

This study has evaluated the clinical acceptability of a new electronic device, IDAS II. The results showed that practicability and acceptability were similar with the IDAS II and the MEMS devices, and the latter is now frequently used in clinical studies. The patients appreciated the MEMS device for its ease of handling and for the reminder function indicating the number of doses taken during the present day, but they appreciated the IDAS II device for drug packaging in the form of the blister pack and the reminder functions indicating the time since last dose. Both devices were considered to be reliable reminders supporting drug intake even though many patients had already established a daily routine for their drug intake. Hence, overall rates of adherence to the prescribed drug therapy was very high and comparable with both devices.

Patients were satisfied with both devices. In our experience this is a rather consistent finding as a positive appreciation of electronic monitoring of drug adherence was also found in another study conducted in epileptic patients followed electronically for 8 months with electronic devices [12]. The favourable appreciation by patients often contrasts with the relative reluctance of physicians to use these systems. In the present study, about half of the patients expressed a willingness to use both devices in the future, and half of them felt supported while being monitored. Patient's acceptation of any device depends on the usefulness and suitability of the device but also on the manner healthcare providers introduce it to the patient. It is worthwhile noting that our patients were not selected to participate in this study because they had drug adherence problems. This may explain why about one third of them did not really consider the devices to be useful.

The overall rates of adherence to the prescribed drug therapy was very high in this study whatever the device. This is well explained by the short duration of the monitoring and probably by the motivation of patients who accepted voluntarily to participate in the clinical study. Moreover, both the pharmacist's intervention and the monitoring of drug adherence have been shown to enhance the adherence to therapeutic regimens [4, 8, 12].

Patients tended to take their drug more regularly when using the IDAS II. This is probably linked to the combined visual and audible reminders of the device. Thus, the IDAS II device might be of help for maintaining a regular timing in patients who take drugs with a narrow therapeutic window and who are supposed to take their medication punctually every day. The audible reminder can be deactivated upon the patient's request; as such, the device remains suitable for confidential circumstances.

One advantage of the IDAS II system is that drugs do not need to be reconditioned and, therefore, they can be used in their original blister pack. However, at the present level of development of the device, this turned out to be a limitation since the IDAS II device could only be used with a one-size blister card. In this study, irbesartan had to be re-packaged by the pharmaceutical company. In clinical practice, the ideal electronic device should accept various blister card sizes. Moreover, one device should ideally enable the monitoring of different drugs simultaneously since most chronic patients take several concomitant drugs. Some patients found the IDAS II to be too large and not practicable to take when travelling or to carry around in the pocket. Nonetheless , the size of the IDAS II did not appear to be a major limitation to its use.

In conclusion, our study shows that IDAS II, a new electronic monitoring device of drug adherence, is well accepted by patients and could represent a valuable device for the clinical management of patients with chronic diseases. The future development of electronic monitoring devices such as the IDAS II is, in our view, an interesting and important approach that assists physicians in diagnosing drug adherence problems in some patients and supports patient adherence in clinical practice.

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References

1. Andrade SE, Kahler KH, Frech F, Chan KA (2006) Methods for evaluation of medication adherence and persistence using automated databases. Pharmacoepidemiol Drug Saf 15:565–574
2. Bertholet N, Favrat B, Fallab-Stubi CL, Brunner HR, Burnier M (2000) Why Objective Monitoring of Compliance is Important in the Management of Hypertension. J Clin Hypertens 2:258–262
3. Burnier M, Santschi V, Favrat B, Brunner HR (2003) Monitoring compliance in resistant hypertension: an important step in patient management. J Hypertens [Suppl] 21:S37–S42
4. Burnier M, Schneider MP, Chiolero A, Stubi CL, Brunner HR (2001) Electronic compliance monitoring in resistant hypertension: the basis for rational therapeutic decisions. J Hypertens 19:335–341
5. Caro JJ, Speckman JL, Salas M, Raggio G, Jackson JD (1999) Effect of initial drug choice on persistence with antihypertensive therapy: the importance of actual practice data. Can Med Assoc J 160:41–46
6. Cramer JA, Mattson RH, Prevey ML, Scheyer RD, Ouellette VL (1989) How often is medication taken as prescribed? A novel assessment technique. JAMA 261:3273–3277
7. DiMatteo MR (2004) Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. Med Care 42:200–209
8. Fallab-Stubi CL, Zellweger JP, Sauty A, Uldry C, Iorillo D, Burnier M (1998) Electronic monitoring of adherence to treatment in the preventive chemotherapy of tuberculosis. Int J Tuberc Lung Dis 2:525–530
9. Haynes RB, McDonald HP, Garg AX (2002) Helping patients follow prescribed treatment: clinical applications. JAMA 288:2880–2883
10. Inui TS, Carter WB, Pecoraro RE (1981) Screening for noncompliance among patients with hypertension: is self-report the best available measure? Med Care 19:1061–1064
11. Jones JK, Gorkin L, Lian JF, Staffa JA, Fletcher AP (1995) Discontinuation of and changes in treatment after start of new courses of antihypertensive drugs: a study of a United Kingdom population. Br Med J 311:293–295
12. Schneider MP, Despland PA, Buclin T, Burnier M (2003) Evaluation of online telemonitoring of drug adherence: a pilot randomised, controlled study in patients with epilepsy. J Inf Technol Healthcare 1:419–435
13. Urquhart J (1997) The electronic medication event monitor. Lessons for pharmacotherapy. Clin Pharmacokinet 32:345–356
14. World Health Organization (2003) Adherence to Long Term Therapies:eEvidence for Action. World Health Organization, Geneva, pp 1–194