

APPLICATION OF ELECTRONIC DIARIES IN PATIENTS WITH SCHIZOPHRENIA AND BIPOLAR DISORDERS

Jochen Mutschler¹, Falk von Zitzewitz², Wulf Rössler¹ & Martin Grosshans³

¹Department of General and Social Psychiatry, Psychiatric University Hospital Zürich, Zürich, Switzerland

²Medical Practice, Ludwigsburg, Germany

³Department of Addictive Behavior and Addiction Medicine, Central Institute of Mental Health, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany

received: 5.2.2012;

revised: 29.3.2012;

accepted: 12.4.2012

SUMMARY

Background: Despite the dissemination of second generation antipsychotics for schizophrenia and bipolar disorder, outcomes remain suboptimal, largely due to poor treatment and drug adherence. The primary aim of the current study was to assess the tolerability, validity and feasibility of the pocket-sized electronic diary Medicus[®].

Subjects and methods: Our case observations attempted to evaluate eighteen patients suffering from schizophrenia and bipolar disorder. All of the patients were treated with the second generation antipsychotic quetiapine. We followed them up in two German medical centers over two years.

Results: The present results display an improvement of mood-stability in all patients treated with quetiapine. All patients were in regular contact to their psychiatrist over a period of 24 months. A complete description of the coherences between the symptoms was essential for estimation, which was conducted by Medicus[®]. Moreover, Medicus[®] seem to be useful for improving compliance within a medication regimen.

Conclusions: Although uncontrolled case observations can only be interpreted with caution, Medicus[®] seems to deserve further investigation and may hold the potential to optimize treatment and drug adherence in patients suffering from schizophrenia and bipolar disorders.

Key words: quetiapine - electronic diary - schizophrenia - bipolar disorders - drug compliance

* * * * *

INTRODUCTION

Outcomes in antipsychotic treatment of bipolar disorders and schizophrenia with drugs remains sub-optimal, mainly due to poor treatment and drug adherence (Goff et al. 2011, Kane 2011, Loga-Zec & Loga 2010). Reduced compliance with antipsychotic medication increases relapse and rehospitalization rates in patients with schizophrenia and bipolar disorders (Laan et al. 2010). The most frequently reasons patient-related factors contributing to the partial compliance are lack of insight into the need for prophylactic medication, lack of insight/denial of illness, feeling embarrassed at taking medication every day, needing someone to remind them to take their medication, cognitive problems, and living conditions inappropriate for compliance (Beck et al. 2011). Main strategies to improve compliance derived from these patient-related factors could be psycho-education and regular drug reminders (Goff et al. 2010, Pitschel-Walz et al. 2011). However, therapist-related factors are also important to improve drug compliance (Dolder et al. 2003, Mutschler et al. 2011, Mutschler et al. 2012). Therefore precise estimates of the current symptoms of psychotic disorders are necessary to evaluate and adapt antipsychotic treatment comprehensively (Agyapong et al. 2009). Relying on recall of symptoms form patients does not allow a longitudinal assessment in naturalistic environments, and fail to incorporate the

multidimensional nature of psychotic symptoms. Electronic diary methods, using real-time data capture, are a tool to serve with those difficulties (Burton et al. 2007, Piasecki et al. 2007). Electronic diaries minimize recall bias by enabling collection of real-time data from patients. Moreover, electronic diaries can remind patients to take their medications by a ring tone (Burton et al. 2007, Piasecki et al. 2007).

However, research on the use of electronic diaries in patients suffering from schizophrenia and bipolar disorders is limited. In this case series the validity and feasibility of the pocket-sized electronic diary Medicus[®] was examined in patients suffering from schizophrenia and bipolar disorders and being treated with the second generation antipsychotic quetiapine. The Medicus[®]-system was sought to determine the ability of the diary to detect mood-instability and improve individual drug compliance.

SUBJECTS AND METHODS

Subjects

All eighteen patients (10 males, 8 females; aged between 18 and 65 years) fulfilled the diagnostic criteria for schizophrenia and bipolar disorder according to ICD-10 and DSM IV, and did not suffer from any other psychiatric disorder (clinical interview by a psychiatrist)

or addictive disorder (except tobacco dependence). We present data of a retrospective case study of persons with schizophrenia or bipolar disorder. Patients with one of the mentioned diagnosis were consecutively asked, if they were willing to use the electronic diary. There were no exclusion criteria. According to the local ethics committee it is permitted to retrospectively analyze anonymous clinical data for research purposes. All patients gave written informed consent.

Medication

All patients were treated weekly to monthly by a psychiatrist in an outpatient setting. Initially, we only intended to observe the patients for 12 months, however, all of them visited our outpatient department regularly up to 24 months. Therefore, we decided to report the full-length observation time. We started quetiapine with 100 mg/day in the evening, dosage adjustment was done according to the clinical effect. Since sedation in quetiapine increases with reduction of dosage (clinical experience), we reduced the dosage in increments of 25 mg/day till sleep was reported to be good. In contrast, we increased dosage up to 200 mg/day in increments of 25 mg/day if the patient reported sleepiness in the daytime. The dosage was adjusted according to clinical response targeting at about 200 mg per evening and ranged from 100 to 200 mg/day.

Electronic diary

Current mood and three sub-classes of mood disorder (tiredness, agitation and anxiety) were assessed by Medicus[®]. Before they were recruited, physician assistants instructed the participants in using the electronic diary-system.

The system was individually programmed with the drug dosages and therapy times of every participant. The patients were reminded by a ring tone when it was time to take the next dosage of quetiapine. Additionally, the participants documented their medication intake as well as their mood-qualities by pressing the keys on the system. Medicus[®] is endowed with four buttons: M documents medication intake, W symptoms and two buttons document diverse steps of condition. Up to 11 degrees are possible. In this study eight steps (--, -, (-), 0, (+), +, ++ and +++) were set to acquire the degree of patient condition. Time and date were automatically registered. The patients' condition and its intensity could be captured at any time. The measured data were visualized by graphics on a computer screen. Compliance and results of treatment were viewable at any point of the treatment. Further details on Medicus[®] are described at <http://medicus.eu/>. All participants gave informed consent.

Statistical analysis

Descriptive statistics are given when appropriate (mean \pm SD).

RESULTS

After a two-year-period of monitoring, the results of this investigation showed that the choice of motivated physician assistants offered the possibility for individuals with schizophrenia or bipolar disorders to use Medicus[®] without problems. The recording-procedures worked well and the participants report that the device is easy to handle. The recorded data gave important insights in the process of disease and could be immediately statistically analyzed by the computer system. A continuous observation of the individual symptoms and drug side effects was possible. The results offer an improvement in mood by treatment with quetiapine. Additionally, some participants of this study suffered from schizophrenia with severe mood swings. By using Medicus[®] data quetiapine dosage was adjusted which was followed by a reduction of mood swings and a stabilized affect. For details see Figure 1 (this example was elected, because it demonstrates a typical course) and Table 1.

In the patients observed, and treated with quetiapine, we found a good clinical overall-response and no serious adverse events have been recorded during the course of the study. As expected, the most prominent adverse event of quetiapine was tiredness and sedation in particular during daytime. It should be noted that in each case, a few weeks after the start of quetiapine and adjustments of the daily dosage administered, tiredness and/or sedation disappeared. Furthermore, our data display good tolerance and safety.

DISCUSSION

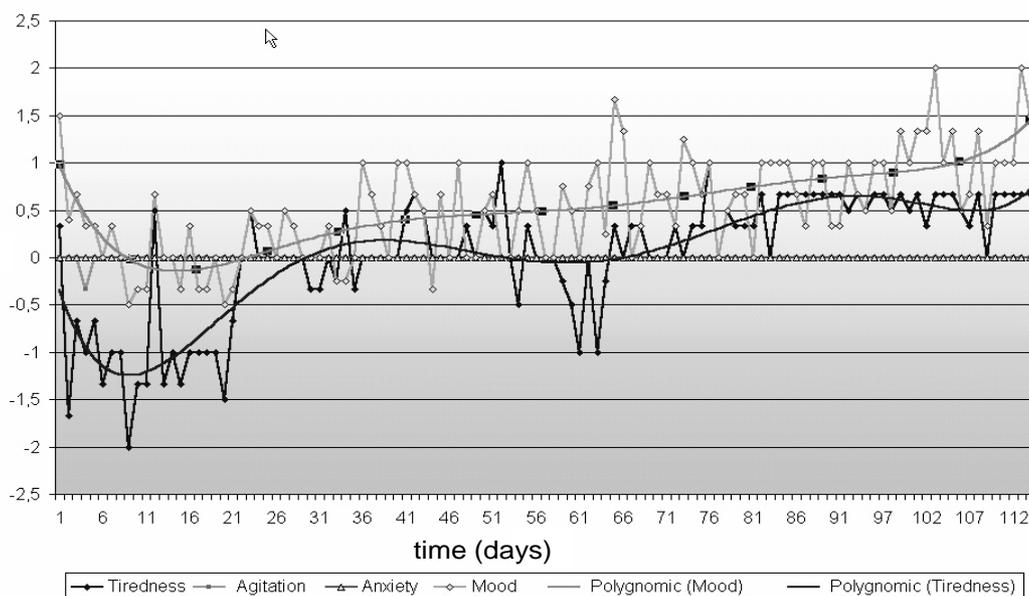
The present study evaluated the feasibility of using a specially designed computerized device, Medicus[®], for the treatment of patients with schizophrenia and bipolar disorders. Our data suggest that many patients are willing and able to use this kind of treatment-supporting technology.

Although many of the participants had never used computers, and many had cognitive limitations, all subjects were successfully trained to use Medicus[®], and were able to use the device on their own at home. This suggests that socioeconomic status, cognitive difficulties, and other variables associated with schizophrenia and bipolar disorders are not limiting factors in using computer devices specifically designed for monitoring patients.

Medicus[®] was useful to improve compliance with medication regimens. All participants could be followed up two years. The patients in this study reported taking their medication more regularly, which is likely to be a result of the monitor's prompting. However, if patients finally took their medications more regularly has not been verified and has to be proven in a future study (e.g., by measuring plasma levels of the medication).

Table 1. Cross-sectional illustration of the subjective scores, indicated the manifestation of the degree of the different emotional states (-- = severe symptoms; - = mild symptoms; 0 = no symptoms/balanced emotional state, + = good; ++ = very good)

Patient	Mood	Tiredness	Agitation	Anxiety
1	+	++	+	++
2	+	-	+	++
3	+	-	++	++
4	+	+	+	+
5	--	+	--	--
6	+	-	+	+
7	++	-	++	-
8	+	++	--	0
9	0	+	+	0
10	+	--	-	0
11	-	--	-	-
12	0	0	0	0
13	(-)	(-)	--	-
14	--	-	+	+
15	++	++	-	-
16	+	++	-	-
17	-	--	--	-
18	++	(-)	(+)	0



The y-axis represents a subjective impression of the different emotional states: -2= severe symptoms; -1= mild symptoms; 0 = no symptoms/balanced emotional state, 1= good emotional state; 2= very good emotional state. On the x scale the recorded time period in days is plotted. A complete description of all parameters was essential for evaluating the coherence of the parameters. Medicus[®] visualized the process in disease and included all parameters. Figure 1 shows an example.

Figure 1. Graphic demonstration of all parameters in patient 8 (paranoid schizophrenia). For evaluation the coherence between mood and tiredness we used polygnomic demonstration

The monitor maybe an effective tool for preventing or reducing relapse in chronic diseased patients, however, this also has to be proven in future studies. It is well known that drug non-compliance is one important factor contributing to the maintenance of

schizophrenia or bipolar disorder (Goff et al. 2011, Laan et al. 2010).

During the trial, if individual symptoms increased, data were reported immediately to the clinical staff. Therefore, clinical interventions were timely, and

targeted the specific symptoms reported by patients. This process allowed clinicians to be efficient and effective and may have prevented relapses among the participating patients.

The combination of elements offered in this study - receiving patient information about symptoms, monitoring the symptoms, and responding quickly to changes - may be particularly helpful for patients with schizophrenia, bipolar disorders or other illnesses in which timely intervention is a key factor in preventing or reducing relapses. The ability to provide rapid, targeted interventions may also be helpful in clinical drug trials, to promote patient adherence to their protocol, and complete the trial more promptly.

An important aspect of this study was the daily transmission of educational facts about the disease and medications. Consequently, the majority of participants reported having learned more about schizophrenia, bipolar disorders, and medication. Furthermore, participants gained increased awareness of the association between individual symptoms and medication adherence, potentially increasing future adherence to medication regimens.

Almost all of the participants in this observation report positive experiences with the Medicus[®]-system. It is likely that patients who believe in the efficacy of the Medicus[®]-system will continue to use it device even during difficult episodes (e.g., symptom exacerbations, personal problems, technical difficulties with the equipment, or simply boredom with the routine). Furthermore, patients who are content with this medical system are more likely to convey these feelings to other individuals suffering from similar diseases. Word-of-mouth plays an important role in engaging potentially resistant patients in a new process, especially in inner city clinics.

The current findings support the use of Medicus[®] not only for clinical practice, but also for future clinical drug trials. Current methods in clinical trials to monitor participants and collecting data often rely upon paper and pencil diaries and/or pill counts to assess parameters like symptom response, side effects, adverse events, and medication compliance. These methods lack the accuracy of a real time data capture, and the daily dose-response monitoring capabilities of a system like Medicus[®]. Traditionally, participants in clinical trials on schizophrenia or bipolar disorders are being instructed with written protocols how to take part in the study. But many of those study participants suffer from cognitive problems which may be a bias in later data analyses, therefore a simple and reliable data recording system might improve the efficacy of this kind of studies.

The next, more sophisticated generation of this system, Medicus II[®] will contain better documentation capabilities in order to evaluate polypharmacological treatment and dose-response-relationships. However, some limitations the investigation presented here should be mentioned. The number of cases is low and we did

not recorded data from a control group. Furthermore, psychopathology was not assessed with standardized questionnaires. One might speculate that the electronic device per se might have an impact on the clinical outcome and compliance. Thus, we strongly recommend controlled clinical trials to further evaluate our preliminary findings.

CONCLUSION

The results of this preliminary study suggest that the use of a specialized electronic device is feasible in clinical monitoring, and in the treatment of schizophrenia and bipolar diseases. All participating patients and clinicians described the system as useful, easy to handle, satisfying, and educational. In addition, future studies should expand the current data by including other populations from a variety of perspectives such as medication adherence, symptom management and education.

Acknowledgements: None.

Conflict of interest : None to declare.

REFERENCES

1. Agyapong VI, Nwankwo V, Bangaru R, Kirrane R: Sources of patients' knowledge of the adverse effects of psychotropic medication and the perceived influence of adverse effects on compliance among service users attending community mental health services. *J Clin Psychopharmacol* 2009; 29:565-70.
2. Beck EM, Cavelti M, Kvrđic S, Kleim B, Vauth R: Are we addressing the 'right stuff' to enhance adherence in schizophrenia? Understanding the role of insight and attitudes towards medication. *Schizophr Res* 2011; 132:42-9.
3. Burton C, Weller D, Sharpe M: Are electronic diaries useful for symptoms research? A systematic review. *J Psychosom Res* 2007; 62:553-61.
4. Dolder CR, Lacro JP, Leckband S, Jeste DV: Interventions to improve antipsychotic medication adherence: review of recent literature. *J Clin Psychopharmacol* 2003; 23:389-99.
5. Goff DC, Hill M, Freudenreich O: Strategies for improving treatment adherence in schizophrenia and schizoaffective disorder. *J Clin Psychiatry* 2010; 71 (suppl 2):20-6.
6. Goff DC, Hill M, Freudenreich O: Treatment adherence in schizophrenia and schizoaffective disorder. *J Clin Psychiatry* 2011; 72, e13.
7. Kane JM: Improving treatment adherence in patients with schizophrenia. *J Clin Psychiatry* 2011; 72, e28.
8. Laan W, Does Y, Sezgi B, Smeets HM, Stolker JJ, Wit NJ, Heerdink ER: Low treatment adherence with antipsychotics is associated with relapse in psychotic

- disorders within six months after discharge. *Pharmacopsychiatry* 2010; 43:221-4.
9. Loga-Zec S & Loga S: Antipsychotics and the quality of life of schizophrenic patients. *Psychiatr Danub* 2010; 22:495-497.
 10. Mutschler J, Dirican G, Gutzeit A, Grosshans M: Safety and efficacy of long-term disulfiram aftercare. *Clin Neuropharmacol* 2011; 34:195-8.
 11. Mutschler J, Eifler S, Dirican G, Grosshans M, Kiefer F, Rössler W, Diehl A: Functional social support within a medical supervised outpatient treatment program. *Am J Drug Alcohol Abuse* 2012 (Epub ahead of print).
 12. Piasecki TM, Hufford MR, Solhan M, Trull TJ: Assessing clients in their natural environments with electronic diaries: rationale, benefits, limitations, and barriers. *Psychol Assess* 2007; 19:25-43.
 13. Pitschel-Walz G, Gsottschneider A, Frobose T, Kraemer S, Bauml J, Jahn T: Neuropsychology of psychoeducation in schizophrenia : Results of the Munich COGPIP study. *Nervenarzt* 2011 [Epub ahead of print].

Correspondence:

Jochen Mutschler, MD
Department of General and Social Psychiatry, Psychiatric University Hospital Zürich
Militärstrasse 8, P.O. Box 1930, 8021 Zürich, Switzerland
E-mail: jochen.mutschler@puk.zh.ch