A short message service (SMS)-based strategy for enhancing adherence to antipsychotic medication in schizophrenia

Jose Manuel Montes [a], Esteban Medina [b], Manuel Gomez-Beneyto [c], Jorge Maurino [b],*

[a] Department of Psychiatry, Hospital Universitario del Sureste, CIBERSAM, Madrid, Spain
[b] AstraZeneca Medical Department, Madrid, Spain
[c] Department of Psychiatry, School of Medicine, University of Valencia, Valencia, Spain

ARTICLE INFO

ABSTRACT

Background: The aim of this study was to assess the impact of a short message service (SMS)-based strategy on adherence to antipsychotic treatment.
Methods: A multicentre, randomised, open-label, controlled, 6-month study with clinically stabilised outpatients with schizophrenia was conducted. The patients assigned to the intervention received daily SMS reminders to take their medication for 3 months. Self-reported medication adherence was determined using the Morisky Green Adherence Questionnaire (MAQ). Secondary outcomes were severity of illness, attitude towards medication, insight into illness and health-related quality of life.
Results: A total of 254 patients were analysed. A significantly greater improvement in adherence was observed among patients receiving SMS text messages compared with the control group. The mean change in MAQ total score from baseline to month 3 was –1.0 (95% confidence interval (CI) -1.02, -0.98) and -0.7 (95%CI -0.72, -0.68), respectively ($P=0.02$). Greater improvement in negative, cognitive and global clinical symptoms at month 3 was observed. Attitude towards medication also significantly improved across the study in the intervention group versus the controls.
Conclusions: An SMS-based intervention seems feasible and acceptable for enhancing medication adherence. Further studies are needed to confirm whether this kind of intervention could be a complementary strategy to optimise adherence in schizophrenia.

© 2012 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Non-adherence to antipsychotic treatments is still an enormous challenge for clinicians in the management of patients with schizophrenia (Velligan et al., 2009). Partial and non-adherence to treatment are associated with poorer prognoses, higher risk of relapse and hospitalisation and suicide attempts (Ascher-Svanum et al., 2006; Leucht et al., 2006). The mean adherence rate with antipsychotic medications is 58%, with a range from 24% to 90% (Cramer and Rosenheck, 1998). Many factors contribute to partial and non-adherence in schizophrenia, including poor insight, a negative attitude towards medication, substance abuse and disorganisation (Lacro et al., 2002; Liu-Seifert et al., 2010).

Different strategies have been used to improve adherence to treatment, including patient and family psychoeducation, motivational interviewing, cognitive and behavioural approaches, assertive community models and other strategy combinations (Patterson et al., 2008; Julius et al., 2009; Goff et al., 2010; Barkhof

et al., 2012). In addition, behavioural components such as reminders, self-monitoring tools, cues or reinforcements have proved to be useful, easy to implement and do not interfere with daily clinical practice (Dolder et al., 2003; Montes et al., 2011). Nevertheless, no specific intervention has demonstrated overwhelming success in improving adherence (Barkhof et al., 2012).

Internet and cell-phone services recently have been implemented to optimise communication between health-care providers and patients (Patrick et al., 2008). New technologies may be a powerful tool to be used as a method for reminding patients to take their medication (Wangberg et al., 2008; Borzekowski et al., 2009; Christensen and Hickie, 2010). Nowadays, mobile devices are extensively used among the population and have shown to be feasible and acceptable approaches for interventions in chronic physical illnesses, such as arterial hypertension, diabetes, malaria chemoprophylaxis or human immunodeficiency virus (HIV) anti-retroviral treatment, as well as to improve compliance with hospital/outpatient appointments (Patrick et al., 2008; Smith et al., 2010). Cell phones incorporate a short message service (SMS) for sending text messages, constituting a cheap, low time-consuming and discreet tool for communication (Patrick et al., 2008; Depp et al., 2010; Ehrenreich et al., 2011; Harrison et al., 2011; Mäkelä et al., 2010; Van den Berg et al., 2011). SMS text

* Corresponding autor at: AstraZeneca Medical Department, Parque Norte. Edificio Roble, Serrano Galvache, 56. 28033 Madrid, Spain
E-mail address: jorgealejandro.maurino@astrazeneca.com (J. Maurino).

messages used to remind patients with schizophrenia and bipolar disorder to take their medication have shown promising results in a non-randomised pilot study (Van Gent and Knoppert Van Der Klein, 2010). Pijnenborg et al. (2010) recently published a randomised trial to assess the efficacy of SMS messages in the cognitive rehabilitation of 62 patients with schizophrenia or related psychotic disorders. Patients achieved more of their goals in daily life. However, prompting with SMS did not lead to a significant increase in therapeutic adherence. Preliminary findings indicate that most patients are willing to use this method of communication and are able to do so with few problems (Spaniel et al., 2008; Humphrey Beebe et al., 2010; Pijnenborg et al., 2010).

The primary aim of this study was to assess the efficacy of sending daily treatment reminders via SMS over 3 months for adherence to antipsychotic medication among outpatients with schizophrenia. We also assessed the impact on other outcome measures, including attitude towards medication, insight into illness, clinical severity and health-related quality of life.

2. Materials and methods

A prospective, randomised, open label, controlled, 6-month study was conducted in 56 outpatient psychiatric centres throughout Spain. These facilities were nominated for their good practice by researchers and experts in psychiatry community care. The study was approved by the institutional review board of the Fundació Catalana dʹHospitals (Barcelona, Spain) (Clinical Trial Registry #NCT00873249). Data were collected from April 2009 to February 2010.

2.1. Subjects

The criteria for patient recruitment were: 18–65 years of age, a diagnosis of schizophrenia according to the Diagnostic and Statistical Manual, fourth edition, text revision (DSM-IV-TR), clinically stable (operationalised as having had either any change in severity or new treatments initiated in the last 6 months), a single oral antipsychotic medication, follow-up as an outpatient, at least one affirmative answer (indicating suboptimal medication adherence) to the Morisky Green Adherence Questionnaire (MAQ) and availability of a cell phone capable of receiving SMS messages.

Those patients receiving long-acting injectable antipsychotic treatment were excluded.

After a complete description of the study to the participants, written informed consent was obtained. Patient confidentiality was maintained, since no identifying data were recorded in the study documentation.

Investigators included the first five consecutive patients that met the inclusion criteria for participating in the study. Competitive recruitment was established among centres. Randomisation codes were computer generated by our statistician and sealed in envelopes labelled with consecutive numbers. The envelopes were opened by the investigator in an ascending order and patients were allocated to the intervention or control group (CG).

2.2. SMS-based intervention

Participants assigned to the intervention received daily SMS reminders on their cell phones to take their medication for 3 months. Group assignment was based on a 1:1 randomisation scheme. The SMS text received by the patients in the intervention group (SMSG) said: "*Please remember to take your medication*". Patients could choose between receiving the message at either 11 a.m. or 2 p.m.

Patients assigned to the CG did not receive SMS messages or any other more intensive approach for increasing adherence than standard of care during the study period.

Between months 3 and 6, all patients were followed-up without receiving SMS messages.

An automated SMS messaging service integrated into a website was created ad-hoc for the study. Participating investigators needed a username and password to access the website and to include the patient cell-phone number and the date of starting the intervention. During each personal website visit, the investigator could check the current status of SMS reception for each patient.

2.3. Outcome measures

Assessments took place at baseline and at 3 and 6 months after randomisation. The primary outcome measure was the change from baseline to month 3 in the MAQ (Morisky et al., 1986) total score compared with the CG. The MAQ addresses how patients may fail to take medication as prescribed due to forgetfulness, carelessness, stopping the drug when they feel better or stopping treatment because they believe it makes them feel worse. It is a self-rated questionnaire consisting of four questions with yes/no answers. When the answer indicates a negative adherence issue, a score of 1 is recorded. The total score ranges from 0 (good adherence) to 4 (poor adherence). MAQ score at a threshold of ≥ 1 may be a valuable tool for identifying non-adherent patients in a cohort where adherence is low (Erickson et al., 2001). The scale has good levels of validity and reliability, and was initially developed to assess compliance in patients with arterial hypertension and occasionally in the context of psychiatric disorders (Gray et al., 2006).

Secondary outcome measures included the change from baseline to month 6 in the MAQ total score (3 months after stopping the SMS-based intervention). Clinical severity was assessed using the Clinical Global Impression – Schizophrenia scale (CGI–SCH) (Haro et al., 2003). The CGI-SCH consists of two categories: severity of illness (CGI–SCH–SI) and degree of change (CGI–SI–DC). The SCH category evaluates the situation during the week prior to the assessment, while the DC category evaluates the change from the previous evaluation (or from the phase preceding the trial). Each category contains five different ratings (positive, negative, depressive, cognitive and global), which are evaluated using a 7-point ordinal scale.

Attitude towards medication was assessed using the Spanish adaptation of the 10-item Drug Attitude Inventory (DAI-10) (Robles et al., 2004). The DAI-10 is a self-rated scale developed to measure subjective responses and attitudes of patients with chronic schizophrenic towards maintenance antipsychotic treatment. A positive total score means a positive subjective attitude (Hogan et al., 1992). Insight was measured using the first three items of the Scale to Assess Unawareness of Mental Disorder (SUMD) (Amador et al., 1994; Ruiz et al., 2008). These items assess subject general insight into having a mental disorder, the effects of medication upon the disorder and general understanding of the consequences of the disorder, respectively. The items are rated on a 5-point Likert scale (1='aware' to 5='unaware'), with higher scores indicating poorer awareness. Health-related quality of life was assessed using the second part of the Spanish version of the EuroQol (EQ-5D) (Badia et al., 1999). This is a self-administered instrument with proven validity for assessing quality-of-life differences in patients with schizophrenia of different degrees of severity (König et al., 2007). EQ-5D part two is a visual analogue scale (VAS) ranging from 0 ('worst possible state of health') to 100 ('best possible state of health').

2.4. Statistics

A sample size of 286 patients was sought to detect differences in a mean MAQ total score of 0.5 between baseline and 3–6-month visits, achieving 80% of statistical power and assuming a standard deviation of 1.5 with a two-sided alpha level of 0.05 (Gray et al., 2006). With an estimated 20% attrition rate, this required a recruitment plan of 360 patients (180 in the intervention and 180 in the CG) at baseline.

To ensure that each participant in the SMS group was properly exposed to the intervention, our study protocol established a cut-off point according to opening or not of the SMS text messages by the patient. We hypothesised that a certain number of patients could have problems interacting with mobile phones due to poor motivation, disorganised daily living activities, etc. Patients with more than 7 consecutive days without properly receiving the SMS reminders on their cell phones were classified as 'not properly exposed' to the intervention, and excluded from the analysis.

Descriptive statistics were used to present patient demographics and clinical information. Independent samples *t*-tests and chi-square analyses were used to compare characteristics between the two study groups. To analyse the changes during the study, a 'last observation carried forward' (LOCF) approach was used, including those patients with a baseline evaluation and at least one posterior evaluation. A two-tailed significance level of 95% was considered for all analyses.

A stepwise linear regression model was constructed including all variables that were significant ($p < 0.2$) in the bivariate analysis to evaluate the association of other covariates in the improvement of adherence as measured by the changes in MAQ total score between visits. All statistical analyses were performed using Statistical Analysis Software (SAS) v.8.02 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Baseline characteristics

A total of 340 patients were included in the study. Twenty patients were excluded from the analysis due to major protocol deviations. An additional group of 66 patients were classified as 'not properly exposed' to the intervention and also excluded.