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ScienceDirect

Comprehensive Psychiatry 55 (2014) 33–39

COMPREHENSIVE PSYCHIATRY

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Should full adherence be a necessary goal in schizophrenia? Full versus non-full adherence to antipsychotic treatment

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Abstract

There is solid evidence of negative consequences of non-adherence in schizophrenia, and recently adherence has been defined as taking more than 80% of prescribed medication. However, the clinical relevance of different degrees of adherence in adherent patients has not been studied. We evaluated sociodemographic, clinical, treatment-related and psychopathological variables in 78 adherent outpatients with schizophrenia, who were classified into two groups: full-adherence (100% adherence) and non-full adherence (80–99.9%). Adherence was evaluated using electronic monitoring (MEMS®), and the injection record in case of injectable antipsychotics. Non-full adherence patients showed more extensive delusions and guilt feelings, as well as trends toward greater somatic concern, disorientation, general psychopathology, and lower number of prior psychiatric hospitalizations. These finding suggest that the 'fullness' of adherence to antipsychotic treatment is a relevant issue, impacting the psychopathological state of adherent patients with schizophrenia. We found that a large proportion of patients can achieve full adherence, and while 'adherence' is an appropriate objective to be pursued with non-adherent patients, 'full adherence' should be the goal among adherent patients.

1. Introduction

Although potentially preventable, non-adherence is still very frequent in psychiatry as well as in the general medical practice [1]. Reported non-adherence rates in schizophrenia range between 41.2% and 49.5% [2]. The clinical consequences of non-adherence include psychotic relapse [3], hospitalization [4,5], worse prognosis [6], higher risk of suicide attempts [5], completed suicide [7], and worsening of psychopathology [1], functional performance and quality of life [2], as compared to adherence to treatment.

Major limitations are found in the related literature, such as the lack of a suitable evaluation method [8,9] or the difficulty of establishing a conceptual and operative definition [10,11]. These limitations have led to marked heterogeneity across studies [10,11]. In this context, the Medication Event Monitoring System (MEMS®; Aprex Corp., Fremont, CA) is considered to be the "reference standard" evaluation method [9,12,13]. It consists of a medication bottle cap with a microprocessor that records the occurrence and time of each bottle opening, thus allowing for subsequent computer analysis.

Current criteria for defining non-adherence are less than 80% of prescribed medication taken or gaps in medication of at least 7 days [14]. Most adherence studies are based on dichotomous designs that compare adherent versus non-adherent patients [4]. This approach has resulted in considerable knowledge of the clinical consequences of non-adherence [14]. However, to our knowledge, there are no studies exploring the possible clinical relevance of different degrees of adherence among adherent patients, according to the current definition (i.e. taking 80% or more of prescribed medication) [14].

In this context, the objectives of the present study were:

1. To evaluate possible differences between adherent patients with schizophrenia on an ambulatory basis who show full adherence versus non-full adherence.
2. To evaluate the prevalence of full adherence among ambulatory patients with schizophrenia.

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http://dx.doi.org/10.1016/j.comppsych.2013.09.005

2. Methods

2.1. Subjects

The sample used in this study was obtained from the total sample used in our earlier study, published elsewhere [15]. All patients were diagnosed with schizophrenia according to the ICD-10 criteria, and were consecutive patients attending our Mental Health Unit (MHU) in Gran Canaria, Spain, between May 1 and December 31, 2006.

The present observational study only included those patients who had adhered to the treatment throughout the evaluation period. The sample finally included 78 patients, who were classified into two groups according to their degree of adherence to antipsychotic treatment: full adherence (100% adherence; n = 39) and non-full adherence (80–99.9% adherence; n = 39).

Participating patients were informed about the procedures and the objectives of the study, and they signed a written consent form. This study was previously approved by the Research Ethics Committee of the Insular University Hospital of Gran Canaria.

2.2. Procedure

Adherence was evaluated for a three-month period. Adherence to oral antipsychotics was evaluated using the MEMS device. Adherence to long-acting or depot injectable antipsychotics (henceforward called "injectable") was evaluated through the injection record on the patient's medical record. All injections were administered at our MHU.

Following recent recommendations [13,14], the adherence threshold was established at 80% of the prescribed medication. Thus, we defined adherence to oral antipsychotic treatment as a number of MEMS bottle-cap openings (independently of the time of the day) at least equal to that of the prescribed regime, recorded on at least 80% of the evaluation days. Excessive opening was not considered to be non-adherence. Adherence to injectable antipsychotic was defined as correct administration of at least 80% of prescribed injections. Administration was considered correct if it took place within three days before or after the scheduled date. For the patients with oral plus injectable treatment, adherence was calculated through the mean of both adherence rates.

Baseline evaluation included: sociodemographic variables (age, sex, marital status, educational level, cohabitation, type of residence); clinical variables (length of illness, current and past substance use or abuse, number of prior hospitalizations, time since last hospitalization); treatment-related variables (type of treatment, type of antipsychotic drug, antipsychotic dose regimen, other psychotropic drugs, number of psychotropic tablets per day); and psychopathological variables. Psychotic symptoms, negative symptoms and general psychopathology were evaluated with the validated Spanish version [16] of the Positive and Negative Syndrome Scale (PANSS) for Schizophrenia [17], and insight was evaluated with the first three items of the Amador Insight Scale [18]. The scale used was the validated Spanish version [19]. Regarding the PANSS scale, we included as variables the positive, negative and general psychopathology subscales, as well as each of the individual items. For patients on injectable treatment, the various reasons for prescribing this type of therapy were evaluated: previous non-adherence, dosing convenience or adverse effects associated with oral dosing.

2.3. Statistical analysis

The following analyses were conducted:

Continuous variables were described by central tendency and dispersion measures: mean, standard deviation, median and range. The one-sample Kolmogorov-Smirnov test was used to verify normality of the distributions. Categorical variables were expressed as absolute and relative frequencies for each category.

Categorical variables were compared between full adherents and non-full adherents using the two tailed Chi-square test and the Fisher's exact test where necessary. Continuous variables were compared using two tailed Student's t-test if the normality hypothesis was fulfilled or the two tailed Mann Whitney U-test if it was not.

Logistic regression models were constructed to identify factors independently associated with the rate of adherence (full adherence or non-full adherence). The model was constructed starting with a complete model and then adjusted using a stepwise procedure based on the likelihood ratio test until obtaining the best model.

Statistical significance was considered as $P < 0.05$, and trend toward significance was defined as $P = 0.05–0.1$. Statistical analyses were conducted with SPSS for Windows version 14.

3. Results

3.1. Characteristics of the sample

Table 1 summarizes the sociodemographic, clinical and treatment-related variables corresponding to the total sample of this study classified according to the type of treatment (oral, oral + injectable, and injectable). Within the patients with other psychotropics (n = 44), the number of patients was distributed as follows: antidepressants (n = 17), anxiolytics (n = 16), hypnotics (n = 21), anticholinergics (n = 7) and mood stabilizers (n = 3).

Full adherence was demonstrated for 39 patients, which accounted for 50% of the adherent patients, included in the present study (n = 78) and 40.2% of the whole sample evaluated in our original study (n = 97) [15]. Full adherence was found in 100% of the patients on injectable treatment alone, 50% in those on injectable + oral treatment, and 27.7% in those with oral treatment only. Non-full adherent patients showed a mean (SD) adherence rate of 95.4% (4.5).

The mean adherence rates in the adherent patients with injectable, injectable + oral, and oral treatment were 100%,