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Research report

Predictors of functional outcome after a manic episode

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ABSTRACT

Background: The identification of functional outcome predictors after acute episodes of bipolar disorders (BD) may allow designing appropriate treatment aiming at restoring psychosocial functioning. Our objective was to identify the best functional outcome predictors at a 6-month follow-up after an index manic episode.

Methods: We conducted a naturalistic trial (MANACOR) focusing on the global burden of BD, with special emphasis on manic episode-associated costs. We observed patients with BD seen in services of four hospitals in Catalonia (Spain).The total sample included 169 patients with chronic DSM-IV-TR BD I suffering from an acute manic episode who were followed-up for 6 months. In this subanalysis we report the results of a stepwise multiple regression conducted by entering in the model those clinical and sociodemographic variables that were identified through preliminary bivariate Pearson correlations and using total scores on the Functioning Assessment Short Test (FAST) at the 6-month follow-up as the dependent variable.

Results: Number of previous depressive episodes (Beta=3.25; t=3.23; p=0.002), presence of psychotic symptoms during the manic index episode (Beta=7.007; t=2.2; p=0.031) and the Body Mass Index (BMI) at baseline (Beta=0.62; t=2.09; p=0.041) were best predictors of functional outcome after a manic episode.

Limitations: The main limitations of this study include the retrospective assessment of the episodes, which can be a source of bias, and the 6-month follow-up might have been too short for assessing the course of a chronic illness.

Conclusions: Psychotic symptoms at index episode, number of past depressive episodes, and BMI predict worse outcome after 6 months follow-up after a manic episode, and may constitute the target of specific treatment strategies.

1. Introduction

Bipolar disorder (BD) is a highly prevalent (Catalá-López et al., 2013; Merikangas et al., 2011) and disabling disease (Huxley and Baldessarini, 2007; Judd et al., 2005; Rosa et al., 2008, 2009). Impairment in functional outcome is commonly observed even when patients are euthymic (Bonnín et al., 2010; Rosa et al., 2010; Tohen et al., 2000) and includes multiple areas of functioning (independent living, interpersonal relationships, occupational and educational achievement, recreational enjoyment and sexual activity) (Goldstein et al., 2009; Kauer-Sant'Anna et al., 2009; Rosa et al., 2009; Rosa et al., 2012). Many factors such as sociodemographic, clinical, pharmacological and neurocognitive variables have been associated with functional impairment (for a review see Sanchez-Moreno et al. (2009)).

Studying the factors associated with functional outcome after an acute episode is relevant because it could help to elucidate potential targets for both pharmacological and psychological treatments (Vieta, 2014). Our group already have performed a 6-month follow-up study using the Functioning Assessment Short Test (FAST) scale as

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the primary outcome in a sample of subsyndromal and syndromal patients with BD (Rosa et al., 2011). Nevertheless, in that study, acute patients were included regardless the polarity of the episode (both manic and depressive) and no multivariate analyses were performed in order to find predictive variables associated with functional outcome. Many studies have evaluated potential predictors of functional recovery after a manic episode, especially after a first manic episode (Conus et al., 2006; Jaeger et al., 2007; Kauer-Sant'Anna et al., 2009; Singh et al., 2000; Smith et al., 2014; Tohen et al., 2000; Torres et al., 2011), but when it comes to patients with multiple episodes the evidence is inconsistent. It is known that patients with first-episode bipolar disorder have better functioning that those with multiple episode at one-year follow-up (Rosa et al., 2012), but determinants of functional outcome in chronic patients still remain unclear. The main objective of the present prospective study was to evaluate the baseline clinical and sociodemographic variables that were significantly associated with functional outcome at 6-month follow-up after an acute manic episode in a sample of multiple episodes bipolar patients.

2. Method

2.1. Study design and participants

This is a subanalysis of a naturalistic trial (MANACOR) which aimed at describing the general burden and costs associated with manic episodes in bipolar patients from four hospitals in Catalonia: Hospital Clínic (Barcelona), Santa Maria Hospital (Lleida), Institut Pere Mata (Reus) and Xarxa Assistencial de Manresa (Manresa). The primary analysis (Hidalgo-Mazzei et al., 2015), combined prospective and retrospective data collection and focused on costs. Clinical data was captured prospectively as a part of the systematic assessment of the Barcelona Bipolar Disorders Program (Vieta, 2013) which was also adopted by the other hospitals involved in the study. Pre-planned subanalyses of the study involved the outcome of BD patients with mixed features (Reinares et al., 2015), pharmacological treatment (Grande et al., 2015), and functional outcome as it is reported in the current study.

In total, the study involved 169 patients with a manic episode, treated clinically and followed-up in four different psychiatric services from Catalonia, Spain. The study protocol was reviewed and approved by the ethical committee of each hospital. Inclusion in this study required meeting: (1) diagnostic criteria for bipolar disorder type I with an index/current manic episode according to DSM-IV-TR and having a Young Mania Rating Scale (YMRS) total score $\geq$ 15 (Colom et al., 2002; Young et al., 1978); (2) to be 18 years or older; (3) the present episode could have been handled in an inpatient or outpatient setting, depending on the patient's clinical severity and psychiatrist's decision. The study started in January 2011 and finished in December 2013.

2.2. Procedure and data collection

Sociodemographic information was extracted from the prospective database. Relevant information about the course of bipolar disorder was specifically reviewed and registered: age and polarity of the first and following episodes, suicide attempts and previous hospitalizations. Date, clinical information, employment-functional status and clinical assessments during the index manic episode were also collected as well as the clinical setting and treatment received.

At baseline and follow-up visits, patients were evaluated through standardized clinical measures, included in the bipolar disorders program protocol of each Hospital involved. The systematic follow-up consisted in periodic appointments (baseline; 1-month; 6-month follow-up) with expert psychiatrists which included a clinical interview and assessment of manic symptoms through the Spanish version of the YMRS and depressive symptoms with the 17-item Hamilton Depression Rating Scale (HAMD) (Hamilton, 1960; Ramos-Brieva and Cordero, 1986). The Spanish version of the Clinical Global Impressions Scale for Bipolar Disorders (CGI-BP) [CGI-BP-M (Spearing et al., 1997; Vieta et al., 2002)] was routinely used as a reference to assess the patient's global clinical state in addition to the FAST (Rosa et al., 2007) which evaluates global functionality. Functional recovery was defined as a FAST total scores $<$ 12. For further details of the study protocol, see Hidalgo-Mazzei et al. (2015).

2.3. Data analyses

Descriptive analyses of sociodemographic variables including age, gender, marital status and employment status, were conducted. Regarding clinical variables, family psychiatric history along with medical and psychiatric comorbidities, polarity of first episode, lifetime psychotic symptoms and rapid cycling were also analyzed through frequencies analyses. Variables related to history of bipolar disorder such as age of onset, number and type of episodes, and number of suicide attempts and hospitalizations/admissions were described by their means and standard deviations. Analyses involved preliminary Pearson bivariate comparisons of the factors associated with the dependent variable, which was the FAST total score at 6-month follow-up. Bivariate associations with qualitative variables were explored using Mann–Whitney U tests. Finally, all the baseline variables that appeared to be associated with the dependent variable, that showed a trend or have demonstrated to be related to functional outcome in previous literature underwent stepwise multiple regression to provide the beta standardized scores of the variables that best predicted FAST scores at 6-month follow-up.

3. Results

3.1. Sociodemographic and clinical characteristics

Of the total sample of 169 bipolar disorder I acute manic patients, 133 were hospitalized (78.7%) and 36 (21.3%) were treated in the outpatient units.

Mean age was 42.5 (12.7) years and men were slightly more prevalent than women (46.2%).

Table 1 shows the demographic and clinical variables of the sample.

At the 6-month assessment, 17% (n=29) of patients were functionally recovered (that is FAST total score $<$ 12). These patients were younger 38.5 (10.9) when compared to the non-functionally recovered group 43.9 (12.8) (p=0.03). Moreover, they presented lower BMI at baseline (23.9 vs. 27.1; p=0.005), fewer number of total episodes (5.1 vs. 8.2; p=0.02) and shorter illness duration (chronicity) (8.5 vs. 15.4; p $<$ 0.001). Both groups did not differ in terms of age at onset (30 vs. 28.5; p=0.47), presence of psychotic symptoms during the index manic episode (45% vs. 56%; p=0.26), or days of hospitalization (17.8 vs. 20.1; p=0.39).

Regarding mood symptomatology, 96 patients (57% of the initial sample) presented full remission from acute symptoms, operationalized as follows: HAMD $\leq$ 8 and YMRS $\leq$ 6. There were no differences in gender regarding symptomatic recovery.

3.2. FAST change and correlations with FAST total score at follow-up

FAST total score decreased significantly (t=8.64; df=147; p $<$ 0.001) from baseline 38.03 (12.3) to the end of follow-up 25.49 (13.8).

FAST total score at the end of follow-up significantly correlated with the following continuous variables collected at baseline: age