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Research report

Guidelines concordance of maintenance treatment in euthymic patients with bipolar disorder: Data from the national bipolar mania pathway survey (BIPAS) in mainland China

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ABSTRACT

Background: Although the treatment guidelines of bipolar disorders (BPD) have spread more than a decade, the concordance with evidence-based guidelines was typically low in routine clinical practice. This study is to present the data on the maintenance treatment of BPD in mainland China.
Methods: One thousand and twenty-three patients who had experienced a euthymia were eligible for entry into this survey on the maintenance treatment of BPD. Guidelines disconcordance was determined by comparing the medication(s) that patients were prescribed with the recommendations in the guidelines of the Canadian Network for Mood and Anxiety Treatments.
Results: Three hundred and sixty-four patients (35.6%) had not been prescribed with the maintenance treatment as guidelines recommendations, and 208 patients (20.3%) were prescribed with the antidepressants. A longer duration of BPD, a depressive episode at first onset, and a recent depressive or mixed episode significantly increased the risk for guidelines disconcordance and prescribing antidepressant. In contrast, a hospitalization history due to manic episode was associated with a significant decrease in the risk for guidelines disconcordance and prescribing antidepressant.
Limitation: This study was a cross-sectional and retrospective investigation based on medical records.
Conclusions: Considering the potentially hazardous effects of inappropriate treatment, individualized psychoeducational strategies for subjects with BPD are necessary to enhance treatment adherence and close the gap between guidelines and clinical practice in mainland China.

1. Introduction

Bipolar disorders (BPD) are chronic, recurrent, debilitating disorders with high lifetime prevalence and significant disease burden across different populations (Merikangas et al., 2007, 2011; Phillips et al., 2009). However, recent advances in pharmacological treatment for BPD remained quite modest. The treatment of bipolar depression is still a major challenge (Geddes and Miklowitz, 2013). Moreover, BPD is frequently unrecognized and misdiagnosed, particularly in patients presenting with their first-episode depression. These patients are often treated with inappropriate and costly regimens (Muzina et al., 2007; Hu et al., 2012; Xiang et al., 2013). There is evidence that greater provider adherence to treatment guideline recommendations was associated with a greater reduction in symptoms and greater improvement in the outcome of diseases (Dennehy et al., 2005; Bauer et al., 2009). For this reason, a number of treatment guidelines have emerged to aid clinicians to make clinical decisions for patients with BPD (American Psychiatric Association, 2002; National Collaborating Center for Mental Health, 2006; Shen et al., 2007; Grunze et al., 2009, 2010, 2013; Mok et al., 2011; Yatham et al., 2013).

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Although the timeline of these guidelines has spread more than a decade, the concordance with evidence-based guidelines in the treatment of BPD was typically low in routine clinical practice, and personal experience appeared in the foreground for the choice of therapies (Bauer et al., 2009; Dennehy et al., 2007; Perlis, 2007; Smith et al., 2008; Altinbas et al., 2011; Samalin et al., 2011; Paterniti and Bisserbe, 2013). The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) reported that the guideline concordant treatments were prescribed in 81.8% of mixed episodes, 81.9% of hypomanic/manic episodes, and 83.4% of depressive episodes (Dennehy et al., 2007). A more recent study in 113 individuals with BPD who were referred to a Mental Health Center from the community found that the rate of treatment not following the guidelines was 31.9% (bipolar I disorder: hypomania 42.9%, depression 16.7% and euthymia 28.6%; bipolar II disorder hypomania 77.8%, depression 8.5% and euthymia 62.5%) (Paterniti and Bisserbe, 2013).

There was no update on Chinese treatment-guidelines for BPD in mainland China since 2007. The Chinese Psychiatry Association conducted a nation survey (Bipolar Mania Pathway Survey, BIPAS) on the treatment of BPD during routine clinical practice in mainland China. As we reported before, the rate of guideline-disconcordant treatments on the acute treatment of mania or mixed episode and bipolar depression was 11.1% and 50.2%, respectively (Wang et al., 2014a, 2014b). This report is to present the data of BIPAS on the maintenance treatment of BPD in routine clinical practice in mainland China.

2. Methods

2.1. Subjects

The BIPAS study was conducted in 26 teaching hospitals (15 psychiatric hospitals and 11 psychiatric departments of general hospitals) across mainland China from the November of 2012 to the January of 2013. All procedures were reviewed and approved by the institutional review boards of Shanghai Mental Health Center and other participating institutions. Written informed consents were obtained from each participant before any study-related procedure was performed. Both inpatients and outpatients who presented with a previous or current manic episode were consecutively screened for the BIPAS study. Diagnosis of bipolar disorder was ascertained with *ICD-10* (International Classification of Disease—10 Edition) diagnostic criteria for bipolar affective disorder (Wang et al., 2014a, 2014b). The patient who had experienced a recent euthymia or a current euthymia after treatment was eligible for entry into this survey on the maintenance treatment of BPD. The euthymia was defined as not suffering from any significant mood disturbance more than two months judged by research psychiatrists according to *ICD-10.*

2.2. Clinical assessments

All patients who were enrolled in the study received a single-round survey with a structured form. During the screening visit, variables including gender, race, mood state at first onset and recent mood episode, current or past co-morbidity with mental disorders and/or physical disorders, family history of a mental disorder(s), hospitalization history due to manic episode, the age at study entry and at first onset, the duration of BPD, and the number of episodes in past year were obtained from the patients, their family members, and the medical records by research psychiatrists and research assistants. The prescribing information (name of psychotropic agents) for a recent mood episode and the maintenance treatment for a recent or a current euthymia was retrospectively obtained from patients' medical records. The collected psychotropic agents included mood stabilizers, antipsychotics, antidepressants, Chinese medicine, and benzodiazepines for treating mental symptoms. Medications for dealing with physical diseases or side effects related to psychotropic agents were not collected (Wang et al., 2014a, 2014b). The research psychiatrists and research assistants made a mutual check to avoid any variable missing.

2.3. Criteria: adherence to treatment guidelines

The Canadian Network for Mood and Anxiety Treatments (CANMAT) and the International Society for Bipolar Disorders (ISBD) guidelines for the management of patients with bipolar disorder updated in 2013 (Yatham et al., 2013) were considered for purposes of evaluating treatment concordant with guidelines. The use of CANMAT guidelines as "standard" was justified because there was no update on treatment-guidelines for BPD since 2007 and the CANMAT guidelines were commonly recommended during continuing medical education and clinical practice in mainland China. Among the available psychotropic agents for BPD in clinical practice in mainland China, mood stabilizer (lithium, lamotrigine and valproate) monotherapy and atypical antipsychotic monotherapy (olanzapine, quetiapine, risperidone long-acting injection, and aripiprazole) were considered as the first-line recommendations, adjunctive or combination therapy of atypical antipsychotics (olanzapine, quetiapine, risperidone or risperidone long-acting injection, aripiprazole and ziprasidone) with lithium or valproate, lithium plus valproate or lamotrigine, and olanzapine plus fluoxetine as the second-line recommendations. In this survey, the maintenance treatment with at least one agent or combination of the first- or second-line recommendations was considered as guidelines concordance, and the addition of benzodiazepines was considered reasonable. Therefore, other treatment option(s) was considered as guidelines disconcordance.

2.4. Statistical analysis

Demographics characteristics, clinical features and treatment options for the maintenance treatment were analyzed with descriptive statistics. A conditional logistic regression among variables by forward procedure was used to study independent predictors for treatment discontinuance, guidelines disconcordance and prescribing antidepressant. Adjusted odds ratios (OR) and 95% confidence intervals (95% CI) indicates the strength of the association between them and risk factors. All candidate variables entered the model were categorical variables. Continuous variables were divided into categories as their medians. Given the exploratory nature of the study, statistical significance was set at $\alpha=0.05$, two-tailed without adjustment for multiple comparisons.

The variables analyzed in the regression model included gender (male vs. female), mood state at first onset (hypomanic/manic episode vs. depressive episode), recent mood episode (hypomanic / manic episode vs. depressive episode vs. mixed episode), co-morbidity with mental disorder (no vs. yes), co-morbidity with physical illness (no vs. yes), family history of mental disorder (no vs. yes), hospitalization history due to manic episode (no vs. yes), age at study entry (≤ 35 years vs. >35 years), age at first onset (≤ 25 years vs. >25 years), duration of disease (≤ 6 years vs. >6 years), and the number of episodes (≤ 4 time vs. >4 time).

3. Results

3.1. Demographics and clinical characteristics of patients with BPD in maintenance treatment

Of the 3906 patients enrolled into the BIPAS study, 1023 patients were eligible for entry into this survey on the maintenance