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Research report

Diagnostic conversions from major depressive disorder into bipolar disorder in an outpatient setting: Results of a retrospective chart review

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ABSTRACT

Background: The aim of the study was to check the stability of a diagnosis of major depressive disorder (MDD) in an outpatient setting, as well as to assess the scope of diagnostic conversions into bipolar disorder (BD).

Methods: Retrospective chart review of 122 patients with a primary diagnosis of MDD.

Results: Diagnostic conversion from MDD into BD was noticed in 40 subjects (32.8%), 25 patients (20.5%) were treatment-resistant. Mean time to the conversion was 9.27 ± 8.64 years. A negative correlation between the age of illness onset and time to diagnostic conversion was observed (-0.41; $p < 0.05$). Earlier onset of MDD was associated with higher risk of diagnostic conversion (< 30vs≥ 30 years of age at onset: 69% vs 28%, $p=0.0001$; < 35vs≥ 35 years of age: 50% vs 25%, $p=0.0065$). Treatment-resistance was more prevalent in the BD conversion group (40% vs 11%; $p=0.0002$). Diagnostic conversion into BD was also related longer duration of treatment received, higher number of illness episodes, and higher number of hospitalizations.

Limitations: Retrospective design of the study.

Conclusions: The problem of diagnosis evolution from MDD to BD was observed in about 1/3 of patients, and was associated with treatment-resistance of depression, earlier onset of depression, longer time of treatment, higher number of depressive episodes and hospitalizations. The variables above may be a useful predictor of bipolar diathesis.

1. Introduction

Providing adequate differential diagnosis between major depressive disorder (MDD) and bipolar disorder (BD) remains an important clinical challenge. Misdiagnosis of BD may imply a variety of negative outcomes, such as inadequate use of antidepressants, greater number of recurrences, more lengthy episodes, and a higher level of social impairment (Perlis, 2005; Dudek and Siwek, 2012). As depression is the predominant phase of the latter disorder (Judd et al., 2002), patients presenting with bipolar syndromes are often misdiagnosed as suffering from MDD.

The rate of subjects with BD receiving inadequate diagnoses in mental health facilities is estimated to be as high as 20–60% (Benazzi, 2003; Manning et al., 1997; Perugi et al., 2000; Rybakowski et al., 2005; Akiskal et al., 2006a,b; Kim et al., 2008). National Depressive and Manic Depressive Association Survey (Hirschfeld et al., 2003) has revealed that as many as 69% of patients with BD had received improper diagnoses, with MDD being the most frequent one. Accordingly, significant delays in delivering correct diagnosis and treatment to those subjects are a widespread problem. Baethge et al. (Baethge et al., 2003) have found that the mean time from the onset of the initial BD symptoms to an adequate diagnosis is as long as 9.6 years. Some authors argue that approximately 40% of patients with BD are not diagnosed correctly at the initial presentation, about 2/3 of subjects belonging to this population receive proper diagnosis after 10 years, and there are about 3–4 incorrect clinical assessments prior to the establishment of the diagnosis of BD (Hirschfeld et al., 2003; Ghaemi et al., 2002). Other researchers have claimed that the 'way to a BD diagnosis' takes 7.5–8.9 years (Ghaemi et al., 1999) or 1.89–2.98 years (Li et al., 2012).

The time to diagnostic conversion from MDD to BD has been analyzed in numerous studies. Sharma et al. have found that out of 61 patients with an initial diagnosis of MDD 35% of them were diagnosed as having BD at the beginning of the trial, and at ≥ 1

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year follow up the prevalence of BD was estimated to be equal to 59% (Sharma et al., 2005). A 15-year follow-up of 74 hospitalized patients with MDD has revealed that 26% of the subjects had developed hypomania, while 19% had undergone ≥ 1 manic episode (Goldberg et al., 2001). The results of studies with a shorter follow-up (up to 10 years) are more modest, with conversion rate between 7 and 12% (Coryell et al., 1995; Li et al., 2012). In course of a prospective Zurich cohort study covering a period of 26 years 39% of subjects with a primary diagnosis of unipolar disorder had been eventually assigned to a bipolar group (Angst et al., 2005). This finding remains consistent with the estimate that a mean rate of diagnostic change from MDD to BD type I or II is equal to 1% or 0.5% per year of observation, respectively (Angst, 2000).

The aim of our study was to check the stability of a diagnosis of unipolar depression in an outpatient setting, as well as to assess the scope of diagnostic conversions into BD.

2. Methods

A retrospective chart review was performed.

2.1. Subjects

157 charts of the subjects diagnosed with depressive disorders were analyzed at baseline. Ultimately, 122 outpatients (97 women [79.5%] and 25 men [20.5%]) with a primary diagnosis of depression consistent with ICD-9 or ICD-10 criteria (depressive episode, major depression, unipolar depression, recurrent depression or endogenous depression) were enrolled in the study. 35 cases were excluded due to insufficient data, comorbid severe medical condition that could contribute to depressive symptoms, or a diagnosis formulated by a junior doctor.

The sample included in the study consisted of patients examined and diagnosed by consultant psychiatrists, admitted to the outpatient clinic of the Department of Psychiatry, Collegium Medicum, Jagiellonian University in Krakow, between 1979 and 2009, including 18 subjects admitted between 1979 and 1989, 94 subjects–between 1989 and 1999, and 10 subjects–between 2000 and 2006.

Patients were included in the analysis if they fulfilled the following criteria: (1) age ≥ 18 years at the onset, (2) first established diagnosis of depression. Patients with a diagnosis of mood disorders due to a general medical condition were excluded. Mean age at the initial admission to the psychiatric outpatient clinic was 39.8 ± 10.9 years. Mean age of the participants (at the time when the analysis was conducted) was 57.5 ± 9.6 years (minimal: 24 years, maximal: 77). Mean follow-up was 18.5 ± 9.5 years (minimal: 5 years, maximal: 37 years). Mean time from the onset of disease to the first admission to our outpatient clinic was 2.61 ± 4.11 years.

2.2. Statistical analyses

The *t*-tests, Chi^2 tests, and correlation tests were used.

3. Results

Diagnostic conversion from MDD into BD was noticed in 40 subjects (32.8% of the total sample), of which 17 subjects (42.5% of the converters) had the diagnosis changed within the first 5 years of the follow-up period. The mean time between a diagnosis and a diagnostic conversion was 9.3 ± 8.6 years.

Mean number of diagnoses prior to the establishment of a diagnosis of BD was 2.2 ± 0.8 (minimal: 1, maximal: 4), the most prevalent previous diagnoses apart from MDD were personality disorders, anxiety disorders, alcohol or benzodiazepine abuse.

A statistically significant negative correlation between the age of illness onset and time to diagnostic conversion was observed (-0.41; $p < 0.05$). Patients with earlier onset of depression (before 30 years of age) had higher conversion rates into BD than patients with later onset of illness: 69% vs 28%, ($p = 0.0001$).

In 25 out of 122 patients (20.5%), depression was resistant to treatment with antidepressants, (defined as lack of significant improvement following at least two adequate antidepressant trials). The diagnoses of treatment-resistant depression were established on the basis of clinical examinations performed by consultant psychiatrists. Treatment-resistance to antidepressants was 3.6 times more prevalent among patients who were eventually diagnosed with BD (40% vs 11%; $p = 0.0002$; Chi^2 test).

Comparison of clinical variables related to patients who had (or had not had) their diagnosis converted from MDD to BD is presented in Table 1.

Patients who had their 'depressive' diagnosis changed into a 'bipolar' one were characterized by a significantly earlier age of illness onset, a longer duration of received treatment, a higher number of illness episodes, as well as a higher number of hospitalizations. Furthermore, subjects who had their diagnosis converted into BD spent more time in hospitals compared to 'truly' unipolar patients. Neither group differs in the duration of the course of the illness in terms of years, in the duration of the first depressive episode, the number of drugs and/or dosage changes during the entirety of the treatment, nor the time elapsed before an occurrence of a second episode of depression.

4. Discussion

The main finding of our study is that about 1/3 of our subjects, diagnosed with depression and primarily outpatients, had their diagnosis converted into BD. The rate of the conversion from MDD into BD in our group of patients was 1.8% of subjects per year (32.8/18.5), which is comparable to previously published results

Table 1
Comparison of clinical variables related to patients who had (or had not) their diagnosis conversed from MDD to BD.

	Conversion	No conversion	*p*
Age of illness onset (years)	36.5 ± 11.0	40.7 ± 8.3	0.022
Duration of observation (years)	17.1 ± 7.0	14.3 ± 5.2	0.016
Number of depressive episodes	8.5 ± 4.2	7.1 ± 3.0	0.043
Number of hospitalizations	3.7 ± 3.2	1.8 ± 2.2	0.0003
Time spent in psychiatric wards (weeks)	26.3 ± 30.1	10.7 ± 17.6	0.0022
Number of relapses	5.4 ± 4.3	5.0 ± 2.6	0.540
Time of illness course (years)	18.9 ± 7.8	17.3 ± 4.7	0.176
Duration of the first depressive episode (weeks)	13.6 ± 4.2	15.0 ± 7.6	0.561
Number of drug changes during the whole treatment	12.3 ± 7.8	10.4 ± 7.2	0.203
Time to the second depressive episode (years)	3.7 ± 5.0	3.2 ± 3.1	0.486