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Bipolar depression: the real challenge

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Abstract

This paper seeks to raise awareness of the impact and burden of bipolar depression and the need to improve its recognition and management in clinical practice. Bipolar depression is commonly misdiagnosed as unipolar depression and consequently, patients may receive inappropriate treatment that could potentially worsen symptoms. The Mood Disorder Questionnaire (MDQ) is a useful screening tool for identifying the range of bipolar spectrum disorders in general and psychiatric populations. Bipolar depression has a significant impact on patients, affecting work, social activities, family and friends. Current treatments for bipolar disorder have focused on mania, yet symptoms of bipolar depression occur more frequently, last longer, are more disruptive and are associated with greater risk of suicide than mania. In comparison with unipolar depression, bipolar depression is more severe, is associated with more frequent hospital visits and causes greater psychosocial impairment. These facts emphasise the importance of improving the diagnosis and treatment of bipolar depression.
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Keywords: Bipolar disorder; Depression; Mania; Mood disorder questionnaire; Diagnosis

1. Introduction

Bipolar disorder is a serious, recurrent illness, which is characterised by mood dysregulation, specifically risk-taking and impulsivity, interpersonal difficulties and depression. While much of the research in bipolar disorder has focused on bipolar I disorder, in which patients experience at least one episode of both depression and mania during the course of their illness, bipolar disorder is increasingly viewed as comprising a wider range of illnesses than pure mania, including hypomania, recurrent brief hypomania, sporadic brief hypomania and cyclothymia (Angst, 1998; Hirschfeld et al., 2003c). Symptoms of hypomania and cyclothymia tend to be more difficult to diagnose than those of mania, and hence many patients with bipolar spectrum disorders have received diagnoses of unipolar depression. In epidemiological studies, the lifetime prevalence rates of bipolar spectrum disorders range from 3.0% to 6.5%, compared with 0.0% to 1.7% for bipolar I disorder (Angst, 1998).

Until recently, research interest in bipolar disorder has tended to focus on mania and its treatment, with little consideration given to the treatment of depression. However, symptoms of depression in patients with bipolar disorder are more frequent and of longer duration than symptoms of mania (Judd et al., 2002; Kupfer et al., 2002). The long-term course of bipolar disorder has been prospectively explored in the National Institute of Mental Health Collaborative Study (mean follow-up 12.8 years). Patients in this study ($n = 146$) experienced symptoms for an average of 47.3% of the study period, with depression accounting for 67% of that time (Judd et al., 2002).

The risk of suicide is much greater while patients are suffering from depression than mania. For example, in a US study involving 2839 patients with bipolar disorder, 46.3% made at least one suicide attempt while suffering from depression compared with 13.4% while suffering from mania (Kupfer et al., 2002).

The purpose of this paper is to raise awareness of the impact of bipolar depression and the need to improve its recognition and management in clinical practice.

2. The challenge in bipolar disorder: correct diagnosis

Bipolar disorder is frequently misdiagnosed, and consequently patients are often inappropriately treated. Several

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problems contribute to the misdiagnosis of bipolar disorder. Patients often consider their manic symptoms to be normal and fail to realise that they might require treatment. Secondly, symptoms are highly variable, ranging from impulsive behaviour or substance abuse, to fluctuations in energy levels, and are often attributed to disorders other than bipolar disorder (Hirschfeld et al., 2000).

2.1. The 1992 and 2000 Depressive and Manic-Depressive Association (DMDA) surveys

Two surveys conducted in the US, involving patients from the National DMDA, reported on the rate of misdiagnosis of bipolar disorder in this sample. The first of these studies was conducted in 1992 (Lish et al., 1994), the second in 2000 (Hirschfeld et al., 2003d). Patient demographics were similar in the two surveys, with approximately two-thirds of patients being female. A high proportion of patients in both surveys reported being initially misdiagnosed. Very little change in the rate of misdiagnosis occurred in the 8 years between the two surveys (73% vs. 69%), with the most common misdiagnosis being unipolar depression (44% vs. 60%). Both surveys revealed that more than a third of patients did not receive a correct diagnosis for at least 10 years after they first sought medical help. In the 2000 survey, although there was a tendency for patients to under-report symptoms, only 28% believed that this under-reporting was associated with their misdiagnosis, whereas 60% believed that misdiagnosis was due to their physician having a poor understanding of bipolar disorder. Although these surveys were limited to self-selected members of a voluntary patient organisation, they do highlight the considerable problems faced by patients with bipolar disorder.

2.2. Bipolar II disorder

The prevalence of bipolar II disorder in outpatients presenting with depression was investigated in a French multicentre study (EPIDEP) (Hantouche et al., 1998). Of the 250 patients enrolled in EPIDEP, 22% were initially diagnosed with bipolar II disorder, with the remainder diagnosed as having unipolar depression (72%). The psychiatrists involved in this study subsequently underwent training in a systemic protocol for hypomania, which included DSM-IV criteria, the Akiskal (soft polarity) criteria, the Angst Hypomania Checklist and several other structured/semi-structured instruments/evaluations. On prospective follow-up, 40% of the study population were diagnosed with bipolar II disorder, nearly double the percentage initially identified.

A second study, carried out in a private clinic in Italy, involved 203 patients who had a DSM-IV diagnosis of major depressive disorder, uncomplicated by schizoaffective or psychotic disorder, dementia, substance abuse or severe personality disorder (Benazzi, 1997). Patients were interviewed using the Comprehensive Assessment of Symptoms and History (CASH), a structured interview for major psychoses and affective disorders which enables diagnoses to be made using a variety of criteria (in this case the DSM-IV criteria for hypomania were applied). The resultant diagnoses were bipolar II disorder (45%), bipolar I disorder (4%) and unipolar depression (51%). An important observation in this study was that the depression phase of bipolar II disorder only differed from unipolar depression in terms of atypical features.

The above findings were confirmed by a longitudinal study of 108 consecutive outpatients diagnosed with various depression or anxiety disorders in a family practice setting in the US (Manning et al., 1997). In this study, physicians specially trained in mood disorders evaluated patients using in-depth semi-structured interviews covering clinical features, family history and treatment response. This approach identified 18% of the sample as having bipolar II disorder, 3% as having bipolar I disorder and 5% as having other bipolar disorders (including cyclothymia). Of the 20 patients diagnosed as having bipolar II disorder, only 1 had previously received this diagnosis.

2.3. Rapid-cycling bipolar disorder

There is similar under-recognition of patients with rapid-cycling bipolar disorder with the most common initial diagnosis being unipolar depression. For example, in a sample of patients ($n = 345$) with rapid-cycling disorder who were entered into a treatment trial, only 45% had previously received a diagnosis of rapid-cycling bipolar disorder. Despite the severity of their symptoms, 18% of patients had received no psychiatric diagnosis, while the remaining 37% of patients had received a diagnosis of unipolar depression (Calabrese et al., unpublished data).

2.4. Consequences of misdiagnosing bipolar disorder

If bipolar disorder is misdiagnosed, patients are likely to receive inappropriate pharmacotherapy. In particular, if a misdiagnosis of unipolar depression is made, conventional antidepressants may be prescribed, which carry a risk of switch into either mania or cycle acceleration. A naturalistic study conducted by Ghaemi and colleagues (Ghaemi et al., 2000) further illustrates the difficulties of correctly diagnosing bipolar disorder, as well as the potential consequences of misdiagnosis. Of the 54 psychiatric outpatients diagnosed with bipolar disorder, 29 (56%) had previously been diagnosed with unipolar depression. Forty-two patients (78%) with bipolar disorder had received a prescription for antidepressants, with only 30 (56%) ever having received mood stabilisers. The mean age at which antidepressants were first prescribed was 30.0 years, whereas mean age when patients received mood stabilisers was 33.2 years. Fifty-five percent of the patients for whom data were available ($n = 38$) had developed mania or hypomania

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