EXPERT REVIEWS

Dilemma for enhancing psychiatrists' adherence to guideline (evidence)-based practice

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Evaluation of: Glauser TA, Cerenzia W, Wiley S, Howson A, Thase M. Identifying psychiatrists' practice patterns when managing depression in patients with bipolar I disorder: a descriptive study to inform education needs. *Postgrad. Med.* 125(1), 144–153 (2013).

Bipolar disorder (BD) is a prevalent and chronic devastating disorder that is associated with considerable psychosocial and economic morbidity. However, its complexity in the clinical course and manifestation of bipolar disorder is still a significant barrier to accurate differential diagnosis from unipolar depression (UD), by which it is still underdiagnosed and undertreated in clinical practice. In community studies, first onset of BD is usually in the adolescent ages, and the occurrence of UD is usually its first clinical manifestation. In addition, reliable criteria for differentiating UD from BD along with validated treatment guidelines for BD are currently not sufficient or adequate, commonly resulting in misdiagnosis and mismanagement of both clinical conditions. Therefore, the study under evaluation results from clinician practice patterns in the real world will substantially enhance the current understanding on the actual situation and unmet needs for accurate and proper diagnosis and management of bipolar depression.

Keywords: bipolar disorder • diagnosis • screen • treatment • treatment guideline • unipolar depression

Bipolar disorder (BD) is a chronic and prevalent mood disorder leading to considerable personal functional impairment as well as resulting in increased disease burden to public heath [1,2]. Despite progress in research fields of nosology, epidemiology, biological background with advancement of research technology, the complicated nature of the clinical course and manifestation of BD is still a significant barrier to accurate differential diagnosis from unipolar depression (UD) [3–5].

According to a recent screening study (n = 85,358), approximately 20% of individuals with positive screens for bipolar I or II disorders reported that they had previously received a diagnosis of BD from a clinician, while 31% reported receiving a diagnosis of UD. An additional 49% reported receiving no diagnosis of either BD or UD. Similar findings were consistently reported across the world and thereby continuous efforts to achieve adequate and appropriate screening, diagnosis and management of potential misdiagnosis in mood disorders should be mandatory [6,7].

Recently, Glauser and colleagues published an interesting article showing clinician factors that should be implicated in misdiagnosis between BD and UD [8]. Glauser and colleagues intended to reveal the current knowledge and practice patterns of US psychiatrists and to identify gaps in knowledge and competence concerning the diagnosis and management of depression in patients with BD [8]. Findings from their study delivered useful information to clinicians about current practice patterns and emerging data regarding the proper diagnosis and treatment of depression in patients with BD [8].

Methods & results

The authors conducted the case-based survey on a random sample of 1149 US psychiatrists obtained from a proprietary database via email between 29 March and 3 April 2012. The survey comprised of two case vignettes to reflect

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symptomatic characteristics of UD and depression in patients with BD. Each case was accompanied by a series of questions to determine how physicians would suspect, diagnose, treat, manage and monitor the patients described in the vignettes. An online survey platform was used to collect the data. Two focus groups were conducted using a nominal group technique via a web interface and teleconference to elicit barriers that psychiatrists face in managing depression in patients with BD. The response rate was quite low (n = 200/1149; 17.4%); the study results clearly showed that there are a number of important knowledge gaps about the diagnosis and proper management of BD, which delivers a significant unmet need of continuing education and practice improvement strategies in clinical practice. According to the results, 67% of the respondents said that they asked depressed patients whether or not they had previously experienced all eight symptoms that define mania in the Diagnostic and Statistical Manual of Mental Disorders-IV, Text Revision. As for the treatment issue in a case with no other clinical factors for BD, 85% of the respondents said that they would use an antidepressant and only 8% of them would prescribe a mood stabilizer; 55% of them did not worry if their treatment would result in a drug-induced manic episode; 5% of the respondents never considered any risk of treatment-emergent manic switch. As for a case with a history of untreated manic episode, 54% of the respondents declared that they would still prescribe an antidepressant as monotherapy; 39 and 23% of the respondents said they would add a mood stabilizer or atypical antipsychotics, while 19% of the respondents said that they would stop antidepressant use. Other interesting points were factors influencing their choice of therapy. A majority of respondents recognized the patient's ability to adhere to a prescribed agent (82%) and the psychiatrists' own clinical experience with a certain agent (81%) as very important factors to choose initial therapy. Only half of the respondents thought that practice guidelines would be very influential, while 41% believed that it was very important that an agent have a regulatory agency-approved indication for the diagnosis. In addition, adequately powered, controlled clinical trial results were also not influential to their routine practice; only a quarter and a half (26 and 53%, respectively) of respondents considered the results of recent clinical trials or practice guidelines to be a very important factor in treatment decision. Finally, only 20% of the respondents followed their patient's clinical course over time using a mood chart.

Discussion & significance

The study results demonstrate that there are a number of important gaps in knowledge about the management of bipolar depression, which in turn helps to clarify objectives of continuing education and practice improvement strategies [8].

According to the study results [8], more than 50% of psychiatrist respondents reported that obtaining an accurate diagnosis was a significant barrier to optimally managing bipolar depression. In fact, there is a longitudinal risk of conversion from UD to BD; approximately more than 10% of the patients who were initially diagnosed as UD ultimately turn out as BD in the longer observation period [9]. In addition, less than 50% of the respondents appropriately selected an antidepressant (AD) for treating a patient who presents with depression [8]; however, when being asked about a specific class of treatment agent for such BD patients, such clinicians picked mood stabilizers or antipsychotics but not AD, indicating the disparity in clinical practice and theoretical choice of treatment agent, as well as uncertainty of treatment recommendations. In addition, 39% of the respondents were not aware of age of onset as a clinical factor differentiating UD from bipolar depression, although age-at-onset has been continuously and strongly suggested to be more clinically useful in delineating BD from UD [10]. These findings indicate that clinicians are not confident in their treatment choices for BD patients with depressive symptoms and they are also not well trained for clinical factors associated with developing BD. According to a recent pooled and systematic review for mood shifts from UD to mania/hypomania/mixed states during AD treatment and rates of diagnostic change from UD to BD [11], a large excess of mood switching associated with AD treatments versus new diagnoses of BD was also evident, based primarily on the occurrence of spontaneous mania/hypomania. The overall risk of mood shifts was 8.2% within 2.4 years of treatment, or 3.4% per year. The overall risk of rediagnosis was 3.3% in an average exposure time of 5.4 years for an incidence rate of 0.6% per year. The mean conversion rate across individual studies was 1.8% per year. The study findings eventually indicate a three- to six-fold excess of mood switches to rediagnoses in all studies they investigated. These trends have been continuously seen in other independent large clinical trials; in fact, threshold switches into full-duration hypomania and mania occurred in 11.4 and 7.9%, respectively, of the acute treatment trials and in 21.8 and 14.9%, respectively, of the continuation trials [12]. However, in some large practical trials, the use of AD, compared with the use of mood stabilizers, was not associated with increased risk of treatment-emergent affective switch [13]. Hence, longer-term outcome studies are needed to fully assess the benefits and risks of AD treatment for BD. Finally, this first randomized discontinuation study with modern ADs also showed no statistically significant symptomatic benefit with those agents in the long-term treatment of BD, along with neither robust depressive episode prevention benefit nor enhanced remission rates [14].

Strikingly, only half of the respondents reported that treatment guidelines should be important in their clinical practice, and they also concluded that clinical trial results were the least influential [8]. Furthermore, only a third of the respondents were familiar with large practical clinical trials and foundations for BD, such as the Systemic Treatment Enhancement Program for Bipolar Disorder trial, Bipolar Affective Disorder: Lithium/Anticonvulsant Evaluation, or the Stanley Foundation Bipolar Network trials. In addition, a fifth of the respondents reported that they were very likely to use a mood chart in their practice [8], although most treatment guidelines advocate the routine use of mood charts or brief self-rating scales for following the clinical course of patients. Despite the clinical benefit of practice guidelines still being questioned, a number of clinical trials comparing clinical outcomes between guideline-based treatment and treatment as usual (TAU)

have clearly demonstrated the utility and feasibility of guideline-based treatment over TAU [15]. An algorithm-based care (ABC) for BD based on the Texas Medication Algorithm Project in the USA should partially address this issue. The Texas Medication Algorithm Project was compared with TAU for patients with BD and UD over 12 months [15,16,101]. ABC and TAU patients showed significant initial decreases in symptoms measured by the 24-item Brief Psychiatric Rating Scale at the 3-month assessment interval, with significantly greater effects for the ABC group [16]. Such superiority of ABC over TAU was also demonstrated in the UD trial [101]. The magnitude of the difference between ABC and TAU was robust in the study (mean Inventory of Depressive Symptoms-Clinical-Rated difference: 4.5 points; mean Inventory of Depressive Symptoms-Self-Rated difference: 7.5 points). The significant advantage of ABC was seen in the first quarter, with no evidence that TAU patients caught up with their ABC counterparts during the ensuing 9-month period. As for the Asian study, Yoshino and colleagues also found a four-step ABC to be superior to TAU in remission rates (60.2 vs 49.7%, respectively) and median number of days to achieve remission (93 vs 191 days, respectively) in UD patients [17]. In fact, a higher rate of lithium augmentation in the ABC group (20.5%) compared with the TAU group (4.7%) may have led to the greater remission rate. Favorable results have also been consistently observed for the collaborative-care model, an evidence-based practice that involves a multidisciplinary depression care team providing guideline-concordant UD treatment in the primary care setting [18,19]. These results clearly indicate the superiority of ABC over TAU in clinical practice. A successful model of measurement-based care using a brief packet, including mood charts and brief rating scales, an evidence-based strategy not based on clinicians' recall and written clinical notes, can substantially assist primary care clinicians in improving the quality of BD management [20,21].

Expert commentary & five-year view

A regular assessment of patients' clinical status and treatment response with short forms of patient-rated self-scales for BD should be a practical help to busy clinicians by providing a more structured and standardized evaluation in private practice. In fact, it was found that clinicians' treatment decisions to change treatment or to make referrals based on self-rating scales was also aligned with guidance from practice guidelines for the monitoring of depression in primary care [22]. In addition, in preparation for evidence-based treatment, it should be emphasized that clinicians should strictly adhere to contemporary practice guidelines during the residency training program to improve clinical practice [23]. However, implementation of such guideline-based treatment should be varied across countries, since crosscultural variations for health-related policy, practice pattern, approved psychotropics, patient attitude and logistics of trained psychiatrists clearly exist [24].

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Key issues

- There is a significant barrier to the accurate differential diagnosis of bipolar disorder from unipolar depression.
- Clinicians need continuous education on the utility of clinical trial data, government-initiated management programs and validated assessment rating scales/mood chart for proper evaluation and management of bipolar disorder patients.
- Evidence-based treatment can substantially enhance the clinical outcomes of bipolar disorder patients.

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