Bipolar II (BP II) disorder is characterized by highly recurrent depressive episodes, a higher suicide rate and a higher frequency of rapid cycling course (Calabrese et al., 2001) when compared to either bipolar I (BP I) depression or unipolar depression.

To date, there is a lack of double-blind, randomized controlled trials specifically designed to address the issue of the management of BP II depression with the co-occurrence of depressive and excitement symptoms (Benazzi, 2004; Calabrese, 2004).

Some studies have shown that major depressive episodes with few co-occurring hypomanic symptoms such as irritability, psychomotor agitation, and crowded thoughts were common among BP II patients (Benazzi, 2004). These patients do not fulfil the DSM-IV criteria for mixed states and cannot be diagnosed within the DSM-IV diagnostic categories. Recent studies pointed out that suicide attempters come mainly from mixed depressives with a predominantly BP II base, showing that decreased self-esteem, racing/crowded thoughts, and psychomotor agitation/activation were independent and clinically significant correlates of suicidal ideation, irrespective of depression severity (Akiskal and Benazzi, 2005; Balazs et al., 2006). However, these patients appear to be relatively frequent and difficult to treat, particularly with respect to the possibility of developing side-effects during antidepressant treatment. In fact, BP II diagnosis implies careful consideration of the possibility of inducing mixed states, mania or hypomania, or rapid cycling when treated with antidepressants alone (Kupka et al., 2003). Current guidelines (APA, 2002) for the treatment of BP II major depressive episode recommend using either a mood stabilizer alone or a combination of a mood stabilizer plus a selective serotonin re-uptake inhibitor (SSRI). The administration of mood stabilizers has been reported to significantly reduce the risk of inducing mania during antidepressant treatment. Recently, we reported a significant association between the absence of mood-stabilizer treatments during antidepressant therapy or treatment with tricyclic antidepressants and the development of antidepressant-induced mania (AIM). This association was significant in both diagnostic subtypes (BP I or BP II) (Mundo et al., 2006).

These results appear to confirm previous literature data on AIM and the protective effect of mood stabilizers (Henry et al., 2001). On the other hand, the role of BP II diagnostic subtype in increasing the risk of developing mania during antidepressant treatment, suggested by some previous studies, still remains controversial (Altshuler et al., 2006; Mundo et al., 2006).

The identification of risk factors for rapid cycling course should also be considered when treating bipolar depression. In addition to some clinical features (BP subtype, female sex, hypothyroidism, hyperthymic temperament), some biological factors (i.e. the serotonin system genes) appear to be relevant in conferring susceptibility to a worse outcome for bipolar depression. The serotonin transporter (SERT) gene has been widely studied with respect to the normal and the abnormal response to antidepressant medication in bipolar patients. In particular, the short variant of the promoter polymorphism of the SERT gene (5-HTTLPR) has been associated with antidepressant-induced mania (Mundo et al., 2001), the development of rapid cycling course (Rousseva et al., 2003), and violent suicidal behaviour (Courtet et al., 2004). The presence of one or two copies of the short variant of 5-HTTLPR implies lower gene expression and, as a consequence, a lower number of transporter sites with higher concentrations of 5-HT in the synaptic cleft. This may be the biological basis of a higher affective instability and of a higher susceptibility to AIM, rapid cycling, and impulsivity.

In conclusion, the difficulties encountered when treating BP II depression should encourage the clinician towards the evaluation of the different clinical and biological factors that may put BP II subjects at risk for course complications. Future studies on the treatment of depression in BP II patients should consider the genetic and biological make-up of subjects and the use of mood stabilizers in ‘at risk’ subjects.

We are currently evaluating the effect of new mood stabilizers (e.g. lamotrigine, olanzapine, quetiapine) in preventing manic switches or mixed states in BP II patients treated with antidepressants (Altamura et al., 2003).
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None.

Statement of Interest

None.

References


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