

## Antidepressant Use and the Risk of Mood Instability

### O Uso de Antidepressivos e o Risco de Instabilidade do Humor

**Keywords:** Antidepressive Agents; Bipolar Disorder; Cyclothymic Disorder

**Palavras-chave:** Antidepressivos; Perturbação Bipolar; Transtorno Ciclotímico

Dear Editor,

Freitas C *et al*<sup>1</sup> recently published a case report on a widely discussed topic in psychiatry, concerning the risk of manic switch with the use of antidepressants. This topic is of the utmost importance especially considering today's widespread use of antidepressants in a wide range of medical conditions. Although the risk of switching with antidepressants is well established, its adverse effects in the management in other clinical conditions are often underestimated in psychiatry. At the core of this issue is the accurate diagnosis of depressive episodes. Today's classification systems on mood disorders are largely based on a polarity dichotomy (unipolar versus bipolar). Frequently it is assumed that any depressive state is synonymous with the diagnosis of unipolar depression, overlooking subsyndromal signs of hypomanic or mixed depressive states. A previous history of treatment resistant depression, irritability, mood lability, mixed features in response to antidepressants is associated with a possible underlying bipolar diathesis.<sup>2</sup> Indeed, some authors propose that up to half of supposedly unipolar depressive episodes presenting in clinical practice might

be diagnosed as depressive mixed states if one takes into consideration criteria excluded from DSM 5 mixed features specifier (such as psychomotor agitation, distractibility, irritability, racing thoughts).<sup>3,4</sup> Radical thinkers go as far as proposing the apparently controversial view that depression is a consequence of manic states.<sup>3</sup> According to this point of view, antidepressants are ineffective and harmful in the treatment of most depressive episodes presenting in clinical practice, and thus contribute to induce further mood instability in these patients. Indeed, most depressive states in clinical practice would involve mixed depressive states, affective temperaments (cyclothymia and hyperthymia) and classical bipolar depression.<sup>5</sup> Misdiagnosis of soft bipolar spectrum disorders or temperamental dysregulations (such as cyclothymia) may lead to frustration amongst clinicians with patients failing to improve and apparently resisting to recommended pharmacological and psychological treatment. The mainstay treatment should include the slow discontinuation of antidepressants and the use of drugs with mood stabilizing properties (lithium, anticonvulsants and second-generation antipsychotics).<sup>4,5</sup> Current evidence would recommend against the use of antidepressant monotherapy in the treatment of bipolar spectrum depression. The key message is to be mindful of associated features and signs that depressive episodes (even in the absence of past mania or hypomania) might not be truly 'unipolar' (Table 1). This might help to prevent misdiagnosis and inappropriate treatment strategies with potential negative long-term prognostic implications (including increased suicide risk).

**Table 1** – Features that might indicate non-unipolar depressive episodes

Symptom profile including irritability, distractibility, inner tension, impulsivity, excitement
Atypical depression (mood reactivity, exaggerated interpersonal sensitivity, increased appetite and hypersomnia)
High comorbidity (anxiety, eating and impulse control disorders, adult attention deficit and hyperactivity disorder, personality disorders with cluster b features, including borderline and histrionic personality disorders)
Early age of onset
Post-partum depression
Seasonal depression
Treatment resistant depression
Family history of bipolar disorder
Hyperthymic or cyclothymic premorbid affective temperament

## REFERENCES

- Freitas C, Barranha R, Abreu T, Von Doellinger O. Mania induzida por mirtazapina: um caso clínico. *Acta Med Port.* 2019;32:671.
- Perugi G, Pacchiarotti I, Mainardi C, Verdolini N, Menculini G, Barbuti M, et al. Patterns of response to antidepressants in major depressive disorder: Drug resistance or worsening of depression are associated with a bipolar diathesis. *Eur Neuropsychopharmacol.* 2019;29:825-34.
- Ghaemi SN, Vohringer PA, Athanasios Koukopoulos' psychiatry: the primacy of mania and the limits of antidepressants. *Curr Neuropharmacol.* 2017;15:402-8.
- Faedda GL, Marangoni C, Reginaldi D. Depressive mixed states: a reappraisal of Koukopoulos' criteria. *J Affect Disord.* 2015;176:18-23.
- Perugi G, Hantouche E, Vannucchi G. Diagnosis and treatment of cyclothymia: the "primacy" of temperament. *Curr Neuropharmacol.* 2017;15:372-9.

Tomás TEODORO✉<sup>1,2</sup>

1. Department of Psychiatry. Centro Hospitalar Psiquiátrico de Lisboa. Lisboa. Portugal.

2. Chronic Diseases Research Center. NOVA Medical School. Universidade Nova de Lisboa. Lisboa. Portugal.

Autor correspondente: Tomás Teodoro. tomasteodoro@chpl.min-saude.pt

Recebido: 06 de outubro de 2019 - Aceite: 07 de outubro de 2019 | Copyright © Ordem dos Médicos 2020

<https://doi.org/10.20344/amp.12917>

