Mood Instability, Bipolar Disorder and Disadvantages of Antidepressants

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Abstract

Objective. To emphasize the clinical importance of mood instability (MI) in the treatment of patients with depression and anxiety, bipolar and substance abuse disorders.
Content. We summarize data to show that MI is common in patients with "neurotic" conditions; in fact, MI may be the central feature of neuroticism. We discuss the association of MI with irritability and suicidal thoughts. We also discuss the assessment of MI in family practice. MI and bipolarity are not well treated by antidepressants, which might actually aggravate the tendency to unstable moods and cycling. Suggestions are made about treatment but firm recommendations about medication are currently outside treatment guidelines.
Conclusion. MI is an important concern in the treatment of anxiety and mood disorders and more research is needed.

Key words: mood instability, bipolar disorder, antidepressants, anxiety.

Introduction

Unstable moods are a common concern of patients with anxiety, depression and bipolar disorders. Unfortunately, when mood (affective) instability is prominent, we have been instructed to think narrowly of borderline personality disorder. Here we describe the relationship of mood instability to mood disorders in general and the consequence for prognosis and treatment.

Definition of Mood Instability (MI)

The APA DSM-IV criteria for major depression require that symptoms be present "most of the day, nearly every day, for at least 2 consecutive weeks"). However, when patients with mood and anxiety problems rate their symptoms prospectively, most will report prominent fluctuations in mood within a day or days (2) (3). We refer to these as Mood Instability (MI) defined as "severe and frequent fluctuations of mood over time" (4).

Unstable moods in depression

Patients with anxiety and depression who rate their symptoms prospectively consistently score higher (Mean 3.072, SD 2.203) than controls (Mean 1.571, SD 1.50) on depressed MI (t 7.99, df 362, $p<0.001$) (2) (3). In these studies, patients rated depressed mood twice a day for 7 consecutive days on visual

analogue scales (10 cm lines). From the successive ratings, we calculated the Mean Square Successive Difference Statistic (MSSD), which is a better measure of point-to-point instability than the standard deviation (5). This gives a precise measure of MI for research but is too cumbersome for everyday clinical use. We have recorded unstable depressed, anxious, irritable and high moods.

Patients might not report these fluctuations spontaneously for several reasons. First, because they are usually not asked; second, there is a negative cognitive bias in depression that can overshadow fluctuations in mood (6), and finally people are often afraid of being labelled "bipolar".

Correlates of MI

MI has been associated with low self-esteem (7), suicidal thoughts (8), borderline personality traits (9), anxiety (3), depression and alcohol abuse (10). We have also shown higher MI in women with premenstrual tension (11) and in pregnant and postpartum women (Bowen et al. submitted for publication) Interestingly, the absence of MI, in other words mood stability, is the best predictor of a sense of well-being (12).

Most psychiatric classifications and textbooks barely mention MI, and when they do, it is relegated to the category of borderline personality disorder (1). The definition of this syndrome rests on instability of relationships and self-image that could both be related to instability of mood as the primary characteristic (9). Anger is another characteristic of the borderline personality disorder, but fluctuating irritability is common in patients with depression and unstable moods (13).

How to inquire about MI clinically

We have used the question: "Do your moods often go up and down?" to elicit reports of mood instability from patients (14) (8). Another question is: "Do you have mood swings?" but patients often interpret this question as an inquiry about irritability; however, irritability is related to mood fluctuations and the bipolar spectrum (13). More recently we have used the short form of the Affective Lability scale to measure MI (15). This is an 18-item questionnaire with questions about mood shifts that correlates well with the MSSD statistic for depressed mood and the question about "moods often going up and down" (8).

Factor analysis of the Eysenck Neuroticism Scale (16) yields a reliable MI factor that is anchored by the same question about "moods often going up and down". This factor predicted suicidal thoughts in a cross-sectional study (8) and also predicted general psychological wellbeing after 7 years in the British Health and Lifestyle study (Bowen et al. submitted for publication). This suggests that MI is the core feature of neuroticism.

Treatment

Not necessarily antidepressants

Depression, even subsyndromal depression, is a highly recurrent condition (17) (55% over 5 years) (18). The SSRI antidepressants alleviate some symptoms of depression over the short term but the evidence for remission of symptoms is not particularly strong (27.5% in the STAR*D trial (19. 20). This is true even when dosing is pushed to the maximum (60 mg citalopram) (20). There is even less evidence that these drugs are effective at preventing the recurrence of depression over the long term (21) (22). The longest studies are about 18 months in duration and by the end of the study, the attrition rate is so high that it is difficult to reach firm conclusions. Recently, it has been suggested that chronic use of antidepressants may induce a form of chronic dysphoria (23).

Bipolarity

We now know that at least half of depressed patients who present for treatment have a bipolar diathesis (13) (24). Chronic exposure to antidepressants is associated with worsening of the long-term course of bipolar disorder due to frequent changes in polarity, mixed symptoms and treatment refractoriness . (25) (26) (27). From the patient's point of view, the typical presentation of hypersomnic, retarded depression can turn into an agitated, anxious mood state with accompanying insomnia and racing thoughts. Consequently, depressed patients should be routinely screened for sub-threshold manic symptoms before the initiation of antidepressants. It may be that the SSRI antidepressants are more useful for symptoms of anxiety that often accompany MI, including mild symptoms of worrying, social anxiety, and obsessionality (28).

Indications of Bipolarity

When the right questions are asked, MI is found to be common among individuals on the bipolar spectrum (24,25,26,27). Therefore, patients presenting with MI or any history of activation should be screened for bipolar disorder. Clues to the bipolar nature of a mood disorder include early age of onset of depression, recurrent episodes, fast onset and brief depressive episodes, atypical depressive symptoms, postpartum depression, concomitant psychotic features, poor antidepressant response or loss of response, antidepressant-induced (hypo)mania, and family history of bipolar disorder in a first-degree relative (29) (30). Unfortunately, there are no studies on the prevalence of MI in bipolar disorder.

Pilot treatment studies

The main reason for inquiring about MI is to improve the mental health of patients, particularly those with anxiety, mood and substance-abuse problems. Patients with anxiety and depression treated with antidepressants tend to have partial improvement on symptom scales after 6 months of treatment, as might be expected (31.). Depressed MI does not improve consistently, however; a few patients become better but others become worse. We are currently conducting an open study with lamotrigine and the early results seem promising for improvement of MI. Preliminary results from other studies suggest that lamotrigine is an effective drug for mood instability in borderline personality disorder (32). It is worth noting that a combination of medications may be necessary.

Why consider alternatives to antidepressants?

It is sobering that depression as a cause of disability days lost is now first or second in importance in developed countries. An equally urgent concern is that suicide continues to be a prominent cause of death, particularly among young people (33). About 50% of young people with suicidal thoughts do not fulfil the criteria for major depression and have not come to the attention of mental health services (34), although most of these have psychiatric symptoms (35). This is a reminder that subthreshold symptoms including MI are important. A relevant question is: "If simple effective treatments are available in the form of antidepressants, why is the outlook for depression not brighter?" In response to this, the emphasis has shifted to enhancing primary care (36) (37). Repackaging and disseminating current treatments will hopefully improve the outlook but does not address the issue that the treatments are not particularly effective. Increased awareness that one-half of depressed patients who present for treatment have a bipolar spectrum disorder will probably also help. Apart from medication, alternative ways of helping to manage MI, such as adequate physical activity, show promise (Bowen et al. in preparation). Because MI is related to neuroticism that is a relatively enduring (but modifiable) trait, it is not likely that it will spontaneously remit over the short term in a particular patient.

The association between MI and Depression

We are not suggesting that MI should replace the concept of "depression" as a general measure of sadness or lack of pleasure. Pooled data from many studies shows that depression correlates consistently but only moderately with MI (N = 161, r = 0.481, p<0.001). (38) This suggests that depression and depressed MI are related concepts but that MI is not redundant (38). Depression might be considered to be a vague term, akin to shortness of breath, and antidepressants are not necessarily the "first-line" treatment for all patients (39) (40). MI is a more specific term but whether it is more clinically useful only more research will reveal.

MI and formal psychiatric diagnoses

Many patients report high subjective distress but do not appear to be severely depressed. This is consistent with the observation that subjective rating scale scores are often higher than observer-rated scales (41). This difference in scores is predicted by "neuroticism" that we have related to MI (41) (8). This means that the patient may be better at assessing his or her own subjective distress than an external observer armed with a diagnostic inventory. In this sense, MI may be a true trans-diagnostic concept that is seen in patients with bipolar, depressive, anxiety, substance abuse and some personality disorders.

Conclusion

Depression is a very general concept but even the diagnosis of major depression lacks the precision necessary for assessing and treating patients effectively. Awareness that one-half of depressed patients have a bipolar disorder will undoubtedly help. Increasingly, evidence suggests that MI is a distressing trait that may affect the long-term outcome of patients with anxiety and mood disorders. The relationship of MI to the bipolar spectrum needs to be determined. Neither bipolar disorder nor MI is well treated by antidepressants alone. A comprehensive program of mood management that includes several medications and lifestyle changes may be necessary. More research on the assessment and treatment of MI and bipolar disorder is needed.

GP Comment

What have I learned from this paper?

Currently within the NHS England QOF indicators ask for a bio-psycho-social assessment at the time of diagnosis. A GP would use PHQ-9 (Patient Health Questionnaire) and GAD-7 (Generalised Anxiety Disorder) at the time of initiation of medication. These questions are repeated during medication reviews and can provide a way of monitoring improvement.

These are helpful tools in assessing the patient objectively at the time and could potentially identify mood instability or deterioration with the commencement of an SSRI.

As a GP I would check the BNF, which does not state an indication or license for lamotrigine. I would therefore rely on consultant psychiatric colleague to consider lamotrigine, as a pharmaceutical option.

Dr Vishal Naidoo, GP.

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