

## Mirtazapine Induced Tremors: A Case Report

Sir,

Mirtazapine is an antidepressant with antagonistic action on alpha 2 noradrenergic receptors and postsynaptic serotonergic receptors (5HT<sub>2</sub> and 5HT<sub>3</sub>).<sup>[1]</sup> It is considered to be one of the safest antidepressants in terms of side effects like involuntary movements. In fact, mirtazapine is one of the medications found useful in alleviating drug-induced akathisia and recommended in Parkinson's disease.<sup>[2,3]</sup> However, there is literature, mostly case reports, suggesting that at least a few subjects are intolerant to mirtazapine and may develop involuntary movement disorders such as akathisia, dystonia, and dyskinesia.<sup>[4]</sup> There is no literature implicating mirtazapine with tremors, chorea, or parkinsonism.<sup>[5]</sup> Here, we describe a case of mirtazapine-induced tremors.

A 60-year-old female came to the outpatient psychiatry department of our hospital with complaints of low mood, reduced interest in daily activities, loss of interest in previously rewarding or enjoyable

activities, restlessness, easy fatigability, and reduced sleep and appetite for last 1 week, precipitated by the death of a close relative. The patient had a history of two depressive episodes in the last 3 years, treated with sertraline for a few months, which she had discontinued after experiencing improvement in her symptoms. There was no family history of psychiatric disorders. She had hypertension and was recently started on telmisartan and hydrochlorothiazide along with cilnidipine. Her blood investigation showed profound hyponatremia (117 mmol/L), and hence, she was shifted to cilnidipine and nebivolol by general physician alongside sodium correction with tolvaptan.

Her psychological condition showed significant improvement within 2 days, with improvement in sodium level (137 mmol/L). She was prescribed oral lorazepam 2 mg/day for residual sleep problems and anxiety. In view of persisting sleep disturbances, at first week follow-up, lorazepam was stopped and mirtazapine 7.5 mg at bedtime was initiated. After 2 days of starting

mirtazapine, she started complaining of restlessness and tremors of both hands. She came back for a consultation a week later because of intolerable movements, which on examination was diagnosed to be both subjective as well as objective signs of akathisia and high amplitude, coarse, low frequency (-4 Hz) resting tremors of both hands. Considering the temporal association with the initiation of mirtazapine, the drug was stopped and oral lorazepam 2 mg/day was restarted. Her restlessness and tremors resolved within a week, but she developed florid depressive symptoms, which promptly responded to agomelatine 25 mg/day thereafter. A Naranjo score of 6 indicated probable adverse drug reaction related to mirtazapine.<sup>[6]</sup>

This is the first case report of tremors caused by mirtazapine. The lady developed akathisia and tremors within 2 days of initiation of mirtazapine, which completely remitted after stopping mirtazapine, and lorazepam helped in the symptomatic alleviation of distressing akathisia.

In general, elderly patients are at increased risk of side effects. This patient presented with probable thiazide-induced hyponatremia, which is known to mimic depression.<sup>[7]</sup> Hence, correcting hyponatremia and symptomatic treatment of anxiety and sleep disturbances was attempted as the first step. On re-emergence of syndromal depression, mirtazapine was started as it has a lower propensity to precipitate hyponatremia. However, because of the intolerable hyperkinetic involuntary movements of akathisia and tremors, it had to be discontinued.

As a recent review, elderly patients are more prone to hyperkinetic side effects with mirtazapine at a dose more than 30 mg/day.<sup>[5]</sup> However, our patient had symptoms at a lower dose of 7.5 mg/day. Onset and remission of these side effects were within the time range observed commonly in the literature. These can start from the first dose to 9 weeks of initiation of mirtazapine and remit within a few hours to 3 weeks of termination.<sup>[5]</sup> As seen in our case, benzodiazepines usually provide symptomatic relief, especially from akathisia.

A meta-analysis showed the efficacy of mirtazapine in antipsychotic-induced akathisia.<sup>[2]</sup> Although rare, paradoxical mirtazapine-induced akathisia has been well reported from all over the world.<sup>[2]</sup> Mirtazapine has been shown to improve resting tremors in Parkinson's disease.<sup>[3]</sup> However, tremors induced by mirtazapine has not been systematically reported earlier. Short-term controlled studies from the United States report the prevalence of tremors to be 2% in patients on mirtazapine in comparison 1%

noted on placebo; the clinical characteristics of the same are not detailed.<sup>[5]</sup> A recent study on a health database showed nearly 3.78 rate ratio of mirtazapine inducing extrapyramidal side effects with respect to age- and follow-up time-matched controls.<sup>[8]</sup> The mechanism of these side effects is largely unknown, but the temporal relationship implicates them to mirtazapine. Effect on the sensitive striatal alpha 2 adrenergic receptors in susceptible subjects could be the potential factor inducing movement-related adverse effects and may be an unusual phenotypic manifestation.<sup>[1]</sup>

Mirtazapine is considered as one of the safest options in elderly with depression. However, clinicians need to be aware of its potential resting tremor and akathisia related movement disorder adversities.

#### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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#### Conflicts of interest

There are no conflicts of interest.

**N. A. Uvais, V. S. Sreeraj<sup>1</sup>, P. Shihabudheen<sup>2</sup>,  
T. P. Mohammed<sup>3</sup>**

Departments of Psychiatry, <sup>2</sup>Medicine and <sup>3</sup>Internal Medicine, Iqraa International Hospital and Research Centre, Calicut, Kerala, <sup>1</sup>Department of Psychiatry, National Institute of Mental Health and Neurosciences, Bangalore, Karnataka, India


**Address for correspondence:** Dr. N. A. Uvais  
Department of Psychiatry, Iqraa International Hospital and  
Research Centre, Calicut, Kerala, India.  
E-mail: druvaisna@gmail.com

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