Mirtazapine Induced Akathisia: Understanding a Complex Mechanism

Sir,

Akathisia is a disabling extrapyramidal adverse effect which can occur with various psychotropic agents. Imbalance between dopaminergic and serotonergic/noradrenergic neurotransmitter systems is considered as a potential mechanism of akathisia.[1] Mirtazapine is a noradrenergic and specific serotonergic antidepressant (NaSSA) which acts by blocking alpha 2 receptors in addition to antagonizing the 5HT2 and 5HT3 receptors selectively.[2] Mirtazapine has been used to treat neuroleptic induced akathisia.[3] Intriguingly, this medication has been associated with occurrence of akathisia as an adverse effect.[4] Here we report the case of a patient with depressive illness who developed mirtazapine induced akathisia which was relieved by discontinuing the drug and by substituting it with another antidepressant.

A 42-year-old year lady with past history of one depressive episode 2 years ago presented with 4 month history of pervasive low mood, marked social withdrawal, anhedonia, ideas of hopelessness, occasional expressing of death wishes, decreased sleep and appetite. Her physical examination was within normal limits. She had diabetes mellitus which was poorly controlled as she was not regular with her antidiabetic medication since the onset of depressive symptoms. She did not significantly improve with tablet fluoxetine up to a dose of 40 mg given for 5 weeks. Subsequently she was started on tablet mirtazapine 15 mg. After initiation of mirtazapine, family members noticed that she was not sleeping at night and was seen pacing restlessly inside the house. On clarifying, the patient reported feeling anxious and jittery. She felt a sense of uneasiness in her feet and felt like walking constantly. She was unable to sit peacefully for more than a few minutes. There were no signs of elevation of mood and hence a possibility of antidepressant induced switch to mania/hypomania was ruled out. A clinical inference of akathisia was made. The Naranjo probability scale suggested a possible relationship between mirtazapine and this adverse event (score 6). Mirtazapine was stopped and the akathisia improved immediately in a couple of days. Barnes Akathisia Rating Scale score dropped from 6 to 0 within 2 days of stopping mirtazapine. The patient was subsequently started on tablet escitalopram 5 mg and gradually increased to 10 mg under close supervision. She did not report of any recurrence of akathisia symptoms and the depressive episode responded to escitalopram 10 mg.

The patient mentioned in this report developed akathisia immediately after the initiation of mirtazapine 15 mg/day and it was relieved promptly after discontinuation of the drug, indicating that the adverse effect was indeed due to mirtazapine. The exact mechanisms for akathisia with mirtazapine is unclear. Mirtazapine has broad range of affinities for adrenergic, serotonergic and histaminergic receptors and this might contribute to its favorable effects in clinical and preclinical models. It has been found that α2 adrenoceptor blockade is a key feature in the mechanism of mirtazapine action. The α2 adrenoceptors are found in prefrontal cortex and striatum.[5] Even though the affinity for mirtazapine in higher for the

prefrontal cortical α2 adrenoceptors, striatal receptor involvement can also potentially occur. It has been hypothesized that the beneficial effect of this medication in akathisia is due to 5HT2A antagonism while the α2 blockade might be responsible for akathisia.[3,4,6] Thus, even though mirtazapine is considered as a therapeutic option in antipsychotic induced akathisia, clinicians also need to be aware that it can produce this distressing extrapyramidal adverse effect.

Dhanya Raveendranathan, Gopal Rao Swaminath

Department of Psychiatry, B. R. Ambedkar Medical College, Bangalore, Karnataka, India

Address for correspondence: Dr. Dhanya Raveendranathan, Department of Psychiatry, Dr. Bhimrao Ramji Ambedkar Medical College, Bangalore - 560 045, Karnataka, India.
E-mail: dhanya.ravi@gmail.com

REFERENCES

1. Adler LA, Angrist B, Reiter S, Rotrosen J. Neuroleptic-induced akathisia: A review. Psychopharmacology (Berl) 1989;97:1-11.
2. Hartmann PM. Mirtazapine: A newer antidepressant. Am Fam Physician 1999;59:159-61.
3. Poyurovsky M, Pashinian A, Weizman R, Fuchs C, Weizman A. Low-dose mirtazapine: A new option in the treatment of antipsychotic-induced akathisia. A randomized, double-blind, placebo- and propranolol-controlled trial. Biol Psychiatry 2006;59:1071-7.
4. Gulsun M, Doruk A. Mirtazapine-induced akathisia. J Clin Psychopharmacol 2008;28:467.
5. Brosda J, Jantschak F, Pertz HH. alpha2-Adrenoceptors are targets for antipsychotic drugs. Psychopharmacology (Berl) 2014;231:801-12.
6. Poyurovsky M, Epshtein S, Fuchs C, Schneidman M, Weizman R, Weizman A. Efficacy of low-dose mirtazapine in neuroleptic-induced akathisia: A double-blind randomized placebo-controlled pilot study. J Clin Psychopharmacol 2003;23:305-8.

Access this article online	
Website: www.ijpm.info	**Quick Response Code**
DOI: 10.4103/0253-7176.168615	