A Case of Visual Illusions Secondary to Mirtazapine Treatment

Virginia Ferrari, MD[a]; Elisa Fontecedro, MD[a];
Matteo Balestrieri, MD, PhD[a]; and Fabio Sambataro, MD, PhD[a,b,*]

Mirtazapine is an antidepressant with presynaptic α_2 antagonist and postsynaptic 5-HT_2 and 5-HT_3 antagonist properties, which result in increased noradrenergic and serotonergic neurotransmission that contribute to its antidepressant effects.[1] Furthermore, this drug has histamine antagonist and anticholinergic properties, which could result in increased appetite and weight gain[2,3] that may be useful for the treatment of nondepressive conditions with cachexia and anorexia.[4,5]

Case Report

Mr A, an 86-year-old man, presented to the emergency department with protracted dysphagia and weight loss and was admitted to a general medicine ward for these complaints. His medical history included hypertension, gastroesophageal reflux disease, subclinical hypothyroidism, and mild cognitive impairment. There was no known history of psychiatric illness or illicit drug or alcohol use. Laboratory workup at admission showed reduced hemoglobin (12.4 g/dL) and hematocrit (38.3%) levels. Barium x-rays and esophagogastroduodenoscopy showed a hiatal hernia with Z-line metaplasia and esophageal diverticulum.

The patient complained of reduced appetite, decreased energy, and significant weight loss for the past 2 months. On the basis of this clinical presentation, depression was also considered. After psychiatric evaluation, a diagnosis of depression was excluded.

Mr A was started on his home medications (pantoprazole 40 mg/d and lisinopril 20 mg/d). After 10 days, he was also started on mirtazapine 30 mg nightly without titration to increase appetite. As soon as Mr A started mirtazapine, he developed visual illusions. These misperceptions began 1–2 hours after taking mirtazapine (8 PM), lasted for about 30 minutes, and disappeared spontaneously with no further intervention. During these episodes, while having clear vision, Mr A saw the hospital room flipped upside down. Notably, the unreality of the visual misperception was always clear to the patient; the sensorium and consciousness were intact as well as memory, attention, and orientation. These misperceptions did not occur during sleep initiation or termination. On the third day, mirtazapine was stopped, and he had no further visual misperceptions.

Discussion

This case suggests a relationship between mirtazapine use and visual illusions. The temporal course of this symptom suggests that these effects may be drug induced. The Naranjo criteria[6] (score: 7/10) indicates that these misperceptions were probably an adverse drug reaction to mirtazapine.

Mirtazapine is rapidly and completely absorbed after a single oral dose and reaches peak plasma levels within 1–2.1 hours.[7] The elderly have higher maximum plasma drug concentration as well as larger area under the curve and longer elimination half-life relative to younger individuals. Notably, Mr A's visual misperceptions always began about 1 to 2 hours after taking an oral dose of mirtazapine.

The literature[8,9] supports the association between mirtazapine and altered visual perception. Mirtazapine-induced auditory and visual hallucinations were reported in elderly patients at the beginning of treatment or during titration.[8] Notably, mirtazapine-induced delirium has also been described in the elderly starting at 30 mg/d, thus suggesting a greater susceptibility to this side effect at higher dosages, especially in light of age-related increases of mirtazapine availability.[9]

Although visual misperceptions have been previously associated with antidepressants, mostly selective serotonin reuptake inhibitors,[10] the mechanism by which mirtazapine can cause these symptoms is still unknown. Altered dopamine signaling may play an important role. Indeed, this neurotransmitter has been implicated in the pathophysiology of psychosis.[11]

Mirtazapine can modulate dopamine tone via 2 mechanisms: blocking α_2 receptors, resulting in increased corelease of norepinephrine and dopamine from noradrenergic terminals in the prefrontal[12] and occipital cortex,[13] and enhancing the output of cortical dopamine via 5-HT_{1A} receptor activation.[14]

In conclusion, mirtazapine is a well-tolerated drug recommended for the treatment of depression in the elderly. Although a potential role of mirtazapine to improve appetite and induce weight gain independent of antidepressant effects has been suggested in underweight elderly patients,[15] future studies on its tolerability in this population are warranted.[16]

[a]Department of Medicine, University of Udine, Udine, Italy
[b]Department of Neuroscience, University of Padova, Padua, Italy
*Corresponding author: Fabio Sambataro, MD, PhD, Department of Neuroscience, University of Padova, Via Giustiniani 2, Padua, Italy (fabio.sambataro@unipd.it).

Prim Care Companion CNS Disord 2020;22(1):19l02500

To cite: Ferrari V, Fontecedro E, Balestrieri M, et al. A case of visual illusions secondary to mirtazapine treatment. *Prim Care Companion CNS Disord*. 2020;22(1):19l02500.

To share: https://doi.org/10.4088/PCC.19l02500

Published online: February 6, 2020.

Potential conflicts of interest: None.

Funding/support: None.

Patient consent: Verbal consent was obtained from the patient to publish the case report, and information was de-identified to protect anonymity.

REFERENCES

1. de Boer T. The pharmacologic profile of mirtazapine. *J Clin Psychiatry*. 1996;57(suppl 4):19–25.
2. Montgomery SA. Safety of mirtazapine: a review. *Int Clin Psychopharmacol*. 1995;10(suppl 4):37–45.
3. Watanabe N, Omori IM, Nakagawa A, et al; MANGA (Meta-Analysis of New Generation Antidepressants) Study Group. Safety reporting and adverse-event profile of mirtazapine described in randomized controlled trials in comparison with other classes of antidepressants in the acute-phase treatment of adults with depression: systematic review and meta-analysis. *CNS Drugs*. 2010;24(1):35–53.
4. Riechelmann RP, Burman D, Tannock IF, et al. Phase II trial of mirtazapine for cancer-related cachexia and anorexia. *Am J Hosp Palliat Care*. 2010;27(2):106–110.
5. Marvanova M, Gramith K. Role of antidepressants in the treatment of adults with anorexia nervosa. *Ment Health Clin*. 2018;8(3):127–137.
6. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30(2):239–245.
7. Timmer CJ, Sitsen JM, Delbressine LP. Clinical pharmacokinetics of mirtazapine. *Clin Pharmacokinet*. 2000;38(6):461–474.
8. Padala KP, Padala PR, Malloy T, et al. New onset multimodal hallucinations associated with mirtazapine: a case report. *Int Psychogeriatr*. 2010;22(5):837–839.
9. Bailer U, Fischer P, Küfferle B, et al. Occurrence of mirtazapine-induced delirium in organic brain disorder. *Int Clin Psychopharmacol*. 2000;15(4):239–243.
10. Marcon G, Cancelli I, Zamarian L, et al. Visual hallucinations with sertraline. *J Clin Psychiatry*. 2004;65(3):446–447.
11. Rogóz Z, Wróbel A, Dlaboga D, et al. Effect of repeated treatment with mirtazapine on the central dopaminergic D2/D3 receptors. *Pol J Pharmacol*. 2002;54(4):381–389.
12. Millan MJ, Gobert A, Rivet JM, et al. Mirtazapine enhances frontocortical dopaminergic and corticolimbic adrenergic, but not serotonergic, transmission by blockade of alpha2-adrenergic and serotonin2C receptors: a comparison with citalopram. *Eur J Neurosci*. 2000;12(3):1079–1095.
13. Devoto P, Flore G, Pira L, et al. Mirtazapine-induced corelease of dopamine and noradrenaline from noradrenergic neurons in the medial prefrontal and occipital cortex. *Eur J Pharmacol*. 2004;487(1–3):105–111.
14. Nakayama K, Sakurai T, Katsu H. Mirtazapine increases dopamine release in prefrontal cortex by 5-HT1A receptor activation. *Brain Res Bull*. 2004;63(3):237–241.
15. Hilas O, Avena-Woods C. Potential role of mirtazapine in underweight older adults. *Consult Pharm*. 2014;29(2):124–130.
16. Cancelli I, Marcon G, Balestrieri M. Factors associated with complex visual hallucinations during antidepressant treatment. *Hum Psychopharmacol*. 2004;19(8):577–584.