

Modafinil-Induced Mania in an Elderly Man

To the Editor: Modafinil is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea, or shift work disorder.¹ There are several reports^{2–8} of modafinil inducing mania in patients with a history of a primary psychiatric or neurologic disorder. We report the case of a 66-year-old man who presented with manic symptoms associated with modafinil therapy. To the best of our knowledge, this report is the first concerning the risk of modafinil to induce mania in an elderly patient with no history of a mood or psychiatric disorder.

Case report. Mr A is a 66-year-old man with no documented psychiatric history admitted involuntarily to our inpatient psychiatric unit after he was found naked and agitated in his neighborhood. At admission, Mr A presented as an obese man with agitation, irritability, grandiosity, pressured speech, and impaired insight. He scored 42 on the Young Mania Rating Scale (YMRS).⁹ He was fully alert and oriented with no clouding of consciousness. Mr A was not intoxicated and had a negative urine drug screen. There was no known history of bipolar illness or other psychiatric disorder in his family. Collateral information from Mr A's wife revealed that he was prescribed modafinil 100 mg/d 2 months ago to manage excessive daytime sleepiness associated with obstructive sleep apnea and started to show symptoms of mania (decreased need for sleep, irritability, racing thoughts, reckless spending) 1 week after initiation. His other medications included a multivitamin supplement, lisinopril 10 mg/d for high blood pressure, and atorvastatin 40 mg/d for high cholesterol. He was taking no other medications or over-the-counter supplements and had no other known medical illnesses.

Head computed tomography, chest radiography, and blood chemistry results were all within normal limits. Given the lack of prior history of mood disorder and the temporal relationship between the manic symptoms and the introduction of modafinil, the treatment team discontinued modafinil and took a wait-and-see approach, deciding not to use an antipsychotic or a mood stabilizer. After 2 days, Mr A began to show improvement in his thought process, his speech became less pressured, and his sleep improved. For the next 3 days, Mr A was no longer grandiose or agitated and gained some insight in recognizing his recent reckless spending. Mr A stayed on our unit for 9 days and improved steadily. On the day of discharge, Mr A scored 1 (sleeping less than normal amount by up to 1 hour) on the YMRS. Mr A was discharged from the hospital for follow-up care with a community psychiatrist and given the diagnosis of modafinil-induced bipolar disorder (DSM-5). Six months post discharge, the patient continued to be free of manic symptoms.

Modafinil is thought to have indirect γ -aminobutyric acid inhibition, dopamine receptor agonism, α_1 -adrenergic agonism, and dopamine reuptake inhibition.¹ In vitro, modafinil binds to the dopamine transporter and inhibits dopamine reuptake. This

activity has been associated in vivo with increased extracellular dopamine levels in some brain regions of animals.¹ Modafinil produces psychoactive and euphoric effects and alterations in mood, perception, thinking, and feelings typical of other central nervous system stimulants in humans. The mechanism of action for induction of mania in patients taking modafinil is currently unknown.¹⁰ We believe that modafinil was the most likely cause of Mr A's manic symptoms because manic symptoms appeared 1 week after the administration of modafinil, and he became euthymic shortly after discontinuation. Currently, there are no guidelines for the treatment of modafinil-induced mania. In our case, removal of the culprit drug was sufficient treatment for symptom resolution. New-onset mania is a possible complication of modafinil use. Patients should be carefully monitored for the onset of manic symptoms when taking modafinil.

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Potential conflicts of interest: None.

Funding/support: None.

Patient consent: Permission was received from the patient to publish this case, and the information has been de-identified to protect anonymity.

Published online: May 24, 2018.

Prim Care Companion CNS Disord 2018;20(3):17102187

To cite: Francois D, Chelidze K. Modafinil-induced mania in an elderly man. *Prim Care Companion CNS Disord*. 2018;20(3):17102187.

To share: <https://doi.org/10.4088/PCC.17102187>

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