New Onset of Compulsive Gambling Associated With Modafinil: A Case Report

To the Editor: We describe a case of compulsive gambling associated with the use of modafinil in a patient with idiopathic hypersomnia. Modafinil is a wakefulness-promoting agent that is approved by the US Food and Drug Administration for hypersomnolence associated with narcolepsy, obstructive sleep apnea, shift work sleep disorder, and fatigue associated with multiple sclerosis.[1] Modafinil prescribing information reports psychiatric adverse experiences including mania, delusions, hallucinations, suicidal ideation, and depression.[1] Tarrant and colleagues[2] have described a case of a patient with minor gambling, who reported a 10-fold increase in his slot-machine use after taking modafinil. However, new-onset impairment of impulse control has been more commonly described in patients receiving dopamine agonist therapy for restless legs syndrome and Parkinson's disease.[3]

Case report. A 46-year-old white woman with history of idiopathic hypersomnia diagnosed in 2005 at another sleep center presented to our sleep clinic as a transfer of care in 2010. She had history of excessive daytime sleepiness dating back to early school years. She had also experienced hypnogogic hallucinations and occasional sleep paralysis. There was no clear history of cataplexy. In 2005, her primary complaint included excessive sleepiness and snoring. She underwent diagnostic polysomnography (PSG) and a multiple sleep latency test (MSLT with 4 naps). Review of these records indicated an unremarkable PSG. Results from a MSLT performed after 8 hours of PSG-documented sleep showed a sleep latency of 4 minutes 45 seconds with no sleep-onset rapid-eye-movement periods. She was diagnosed with narcolepsy without cataplexy (based on *International Classification of Sleep Disorders*, second edition[4]), and modafinil was started at a dose of 200 mg in the morning and a 100-mg additional dose if needed for residual daytime sleepiness. She had a good response to the medication and no longer required daily naps.

The patient's hypersomnolence symptom remained stable on a dose of 200 mg of modafinil for a year when she developed impulsive gambling. She was not taking any other medications at that time. She tried to curtail her gambling, but could not, and would go to casinos and lose significant amounts of money until she was seen in our sleep center in 2010.

She described losing up to $1,000 each time and reported losing $20,000 in the past 5 years prior to the visit to our clinic. She has tried behavior modifications such as talking to her husband when there was an urge to gamble, but had little success. In the year 2010, she was switched from modafinil to methylphenidate, which helped resolve gambling severity within a month. She was never restarted on modafinil after this as she did not want to risk having another episode of gambling again.

On a follow-up visit the next year, she reported improvement in the compulsive gambling. She still had urges, but was able to exercise control over the impulses. In regard to her hypersomnolence symptoms, however, she had better results with modafinil. A more divided dose of methylphenidate was recommended during the visit. The patient has continued to take methylphenidate since 2010 and has had no reported side effects. She was taking a sustained dose of methylphenidate with good response.

Impulse-control disorders (ICD) are characterized by excessive rumination and/or unwanted behaviors that lead to dysfunction or interference with work or social functioning.[5]

In a group of patients treated with dopaminergic agents, up to 17% of patients developed ICDs, of which 5% was pathological gambling. Mean time to onset of symptoms was 9.5 months.[6]

Modafinil is a non-amphetamine stimulant medication, and the exact mechanism of action is unknown.[7] The wakefulness-promoting action useful in narcolepsy treatment could be due to activation of orexin neurons in the hypothalamus.[6] In addition, modafinil has been shown to inhibit dopamine transporter and increase cortical and caudate dopamine concentrations.[8] The effects of modafinil on impulse control are poorly studied. Zack and Poulos[9] found that modafinil can have bidirectional effects on pathological gambling patients, ie, it can increase desire to gamble, disinhibition, and risky decision-making in low-impulsivity subjects, while decreasing these indexes in high-impulsivity subjects.

In our patient, a previous history of gambling was not associated with disruption in her life. Moreover, there was no previous psychiatric comorbidity. She did not describe episodic hypersomnia, suggestive of Kleine-Levin syndrome, which commonly is associated with behavioral disturbances. However, the patient developed a new-onset pathological gambling and an inability to stop despite financial and social repercussions. Symptoms began after the use of modafinil, with significant improvement in gambling preoccupation and urges once the medication was stopped. While the majority of patients who develop ICDs while using dopaminergic agents for Parkinson's disorder will have remission of symptoms, ICDs, particularly pathological gambling, can persist.[10]

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