General Hospital Psychiatry 37 (2015) e7–e8

Contents lists available at ScienceDirect

General Hospital Psychiatry

journal homepage: http://www.ghpjournal.com

E-only Letter

Compulsive modafinil use in a patient with a history of alcohol use disorder

To the Editor,

The mechanism of action of modafinil, a nonamphetamine stimulant, remains unknown [1,2]. Modafinil is prescribed for a variety of medical conditions including narcolepsy, obstructive sleep apnea, shift work sleep disorder and bipolar depression [3,4].

Modafinil is a dopamine transporter inhibitor [5] with low abuse liability; its efficacy has been investigated for the treatment of cocaine, methylphenidate and alcohol addiction [6–8]. However, few studies have been conducted on the addictive potential of modafinil, although it has been suggested that modafinil should be used with caution [2,3,8]. An association between modafinil use and pathological gambling has been reported, possibly due to the potentiation of the dopaminergic system [9]. To the best of our knowledge, the case described herein represents the first report of compulsive modafinil use, which occurred following 2 years of modafinil treatment.

A 34-year-old male presented with a history of recurrent depression and alcohol addiction for 11 years. He was admitted to our clinic and diagnosed with major depression with psychotic features 3 years previously; psychiatric outpatient follow-up was irregular. The patient was treated with various psychotropic medications (e.g., Selective serotonin reuptake inhibitors (SSRIs), Serotonin-norepinephrine reuptake inhibitors (SNRIs) and Tricyclic antidepressants (TCAs) antidepressants, benzodiazepines and carbamazepine). Due to abuse, benzodiazepine treatment was discontinued 2 years previously. The patient complained of oversleeping, fatigue and anhedonia not relieved by medication. Laboratory analysis revealed no abnormalities, and neurological evaluation was normal. Two years previously, modafinil was added to his treatment regimen, which comprised duloxetine at 60 mg/day, bupropion at 150 mg/day, modafinil at 200 mg/day and amisulpride at 400 mg/day. This regimen was maintained for 1.5 years; the patient reported that it increased his energy levels.

Following a 6-month absence, the patient reported to our clinic stating that he had increased the dose of modafinil to 35 tablets per day (3500 mg/day), using tablets prescribed at nonpsychiatric and psychiatric outpatient clinics or purchased without prescription. We offered hospitalization or outpatient follow-up; the patient declined to be hospitalized. No signs of modafinil addiction were detected, and we altered his treatment regimen as follows: modafinil dose was gradually decreased; duloxetine was increased to 90 mg/day; bupropion and amisulpride doses were maintained at current levels; and carbamazepine was added at 600 mg/day,

Modafinil dopamine receptor affinity is similar to that of methylphenidate, suggesting possible abuse liability [2,10]. In the present case, modafinil was used for treatment-resistant depression, and it ameliorated oversleeping, fatigue and anhedonia. However, the patient reported that dose escalation was necessary to maintain his improved mood. We suggested that the duloxetine dose be increased instead and that the dose of modafinil be decreased gradually, given its stimulant action. To reduce impulsivity, we suggested carbamazepine as more appropriate compared with modafinil dose escalation because modafinil shares structural similarities with cocaine [11]. According to the most recent psychiatric records obtained from another hospital, the patient applied to other psychiatric clinics and decreased his modafinil dosage to five tablets per day (500 mg/day) in accordance with our suggested treatment regimen. At the most recent psychiatric follow-up, also at another clinic, amisulpride was ceased following consultation with our unit.

During sensitization, behavioral and neurochemical responses after substance abuse are potentiated [12], a process that can underlie addictive behavior. D1 receptors represent one possible mediator of sensitization [13]. Amisulpride exhibits only marginal affinity for the postsynaptic D1 receptor [14], but this would be exacerbated by the dopamine reuptake inhibitory effects of bupropion [15] and modafinil. Compulsive modafinil use may be associated with the increase in synaptic dopamine transmission that preferentially stimulates postsynaptic D1 receptors.

Modafinil may exert different effects in accordance with personality profile [16]; no personality measurement instruments were applied in the present case, which represents a limitation to the study.

In conclusion, in patients with a history of addiction and low treatment compliance, dopamine-enhancing medication should be used with caution; potential interactions with other prescribed drugs should be considered to reduce the likelihood of compulsive use.

Melek Cengiz Mete, MD
Ömer Şenormancı, MD
Özge Saraçlı, MD
Nuray Atasoy, MD
Levent Atik, MD
Professor, Bülent Ecevit University School of Medicine, Psychiatry
Zonguldak, Turkey
E-mail address: senorman_7@hotmail.com

http://dx.doi.org/10.1016/j.genhosppsych.2015.01.001

References

[1] Wisor J. Modafinil as a catecholaminergic agent: empirical evidence and unanswered questions. Front Neurol 2013;4:139.
[2] Schmitt KC, Reith ME. The atypical stimulant and nootropic modafinil interacts with the dopamine transporter in a different manner than classical cocaine-like inhibitors. PLoS One 2011;6:25790.
[3] Davies M, Wilton L, Shakir S. Safety profile of modafinil across a range of prescribing indications, including off-label use, in a primary care setting in England: results of a modified prescription-event monitoring study. Drug Saf 2013;36:237–46.

[4] Goss AJ, Kaser M, Costafreda SG, Sahakian BJ, Fu CH. Modafinil augmentation therapy in unipolar and bipolar depression: a systematic review and meta-analysis of randomized controlled trials. J Clin Psychiatry 2013;74:1101–7.
[5] Mereu M, Bonci A, Newman AH, Tanda G. The neurobiology of modafinil as an enhancer of cognitive performance and a potential treatment for substance use disorders. Psychopharmacology (Berl) 2013;229:415–34.
[6] Sofuoglu M, DeVito EE, Waters AJ, Carroll KM. Cognitive enhancement as a treatment for drug addictions. Neuropharmacology 2013;64:452–63.
[7] Schmaal L, Goudriaan AE, Joos L, Krüse AM, Dom G, van den Brink W, et al. Modafinil modulates resting-state functional network connectivity and cognitive control in alcohol-dependent patients. Biol Psychiatry 2013;73:789–95.
[8] Shuman T, Cai DJ, Sage JR, Anagnostaras SG. Interactions between modafinil and cocaine during the induction of conditioned place preference and locomotor sensitization in mice: implications for addiction. Behav Brain Res 2012;235:105–12.
[9] Tarrant N, Cavanna AE, Rickards H. Pathological gambling associated with modafinil. J Neuropsychiatry Clin Neurosci 2010;22:E27–8.
[10] Kim W, Tateno A, Arakawa R, Sakayori T, Ikeda Y, Suzuki H, et al. In vivo activity of modafinil on dopamine transporter measured with positron emission tomography and [^{18}F]FE-PE2I. Int J Neuropsychopharmacol 2014;17:697–703.
[11] Llopis Llácer JJ, Castillo Aguilella A. Efficacy of oxcarbazepine treatment in patients diagnosed with cocaine abuse/dependence. Adicciones 2008;20:263–70.
[12] Vanderschuren LJ, Kalivas PW. Alterations in dopaminergic and glutamatergic transmission in the induction and expression of behavioral sensitization: a critical review of preclinical studies. Psychopharmacology (Berl) 2000;151:99–120.
[13] Hummel M, Unterwald EM. D1 dopamine receptor: a putative neurochemical and behavioral link to cocaine action. J Cell Physiol 2002;191:17–27.
[14] Möller HJ. Amisulpride: limbic specificity and the mechanism of antipsychotic atypicality. Prog Neuropsychopharmacol Biol Psychiatry 2003;27:1101–11.
[15] Fava M, Rush AJ, Thase ME, Clayton A, Stahl SM, Pradko JF, et al. 15 years of clinical experience with bupropion HCl: from bupropion to bupropion SR to bupropion XL. Prim Care Companion J Clin Psychiatry 2005;7:106–13.
[16] Zack M, Poulos CX. Effects of the atypical stimulant modafinil on a brief gambling episode in pathological gamblers with high vs. low impulsivity. J Psychopharmacol 2009;23:660–71.