Psychiatria Danubina, 2019; Vol. 31, No. 3, pp 369-370 https://doi.org/10.24869/psyd.2019.369 *Case report*

MODAFINIL INTOXICATION INDUCED PERSISTENT PSYCHOSIS: CASE REPORT

Ebru Şahan & Özgür Bölükbaşı

Bezmialem Vakif University, Department of Psychiatry, Istanbul, Turkey

received: 27.5.2019; revised: 19.7.2019; accepted: 30.8.2019

* * * * *

INTRODUCTION

Modafinil is a psychostimulant drug used in narcolepsy and other daytime sleep disorders. Its dopaminergic, histaminergic, noradrenergic, glutamatergic, GABAergic, and serotonergic actions may be associated with various neurochemical and behavioral effects.

Very few papers have been published on neuropsychiatric diseases resulting from modafinil intoxication. Most of the cases are on acute psychotic manifestations after modafinil use even in small doses (Aytas & Dilek Yalvac 2015, Mariani & Hart 2005, Narendran et al. 2002, Prado et al. 2012, Rudhran et al. 2013, Wu et al. 2008). In this manuscript, we aimed to present a patient who attempted suicide with 12 gr of modafinil and stayed in intensive care unit for a month, later presented to a psychiatrist with psychosis.

CASE

A 17-year-old girl preparing for the university entrance exams admitted to neurology outpatient clinic with daytime sleepiness complaints. She had no previous medical and psychiatric history and no family history of narcolepsy or hypersomnia; the diagnosis of idiopathic hypersomnia was made. She was started on 100 mg/day of modafinil and one month later because of partial response it was raised to 200 mg/day. Due to various stressors and exam anxiety, she committed suicide with 12 blister packs of 10 tablets each containing 100 mg modafinil (0.18 gr/kg, 12 gr of modafinil in total) and was brought to the emergency department with altered consciousness. She was lethargic and immediately transferred to the intensive care unit with toxic encephalopathy and stayed there for one month. After discharge, she rejected eating, had visual and auditory halucinations and admitted to many psychiatrists. She had been treated with high potency antipsychotics: haloperidol decanoate 50 mg/ml gluteal injection once in a month and risperidone 4 mg/day orally with biperiden 2 mg/day. Despite using these for six months, she had no clinical improvement and admitted to our outpatient clinic. In clinical examination, she had antipsychotic-induced akathisia, anger, irritability, restlessness, impulsivity including self-harm, sleep disorders, perseverative movements, visual and auditory hallucinations. She was hospitalized in our psychiatry inpatient clinic.

After an initial assessment, in consideration of antipsychotic related akathisia, patient's high potency antipsychotic treatment was stopped and she was started to lorazepam. Magnetic Resonance Imaging (MRI) of the brain showed cerebral volume loss, enlargement in the ventricular system and cortical atrophy. Neurology consultation was requested for patient's bradykinesia, rigidity, bradymimic eye movements, loss of automatic movements of arms. She was walking with short steps and had a prolonged reaction time. Positron Emission Tomography (PET) scan of the brain was taken, the left parietal and temporal regions were partially hypometabolic compared to right side and mild hypometabolism was found in the frontal cortex and anterior cingulate gyrus. In the following days, patient's akathisia improved. Considering her brain damage we decided to start treatment with antipsychotics with low risk of extrapyramidal symptoms. Quetiapine 200 mg/day was started and increased to 1000 mg/day within 3 weeks.

The patient was scheduled to undergo neuropsychological tests. Her Mini-Mental Status Exam (MMSE) test score was 22. She could not co-operate on the subsequent tests at first week because of her hallucinations and anxiety. When these symptoms were relieved, we repeated the neuropsychological tests and mild deficits in the mental trail, maintenance of attention and visual-spatial working memory were observed.

Considering the neuropsychiatric symptoms such as personality change, depression, hallucination, anxiety, and mild neurocognitive impairment, the limbic encephalitis took a part in the differential diagnosis. Testing for the NMDA receptor antibodies had been done and it was negative.

After three weeks of treatment with quetiapine, her symptoms were remarkably reduced. Due to her emotional instability and intermittent explosions during her inpatient stay, valproate 500 mg/day was added both for mood stabilization and neuroprotection. In her post-discharge follow-up, patient's hallucinations were disappeared and she experienced fewer anger attacks.

DISCUSSION

It is known that modafinil increase extracellular dopamine, norepinephrine and serotonin concentrations in the neocortex (Minzenberg & Carter 2008). Additionally, it has an effect on glutamate increase and gamma-aminobutyric acid (GABA) decrease both on hippocampus and hypothalamus. Also, by stimulation of hypocretin neurons, it induces an increment on histamine release (Neuman et al. 2009). Apart from other wake-promoting agents such as amphetamines, modafinil is highly active and selective to Dopamine and/or Norepinephrine Transporters (DAT, NET). At clinically recommended doses, it is shown that modafinil binds and inhibits DAT and/or NET and promotes wakefulness on hypothalamus-based circuits (Madras et al. 2006). On the other hand, in toxic doses, it may evoke dyskinesia which suggests the dopaminergic role of modafinil (Neuman et al. 2009). Although modafinil overdose is rarely seen, it is generally of moderate severity. Most commonly seen side effects are tachycardia, agitation, increased anxiety, headache, hypertension, dizziness, insomnia, tremors, and dystonia. Major clinical effects, cardiac dysrhythmias, toxic encephalopathy or death have not been reported yet. Our patient may have had the signs and symptoms of CNS toxicity, toxic encephalopathy from modafinil overdose.

Clinical management of modafinil overdose is generally supportive including cardiovascular monitoring and surveillance of the patient's psychomotor condition until the symptoms relieved (Spiller et al. 2013).

With reported ingestions of doses up to 8 g, as far as we know, our case has a very high intoxication dose which is 12 g of modafinil. Although 60 times of recommended dose of modafinil was ingested, it did not cause mortality but seems to have evoked an organic mental disorder in our case. The modafinil intoxication induced toxic encephalopathy in this case may have caused brain damage which might have a role in psychosis.

There have not been an enough follow-up period for modafinil intoxicated cases to see which neuropsychiatric symptoms are transient and which are persistent yet.

Clinical studies investigating if any difference exists in characteristics and prognosis of modafinil overdose induced psychosis cases who were with or without encephalopathy at the time of intoxication are needed.

Fortunately, the outcome of 12 g of modafinil ingestion was not fatal for this 17-year-old girl but the patient had long term damage from modafinil adverse effects resulting in encephalopathy and psychotic disorder.

Acknowledgements: *None.*

Conflict of interest: *None to declare.*

Contribution of individual authors:

Ebru Şahan & Özgür Bölükbaşı made substantial contributions to conception and design, acquisition of case history, analysis and interpretation of physical and psychiatric examination, laboratory and radiological findings, participated in drafting the article, and gave final approval of the version to be submitted.

Ebru Şahan revised the article critically for important intellectual content.

References

1. *Aytas O, Dilek Yalvac H: Modafinil-Induced Psychosis: A Case Report. Noro Psikiyatr Ars 2015; 52: 99-101*
2. *Mariani JJ, Hart CL: Psychosis associated with modafinil and shift work. Am J Psychiatry 2005; 162: 1983*
3. *Narendran R, Young CM, Valenti AM et al.: Is psychosis exacerbated by modafinil? Arch Gen Psychiatry 2002; 59:292-293*
4. *Wu P, Jones S, Ryan CJ et al: Modafinil-induced psychosis. Intern Med J 2008; 38: 677-678*
5. *Prado E, Paholpak P, Ngo M et al: Agitation and psychosis associated with dementia with lewy bodies exacerbated by modafinil use. Am J Alzheimers Dis Other Demen 2012; 27: 468-473*
6. *Rudhran V, Manjunatha N, John JP: High-dose, self-administered modafinil-related psychosis: is it the pedal in the prodrome of psychosis? J Clin Psychopharmacol 2013 33: 576-577*
7. *Minzenberg MJ, Carter CS: Modafinil: A Review of Neurochemical Actions and Effects on Cognition. Neuropsychopharmacology 2008; 33: 1477-1502*
8. *Neuman G, Shehadeh N, Pillar G: Unsuccessful Suicide Attempt of a 15 Year Old Adolescent with Ingestion of 5000 mg Modafinil. Journal of Clinical Sleep Medicine : JCSM : Official Publication of the American Academy of Sleep Medicine 2009; 5: 372-373*
9. *Madras BK, Xie Z, Lin Z et al: Modafinil Occupies Dopamine and Norepinephrine Transporters in Vivo and Modulates the Transporters and Trace Amine Activity in Vitro. Journal of Pharmacology and Experimental Therapeutics 2006; 319: 561-569*
10. *Spiller HA, Hays HL, Aleguas A, Jr.: Overdose of drugs for attention-deficit hyperactivity disorder: clinical presentation, mechanisms of toxicity, and management. CNS Drugs 2013; 27: 531-543*

Correspondence:
Ebru Şahan, MD
Department of Psychiatry, Bezmialem Vakif University
Adnan Menderes Boulevard (Vatan Street) P.K. 34093 Fatih / İstanbul, Turkey
E-mail: ebrushaan@hotmail.com