



Modafinil Dependence: A Case with Attention-Deficit/Hyperactivity Disorder

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Modafinil is generally known as a drug with low addiction potential. There are few case reports in the literature demonstrating that Modafinil, stated being capable of diminishing symptoms of attention deficit/hyperactivity disorder (ADHD), causes addiction. In the present article a Modafinil addicted ADHD case, consuming usurious doses (5,000 mg/per day) of Modafinil is presented. The case presented to our psychiatry outpatient clinic due to: requirement of in taking high dose Modafinil in order to achieve the initial effects, difficulty in obtaining the drug, irritability, anxiousness, sleep irregularities, fatigue and unpleasant vivid dreams when he did not use the drug. It was realized that the patient, himself increased doses of Modafinil incrementally, in order to keep its effects on attention symptoms at the same level. It has to be kept in mind that ADHD patients can develop Modafinil addiction. It is necessary to carry out systemic studies on this subject.

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Key Words Modafinil, Dependence, Attention-deficit/hyperactivity disorder.

INTRODUCTION

Modafinil is a non-amphetamine type stimulant used in narcolepsy, obstructive sleep apnea syndrome and circadian rhythm disorder.¹ Modafinil has also been tried for disease-related fatigue, attention-deficit disorder, Alzheimer's disease, age-related memory decline, depression, cognitive impairment in schizophrenia, idiopathic hypersomnia, myotonic dystrophy, post-anaesthesia grogginess and everyday cat-napping.² Even though the action mechanism is not clear, it is thought to be distinct from other stimulant drugs.³ Modafinil is known to act via its effects on noradrenergic (activation of alpha-1 receptors)⁴ and dopaminergic⁵ neurotransmission. Its wakefulness and activity-promoting properties are mostly related to its effects on these neuromediators.⁶

Due to its dopaminergic activity and low abuse potential, Modafinil has been used in treatment of cocaine⁷ and meth-

amphetamine⁸ abuse and correction of disturbed cognitive functions in alcohol dependent subjects.⁹ Even though Modafinil abuse is not frequent, it's still possible to encounter patients abusing the substance.¹ There are rare reports of Modafinil abuse in literature. In two of the three case reports that we encountered, subjects with Modafinil abuse concurrently had history of alcohol and benzodiazepine dependence, whereas a case who had schizoaffective disorder did not have history of alcohol or drug abuse. Maximum amount of Modafinil intake of the cases in these reports was 3,000 mg/day.¹⁰⁻¹²

In this report, we present a case with high-dose (5,000 mg/day) Modafinil dependence who had no history of alcohol or substance abuse and was diagnosed with attention deficit hyperactivity disorder (ADHD).

CASE

Twenty-four years old male, single student, living in county town with his parents stated, in his own words that; he had been facing difficulty in listening to classes since primary school, had issue in concentrating, difficulty in making friends, had low academic success, had coerced particularly during transition to higher education and due to performance anxiety had clinical psychologist visits. Developmental and past psychiatric history, corroborated by his parents confirmed these

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complaints. During childhood he was obviously more active than peers, and he was easily distracted by external stimulus. The parents reported that, when he was 10 years old, they admitted to a child psychiatry policlinic complaining of inattention, difficulty in completing school work, organizing activities, following instructions, committing frequent mistakes, losing belongings and forgetting daily routines. He was diagnosed with ADHD by the child psychiatrist and stimulant medication was indicated. However, parents refused medical treatment due to concerns related to side effects. No further treatment was searched.

Patient reported that approximately 5 years ago, he began consuming omega 3-6-9 preparations and vitamin supplements in order to increase his social and academic performance. Subsequently approximately 3 years ago, without any doctor suggestion, he commenced taking Modafinil in 50 mg/day dose, and gained improvements in attention, self-reliance, academic success and social activity. After a while, in order to be able to maintain initial effects, he necessitated increasing the dose and went on using Modafinil at 300–400 mg/day dose during 2 years. It was ascertained that since his ailments were not totally resolved and his exam load increased, 1 year ago he presented to a different psychiatry clinic than ours, where 20 mg/day short-acting Methylphenidate was initiated for attention deficiency and hyperactivity disorder diagnose. It's realized that, as an addition to Modafinil he used short-acting Methylphenidate 60 mg/day. The patient stated that, even though he benefited from the Methylphenidate treatment, he did not use regularly and discontinued the drug. During the last year, he increased the Modafinil dose, in order to achieve the initial effects Modafinil and resulted in consuming 100 mg tablets, 5 times a day and 10 tablets most of the time. Whenever he quit using Modafinil or diminished the amount, he experienced irritability, anxiousness, sweating, tremor and an urge to take excessive Modafinil. The case presented to a different psychiatry clinic with a desire to quit Modafinil, where Modafinil was stopped and Venlafaxine at 75 mg/day, Risperidone 2 mg/day, Propranolol 80 mg/day and Olanzapine 5 mg/day were initiated. After discontinuation of Modafinil, he experienced fatigue, vivid and unpleasant dreams, sleeping irregularities, anxiousness, and functionality impairment, as previously. Since, despite the given treatment his complaints did not subside, he abandoned treatment and revert using Modafinil.

Modafinil that could be purchased over the counter before, became a prescription medicine with recent regulations in Turkey. Therefore the patient encountered difficulty in accessing the drug and presented to our polyclinic. During his anamnesis he presented his complaints as necessity to consume usurious doses of Modafinil, to be able to achieve the initial

effects, difficulty in obtaining the medicine, irritability, tremor, anxiety, sleep disorder, fatigue, and unpleasant vivid dreams when he did not use the drug. It was realized that he was consuming 5,000 mg/day Modafinil since 1 month. After evaluation, he was admitted to our psychiatry ward with the initial diagnosis of “stimulant use disorder” according to DSM-5 classification.

During mental state examination performed in our clinic, he appeared at his age, was self-sufficient, his associations were normal, his speaking rate and amount was partially increased, and was anxious. He did not have active psychotic thought content, evaluation of actuality was normal. He had irregular sleeping pattern, decreased appetite and normal libido.

Family history revealed that his elder brother previously had alcohol addiction.

In our psychiatry ward, the patient was introduced Lorazepam 2.5 mg/day, Risperidon 1 mg/day and Ketiapin 25 mg/day. Following abandoning of Modafinil, cravings, psychomotor agitation, sweating, tremor, fatigue were observed. Therefore his treatment was modified to Diazepam 15 mg/day, Ketiapin 100 mg/day, Risperidon 2 mg/day. On the third day of his admission, the patient was discharged from the ward upon his own will. During his first control in outpatient clinic, it was realized that, although he had some benefits from treatment, his compliance to medication was poor. He requested prescription of Modafinil, and he did not attend to further control visits.

DISCUSSION

Due to weak inhibition of dopamine reuptake pumps, Modafinil increases dopamine in some areas of the brain, mainly the cortex, striatum and nucleus accumbens.¹³ Studies investigating this mechanism revealed that, cortex and striatum are diffusely activated following amphetamine administration to rats. With Modafinil use, activated areas are restricted with paraventricular and suprachiasmatic nuclei, anterior hypothalamus, amygdala and tuberomamillary nucleus.¹⁴ Modafinil increases the effects of dopamine and norepinephrine by binding to carrier proteins of these catecholamines.¹⁵ Unlike amphetamine, Modafinil does not have an influence on dopamine release and cycle in mouse striatum, has very little influence on blood flow to the brain cortex, and results in a metabolic activation that is different from amphetamine.⁶ This may be the explanation for its low abuse potential. Despite all these diversities, Modafinil's effect related with stimulation and behavioral activity are supposed to be at least partially involving dopamine.¹⁶ D1 and D2 receptors also take role in effects of Modafinil on cognitive functions and behavior.⁶

Affinity of Modafinil to dopamine receptors resembles methylphenidate. This can be reason of possible risk for abuse.^{13,17} Modafinil dependence may be related to its dopamine increasing effect in dopaminergic areas of the brain via reuptake inhibition.⁵ Postsynaptic D1 receptors are one of the mediators of sensitization; increased dopamine transmission results in increased stimulation of D1 receptors, compulsive use of Modafinil may be related to this.¹⁸⁻²⁰

Modafinil is thought to enhance cognitive functions such as attention, learning and memory via acting differently from the typical psychostimulants.⁵ Promotion of cognitive functions by Modafinil has been investigated in many mental disorders that result in decreased cognitive functions.⁶ As an example, a study with schizophrenic patients using Modafinil, in addition to antipsychotic treatment, aiming to decrease cognitive functions had promising results.²¹ Our case had symptoms of ADHD that impaired cognitive functions, such as lack of attention, difficulty in concentrating and difficulty in educational life. Modafinil was helping him to overcome these symptoms. There are also studies that presented Modafinil to be effective in treatment of ADHD.^{22,23} Illegal use of Modafinil has been reported in substance abusers and patients with organic mental disease in order to enhance cognitive functions. This is also supported with the fact that two of the previously reported cases had history of alcohol and benzodiazepine addiction, and the third reported case had schizoaffective disorder.²⁴

One report from India mentioned 1,200 mg/day Modafinil dose, whereas one report from Turkey mentioned 3,000 mg/day Modafinil dose.¹⁰⁻¹² In the present case, utilization of Modafinil at extremely high doses up to 5,000 mg/day may be due to a self-medication in order to reinforce its cognitive enhancing property and to treat symptoms of ADHD. High doses of Modafinil can cause several side effects like agitation, insomnia, tachycardia and elevated blood pressure.²⁵ Our case described palpitations, agitation and insomnia after using high doses of Modafinil. This was one of the reasons whys for seeking treatment. These symptoms were taken into account during his treatment planning. There is no controlled study on Modafinil dependence; treatment with antidepressants like Bupropion and Duloxetine and treatment with benzodiazepines like Clonazepam had been attempted in previously reported cases.¹⁰⁻¹²

There are 2 case reports in the literature stating that Modafinil dependence can occur in patients with previous history of addiction.^{10,11} ADHD patients are known to be more prone to addiction, however as far as we know, this is the first study demonstrating Modafinil dependence of a case with ADHD. Recent suggestion on Modafinil use for ADHD increases the significance of the present case report.²³

Another important point in this case report is that, to our knowledge, there is no report in the literature demonstrating Modafinil use as high as 5,000 mg/day. Despite symptoms presenting at high dose, the drug did not cause any life threatening condition.

It has to be kept in mind that Modafinil can cause dependence in patients with ADHD. Systematic studies are necessary on this field.

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