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CASE REPORT

# Unsuccessful Suicide Attempt of a 15 Year Old Adolescent with Ingestion of 5000 mg Modafinil

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Modafinil (Provigil) is a wake-promoting drug approved for patients with narcolepsy or other causes of excessive daytime sleepiness. Each pill is 100 to 200 mg; maximal daily dose of modafinil in adults is 400 mg (the medication is not approved by the FDA for children younger than 16 years of age). We report the case of an adolescent who attempted to commit suicide by ingesting 50 pills of modafinil. The medication was prescribed for her mother to treat symptoms associated with multiple sclerosis. Approximately 2 hours following ingestion the patient complained of headache, nausea and abdominal pain. Her ECG demonstrated prolonged QTc interval. Observation for 72 hours revealed 24 hours of inability to sleep, tachycardia, and dyskinesia. There was no deterioration of kidney or liver functions, and no change in complete blood count or blood pressure.

**Keywords:** Modafinil, suicide attempt, adolescent

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Modafinil, or 2-[(diphenylmethyl)-sulfinyl] acetamide, is a FDA approved wake-promoting agent shown to improve wakefulness in patients with excessive daytime sleepiness associated with narcolepsy, shift work sleep disorder, and obstructive sleep apnea. It is a non-amphetamine stimulant, which acts via several mechanisms in the brain. We report a case of a patient presenting to the pediatric emergency department after a suicide attempt, in which she ingested 5 grams of modafinil.

## REPORT OF CASE

A 15-year-old female was brought to the pediatric emergency department after ingesting 5 grams of modafinil as a suicide attempt. The drug was prescribed to treat symptom's of her mother's multiple sclerosis.

On arrival, the patient was fully awake. Her vital signs were as follows: blood pressure 123/82 mm Hg; heart rate 106 bpm, regular; oxygen saturation 99%; body temperature 36.7°C. The patient's weight was 49 kilograms. She looked distressed and complained of severe headache, nausea, and abdominal pain. There was no evidence of respiratory or cardiovascular distress, and physical examination revealed no abnormalities.

Complete blood count and liver and kidney function tests were taken; all were normal. A 12-lead electrocardiogram was performed, demonstrating a normal sinus rhythm with prolonged QTc interval (457 and 460 milliseconds on 2 different manual measurements). The patient was admitted to the pediatric ward.

During her hospitalization, she was monitored with a 3-lead ECG, with no abnormal events. Twelve hours after her admission a second 12-lead ECG revealed a normal QTc interval (436 milliseconds). Several hours after her admission the patient developed dyskinesia involving mostly the shoulders, upper limbs, and back, which subsided spontaneously. The patient's headache and abdominal pain completely resolved 15 h after admission. The patient reported no sleep at all in the first night in the ward. On the subsequent nights her sleep was undisturbed.

The patient underwent complete psychiatric evaluation and intervention.

Before her discharge, the patient felt well and was determined to have stable hemodynamic and respiratory status.

## DISCUSSION

No broad consensus exists on the underlying mechanisms of modafinil pharmacology. Several mechanisms are probably involved.[1] The present data raise the possibility that modafinil affects wakefulness by interacting with catecholamine transporters in the brain, in particular dopamine and possibly norepinephrine.[1] The finding of dyskinesia in our case may support the role of modafinil in the dopamine metabolism. Furthermore, modafinil has been found to decrease GABA release in the brain, increase glutamate secretion, and activate hypocretin neurons, thus increasing the release of histamine in the brain.[1] Modafinil triggers activation of neurons in the hypothalamus-based wakefulness circuits, as opposed to amphetamines, that produce diffuse neuronal activation.[1] Therefore, modafinil is

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**Table 1—**Reported Side Effects of Modafinil, When Taken in Recommended Doses for Approved Indications, as Compared to Placebo

| Side effect | Treatment group | Placebo group | Study patient |
|---|---|---|---|
| headache | 34% | 23% | yes |
| nausea | 11% | 3% | yes |
| nervousness | 7% | 3% | yes |
| insomnia | 5% | 1% | yes |
| anxiety | 5% | 1% | no |
| anorexia | 4% | 1% | no |
| dry mouth | 4% | 2% | no |
| chest pain | 3% | 1% | no |
| hypertension | 3% | 1% | no |
| tachycardia | 2% | 1% | yes |
| vasodilation | 2% | 0% | no |
| dizziness | 5% | 4% | no |
| paresthesia | 2% | 0% | no |
| pharyngitis | 4% | 2% | no |

The side effects that occurred in our patient are noted as well.

considered as a "wakefulness promoting agent" rather than a classic amphetamine-like stimulant. The normal elimination half-life of modafinil in humans is 12 to 15 hours.

The United States Food and Drug Administration (FDA) approved modafinil for the treatment of narcolepsy, obstructive sleep apnea, and shift work sleep disorder. In some countries, it is also approved for idiopathic hypersomnia. Modafinil is also indicated, though not approved, in the treatment of attention deficit hyperactivity disorder (ADHD), depression, cocaine addiction, Parkinson disease, schizophrenia, and disease-related fatigue.[2]

Reported side effects of modafinil (when prescribed in recommended doses for approved indications) are listed in Table 1. A single case of premature ventricular contractions appeared causally linked to administration of modafinil.[3]

Modafinil toxicity levels vary widely among species. In clinical trials on humans,[4] taking up to 1200 mg/day for 7 to 21 days or one-time doses up to 4500 mg did not appear to cause life-threatening effects, although a number of adverse experiences were observed, including excitation or agitation, insomnia, anxiety, irritability, aggressiveness, confusion, nervousness, tremor, and palpitations; cardiovascular changes such as tachycardia, bradycardia, hypertension and chest pain; sleep disturbances; and nausea, and diarrhea. As of 2004, FDA was not aware of any fatal overdoses involving modafinil alone in adults. Overdoses involving multiple drugs including modafinil have resulted in fatal outcomes. Cases of accidental ingestion/overdose have been reported in children as young as 11 months of age. The highest reported accidental ingestion on a mg/kg basis occurred in a 3-year-old boy who ingested 800-1000 mg (50-63 mg/kg) of modafinil. The child remained stable. The symptoms associated with overdose in children are similar to those observed in adults. In a recently reported case series, a retrospective multi-poison center chart review of patients from 11 states in the US was performed; there were 137 patients with single-substance ingestions of modafinil. The most frequently reported clinical effects were tachycardia, insomnia, agitation, dizziness, and anxiety.[5]

A suicide attempt with modafinil overdose has not been described before. Our patient ingested 5000 milligrams of modafinil at once (102 mg/kg, an ingestion higher than previously reported). The outcome was not fatal. The occurrence of prolonged QTc and dyskinesia may have a causal relationship with ingestion of very high doses of modafinil. The occurrence of dyskinesia is suggestive for the role of modafinil in dopamine metabolism. The prolonged QTc interval may be associated with the sympathetic system, as no changes in the potassium or calcium levels were noted. Further research is required in order to establish more thorough data regarding the adverse effects of very high doses of modafinil.

## DISCLOSURE STATEMENT

This was not an industry supported study. Dr. Pillar has received research support from Cephalon and Actelion and has consulted for Itamar. The other authors have indicated no financial conflicts of interest.

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