Panic Disorder Induced by a “Herbal” Product Containing Sibutramine: Case Series with Review of Literature

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ABSTRACT:
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Sibutramine is a serotonin and noradrenaline reuptake inhibitor which has been used for weight loss in obese patients. There are slimming products on the market claiming to be ‘natural’ which nevertheless contain sibutramine. In this report, we present three cases where panic attacks were associated with the use of a product and persisted even long after its discontinuation.

Keywords: sibutramine, panic attacks, panic disorder, substance, induced anxiety

INTRODUCTION

Sibutramine is a centrally acting serotonin, noradrenaline and, to a lesser degree, dopamine reuptake inhibitor which augments weight loss by enhancing satiety. Until a recent report about its cardiovascular risks, which resulted in its withdrawal from the European and United States markets, it was widely used in obesity¹. It has been reported that sibutramine and its analogues were detected in a herbal product called Lida, claimed to be a natural appetite-reducing agent, which can be readily obtained via the Internet or in shops². Sibutramine has been reported to have severe adverse psychiatric effects, such as memory impairment³, psychotic episodes⁴,⁵, hypomania when used in combination with citalopram⁶, and a manic episode in a bipolar patient has been described⁷. It is also associated with increases in blood pressure and heart rate⁸. Two cases with sibutramine-induced panic attacks have been reported⁹,¹⁰. However, we report three cases with onset of panic after using “Lida”, who showed continued symptoms even long after discontinuation of the substance and required treatment with SSRIs.

CASE 1

Mr. F, a 50-year-old man, presented to the...
psychiatric unit with complaints of anxiety, inability to leave his house because of palpitations which he interpreted as a sign of a possible heart attack, and difficulty in concentrating. He had been referred by the general emergency unit, where he had presented the day before with palpitations, dry mouth and anxiety. The physical examination, electrocardiography, CBC and cardiac enzymes were found to be normal. Due to his anxiety, he was given 5 mg diazepam PO, after which he felt somewhat better. However, when the symptoms started again the next morning, he decided to seek help in the department of psychiatry, as advised by the general emergency physician.

His psychiatric examination revealed that he had a history of a specific phobia, of the situational type, that caused avoidance of elevators and underground transportation. However, he did not report any previous panic attacks. Upon further investigation we found out that four days earlier, he had started using a “herbal” slimming medication called “Lida” every morning before having breakfast. His panic attacks appeared out of the blue and were not related to any situational or environmental triggers.

His provisional diagnosis was substance-induced anxiety disorder, since attacks were considered to be the result of using “Lida”, rather than being related to his specific phobia. The herbal product was discontinued, and the patient was informed about the possibility that it could trigger his panic attacks and about such attacks in general. Alprazolam 1 mg/day was prescribed, and gradually tapered within 10 days. The symptoms decreased within three days. But 10 days after the cessation of alprazolam, his panic attacks re-emerged. They were accompanied by agoraphobia and anticipatory anxiety. He was still experiencing panic attacks one month after the discontinuation of “Lida”.

As the patient fulfilled the panic disorder criteria, he was prescribed Fluvoxamine 100 mg. After 1 month of treatment, his symptoms decreased and he was able to work again. Fluvoxamine was used for 6 months, and then it was tapered. In the follow-up, he did not report any panic attacks. He has been able to use underground transportation, but still has difficulty in using elevators, except in urgent situations.

**CASE 2**

Ms. D, a 26-year-old woman was seen in the emergency department, with some suspicion of attempted suicide. She reported taking five tablets of alprazolam (a total of 2.5 mg) within half an hour to help her with an anxiety attack. She had then come to the emergency department fearing an overdose. The psychiatric evaluation was made after gastric lavage. She reported no previous suicide attempts, but had a history of problems with anger and impulsivity under stress. She reported that she had undergone anger management therapy with a psychologist for a few months. She had started using “Lida” for weight management a week before and had taken one capsule a day for a week. She reported an increase in anxiety after she started the product, which on the day she went to hospital had progressed to a full-blown panic attack. Later, it was found out that she had taken some of the alprazolam that had been prescribed for her mother in an effort to reduce the anxiety, but with no intention of suicide.

After being given some general information and advice, she left the hospital. The patient acknowledged the role of “Lida” in her panic attacks and agreed to discontinue the product. However, after 6 weeks, she was seen in the outpatient department with panic attacks and severe anxiety, which had resulted in frequent visits to the emergency department at night. She was prescribed sertraline 50 mg, a dose which was gradually increased to 100 mg. Her symptoms resolved three weeks later. She stopped visiting the outpatient department after 3 months. One year later, she was referred by another physician who wanted to rule out a psychiatric etiology for her gastric complaints. She stopped taking the antidepressant after 5 months and has been symptom free for 4 years.
CASE 3

Ms. S was a 47-year-old woman who was first seen in the emergency department for a panic attack. Her panic symptoms were palpitations, fear of losing control, nausea, difficulty in breathing and fear of dying. She reported a history of fibromyalgia and sleep problems due to night sweats associated with peri-menopause, and she and her family described her as a generally anxious person, although she had never sought psychiatric help before and her symptoms had never been clinically significant. She had used “Lida” during the previous week in order to lose weight. Her physical examination and laboratory results were normal.

She was given a single dose of Diazepam 5 mg and was informed about the possible effect of “Lida” on her anxiety. The product was immediately discontinued. However, she went on experiencing severe anxiety and panic attacks in the following days. Alprazolam 1.5 mg/day was prescribed, but later it could not be tapered off, because at every attempt, her anxiety resumed. After 1 month, we added paroxetine 20 mg/day to her treatment. Alprazolam was tapered after six weeks. She used paroxetine for 7 months. After stopping the paroxetine, she experienced only one period of anxiety and one panic attack after a major life event. Only her sleeping problems remained, but in the last 6 months these symptoms have been managed only by over-the-counter hypnotics.

DISCUSSION

Sibutramine has been lately withdrawn from the market in many countries, but as long as “Lida”, a so-called “herbal” product which has been shown to contain this agent, can still be obtained easily, psychiatrists and doctors working in emergency wards will have to deal with its diverse psychiatric complications, such as acute manic episodes, acute psychosis or, as is the case with our patients, panic attacks. Our cases depict how physical factors or drugs can trigger long-lasting psychiatric problems. In all of our cases, the patients reported some psychiatric symptoms in the past, but they had never experienced any panic attacks. In a previous case report, sibutramine-induced panic attacks were reported in a patient who had a history of panic disorder, but who had been panic free without treatment for thirty years. In this case, the panic symptoms were solved a few days after the discontinuation of sibutramine. In the second report linking sibutramine and panic attacks, the panic symptoms did not stop after the discontinuation of sibutramine

In our cases, the patients were informed about the nature of panic attacks and how they might be triggered by the slimming capsules, and SSRIs were not prescribed immediately, but the patients continued to experience panic attacks and anticipatory anxiety even long after the discontinuation of sibutramine. The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria state that if the symptoms persist for a substantial period of time (e.g. about a month) after discontinuation of the substance or are substantially in excess of what would be expected given the type or amount of the substance used or the duration of use, then the symptoms are better accounted for by a specific anxiety disorder rather than substance-induced anxiety disorder. In our cases, panic attacks did not disappear within the first month of discontinuation of “Lida” even though the product had been used for a short period of time. Therefore, we diagnosed all our three cases with panic disorder instead of substance-induced anxiety disorder.

In two longitudinal studies investigating the cardiac outcomes of sibutramine treatment on more than 25,000 subjects, it was found that tachycardia was one of the most important non-fatal cardiac events in this population. There is evidence that panic attacks result from the catastrophic misinterpretation of certain bodily sensations, such as increased heart rate. The development of panic attacks after the use of “Lida” in our patients may be the result of tachycardia due to the effects of sibutramine, leading to a catastrophic misinterpretation of
these bodily symptoms. There have been some reports of the occurrence of panic attacks or panic-like symptomatology after the use of cocaine, caffeine and methamphetamine\textsuperscript{14-16}. Cocaine and methamphetamine are sympathomimetic drugs, and sympathetic activation might also be another reason for sibutramine’s panic-provoking properties.

Although there are many reports of substance-induced panic attacks, as far as we know, there have been no reports of full-blown panic disorder triggered by an agent which causes tachycardia. One possible explanation for this may be high anxiety sensitivity at baseline. It is known that anxiety sensitivity may be a risk factor for the onset of panic attacks\textsuperscript{17}. Although none of our cases reported any previous panic attacks, they all had a history of psychiatric symptoms such as specific phobia, problems with impulsivity or nonspecific anxiety symptoms. Unfortunately, standardized measurements for anxiety sensitivity were not used. Another confounding factor in our cases might be the possibility that “Lida” contains other substances apart from sibutramine that can induce panic attacks.

Although many patients describe psychological or physical triggering events at the beginning of their illness, the current data on the nature of these events and their contribution to the development of panic disorder is limited. These cases suggest that drugs which increase anxiety or cause tachycardia or palpitations may increase the risk of developing panic disorder in individuals who tend to misinterpret bodily symptoms or have high anxiety sensitivity, even when appropriate psychiatric interventions are immediately made. Longitudinal studies on the relationship between medical or pharmacological triggers of panic attacks, anxiety sensitivity and future risk for panic disorder are needed.

References: