Banned, but Not Forgotten: A Case of Ephedrine-Induced Psychosis

Sir: In February 2004, the U.S. Food and Drug Administration (FDA) prohibited the sale of dietary supplements containing ephedrine alkaloids.[1] This final ruling, which took effect in April 2004, garners its regulatory authority under the Dietary Supplement Health and Education Act of 1994 (DSHEA).[2] The DSHEA bypasses usual regulatory practices for agents classified as dietary supplements. It requires instead that supplements demonstrate a "significant or unreasonable risk" prior to any formal action.

Accordingly, ephedrine has repeatedly been implicated in adverse and sometimes fatal outcomes despite compliance with recommended dosages.[3,4] Ephedrine has been likened to other sympathomimetics and controlled stimulants,[5] and the FDA cited significant cardiovascular risk in support of their final rule to ban its sale.[1] In the wake of this FDA decision, a case of ephedrine-induced psychosis is presented. The case underscores both the likelihood of continued ephedrine consumption and the varied clinical presentations associated with adverse reactions to this supplement.

Case report. Ms. A, a 28-year-old white woman, was escorted to the emergency department by police after being found disheveled, wandering the streets, and exhibiting "bizarre behavior." Medical evaluation revealed elevated blood pressure (168/99 mm Hg), tachycardia (122 bpm), and mydriatic pupils. Results of her physical examination were otherwise unremarkable. Results of basic serum laboratory work were within normal limits. The patient's serum alcohol level was undetectable. Urine toxicology was notably positive for caffeine, nicotine, and sympathomimetics. Illicit agents screened for and not detected included phencyclidine, cocaine, benzodiazepines, barbiturates, opiates, amphetamines, and marijuana.

Following medical clearance, Ms. A was transferred to the psychiatric emergency department. She reported being in New Orleans, La., on vacation. Four days prior to presentation, a night "out on the town" was reportedly followed by the theft of her car. Ms. A then recalled becoming increasingly concerned about "people [being] after [her]." This led to 3 days of "no sleep" and wandering on foot from one hotel to another attempting to evade her alleged pursuers. When asked about her pursuers, she said that members of an organized crime family had been following her. The patient was without formal or significant medical, surgical, or psychiatric history. Her family history was noncontributory except for reported obesity among multiple family members. Neither Ms. A nor her parents reported symptoms or behaviors suggesting mood disturbances, specifically bipolar disorder, in Ms. A or any family member. She reported consuming a glass of wine with dinner 2 to 3 nights per week, but not to intoxication. She admitted to current tobacco use and remote marijuana use. She otherwise denied illicit substance use.

Initially reporting vitamins in her medication history, upon repeat inquiry the patient revealed a 2-month history of use of an over-the-counter "herbal weight-loss pill." Results of a mental status examination were notable for a thin woman who, though now disheveled, appeared to be recently well groomed. She further exhibited significant paranoia with a guarded affect. She was observed to repeatedly scan the room, suggesting that she was responding to hallucinations. On multiple occasions, she demanded that staff provide the names of other patients because "they could have followed [her] here." Clarification of her urine toxicology results identified ephedrine as the sole agent present. Collateral information obtained from Ms. A's family revealed a remote history of anorexia as a teenager, but no other psychiatric difficulties. Her family was unaware of any past or current use of weight-loss products. They were, however, able to report "strange behavior" prior to her New Orleans trip that led to termination of Ms. A from her job. They also reported that their daughter had recently ended her engagement and considered this part of her "strange behavior."

Ms. A reluctantly accepted 10 mg of zolpidem and slept for approximately 5 hours. She voluntarily consented to hospitalization but proceeded to refuse all offered medications. Despite her medication refusal, full symptom resolution was noted by day 2 of hospitalization. An Internet search by the authors revealed that the brand of herbal weight-loss supplement that Ms. A had mentioned taking contained ephedrine as the primary ingredient. She reported taking the supplement at the dosage and frequency recommended on the product's label, approximated to be 50 mg/day. Ms. A further disclosed that she had been experiencing threatening auditory hallucinations and frank paranoia for approximately 24 hours prior to her presentation to the hospital emergency room.

Ms. A was discharged on day 4 of hospitalization with the diagnosis of an ephedrine-induced psychosis (DSM-IV criteria) that had resolved with discontinuation of the dietary supplement. Results of her discharge mental status examination were notable for a complete absence of psychotic symptoms. Her vital statistics and physical examination results were reportedly also without notable aberration, though her medical records were unavailable for review.

Used for over 5000 years by Chinese herbalists, ephedrine was introduced into Western medical practice in the 1930s for the treatment of asthma. Ephedrine use grew exponentially in the latter part of the 20th century after discovery of its utility in weight loss and athletic performance.[6] Ephedrine acts via catecholamine release into the synapse, as well as via postsynaptic α-, β_1-, and β_2-adrenergic receptor stimulation.[7] These properties have resulted in significant and potentially fatal adverse effects that outweigh purported benefits, which lack rigorous scientific support.[1]

Despite the FDA's recent ban on ephedrine-containing dietary supplements, American preoccupation with body image suggests that ephedrine consumption will most likely not change. Due to demand for the supplement and unregulated access through Internet distributors, ephedrine-containing supplements will continue to be sought after for weight loss and athletic performance. Clinicians should therefore be prepared to readily identify adverse reactions related to ephedrine use, including psychiatric complications.

Drs. Kim and LeBourgeois report no financial affiliation or other relationship relevant to the subject matter of this letter.

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