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**FILE: ■ Ephedra (*Ephedra sinica*)
■ Psychiatric Adverse Events**

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RE: Psychiatric Effects of Ephedra

Maglione M, Miotto K, Iguchi M, Jungvig L, Morton SC, Shekelle PG. Psychiatric effects of ephedra use: an analysis of Food and Drug Administration reports of adverse events. *Am J Psychiatry*. 2005;162:189-191.

Ephedra (*Ephedra sinica*), also known as Ma Huang, has been used for thousands of years in China as a treatment for bronchial ailments.¹ In recent years, ephedra products have been marketed as weight loss aids and metabolism boosters. In December 2003, the US Food & Drug Administration (FDA) banned ephedra products due to concerns regarding the herb's safety.² Germany's Commission E warns that ephedra can produce psychiatric and nervous system side effects including insomnia, motor restlessness, headaches, and dependency.¹ Additionally, the Commission E monographs document a drug-herb interaction between the monoamine oxidase inhibitor class of antidepressants and state that use of ephedra is contraindicated in people experiencing anxiety and restlessness.¹

The active constituent of ephedra is ephedrine, a phytochemical classified as a CNS stimulant. Ephedrine stimulates a release of the neurotransmitters dopamine and norepinephrine. There are numerous reports of psychiatric adverse events with ephedra containing bronchial medications but few case reports from use of herbal ephedra users. In this article, the authors summarize the case reports on serious psychiatric adverse events received by the FDA. The authors state "Case reports are useful to establish the *potential* for a causal relationship..." but that they could not be considered to "...be conclusive evidence of a cause-and-effect relationship."

The authors reviewed 1,820 FDA MedWatch case reports of adverse events linked to ephedra that were reported as of September 30, 2001. Of these reports, 57 involved serious psychiatric adverse events. The majority of psychiatric adverse events involved psychosis (n=32, 56.1% of psychiatric adverse event reports), severe depression (31.6%), or mania or severe agitation (26.3%). Other psychiatric adverse events involved hallucinations, sleep disturbance, or suicidal ideation (22.8% each). These adverse events were not necessarily mutually exclusive; some case reports involved more than one type of event.

Of the 57 adverse event case reports, 26 (45.6%) required hospitalization. In 55 of the case reports, gender was reported; 60% of these reports involved women. The average age of the ephedra users in the case reports was 31 years of age.

The authors note "Of importance, two-thirds of the 57 cases involved patients with preexisting psychological/psychiatric conditions and/or use of other mood-altering medications of illicit substances." Of the 57 cases, 13 had a documented history of depression, and 12 were taking antidepressants classified as selective serotonin reuptake inhibitors. Case reports also involved patients with documented histories of substance abuse, premorbid eating disorders, anxiety, attention deficit hyperactivity disorder, bipolar disorder, post traumatic stress disorder, and borderline personality disorder.

The authors found relatively few sentinel events, defined as case reports involving patients who were not using medications or other substances that could have caused the event and who had no history of psychiatric illness. Four cases were sentinel events, and six cases were possible sentinel events due to limited medical histories in the case reports. Two of the four sentinel cases involved symptoms that began within the first three weeks of ephedra use. Three sentinel cases required psychiatric hospitalization.

A limitation of this review is that the nervous system stimulant caffeine is included in many ephedra products potentially contributing to the psychiatric adverse events reported. In addition, a large number of herbal medicine adverse events are never reported because such reporting is not mandatory in the US. The Inspector General estimates that less than 1% of all reactions from use of dietary supplements are reported at this time.

Although a link between ephedra use and severe psychiatric events cannot be established based solely on these Medwatch case reports, the authors conclude that clinicians should be aware such a link is possible. This possibility is strongest for patients with a history of psychiatric illness and/or substance abuse and patients taking psychiatric medications.

—*Marissa Oppel, MS*

REFERENCES

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2. Blumenthal M. FDA announces ban on ephedra supplements: federal move follows bans by California, Illinois, and New York. *HerbalGram*. 2004;61:0.

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