

phetamine salts for 6 additional weeks. We made no claims of efficacy for open divalproex treatment, only that it was associated with a benefit in this group. The elicited and spontaneously reported side effects in the entire trial were very low, perhaps because we did not aggressively "load" the divalproex and we used relatively low doses of mixed amphetamine salts in the crossover study. In the open extension (when the dosing of mixed amphetamine salts was not limited), the average dose remained low, at 14.5 mg/day, suggesting that this relatively low dose was clinically useful.

The use of the last observation carried forward is considered the most rigorous way to look at data from clinical trials. The divalproex responders were, in fact, all study completers. The only patient with a response who did not complete this phase of the study was one who improved so much during the first arm of the mixed amphetamine salts/placebo crossover study that the child's mother did not want to risk a change in treatment. This patient was treated with mixed amphetamine salts outside the study and did very well.

As to adverse events, one other patient developed mania: this was clearly stated in the article and the abstract. There were no serious adverse reactions: this was clearly stated in the article. Three patients were hospitalized very early in the course of the open-label divalproex treatment, likely before these patients had adequate opportunity to respond to divalproex.

We do believe that this small, well-controlled study provides a basis for considering larger, more definitive and generalizable trials. Given the clear lack of efficacy of divalproex for ADHD symptoms and the positive effects of mixed amphetamine salts (versus placebo) in a randomized blinded comparison, we believe that such a combination approach (divalproex followed by mixed amphetamine salts) seems promising, and at least with the group and follow-up data that were available, reasonable tolerability and safety can be expected (at the doses used). We certainly believe that this first study should be followed by larger, more definitive controlled trials to better assess generalizability and tolerability in a larger group.

Reference

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Psychiatric Effects of Ephedra: Addiction

TO THE EDITOR: I wish to extend my support to Margaret Maglione, M.P.P., et al. (1) for their article. The issue of the safety of dietary supplements, and specifically ephedra alkaloids, has been long problematic but only recently addressed (2). Although psychosis was found to be the most frequent psychiatric adverse event reported in their review of the database of the Food and Drug Administration (FDA), I offer that substance (ephedra) abuse, and sometimes dependence, is a more frequent occurrence in society.

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As addressed in their article, this is known to occur (FDA data: 8.6%) but is only rarely reported in the medical literature (3). This may be due, in part, to the possibility that psychosis is highly likely to be recognized as an adverse event by clinicians (whether for FDA reporting or for the purposes of medical literature), but addiction is not—despite its more long-lasting, well-documented, and devastating personal and societal consequences. Moreover, be aware that ephedra products have been aggressively marketed as legal alternatives to illegal stimulants, with some ephedra products testing positive for controlled substances of abuse (4). Thus, these products are perhaps more likely to be consumed by those at risk of developing substance use disorders. Since our original case report was published in *Psychosomatics* (5), I have encountered two additional cases of ephedra dependence.

My own experience with the FDA's Internet and telephone-based reporting "portholes" during attempts to report a highly detailed case report of an ephedra addiction/adverse event led only to dead ends and no returned calls, despite three attempts. My best recourse was to publish this case in the medical literature (5). This data input access issue further complicates the FDA's well-intended data, data that may only represent 1% of the actual adverse event reports in society.

Thus, I hypothesize that ephedra abuse/dependence is a more common adverse event than FDA data indicate, and quite possibly more common than psychosis. Nevertheless, this article summarizing the FDA data and alerting clinicians cannot be overstated in terms of its value and practical worth to psychiatrists and general practitioners. I am very thankful for the authors' product.

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The Multiple Sleep Latency Test in the Diagnosis of Narcolepsy

TO THE EDITOR: We read with interest the clinical case conference by Lois E. Krahn, M.D., and Heydy L. Gonzalez-Arriaza, M.D. (1). Excessive daytime sleepiness is a common symptom of many sleep disorders, including narcolepsy. It can be difficult to make a firm diagnosis of narcolepsy, especially when the pathognomonic symptom of cataplexy is absent. Even when present, cataplexy rarely occurs in a physician's office.