

## A Case of Suicidal Thoughts With Alprazolam

**To the Editor:** This is the first report, to our knowledge, of suicidal thoughts emerging after a dose of alprazolam.

**Case report.** Ms A, a woman in her late 20s, presented for the first time in 2008 and was diagnosed with obsessive-compulsive disorder with panic attacks (*DSM-IV* criteria) and was prescribed fluoxetine 20 mg in the morning and alprazolam 0.25 mg 3 times a day as needed. She was not depressed and had not experienced suicidal thoughts in the past. After a single dose of both alprazolam 0.25 mg and fluoxetine 20 mg, she experienced grogginess and sleepiness that lasted for 24 hours. She continued taking only fluoxetine for the next 2 weeks without any side effects. However, as she still experienced panic-like symptoms, she tried taking half the initial dose of alprazolam (half a tablet of alprazolam 0.25 mg) together with fluoxetine 20 mg. This time, she described the “grogginess and sleepiness” as less severe than the first time with alprazolam 0.25 mg. The next morning, she repeated the same doses of alprazolam with fluoxetine and reported “feeling worse in a different way.” She had thoughts of jumping down from her apartment. These thoughts lasted “till the effects wore off,” referring to the grogginess and sleepiness. Subsequent to this, she has stopped taking alprazolam completely and continued with fluoxetine without experiencing similar symptoms.

The product literature on alprazolam does not report suicidal thoughts or ideation.<sup>1</sup> A meta-analysis of controlled trials of alprazolam in treatment of depression does not suggest that alprazolam is associated with increased risk of suicidality.<sup>2</sup> The majority of those treated with alprazolam experienced improvement of suicidal ideation, and that rate of improvement was significantly greater for those taking alprazolam compared to those taking placebo (71.9% vs 57.7%).

However, there are reports indicating that all benzodiazepines have been associated with the emergence or worsening of depression<sup>3,4</sup>; whether they were causative is unknown. Benzodiazepines have also been observed to precipitate suicide in already depressed patients.<sup>5</sup> The American Psychiatric Association report on benzodiazepines warns, in discussing toxicity, that benzodiazepines have been reported to cause or exacerbate symptoms of depression. This is not a frequent side effect, but depressive symptoms can be potentially serious.<sup>6</sup>

The United Kingdom's Committee on Safety of Medicines recommends that benzodiazepines should not be used alone to treat depression or anxiety associated with depression. Suicide may be precipitated in such patients.<sup>7</sup>

In another report,<sup>8</sup> there were 6 patients, previously emotionally stable, who experienced suicidal ideation with a cluster of other symptoms; however, all of these patients had taken greater than maximally recommended doses of diazepam (above 40 mg a day) primarily for medical conditions.<sup>8</sup>

Coadministered fluoxetine can increase serum alprazolam concentrations.<sup>9,10</sup> The interaction effect is an increased risk

of alprazolam toxicity with symptoms such as somnolence, dizziness, ataxia, slurred speech, hypotension, and psychomotor impairment. In the study by Greenblatt et al,<sup>9</sup> 12 healthy male volunteers were given fluoxetine 20 mg twice a day or placebo and a single dose of alprazolam 1 mg on days 3 and 24 of the 31-day, double-blind, crossover study. Fluoxetine significantly increased the half-life of alprazolam from 17 hours to 20 hours and significantly decreased its clearance from 61 mL/min to 48 mL/min. The mechanism of action is thought to be through inhibition of the cytochrome P450 3A4 isoenzyme, which is responsible for alprazolam metabolism.

Whether alprazolam actually triggered the suicidal thoughts or whether these were in relation to the side effects this patient experienced cannot be clearly determined. However, there is high probability, given the risks associated with benzodiazepine use, that alprazolam contributed to the emergence of suicidal thoughts in this patient. The combination of fluoxetine with alprazolam should be used with caution in patients with anxiety disorders.

## REFERENCES

1. Xanax (alprazolam) tablets. Pharmacia Limited, UK, June 2003. <http://www.medicines.org.uk>. Accessed January 21, 2009.
2. Jonas JM, Hearron AE Jr. Alprazolam and suicidal ideation: a meta-analysis of controlled trials in the treatment of depression. *J Clin Psychopharmacol*. 1996;16(3):208–211.
3. Ashton H. Toxicity and adverse consequences of benzodiazepine use. *Psychiatr Ann*. 1995;25:158–165.
4. Breggin PR. Analysis of adverse behavioral effects of benzodiazepines with a discussion on drawing scientific conclusions from the FDA's spontaneous reporting system. *J Mind Behav*. 1998;19:21–50.
5. Ashton HC. Protracted withdrawal from benzodiazepines: the post-withdrawal syndrome. *Psychiatr Bull*. 1995;25(3):174–179.
6. Salzman C. The APA Task Force report on benzodiazepine dependence, toxicity, and abuse. *Am J Psychiatry*. 1991;148(2):151–152.
7. Ashton H. Benzodiazepines: how they work and how to withdraw. <http://www.benzo.org.uk/manual/>. Accessed March 23, 2009.
8. Hall RCW, Joffe JR. Aberrant response to diazepam: a new syndrome. *Am J Psychiatry*. 1972;129(6):738–742.
9. Greenblatt DJ, Preskorn SH, Cotreau MM, et al. Fluoxetine impairs clearance of alprazolam but not of clonazepam. *Clin Pharmacol Ther*. 1992a;52(5):479–486.
10. Lasher TA, Fleishaker JC, Steenwyk RC, et al. Pharmacokinetic pharmacodynamic evaluation of the combined administration of alprazolam and fluoxetine. *Psychopharmacology (Berl)*. 1991a;104(3):323–327.

**Rathi Mahendran, MMed(Psych)**

rathi\_mahendran@imh.com.sg

**Emily Liew, BPharm**

**Author affiliations:** Department of General Psychiatry (Dr Mahendran) and Department of Pharmacy (Ms Liew), Institute of Mental Health/Woodbridge Hospital (IMH/WH), Singapore.

**Potential conflicts of interest:** None reported.

**Funding/support:** None reported.

**Published online:** May 27, 2010 (doi:10.4088/PCC.09l00865blu).

*Prim Care Companion J Clin Psych* 2010;12(3):e1

© Copyright 2010 Physicians Postgraduate Press, Inc.