

Paroxetine Shows No Effect on Drinking

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CHICAGO — Paroxetine can take the anxiety out of the drinker, but it cannot take the drinking out of the anxious person.

The drug did uncouple anxiety and drinking in patients who use alcohol to cope with severe generalized social anxiety, Dr. Sarah Book said at the annual meeting of the Research Society on Alcoholism. But compared with placebo, paroxetine (Paxil) had no effect on overall alcohol consumption.

"These patients were precontemplators for their alcohol use disorder," said Dr. Book, a psychiatrist at the Medical University of South Carolina, Charleston. "They wanted us to fix their anxiety symptoms but weren't interested in addressing their alcoholism."

Her 16-week randomized controlled trial, funded by the National Institute of Alcohol Abuse and Alcoholism, pitted paroxetine (60 mg) against placebo in 42 patients with severe generalized anxiety and comorbid alcohol use disorders. The patients could have had no previous alcohol detoxification treatment. "We wanted to examine the effect of the drug in people who were early in their alcoholism career, to see if we could intervene in the progression," she said.

The patients' average age was 29 years; 50% were male. At baseline, their mean score on the Liebowitz Social Anxiety Scale (LSAS) was about 90, indicating severe social anxiety. Anxiety had its onset at age 12 years in these patients; the use of alcohol to cope with symptoms followed about a decade later. They were moderately dependent on alcohol, consuming about 15 drinks per week.

By week 16, patients in the treatment group had a far greater decrease in their LSAS scores than did those in the placebo group (53% vs. 32%). But a different picture emerged when Dr. Book examined the drug's effect on drinking.

All patients completed a study-specific questionnaire that asked how often they drank to cope before and during social situations. At week 16, those in the paroxetine group had significantly lower scores than did those in the placebo group, with 20% (vs. 40%) saying they still drank to cope with social situations, and 30% (vs. 70%) saying they would avoid such situations if they couldn't drink.

But when Dr. Book examined the total overall drinking, no differences were found between the groups in either frequency of drinking or quantity consumed.

GlaxoSmithKline Inc. provided the study medication. ■

Women Want One Doctor for Substance Abuse, Obstetric Tx

MIAMI — Women with problematic substance use during pregnancy prefer integrated treatment over separate obstetric and substance use care, according to a presentation at the annual conference of the American Society of Addiction Medicine.

The investigators found that women attending one of two integrated programs reported feeling less stigmatization about their substance abuse. They also liked the care they received from consistent providers. In contrast, those who received isolated substance abuse treatment at a traditional center and obstetric care at a general hospital reported harsh and punitive treatment from hospital staff that made them feel marginalized, Dr. Lisa G. Lefebvre said during an interview at a poster session.

"Patients tour the maternity ward in advance, and everyone on the staff is trained to be sensitive to their substance use," said Dr. Lefebvre, who is an addiction medicine consultant with the department of family and commu-

nity medicine, University of Toronto. "The women like this [integrated] model," she said. "They have one doctor who treats pregnancy and everything you'd do for addiction."

In 2005, researchers used focus groups in Toronto to assess satisfaction among women attending one of two integrated programs—the Toronto Center for Substance Use in Pregnancy or the Herzl Family Practice Centre. Transcripts of these sessions were coded for recurring themes.

The researchers compared the subjects' satisfaction with that of women recruited from the obstetrics department at a general hospital in 1995. Women in the latter group also attended a community substance use treatment center.

Women who attended separate programs were less likely to report a good birth experience. "Is it possible that the stigma of substance use was worse in 1995? Even in 2005, when they ended up in another facility, they felt stigma," she said.

—Damian McNamara

EVIDENCE-BASED PSYCHIATRIC MEDICINE

Abuse of Bupropion

The Problem

You work in one of America's contemporary long-term psychiatric treatment centers, also known as a state prison. Inmates who come to outpatient appointments and complain of depressive symptoms frequently request bupropion (Wellbutrin). The history they provide is speciously similar: "It's the only antidepressant that's ever worked." You start to inquire about how this medication is used in the prison yard, and some of your more frank patients say it is snorted to provide a methamphetamine-like high.

The Question

What is known about the abuse potential of bupropion outside of the prison environment?

The Analysis

We looked at popular culture first by doing Google searches for "Wellbutrin snort" and "snorting Wellbutrin." Some Web sites describe the effects of snorting bupropion (www.erowid.org/experiences/exp.php?ID=9266) and some give advice on extracting bupropion from Wellbutrin SR tablets for the purpose of insufflation (<http://bupropion.home.comcast.net>).

Wondering what has been published on this topic in the medical literature, we first searched the Cochrane Database of Systematic Reviews (www.cochrane.org/reviews) without result. We then searched Medline, combining "bupropion" and "abuse or misuse."

The Evidence

Bupropion's amphetamine-like abuse potential was suggested in preclinical trials in which animals substituted bupropion for amphetamine in a drug-discrimination task, and in another study in which it was self-administered intravenously by monkeys.

We were able to find two case reports (N. Engl. J. Med. 2002;347:951; J. Child Adol. Psychopharm. 2004;14:157-8) that described adolescents who insufflated bupropion in an attempt to obtain an amphetamine-like effect. One 16-year-old boy insufflated 600 mg of sustained-release bupropion and experienced a seizure. A 15-year-old girl snorted an unspecified amount of sustained-release bupropion and reported a marijuanalike buzz that only lasted a few seconds.

In a double-blind crossover study conducted to determine the amphetamine-like abuse potential of bupropion, 13 male subjects (aged 22-31 years) with "substantial" histories of psychostimulant abuse were randomized to receive, at intervals of at least 3 days, bupropion (100 mg, 200 mg, and 400 mg); d-amphetamine (15 mg and 30 mg); and placebo (J. Clin. Psychiatry 1983;44:206-8).

Drugs were administered at 8:00 a.m., with physiologic measures taken a half hour before administration and then hourly post dose. Bupropion had no measurable effect (relative to placebo) on blood pressure, pulse rate, respiratory rate, temperature, pupil size, appetite,

caloric intake, or sleep. On self-rating scales, bupropion was perceived as an active drug only as often as placebo. The investigators concluded, "It is unlikely that bupropion will give rise to [amphetamine-like] patterns of abuse among normals or among those predisposed to psychostimulant abuse." (The study came from the Baylor College of Medicine, the Houston Veterans Administration Medical Center, and the Burroughs Wellcome Research Laboratories.)

A double-blind, placebo-controlled, crossover study conducted at the Medical University of Innsbruck (Austria) examined the abuse liability of bupropion using caffeine as a positive control (Pharmacology 2004;70:206-15).

In all, 60 male smokers, aged 18-65 years, were enrolled; 50 completed the trial. The subjects were given two doses, 6 hours apart, of placebo, caffeine (178 mg), or bupropion slow-release (Zyban, 150 mg). They completed standardized telephone questionnaires at hourly intervals. Of the 50 subjects, 50% were able to report "any effect" to caffeine or bupropion. In those who reported "any effect" to caffeine, bupropion was reported as having essentially no effect. Subjects who reported effects from bupropion reported "much more intense effects" after bupropion than caffeine. The authors concluded that bupropion might be of some abuse liability.

The authors of this study cited another study, not picked up by our search, which was in part sponsored by a pharmaceutical company. That study compared bupropion with dexamphetamine and showed essentially no abuse liability of bupropion (Br. J. Clin. Pharmacol. 1979;7:469-78).

Investigators at the University of Chicago conducted a double-blind, placebo-controlled crossover study examining the effects of d-amphetamine and bupropion on cigarette smoking (Psychopharmacology 2001;157:243-53). In this study, 17 subjects, aged 19-54 years, received d-amphetamine (10 mg and 20 mg); bupropion (150 mg and 300 mg); and placebo. Subjective, physiologic, and behavioral effects were monitored, and amphetamine and bupropion increased self-reports of arousal, mood, and euphoria.

The Conclusion

The two university sponsored studies found an abuse liability of bupropion, and the two studies that were partly sponsored by pharmaceutical companies found no abuse liability. Our experience suggests that ingenious and determined patients have found ways, overlooked by published studies, to bypass bupropion's first-pass metabolism and achieve highs similar to amphetamine.

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