PRACTICAL PSYCHOPHARMACOLOGY

Treat Substance Use/ADHD With Due Caution

Although complete abstinence is elusive, substance use should be controlled before addressing ADHD.

Substance use disorder and attention-deficit/hyperactivity disorder often go together. Alcohol abuse or dependence has been reported in 17%-45% of adults with ADHD, and drug abuse or dependence has been reported in 9%-30%. Conversely, an estimated 15%-25% of individuals with SUD have ADHD (Am. J. Psychiatry 2006;163:2059-63).

Their conjunction demands nuanced clinical judgment. The first-line drugs for ADHD, psychostimulants, are frequently abused and must be used with care in the context of SUD; yet withholding them unnecessarily does patients a disservice.

Simply detecting ADHD in substance-abusing patients can be a challenge. "Many psychiatrists were not trained to think of ADHD in adults—up to the early 1990s, there were questions about the validity of the diagnosis—and the way symptoms are phrased [in DSM-IV] may not be developmentally appropriate," said Dr. Frances R. Levin, Kennedy-Leavy professor of clinical psychiatry at Columbia University, New York.

Taking a good developmental history is essential, but the standard age-of-onset criterion (symptoms before age 7 years) should be relaxed in light of the difficulty substance-abusing patients may have in recalling their early years, Dr. Levin said. One recent study found that the pattern of substance use was markedly similar in adults who met all criteria for ADHD and those who met all but age of onset (Am. J. Addict. 2007;16[suppl. 1]:24-32).

In the absence of a documented earlier diagnosis, ADHD (like other psychiatric disorders) cannot be conclusively identified while substance use is ongoing or during withdrawal, when anxiety, confusion, and poor concentration can obscure the picture. "Wait for at least a week of abstinence from alcohol, marijuana, or cigarettes; 2 weeks for cocaine," said Dr. Himanshu P. Upadhyaya, director of the addiction psychiatry fellowship program at the Medical University of South Carolina, Charleston.

Even if complete abstinence is elusive, though, it may be possible to establish a tentative diagnosis, said Dr. Timothy Wilens, director of substance abuse services in the clinical and research program in pediatric psychopharmacology at Massachusetts General Hospital, Boston. "There are some data that symptoms of ADHD remain stable, without much exaggeration, through substance abuse," he said.

Dr. Upadhyaya suggested asking whether ADHD symptoms occurred during periods of sobriety. Other clues are family history—frequently a child in the family was diagnosed first—and excessive, circumstantial speech.

Psychostimulants are frequently abused and must be used with care in the context of substance use disorder; yet withholding them unnecessarily does patients a disservice.

Substance use should be controlled before addressing ADHD. "There have been four placebo-controlled studies showing that if you just blast through the addiction, treatment [for ADHD] has no effect on ADHD or substance use," Dr. Wilens said. "Most people recommend getting at least a toehold on the addiction first."

From a practical point of view, "you simply can't tell if medication for ADHD is having any effect if the patient is intoxicated," said Dr. William Dodson, a psychiatrist in private practice in Denver.

In addition, other comorbidities may require treatment before ADHD is treated. Mood and anxiety disorders are highly prevalent in the context of ADHD, Dr. Wilens pointed out, and, when severe, may demand more urgent attention.

Although complete abstinence before initiating ADHD treatment is ideal, it is not always possible. ADHD symptoms such as impulsiveness may interfere with recovery, and concurrent treatment should not be ruled out. "Never say never," Dr. Levin said. "Every case is individual."

With a recent history of SUD, "using a nonstimulant makes sense for a first trial," Dr. Wilens said. Atomoxetine (Strattera) is a good initial choice. A recent trial involving patients who had been abstinent from alcohol for less than a month had positive results with no severe adverse events, he said.

Dr. Dodson prefers bupropion. At a dosage of 400-450 mg/day it is comparably effective and better tolerated by adults than is atomoxetine. Dr. Levin noted that bupropion's efficacy for depression and smoking cessation are other advantages.

When prescribing atomoxetine to those with a history of alcohol abuse, it is wise to monitor liver function, Dr. Levin said. Dr. Upadhyaya noted that both atomoxetine and bupropion tend to be activating, and may exacerbate irritability and dysphoria in some patients still in drug or alcohol withdrawal, or shortly after. "If you alert the patient that this initial reaction can occur but tends to go away after the first week, they're more willing to stick with the medication," he said.

The stimulants methylphenidate and amphetamine are the first-line treatments for ADHD, but concerns about reigniting substance abuse problems persist. Four to six months of abstinence seems an acceptable margin of safety to many experts, Dr. Wilens said, "and this could be too conservative. More studies are needed to see if prescribing these drugs within 2 or 3 months or even while the patient is still using is helpful, or at least makes things no worse."

Motivation behind previous drug or alcohol misuse is worth investigating. A recent study found that about two-thirds of adolescents and young adults with ADHD who abused substances did so for self-medication, and about one-fourth to get high—the same proportion as in a non-ADHD group (Am. J. Addict. 2007;16[suppl. 1]:14-21).

"I'd ask a patient what he got out of substance use," Dr. Dodson said. "When I hear it served some sort of adaptive function—to help study, sleep, slow down enough to sit in class—I'll consider a first-line agent. If I hear a lot of euphoric recall, I won't." Factors like social support, reliability, and stability of the patient's living situation should also be weighed, he said.

Long-acting preparations—extended-release and transdermal formulations and the prodrug lisdexamfetamine (Vyvanse)—have minimal potential to be misused and are preferable to immediate-release forms, Dr. Wilens said. Amphetamines in any form should not be given to formerly abusing patients who have had a psychotic reaction to such drugs, although methylphenidate appears to be safe, he said.

"You'll want to see patients more often, and talk to them about substance use as well as ADHD," he said. "Ask about cravings. It occurs, although infrequently, that in someone with an SUD history, stimulants trigger cravings for another drug."

A real danger, Dr. Wilens said, is the overly conservative approach that withholds effective treatment from those who would benefit. "I'm concerned about a clinician who is afraid to prescribe stimulants for a 35-year-old patient who was addicted to marijuana in college. It's remarkable how many [clinicians] discriminate against patients with a past history of SUD, and no current or even proximal problems." ■

By Carl Sherman, contributing writer

Women and Men May Respond Differently to Naltrexone

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

CHICAGO — Naltrexone may have little positive effect either on drinking behavior in older women with alcoholism comorbid with depression or on drug-using behavior in women with alcoholism and comorbid cocaine dependence.

Data presented at the annual meeting of the Research Society for Alcoholism—a subanalysis of a 2005 drug trial and a preview of a trial in press—hint that naltrexone may have very different effects in women than men, according to William Dundon, Ph.D., of the University of Pennsylvania, Philadelphia.

"Women metabolize alcohol differently than men, and respond to naltrexone differently as well," he said in an interview. Although most trials haven't seen a significant difference in gender response to the drug, that may reflect a demographic problem rather than a true drug response. "The number of women in most of these studies is generally less than men, so these studies are not necessarily powered to see a gender effect," Dr. Dundon said.

Naltrexone blocks the mu-opiate receptors, moderating the sense of euphoria that alcohol provides, said Dr. Dundon, a researcher at the university's Center for the Studies of Addiction. Genetic makeup may also play a significant part in a given patient's response to the drug. Dr. David Oslin, also of the university, has recently identified a genetic variant—a polymorphism of the mu-receptor gene—that seems to predict naltrexone response (Addict. Biol. 2006;11:397-403).

Dr. Dundon presented a recent gender subanalysis of a 2005 study by Dr. Oslin, demonstrating a poor naltrexone response in older women with comorbid alcoholism and depression (Am. J. Geriatr. Psychiatry 2005;13:491-500).

This study comprised 74 older adults (mean age 63 years) with alcohol dependence and depressive disorder. Most subjects (59) were male; there were only 15 female subjects. All of the patients received sertraline (Zoloft) 100 mg/day for their depression, as well as 10 sessions of therapy focused on both alcohol use and depression. They were also randomized to either placebo or naltrexone (50 mg/day).

At the end of the 12-week trial, 42% of the patients were considered well, with no relapse to heavy drinking and with remission of depressive symptoms. An additional 24% remained depressed, but did not have a drinking relapse.

There were no significant differences between the placebo/sertraline group and the naltrexone/sertraline groups in terms of outcome measures: relapse to heavy drinking, abstinence, remission of depression, or overall improvement.

The gender subanalysis showed a slightly different picture, Dr. Dundon said.

Men with positive outcomes did equally well on either regimen, with 40% of the placebo/sertraline and 45% of the naltrexone/sertraline groups considered well by 12 weeks. In women, though, only about 25% of those in the naltrexone/sertraline group were considered well by the trial's end, compared with 70% of those in the placebo/sertraline group.

Because so few women were in the trial, Dr. Dundon said it's impossible to make clinical recommendations about naltrexone's suitability for older women with comorbid depression and alcoholism. ■