

PRACTICAL PSYCHOPHARMACOLOGY

Medications 'Ancillary' in Eating Disorder Tx

BY CARL SHERMAN
Contributing Writer

For the treatment of eating disorders, medication takes a back seat. "Pharmacotherapy is important but ancillary," said Dr. Scott J. Crow, president of the Academy for Eating Disorders and professor of psychiatry at the University of Minnesota, Minneapolis. "It's very much less central than in other psychiatric disorders."

The primary approach is psychotherapy and nutritional rehabilitation, and when medication is prescribed, it is often for comorbid disorders, he said.

The data are least where the need is greatest—in anorexia nervosa, Dr. Crow said. The mortality from this condition is 5% per decade of illness, making anorexia the leading cause of death from a psychiatric disorder among women (Int J. Eat. Disord. 2005;37:S60-3). "It's a sobering statement, but no evidence-based research supports any pharmacotherapy for acute treatment of anorexia nervosa," said Dr. Allan S. Kaplan, professor of psychiatry at the University of Toronto and head of the eating disorders program at Toronto General Hospital.

Many drugs have been tried, and all have been found wanting. "I'm not being simplistic when I say the drug of choice is food. Nutritional depletion changes brain chemistry, and refeeding is critical to alleviating many of the core symptoms of anorexia, although the drive for thinness and body image distortion are tenacious symptoms and often the last to change," he said.

Even medication for comorbid disorders—anxiety and mood disorders are "the rule rather than the exception," Dr. Kaplan notes—often works less well for these patients. Some evidence suggests that selective serotonin reuptake inhibitors (SSRIs)

are ineffective here because the seriously underweight state compromises serotonin production in the brain, he said.

One drug that some think shows particular promise for acute anorexia treatment is olanzapine (Zyprexa). Interest in the use of antipsychotics for anorexia dates back to the 1960s, and positive results with olanzapine, notably weight gain and reduction in anxiety, have been seen in several recent case series and open label trials. A randomized controlled trial is underway.

An obvious explanation for olanzapine's apparent benefit is the tendency to induce weight gain, but the drug may be appropriate for other reasons. Dr. Pauline S. Powers has suggested that psychotic or near-psychotic symptoms are not uncommon in anorexia patients: patients' misperceptions that they are overweight when they are actually emaciated can resemble hallucinations. Some describe hearing voices telling them not to eat, she pointed out.

About one-fourth of the patients she treats in a tertiary care center have such psychotic features, Dr. Powers said.

"I'd prescribe olanzapine more readily for a patient whose symptoms appear to be psychotic," she said. "I also sometimes give it to people who have made the commitment to get well and recognize that they have to gain weight but find it difficult to take the calories they need."

She gradually goes from a low dosage to a maximum of 10 mg (5-7.5 mg/day is typical). "Once people decide to try it, they feel calmer with olanzapine," she said.

Interest also has developed around the

use of SSRIs for maintenance in patients who have gained weight. An open controlled trial found lower relapse rates with fluoxetine than placebo (Biol. Psychiatry. 2001; 49:644-52), although methodologic questions have been raised about this study, and other research has had inconsistent results.

Dr. Kaplan and Dr. B. Timothy Walsh recently completed a larger randomized controlled trial to test this hypothesis, but the data have not yet been analyzed.

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DR. WALSH

The picture for bulimia nervosa is a lot brighter, with fluoxetine—the only drug approved for any eating disorder—shown in several large trials to affect the core symptoms of bingeing and purging. "Many of us will start with cognitive-behavioral therapy or interpersonal therapy, and add an SSRI quickly if it isn't working," Dr. Crow said. He might medicate at the outset if appropriate psychotherapy is not available, or if comorbidity is prominent. "There are high rates of obsessive-compulsive disorder and panic in bulimia, and the majority of people will have depression at some point," he noted.

Dr. Kaplan observed that, while bingeing and purging are significantly reduced with pharmacotherapy, they rarely remit altogether, and symptoms often break through after 6 months of treatment. "The combination of cognitive-behavioral therapy and medication seems to be more effective than either alone," he said.

Most clinicians try fluoxetine first, and Dr. Walsh, professor of psychiatry at Columbia University, New York, and director of the eating disorders research unit at

New York Psychiatric Institute, is no exception. "But if someone has had a bad reaction to that drug, or if I want an agent with a shorter half life, it would push me toward another SSRI," he pointed out.

He uses standard antidepressant dosages at the high end of the therapeutic range—60 mg/day of fluoxetine, for example—and gets there after a brief titration, if any.

If an adequate trial of an SSRI isn't effective, a trial with the serotonin-norepinephrine receptor inhibitor (SNRI) venlafaxine (Effexor) often comes next. Sibutramine (Meridia)—an SNRI with superior appetite suppression properties—is also worth considering, Dr. Walsh said.

He considers topiramate (Topamax) a third- or fourth-line drug, prescribing it at 200-300 mg/day. Two controlled trials have shown it to be superior to placebo in reducing core bulimia symptoms, and the drug facilitates weight loss as well.

Acceptability is a limiting factor. "We use topiramate, but not often, because people don't tolerate it really well," Dr. Powers said. Cognitive problems, including word loss, memory loss, and confusion, are generally the most distressing side effect. "When people want to lose weight, almost anything that does this will make them happy. But they don't seem happy about using topiramate," she said.

Binge eating disorder, which has uncertain nosological status in a DSM-IV appendix, responds to a host of interventions, including those prescribed for bulimia, Dr. Walsh observed. At least the cardinal symptom, binge eating, does. For most patients, obesity is an important and more recalcitrant therapeutic target, he said.

"We'll probably go through the same drugs we use for bulimia, but move more rapidly to those associated with weight loss—sibutramine and topiramate," he explained. ■



Depression Rates High in Patients With Eating Disorders

BY KERRI WACHTER
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BALTIMORE — Depression frequently co-occurs with eating disorders, making treatment challenging, Dr. Graham W. Redgrave said at a symposium on mood disorders sponsored by Johns Hopkins University.

"There are high rates of concurrent major depressive disorder in anorexia," said Dr. Redgrave of the Johns Hopkins University in Baltimore. Among patients with the restricting type of anorexia, 15%-50% also have major depressive disorder (MDD). The rates among patients with the binge-eating/purging type of anorexia are even higher at 46%-80%. The rates are higher still when these patients are asked whether they have ever had depression.

Numbers like these suggest that anorexia might simply be a behavioral manifestation of an underlying mood disorder. However, controlled family studies have provided good evidence that these disorders are different and independent, Dr. Redgrave said.

One reason so much overlap exists between anorexia and MDD is that starvation produces a host of psychiatric conditions in the body, such as mood lability, irritability, anxiety, apathy, obsessiveness, poor concentration, social withdrawal, and decreased libido.

Patients with anorexia aren't the only ones suffering from comorbid depression. Among patients with bulimia, 30%-60% have concurrent MDD and 50%-65% have had a lifetime occurrence of depression.

In patients with bulimia, starvation can magnify feelings of guilt, shame, and hopelessness, Dr. Redgrave said. Increased frequency in the binge and purge cycles decreases the ability to concentrate, because the fear of being overweight increases in importance.

Depression also is high among patients with binge-eating disorder, with 36%-60% of these patients also having MDD. In addition, 48% of obese women who binge also have MDD, compared with only 26% of obese women who do not binge. "It's not just the obesity. There's something about the psychopathology of depression and the binge eating that seems to be related," Dr. Redgrave said.

Treatment of patients with eating disorders and depression can be a challenge because "when you are treating an eating disorder, you are asking your patient to give up something that is very rewarding," he said. Patients

can recognize that what they're doing is problematic but have a hard time giving it up.

"Imagine if you have a parallel mood disorder that is making your thoughts about yourself more hopeless and self-deprecating. ... How much harder would it be to give up behavior that is rewarding?", Dr. Redgrave said at the symposium, also sponsored by the Depression and Related Affective Disorders Association.

Treatment for an eating disorder focuses first on behaviors and then on thoughts and feelings. Underlying connections and associations are addressed only when the patient is stabilized. When the patient's health is in jeopardy, "you can't be worried about why this happened, you just

have to fix it, and then worry about the why," he said.

Pharmacotherapy is primarily an adjunctive treatment for patients with anorexia. Antidepressants are of modest but important benefit in bulimia nervosa, Dr. Redgrave said. Fluoxetine at high doses is especially useful, though most antidepressants can be useful in this population. Bupropion is contraindicated because of the risk of seizures. ■

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