'Think Outside the Box' in Treating Anorexia

BY PATRICE WENDLING

FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF PSYCHIATRISTS

FT. LAUDERDALE, FLA. — What do atypical antipsychotics, an analeptic, and targeted magnets have in common? They all might play a role in the treatment of anorexia nervosa.

"When you have a disorder that is so treatment resistant, it's like metastatic breast cancer; you have to think outside the box for new interventions," Dr. Allan S. Kaplan said at a workshop on eating disorders at the meeting.

Current statistics indicate that 20% of patients diagnosed with anorexia are resistant to any intervention, and remain chronically ill and disabled. The needs of these patients have been largely neglected by the field, even though their numbers continue to grow as a result of the mortality gradually decreasing from 22% in older studies to about 8%-10% today, said Dr. Kaplan, the Loretta Anne Rogers Chair in Eating Disorders and professor of psychiatry at the University of Toronto.

In his experience, many of these patients are now in their 40s and 50s, and have been ill for 20-30 years. Most suffer from significant medical complications, including renal failure, cardiac arrhythmias, and osteoporosis with resulting hip fractures that have left them wheelchair-bound.

"They are unbelievably disabled," he said. "They are more disabled on quality-of-life measurements than a comparative group of schizophrenics in the hospital. It's a sobering experience to spend time with these patients."

One novel approach that might be useful is use of repetitive transcranial magnetic stimulation (rTMS), which has been shown to be effective in some patients with depression, schizophrenia, and obsessive-compulsive disorder. Current magnets stimulate superficial cortical areas of the brain, but Dr. Kaplan suggests that a better target might be the insula—a cerebral cortex structure located deep within the lateral fissure that plays a role in interoceptive awareness and motor control. His group recently completed an unpublished meta-analysis of neuroimaging studies in anorexia that provides evidence for overactivity in the insula.

The team members have subsequently contracted with an Israeli biotechnology firm to construct a patented magnet for rTMS that will specifically target the insula. They also plan to launch an open-label pilot trial of rTMS for anorexia shortly.

The approach is not without controversy, Dr. Kaplan acknowledged. Although the seizure rate with rTMS is very low in patients with depression, patients with anorexia are at an increased risk for seizures at a rate of about 10% in general.

"It's a bit of a shot in the dark, but when you have no other effective treatment, you have to do that," he said.

Atypical antipsychotics have come under increased scrutiny for anorexia, but with limited success in the few small studies and case reports to date. A recent meta-analysis of 43 publications concluded that there is not enough evidence in anorexia to confirm that these medications increase weight (Eur. Eat. Disord. Rev. 2010;18:10-21).

Olanzapine is an atypical antipsychotic that has been the most reported drug in the literature for treating anorexia and has been the subject of three small randomized, controlled trials. Researchers in Ottawa showed that 10 weeks of olanzapine plus intensive day treatment resulted in faster weight gain and a greater decrease in obsessive symptoms compared with placebo in 34 patients with anorexia, but the amount of weight gain was the same overall (Am. J. Psychiatry 2008;165:1281-8).

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DR. KAPLAN

Dr. Evelyn Attia from New York State Psychiatric Institute/Columbia University and Dr. Kaplan reported in a separate unpublished trial supported by a developmental grant from the National Institute of Mental Health in 2005 that patients gained a mean of almost 2 kg after 8 weeks of up to 10 mg olanzapine. Patients credited this weight gain not to an increase in hunger, but to being less anxious and consumed by thoughts of weight and shape. Importantly, there was absolutely no change in lipids, glucose, or insulin sensitivity, suggesting something might be different about the way the anorexic brain handles these drugs, Dr. Kaplan said. The problem with olanzapine, however, is compliance, said Dr. Kaplan, noting that patients with eating disorders are well-informed of its side effect of stimulating weight gain. Aripiprazole has been found to be less likely to cause significant weight gain in schizophrenia patients and was more acceptable in another small unpublished trial reported by Dr. Kaplan and his associates in 2005. Unfortunately, it had little impact on weight or measures of anxiety or depression in the eight patients in which it was tried, he said.

Positive results on both weight gain and cognition have been seen with ziprasidone and quetiapine, but their use has been limited by concerns about QT interval prolongation, which is already an issue for anorexics. Because of this concern, olanzapine was selected instead of ziprasidone as the study drug for a large multicenter anorexia trial that is planned, he said.

The rationale for using atypical antipsychotics in anorexia lies not just in their potential side effect of weight gain, but also in their ability to ameliorate the core disturbances in cognition, affect regulation, and motor activity seen in patients with anorexia nervosa, Dr. Kaplan explained.

"Anorexia is often underestimated as being a disturbance of motor activity," he said. "Our patients are hyperactive in the face of increasing emaciation, which you don't see in any other condition."

Finally, workshop attendee Dr. Charles Price reported an acute response in a single patient with anorexia given modafinil and followed for 6 months. In a counterintuitive finding, the drug did not have the weight loss aspects observed with other stimulants.

"Basically, it cured her anorexia; now it is an 'N' of one," said Dr. Price, who is in private practice in Reno, Nev.

"It's still worth writing up as a case report," Dr. Kaplan said to the agreement of the audience. ■

Disclosures: *Dr. Kaplan reported having no conflicts of interest. Dr. Attia reported having received research support from Pfizer and Eli Lilly.*

Combo Therapies Were Most Effective in Smoking Cessation

BY HILLEL KUTTLER

FROM THE ANNUAL MEETING OF THE SOCIETY FOR RESEARCH ON NICOTINE AND TOBACCO

BALTIMORE — Utilizing a nicotine patch or bupropion together with a nicotine lozenge was the most effective of five therapies tested for promoting smoking abstinence and avoiding a lapse or relapse into smoking behaviors, according to a prospective study of 1,504 smokers.

All five therapies were "significantly better than placebo in promoting initial abstinence" from cigarette smoking, Sandra Japuntich, Ph.D., reported at the meeting.

'The strongest treatment effects are happening in the first week or two. … If you get past the first week or two on medication and you haven't lapsed, then the medication is working.'

The therapies also were effective at preventing relapse, said Dr. Japuntich, a postdoctoral fellow at Massachusetts General Hospital's Mongan Institute for Health Policy, Boston.

The study was important because it examined the effects of each therapy closer to the smokers' targeted quit dates than previous studies have done, Dr. Japuntich said.

The placebo-controlled trial sought to identify the effects on milestones of smoking cessation of five pharmacologic therapies: nicotine lozenge, nicotine patch, bupropion, bupropion with a nicotine lozenge, and nicotine patch with a nicotine lozenge.

The milestones were one period of 24-hour abstinence within 2 weeks of a target quit date, lapsing with at least one cigarette, and relapsing into regular smoking for at least 7 consecutive days.

A total of 70% of smokers on placebo initially abstained, compared with 92% of those using a nicotine patch with a nicotine lozenge, 86% on bupropion with a lozenge, 81% on bupropiona alone, 81% on a lozenge alone, and 88% on a nicotine patch alone.

Among the smokers who initially abstained, 83% on placebo lapsed, compared with 70% of smokers who used a nicotine patch with a lozenge, 71% on bupropion with a lozenge, 74% on bupropion alone, 73% on a lozenge alone, and 76% on a nicotine patch alone.

Of the smokers who relapsed, 69% on placebo relapsed, compared with 61% using a nicotine patch, 64% on bupropion with a lozenge, 63% on bupropion, 62% on a lozenge, and 61% on a patch with a lozenge.

The study's method provided understanding into the "more precise timing about when medications have effects," Dr. Japuntich said. "That's important, because it informs treatment.

"According to our study, the strongest treatment effects are happening in the first week or two," she said. "We should know whether medication is working [by then]. If you get past the first week or two on medication and you haven't lapsed, then the medication is working."

On the other hand, for those who do not stay abstinent, "it could be that lapsing and relapsing is an indication that the medication isn't working, and that the patients might need to try something else," she said. ■

Disclosures: *Dr. Japuntich had no conflicts of interest to report. One of her coinvestigators, Timothy B. Baker, Ph.D., has served on research projects sponsored by pharmaceutical companies including Pfizer, Glaxo Wellcome, Sanofi, and Nabi Pharmaceuticals.*