Stick With Positive Trial Results When Prescribing Antidepressants

BY DAN HURLEY

NEW YORK — Sticking with medications that have shown positive results in randomized trials is important when it comes to treating pediatric depression, according to Dr. Karen Dineen Wagner.

The Food Drug Administration has approved only two drugs for treatment of pediatric depression—fluoxetine for patients aged 8 to 17 years, and escitalopram for those aged 12 to 17—but she pointed out that citalopram also showed positive results in a published trial, and that sertraline has shown positive results in ages 6 to 17 in an a priori pooled analysis of two studies (even though the individual trials were negative).

"Keep within those we know about," Dr. Wagner advised at a pharmacology update, sponsored by the American Academy of Child and Adolescent Psychiatry (AACAP). She pointed out that budeprion, although widely prescribed, has not been shown effective in any published trial of a pediatric population. "Some parents want to know: Is this drug FDA approved [for use in children]? If you use medications that are not FDA-approved, you want to stay as best you can with those that have shown some efficacy [for use] in children, in the age group you're treating."

Dr. Wagner said the only published trial of omega-3 fatty acids in prepubertal depression was small—involving 28 children—and while 70% of those in the treatment arm showed at least a 50% improvement, none of those on placebo did so (Am. J. Psychiatry 2006;163:1098-100).

"Never in any study I've been involved in has there been a zero placebo response rate," said Dr. Wagner, who is the Marie B. Gale Centennial Professor and vice chairwoman of the department of psychiatry and behavior sciences at the University of Texas Medical Branch in Galveston. "But who knows? It was published."

Many of the trials that failed to show positive results, she said, did so not because the treatment arms showed low response rates, but because the placebo arms showed high improvement rates.

"What makes the placebo response rates so high in children?" Dr. Wagner asked. She cited a recent meta-analysis showing that the chief predictor of a high placebo response rate is the number of study sites (Am. J. Psychiatry 2009;166:42-9).

"Another predictor of a high placebo response rate is the baseline of severity. If a child is enrolled with moderate depression, it's very likely they'll respond to placebo as well as to medication."

Although the Treatment for Adolescents With Depression Study (TADS) showed that cognitive-behavioral therapy (CBT) can be as effective as medication in improving symptoms at 36 weeks, Dr. Wagner noted that it was less effective at 12 weeks (Arch. Gen. Psychiatry 2007;64:1132-44; Am. J. Psychiatry 2009;166:337-44).

"What [the study] shows is that CBT is effective, but it takes a while to work," she said. "Parents have to be advised about that. Some will get better early, but for the most part it will take time. The medication will work faster. For moderate to severe depression, CBT just may take too long."

She pointed to another analysis of TADS that found that the rate of attempted suicides or suicidal ideation between those on medication and those on placebo did not vary over the course of the study (J. Clin. Psychiatry 2009;70:741-7). "You would think if there was a drug effect, there would be a timing to it," she said.

One of the key predictors of suicidal attempts or ideation in TADS was acute interpersonal conflict. "Usually, it was a fight or conflict with a parent," Dr. Wagner said. "This needs to be discussed with parents. Keeping conflict low is important."

In addressing the question of whether to switch to another selective serotonin reuptake inhibitor or to another class of drugs when an adolescent fails initial therapy, Dr. Wagner asked for a show of hands from the psychiatrists in attendance as to which strategy they would prefer.

"Everybody who raised their hand was correct," she said, citing recent evidence from the Treatment of SSRI-Resistant Depression in Adolescents (TORDIA) trial (JAMA 2008;299:901-13). "If your child fails an SSRI, they have a 50% chance of doing well on another SSRI and a 50% chance of improvement on a different class. Adding CBT increases the chances of improvement by about 11%."

Like TADS, the TORDIA trial also found that family conflict is a leading predictor of suicide attempts, as is baseline suicidal ideation.

"Ideation in the face of family conflict is a group to watch very carefully," she emphasized.

Guidance on how long a clinician should wait before deciding whether an initial treatment needs to be changed or supplemented came from study that was published last year (J. Am. Acad. Child Adolesc. Psychiatry 2009;48:71-8).

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According to that study, Dr. Wagner said, "If by week 4, they haven't had a 58% improvement—if they're not more than 50% improved—they're unlikely to go on to remit. It's time to up the dose or switch."

A successful therapy should be maintained for at least a year before attempting to cease treatment, Dr. Wagner said (J. Child. Adolesc. Psychopharmacol. 2008;18:389-94). "A year from the time you start treatment would be a bare minimum. I know a lot of parents want it short, but then it's important that they understand and assume the risk," she said.

As to the box warnings on suicide risk that were issued by the FDA in 2004 and 2007, she referred to findings that showed a 44% decrease in primary care providers' diagnoses of depression after the warnings were issued and a 10% reduction in prescriptions of SSRIs (Arch. Gen. Psychiatry 2009;66:633-9).

"Where did those children who were previously being diagnosed with depression go?" Dr. Wagner asked. "The suicide rate is now 5% higher than it has been in the previous 20 years. It's worrisome that diagnosis … and treatment has dropped. There's increasing evidence that those trends could be an unintended consequence of the FDA's box warning."

She concluded by citing another study that showed that the number of children needed to treat with antidepressants to achieve one remission is 10, while the comparable number needed to harm due to suicidal ideation or attempts is 112 (JAMA 2007;297:1683-96).

"That's not committing suicide but having suicidal attempts or ideation," she emphasized. "They are 11 times more likely to get benefit than to develop suicidality. From my perspective, that's an excellent ratio."

Dr. Wagner disclosed that she has received honorarium and travel support from AACAP, research support from National Institute of Mental Health, and other support from the American Society of Clinical Pharmacology. ■

Psychotropic Drug Use in 31% Seeking Bariatric Surgery

BY HEIDI SPLETE

WASHINGTON — Almost one-third of adolescents who were approved for bariatric surgery reported using psychotropic medications, but the use of substances such as drugs and alcohol was lower than expected, according to data from 82 subjects collected as part of a larger longitudinal study.

"Some of the worst consequences of extreme obesity are psychosocial," Meg H. Zeller, Ph.D., a psychologist at Cincinnati Children's Hospital Medical Center, said at the annual scientific meeting of the Obesity Society.

Longitudinal psychosocial assessment helps document changes associated with bariatric surgery and identify factors that might predict optimal mental and physical health in adolescents after surgery, she said.

To determine the baseline psychosocial characteristics of teens undergoing bariatric surgery, Dr. Zeller and her colleagues reviewed data from adolescents aged 19 years and younger within 30 days before surgery. The average age of the members in study group was 17 years, and the average body mass index was 56 kg/m^2. Most of the patients (77%) were girls, and a majority (68%) were white.

VITALS

Major Findings: Depressive symptoms were reported by 76% of adolescents seeking bariatric surgery.

Data Source: A review of baseline psychosocial characteristics of 82 teens undergoing bariatric surgery.

Disclosures: The study was supported in part by a grant from the National Institute of Diabetes and Digestive and Kidney Diseases.

The researchers used several validated questionnaires, including the Beck Depression Inventory (BDI), the Impact of Weight on Quality of Life–Kids (IWQOL-Kids), and the Questionnaire on Eating and Weight Patterns–Revised (QEWP-R). The adolescents also responded to questions about substance use and use of mental health services within the previous 12 months.

Overall, 76% of the adolescents reported depressive symptoms based on the BDI. Based the QEWP-R, 11% met screening criteria for binge eating disorder and 6% reported alcohol use, Dr. Zeller said. However, 31% reported use of a psychotropic medication, 28% were taking antidepressants, and 11% were taking mood stabilizers. In addition, data from IWQOL-Kids showed significant and global impairments in weight-related quality of life issues crossing physical, social, emotional, and body-esteem domains.

The low use of drugs and alcohol in the study population may reflect less exposure to peer contacts and peer pressure because of the patients' extreme weight, and it's not unusual for very obese adolescents to be home schooled, Dr. Zeller noted.

"What is critical and ongoing is our follow-up, 6, 12, and 24 months after surgery," Dr. Zeller added.

The adolescents are part of the ongoing Teen–Longitudinal Assessment of Bariatric Surgery (Teen-LABS).

Teen-LABS includes five clinical centers collaborating to facilitate clinical, behavioral, and epidemiologic studies of bariatric surgery in adolescents, and to study the causes and effects of severe obesity in teens, according to the group's Web site, www.teen-LABS.org. ■