Choose Nonstimulants With Care in ADHD

BY NANCY WALSH
New York Bureau

NEW YORK — Options are available for children with attention-deficit hyperactivity disorder who do not respond to treatment with stimulants or are troubled by side effects, but they must be chosen and used carefully, Laurence L. Greenhill, M.D., said at a psychopharmacology update sponsored by the American Academy of Child and Adolescent Psychiatry.

First the diagnosis should be reviewed, as many conditions that will not respond to stimulants can overlap or mimic ADHD. These include oppositional defiance disorder, anxiety problems, depression, occasionally bipolar disorder, and psychotic conditions.

"And don't forget substance abuse disorder, which is a pretty good neutralizer of some stimulant treatments," said Dr. Greenhill, who is professor of clinical psychiatry at Columbia University, New York, and director of research for the pediatric psychopharmacology unit at the New York State Psychiatric Institute.

The preferred second-line drug is atomoxetine (Strattera), a nonstimulant, highly specific norepinephrine reuptake inhibitor. This is not a controlled substance, so it also is useful for parents who are uncomfortable giving their child a schedule II drug, he said.

As a 24-hour drug, atomoxetine significantly improves behavior and activities in both evening and early morning.

"The most important thing you can do for your patients is to start this drug slowly and give it twice a day when you are titrating it," Dr. Greenhill said. Patients are much less likely to experience severe somnolence if the drug is titrated over a week, despite the fact that the labeling says upward titration to a full dose of 1.2 mg/kg per day can begin after 3 days on the initial dose of 0.5 mg/kg per day.

If the full dose is given rapidly, there is a good chance that a formerly disruptive ADHD child will fall asleep in class. "As much as that might be a refreshing change for a teacher who's been battling the noise, nothing gets a parent out of work faster than the school nurse calling and saying, 'We can't keep your son awake—come and get him.' That only has to happen once and the parents will stop the atomoxetine really fast, because they've never had this problem before," Dr. Greenhill said.

Third-line treatments include the α-2 agonists and bupropion. Clonidine (Catapres) may be useful in treating very hyperactive or aggressive patients, but it may take several weeks to take effect and does not improve inattention symptoms. There also are risks of cardiovascular adverse effects, depression, and decreased glucose tolerance.

Guanfacine (Tenex) is a longer acting α-2 agonist that has a more favorable side effect profile than clonidine, but it has been studied only in open trials. Studies of this drug in primates suggest that it acts more on postsynaptic α-2 receptors in the prefrontal cortex than in the brainstem where clonidine works. This may prove helpful, but there's much more work to be done, Dr. Greenhill said.

Bupropion may be useful for comorbidities and is not a controlled substance, but the effect size of this drug appears to be limited. Adverse effects include irritability, insomnia, and tics.

The usual effective dose is about 300 mg/day, but seizures can result if the dose exceeds 450 mg/ day. "So make sure the patient hasn't been prescribed Zyban, the other form of bupropion, for smoking cessation," he said.

Dr. Greenhill disclosed that he has relationships with several manufacturers of drugs used to treat ADHD, including Eli Lilly & Co., the manufacturer of atomoxetine. ■

ADHD Stimulants: No Link to Propensity for Later Drug Abuse

BY DOUG BRUNK
San Diego Bureau

YOSEMITE, CALIF. — Will my child become a dope fiend?

That's a common question Robert S. McKelvey, M.D., fields from parents of children who are prescribed a class II stimulant for attention-deficit hyperactivity disorder (ADHD).

"The answer is 'no,' " Dr. McKelvey said at a pediatric conference sponsored by Symposia Medicus. "The risk of kids who have properly diagnosed ADHD taking stimulants and becoming dope fiends is no different than [it is for] kids who do not have ADHD. The kids at risk are those who have ADHD" and are not on a prescribed drug treatment. "They have three times the likelihood of developing substance abuse problems," he said.

'The kids at risk are those who have ADHD' and are not on a prescribed drug treatment.

DR. McKELVEY

Nonstimulant medications are an option for antisocial teens with ADHD, "although, at least in my view, they're not as effective as stimulants," noted Dr. McKelvey, director of child and adolescent psychiatry at Oregon Health and Science University, Portland. Nonstimulant choices include atomoxetine, bupropion, clonidine, guanfacine, and the tricyclic antidepressants imipramine and nortriptyline.

Another question he commonly fields from parents is the effect of stimulants on children who have a chronic tic disorder such as Tourette's syndrome. "When I was in training, if you had tics, you had a history of tics, or even a family history of tics, we didn't start you on stimulant medication," he said. "Now there are a couple of studies that show that if you have tics and you take stimulants, it's probably OK as long as the tics don't worsen. In many cases, the tics seem to [decrease in severity]."

Drug preparations in the stimulant class are derived from methylphenidate or dextroamphetamine. Methylphenidate is more widely used in the United States, but Dr. McKelvey noted that both agents are equally effective.

"You can't yet predict response, but it's possible that pharmacogenetics studies will give us a hand on that," he said. "If one of them doesn't work, you try the other."

A key point to remember about both agents is that they have very short half-lives. Maximal benefit on behavior occurs in 1-2 hours for agents derived from methylphenidate and 3-4 hours for agents derived from dextroamphetamine.

The sustained-release formulations appear to be as effective as the standard short-term formulations. The doses vary with the individual. There is some thought that academic performance (such as that associated with inattention) may respond to a lower dose than do restlessness and impulsivity, he said.

New, long-acting preparations enable once-daily dosing. These include Concerta, Metadate CD, Adderall XR, Methy-Patch, and Focalin.

The most common adverse effect of stimulants is decreased appetite, which occurs in about 80% of children who take them. "The decreased appetite and weight loss can be stunning in some kids," he remarked. "I've seen some very skeletal-looking little boys, and it can make you quite nervous."

Long-term stimulant use may result in about a 1-cm decrease in height per year during the first 3 years of use, "but some of that is caught up," Dr. McKelvey said. "More recent studies suggest there is perhaps a 1-cm decrease [in height] overall if you take stimulants long term."

Insomnia is another common side effect, "so you tend to give it earlier in the day. You have to monitor heart and blood pressure. The things you're monitoring are height, weight, and blood pressure. It's pretty straightforward, but yearly, I usually check the white blood cell count," he said.

He also warned against unproven therapies for ADHD, including megavitamins, biofeedback, sensory integration training, and optometric vision training. "There's a lot of malarkey out there." ■

Anxiety Disorders Place Huge Burden on Child's Entire Family

BY MARY ELLEN SCHNEIDER
Senior Writer

ATLANTA — A significant burden is placed on the family members of children and adolescents with anxiety disorders, regardless of the age of the child, Catherine Mancini, M.D., said in a poster presentation at the annual meeting of the American Psychiatric Association.

The research shows that an anxiety disorder affects various areas of family functioning, including the physical and mental health of family members and family closeness, wrote Dr. Mancini and her associates at McMaster University in Hamilton, Ont.

The study included 24 outpatient children (8-17 years old) with an anxiety disorder and 24 family members. The family members—4 fathers and 20 mothers—each completed self-rated questionnaires on the impact of the child's illness on various areas of family functioning.

Primary obsessive-compulsive disorder rated significantly higher on the overall family burden scale than did other primary conditions.

Among the family members in the study, 50% reported some degree of family burden, 50% reported an effect on family health, and 25% reported an impact on family closeness.

A total of 17 of the 24 family members reported that their ill child had become "distressed/anxious/angry when we have not provided assistance." The study results showed that family members also reported disruption of routine activities because of the child's illness and care, or "irrational demands."

Ten of the 24 parents reported that they or another family member had experienced physical change because of the child's illness, including weight loss, back pain, headaches, or sleeping problems, the investigators said.

Dr. Mancini and her associates did not find any significant differences on family burden scales between children aged 9-12 and adolescents aged 13-17.

Although the type of primary diagnosis did not make a significant difference in the family's burden, the researchers did report that primary obsessive-compulsive disorder rated significantly higher on the overall family burden scale than did other primary conditions.

In addition, anxiety disorders in male youths might be associated with higher rates of overall burden and impact on family closeness, Dr. Mancini and her associates found. ■