Stimulants for ADHD: No Link to 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.

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 parents ask is what effect stimulants have on children with 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. Often, the tics seem to [decrease in severity]."

Drugs 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. There is some thought that academic performance (such as that associated with inattention) may respond better 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.

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DR. McKELVEY

The most common adverse effect of stimulants is decreased appetite, which occurs in 80% of children. "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." ■

Health Canada Reinstates Adderall XR After Review of Children's Deaths

Patients in Canada with attention-deficit hyperactivity disorder are now able to obtain Adderall XR.

Sales of the drug, distributed by Shire Pharmaceuticals Group PLC, had been suspended earlier this year in Canada after the release of postmarketing reports of sudden death in 12 children in the United States who had taken the drug between 1999 and 2003.

At Shire's request, Health Canada, that country's drug regulatory agency, convened the New Drug Committee, a three-member panel of experts in pediatric cardiology, pediatric development, and pharmacoepidemiology, to review the suspension of the drug. The committee's recommendation to reinstate Adderall XR, which came in late August, hinged on the adoption of revisions to the Canadian version of the product monograph and to the patient leaflet.

The committee also recommended a Dear Healthcare Professional letter, as well as continuing medical education about sudden death in otherwise healthy children. The product label had been changed in August 2004 to include a warning that patients with underlying heart disease might be at increased risk for sudden death.

—Heidi Splete

No Withdrawal Syndrome Seen With Modafinil for ADHD

BY DAMIAN McNAMARA
Miami Bureau

BOCA RATON, FLA. — Children and adolescents with attention-deficit hyperactivity disorder did not experience withdrawal or discontinuation syndrome after abrupt cessation of modafinil film-coated tablets in a phase III, double-blind, multicenter trial.

Researchers also found efficacy as early as 1 week in this 9-week study of 6- to 17-year-olds with attention-deficit hyperactivity disorder (ADHD). The Food and Drug Administration has approved modafinil (Provigil) for treatment of narcolepsy and is currently reviewing a special pediatric formulation for ADHD.

"This is not surprising. Modafinil is a medication that improves vigilance and alertness and could improve similar symptoms in ADHD," Joseph Biederman, M.D., said in an interview at his poster presentation during a meeting of the New Clinical Drug Evaluation Unit sponsored by the National Institute of Mental Health.

Dr. Biederman and his associates compared efficacy using the school and home versions of the ADHD Rating Scale-IV, the Clinical Global Impression of Improvement (CGI-I) scores, and adverse event reporting by 125 patients taking the pediatric formulation of modafinil and 64 taking a placebo.

The modafinil group had significantly improved school rating total scores, compared with those of the placebo group at 1 week, an effect that was maintained through week 7. The final 2 weeks of the study was a washout phase. Mean reduction from baseline was 17 points with modafinil versus 8 points with placebo. Significant reductions in home rating total scores also were observed with modafinil at all visits, according to Dr. Biederman, chief of the joint program in pediatric psychopharmacology, Massachusetts General Hospital, Boston.

A significantly greater percentage of modafinil patients was rated as "much" or "very much" improved on the CGI-I (49%) than were placebo patients (25%).

Modafinil was abruptly discontinued in 37 patients. Abrupt cessation was not associated with symptom rebound, and no evidence of withdrawal or discontinuation syndrome was seen.

This and other phase III study results were submitted to the FDA in December 2004. "I don't see any reason why they wouldn't approve it," said Dr. Biederman, who reported no affiliation with Cephalon Inc., the manufacturer and sponsor of the study. ■

Sleep-Disordered Breathing and Inattention Are Linked in Teens

BY BRUCE JANCIN
Denver Bureau

DENVER — Adolescents with symptoms of sleep-disordered breathing had a 2.5-fold increased prevalence of inattention-type attention-deficit hyperactivity disorder in the first large, population-based study to examine this relationship, Eric O. Johnson, Ph.D., reported at the annual meeting of the Associated Professional Sleep Societies.

In contrast, sleep-disordered breathing (SDB) was not linked to hyperactivity-type ADHD in the survey of 1,014 Detroit-area youths aged 13-16 years and their parents, according to Dr. Johnson of the Henry Ford Health System, Detroit. The observed association between SDB and inattention-type ADHD was independent of potential confounders including race, body mass index, the presence of conduct or oppositional defiant disorder, and asthma.

Participants were randomly selected from a large Detroit-area HMO. Computer-assisted structured interviews conducted separately with the teenager and one parent showed good concordance with regard to the presence of SDB.

Roughly 6% of the adolescents experienced the classic symptoms of loud snoring, periods of stopped breathing, and/or choking or gasping sounds during sleep at least once a week. The prevalence of SDB symptoms was twice as high among African American teenagers as among Caucasians.

By the adolescents' own reports, 4.5% met DSM-IV criteria for lifetime diagnosis of ADHD. By their parents' accounts, the rate was 7.8%. Most cases were of the inattention type. By applying the statistical tool known as generalized estimating equations, it was possible to account for the differing parental and adolescent estimates and essentially split the difference.

Although this was the first large, population-based study to examine SDB and ADHD in a teenage population, several small, clinic-based studies have suggested that SDB in young children is associated with both hyperactive- and inattention-type ADHD. Obstructive sleep apnea in adults is typically associated with inattentive types of behavior rather than hyperactivity. The new Detroit survey suggests that by the time children with SDB reach the age of 13 to 16, the dominant manifestation has shifted from hyperactive- to inattentive-type behaviors for many individuals.

But it must be emphasized that it is unclear from these data whether SDB causes inattention or whether inattentive-type ADHD somehow predisposes individuals to SDB, Dr. Johnson noted.

The study was funded by the National Institutes of Health. ■