Screen ADHD Patients for Problems With Sleep

Clonidine, antihistamines prescribed most often by child and adolescent psychiatrists for insomnia.

BY NANCY WALSH
New York Bureau

NEW YORK — Insomnia is a real and pressing concern for children with attention-deficit hyperactivity disorder and their families, Judith A. Owens, M.D., said at a psychopharmacology update sponsored by the American Academy of Child and Adolescent Psychiatry.

"At least 60% of the kids in our ADHD clinic have significant problems with sleep that really impact their quality of life," said Dr. Owens of the department of pediatrics at Brown University, and director of the pediatric sleep disorders clinic, Hasbro Children's Hospital, Providence, R.I.

The problem is multifaceted and bidirectional. Insufficient or fragmented sleep can lead to excessive daytime sleepiness, which in turn can result in ADHD-like symptoms. The medications themselves, such as psychostimulants used to control ADHD, can affect sleep onset and continuity. Methylphenidate, for example, has been shown to delay sleep onset by 30 minutes, Dr. Owens said.

Other psychotropic medications can affect sleep architecture, altering percentages of rapid eye movement (REM) and slow-wave sleep, and can interfere with the neurochemicals responsible for regulation of sleep and wakefulness.

Comorbid conditions may further complicate the situation, with bedtime resistance seen in oppositional defiant disorder, insomnia and early awakening in depression, and night waking in anxiety disorders.

A subset of children with ADHD may have a primary sleep dysfunction involving homeostatic dysregulation, she said.

"But no sleep medications are approved for use in the pediatric population, which some of us have been trying to change," she said. This has proved difficult, at least in part because of the perception that insomnia in ADHD children is largely a parent-driven complaint. "It has been very difficult to convince the Food and Drug Administration that there is a need for these," Dr. Owens said.

The lack of approved drugs leaves clinicians relying on drugs that are less than effective and those that may have problematic side effects and questionable long-term safety.

Preliminary data from a recent survey of 1,271 practicing members of the American Academy of Child and Adolescent Psychiatry suggest that 51% use insomnia medications in more than half of their ADHD patients, she said.

On the list of drugs used, clonidine (Catapres) topped the list, with 86%, followed by antihistamines, at 67%.

The central α_2-agonist clonidine has various effects on sleep architecture, including slowing sleep-onset latency, increasing slow-wave sleep, and decreasing REM sleep, she said. Its side effects include hypotension, bradycardia, anticholinergic effects, and dysphoria. It can interact with CNS depressants and stimulants, and tolerance often develops.

"I don't have a lot of arguments to suggest that other things are much better, but I do think there are some problems with this drug," Dr. Owens said. Interestingly, recent reports have identified a 10-fold increase in overdoses seen in emergency rooms, she said.

Antihistamines generally are viewed as benign by parents and physicians, and they are used quite often in cases when sleep-onset latency problems are less severe. "But they're not terribly effective," she said.

Trazodone (Desyrel) is also used, though it tends to cause morning hangover. Benzodiazepines are little used in children, nor are zolpidem (Ambien) and zaleplon (Sonata), although the latter appear to be safe and well tolerated in adults and have little effect on sleep architecture.

"We worry about sleep architecture in children because if slow-wave sleep is suppressed, it can alter their production of growth hormone," she said.

Melatonin is being evaluated as a possible sleep aid for children, but much more information is needed before this dietary supplement can be recommended. Among the concerns with melatonin are reports that it may suppress the hypothalamic-gonadal axis. There have been case reports of its withdrawal triggering precocious puberty, Dr. Owens said.

"The most important thing is that whenever you are evaluating any child, be sure to screen for sleep problems. I never cease to be astonished that, if you don't ask the question, the parents just think it's something they have to live with and won't volunteer the information," she said. "Do this in some simple systematic way, and you will be addressing a huge issue for families." ■

Methylphenidate Appears Safe in Preschoolers

BY KERRI WACHTER
Senior Writer

WASHINGTON — Methylphenidate appears to be effective and safe for the treatment of attention-deficit hyperactivity disorder in preschool-age children, according to preliminary data presented at the annual meeting of the American Academy of Child and Adolescent Psychiatry.

The results come from the Treatment of Attention Deficit Hyperactivity Disorder in Preschool-Age Children study (PATS), sponsored by the National Institute of Mental Health.

Several studies have previously suggested that preschool-age children with ADHD would respond to and tolerate methylphenidate, and this multisite study is the first major effort aimed at directly assessing the safety and efficacy of a stimulant for the treatment of attention-deficit hyperactivity disorder in children aged 3-5 years.

"The take-home message is that 85% of the children responded to the methylphenidate," during the 5-week crossover period to determine the optimal dosing for each of the children, said study investigator Howard B. Abikoff, Ph.D., of the New York University Child Study Center.

The optimal dose for each child was determined during a 5-week period. Over that period, all of the children were given a placebo or a dose of 1.25 mg, 2.5 mg, 5 mg, or 7.5 mg three times daily for 1 week each. Overall, 144 children completed this 5-week trial. Each week, a composite score of symptom severity was assigned based on parent and teacher responses to the Conners, Loney, and Milich (CLAM) Questionnaire and the Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) rating scale.

Two blinded assessors were then asked to identify the best dose for each child. A full panel of all investigators decided upon the appropriate dose when the two assessors did not agree. Just over half (51%) of the children were referred to the full panel of investigators to determine the optimal dose.

Children also could be evaluated at a 10-mg dose if investigators agreed that there was a good chance that the child would have an even better response with a higher dose. This happened in 15 of the cases.

"First of all, we got a very significant effect per dose relative to placebo," said Dr. Abikoff. For the 2.5-mg, 5-mg, and 7.5-mg doses, the children's composite scores were significantly lower than for placebo.

"We got small to moderate effect sizes at the intermediate doses [2.5 mg and 5 mg] and a reasonably robust effect size at the 7.5-mg dose," Dr. Abikoff said. There was also a trend toward significantly lower scores for children in the 1.25-mg group.

After the 5-week crossover period, 113 children were randomized to receive either the optimal dose (61 children) or placebo (52 children) for 4 weeks. In the analysis of this portion of the trial, all children were included even if they left the trial early, with the last observation for that child carried through.

In the second portion of the study, a statistically significant difference was found in the composite scores—1.79 points for those in the placebo group and 1.49 points for those receiving the optimum dose of methylphenidate. "The effect sizes are linear from 1.25 mg up to 7.5 mg. … The effect size for 10 mg was somewhat lower," said Dr. Abikoff.

Over the course of the trial there were 39 adverse events, including difficulty falling asleep, decreased appetite, emotional outbursts, and stomach discomfort, he said.

Safety was a significant concern, given the age group involved. The researchers worked closely with the Food and Drug Administration in designing the trial to ensure safety. In fact, the original study design was altered to account for the concern that children in this age group might be uniquely sensitive to stimulants and have a number of adverse events. Originally, the lowest dose of methylphenidate was planned to be 2.5 mg three times a day, but the dose was lowered to 1.25 mg three times daily to ease FDA concerns about adverse reactions.

There was also a 40-week open-label maintenance phase, with children receiving a mean total daily dose of 14 mg. During this phase, the child was given the dose that the clinician thought was appropriate. "What's interesting is that we see a noticeable increase of 23% in absolute dose," Dr. Abikoff said.

At the end of this maintenance period, the optimal dose had increased to 20 mg/day. This suggests "the doses used here were a bit low in terms of clinical optimization," he said. ■

Romantic Stress Tied to Depression In Sensitive Girls

BALTIMORE — Highly sensitive teenage girls are more likely to develop depression in response to romantic stress, Shannon E. Daley, Ph.D., said at a meeting sponsored by the Society for Research on Adolescence.

In this longitudinal study, 87 girls were studied using questionnaires and telephone interviews; 21% were African American, and 79% were Hispanic. Data were collected 6 months apart, and the measuring tools used were the Structured Clinical Interview for DSM-IV, the Interpersonal Sensitivity Measure, the Chronic Strain Interview, and the Episodic Stress Interview.

Participants, who were 16 years old, were questioned about romantic life events, and their lifetime history of unipolar depression was evaluated at the start of the study. Chronic romantic stress was assessed over the 6-month follow-up period, along with any more depressive symptoms, Dr. Daley, of the University of Southern California, said in an interview.

Through logistic regression analyses, Dr. Daley and her colleague at the university, doctoral candidate Christie J. Rizzo, determined that interpersonal sensitivity moderated the relationship between episodic and chronic romantic stress and clinical depression.

"Girls who experience a heightened sensitivity to interpersonal processes are especially likely to become depressed when confronted with romantic stress or low-quality romantic relationships," they said.

—Deeanna Franklin