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 percent-ages of rapid eye movement (REM) and slow-wave sleep, and can interfere with the normal sleep-wake rhythm. The newness of this drug was respected even for regulation of sleep and wakefulness.

Comorbid conditions may further complicate the situation, with bedtime resis-tance seen in oppositional defiant disorder, insomnia and early awakening in depres-sion, and night wakening in anxiety disorders. A subset of children with ADHD may have a primary sleep dysfunction involv-ing 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, in part because of the perception that in-somnia in ADHD children is largely a par-ent-driven complaint. It has been very diffi-cult to convince the Food and Drug Administra-tion that there is a need for these,” Dr. Owens said.

The lack of approved drugs leaves clini-cians relying on drugs that are less than effective and those that may have prob-lematic 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 Psy-chiatry suggest that 51% use insomnia medications in more than half of their ADHD patients, she said.

Other medications used, clonidine (Catapres) topped the list, with 86%, fol-lowed by antihistamines, at 67%.

The central α2 agonist clonidine has var-i-ous effects on sleep architecture, includ-ing slowing sleep onset latency, increasing slow-wave sleep, and decreasing REM sleep, she said. Its side effects include hy-potension, bradycardia, anticholinergic ef-fects, and dizziness. It can interact with CNS depressants and stimulants, and tol-erance often develops.

“I don’t have a lot of arguments to sug-gest, other than things that are useful, but I do think there are some problems with this drug,” Dr. Owens said. Interestingly, recent reports have identified a 10-fold in-crease 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-on-set latency problems are less severe. “But they’re not terribly effective,” she said.

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

“Don’t even consider zolpidem in children because if slow-wave sleep is sup-pressed, it can alter their production of growth hormone,” she said.

Melatonin is being evaluated as a possi-ble 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 hypo-thalamic-gonadal axis. There have been case reports of its withdrawal triggering precarious puberty, Dr. Owens said.

“Melatonin is being offered as a treat-ment option 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, parents won’t volunteer the information,” she said. “Do this in some simple systematic way, and you will be addressing a huge is-sue 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 hyperac-tivity disorder in preschool-age children, according to preliminary data presented at the annual meeting of the American Academy of Child and Adolescent Psy-chiatry.

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

Several studies have previously sug-gested 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 opti-mal 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 de-termined during a 5-week period. Over that period, all of the children were giv-en a placebo or a dose of 1.25 mg, 2.5 mg, 5 mg, or 10 mg (or 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, Kockin, 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 signifi-cantly lower scores for children in the 1.25 mg group.

After the 5-week crossover period, 113 children were then asked to receive ei-ther 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 ef-fect 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, emo-tional outbursts, and stomach discomfort, he said.

Safety was a significant concern, giv-en the age group involved. The re-searchers worked closely with the Food and Drug Administration in designing the trial to ensure safety. In fact, the original study design was altered to ac-count for the concern that children in this age group might be uniquely sensi-tive 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 dai-ly to ease FDA concerns about adverse reactions.

There was also a 40-week open-label maintenance phase, with children re-ceiving a mean total daily dose of 14 mg. During this phase, the child was given the dose that the clinician thought was ap-propriate. “What’s interesting is that we see a noticeable increase in 23% in ab-solute dose,” Dr. Abikoff said.

“At the end of this maintenance period, the median dose had increased by 25 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 meet-ing 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 col-lected 6 months apart, and the measuring tools used were the Structured Clinical In-terview for DSM-IV, the Interpersonal Sensitivity Measure, the Chronic Strain Inter-view, and the Episodic Stress Interview.

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

Through logistic regression analyses, Dr. Daley and her colleague at the uni-versity, doctoral candidate Christie J. Riz-zo, determined that interpersonal sensi-tivity moderated the relationship between episodic stress and depressive symptoms and clinical depression.

“Girls who experience a heightened sen-sitivity to interpersonal processes are es-pecially likely to be depressed when they are confronted with romantic stress or low-quality romantic relationships,” they said.

—Deanna Franklin