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

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 4-5 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, 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 all 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 then assigned 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 carried forward 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 concerns in 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 daily, 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 ab sole 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.

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 children, according to preliminary data presented at the annual meeting of 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.

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.

"We worry about sleep architecture, including slow-wave sleep onset latency, increasing slow-wave sleep, and decreasing REM sleep, 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 generalizing things are must be true, but I do think there are some problems with this drug," Dr. Owens said. Interestingly, recent reports have identified a 10-fold increase in cases of sudden cardiac death in emergency rooms, she said.

Evidence cited in the study indicates 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, that’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."