ADHD: Switching to Atomoxetine Can Help

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

TORONTO — Children with attention-deficit hyperactivity disorder can be successfully cross-tapered from a stimulant to atomoxetine with significant improvements in their ADHD symptoms, Dr. Humberto Quintana reported in a poster at the joint annual meeting of the American Academy of Child and Adolescent Psychiatry and the Canadian Academy of Child and Adolescent Psychiatry.

Slightly more of the children in the group (52%) were taking methylphenidate at baseline; the rest were taking an amphetamine.

Switching from a stimulant to the serotonin norepinephrine reuptake inhibitor atomoxetine also was safe, said Dr. Quintana of the Louisiana State University Health Sciences Center, New Orleans. The study found slight, but statistically significant, increases in blood pressure and heart rate, but the safety findings otherwise were unremarkable.

The study, funded by Eli Lilly & Co.—for whom Dr. Quintana is an investigator—included 62 children aged 6-17 years. Just over half of the children (53%) were switching to atomoxetine because of inadequate response to their current medication; the rest (47%) switched because of adverse events.

Slightly more of the group (52%) were taking methylphenidate at baseline; the rest were taking an amphetamine.

During the first week of the transition period, patients received the full dose of their current medication daily, plus 0.5 mg/kg per day of atomoxetine. During the second week, they received a half-dose of their stimulant each day, plus 1.2 mg/kg per day of atomoxetine. During the final 5 weeks of the study, the patients received 1.2 mg/kg per day of atomoxetine and no stimulant.

At the end of the study, patients experienced a significant decrease in ADHD symptoms as reported by parents on the ADHD Rating Scale. The mean total score decreased from 32 to 22.5, the inattention score decreased from a mean of 17 to a mean of 13.5, and the mean hyperactivity score decreased from 13 to 9.

Most of the children (65.5%) said they preferred atomoxetine over their previous stimulant medication. When surveyed after the study, parents clearly preferred atomoxetine. Parents said they were satisfied with the drug's effect overall, as well as with its effect in both morning and evening hours. They were very satisfied with the drug's ability to "allow the child to be himself" during treatment.

Significant increases in blood pressure and heart rate were found for most of the 62 children; 53 experienced an average increase of 2.4 mm Hg in both diastolic and systolic blood pressure. Fifty-seven children experienced an average increase in heart rate of 9 beats per minute. There were no other ECG changes, including in the QT interval. ■

Some Patients Respond Well to Reduced Doses of Atomoxetine

TORONTO — Reducing the dose of atomoxetine may be possible for children with attention-deficit hyperactivity disorder who have responded well to the medication, Dr. Jeffrey Newcorn reported in a poster at the joint annual meeting of the American Academy of Child and Adolescent Psychiatry and the Canadian Academy of Child and Adolescent Psychiatry.

Dr. Newcorn, of the Mount Sinai Medical Center, New York, investigated low-dose response rates in 229 children aged 6-16 years who had responded well to atomoxetine (Strattera) doses of up to 1.8 mg/kg per day in a previous trial. These children were randomized to continue their same dose of atomoxetine (mean 1.43 mg/kg per day) or to take a reduced dose (mean 0.46 mg/kg per day), and were followed for up to 8 months.

Only three children in the previous-dose group (2.6%) and three (2.5%) in the low-dose group relapsed. However, significantly more children in the low-dose group were no longer considered medication responders; i.e., they no longer had a symptom reduction of at least 40%. The rates of nonresponders were 17% (20/115) in the previous-dose group and 23% (25/109) in the low-dose group.

Tolerability was not a major issue in the study, Dr. Newcorn wrote, although adverse events were less common in the low-dose group. Headache was the most common adverse event, experienced by 21% and 16%, respectively.

"These data suggest that it is possible to maintain initial treatment gains at lower doses during continuing treatment," he wrote. "However, they do not provide definitive evidence that the dose should be lowered during continued treatment."

Still, he said, "The option of lowering the dose during maintenance therapy may be important for patients who respond well to initial treatment but who experience troublesome side effects."

Dr. Newcorn is a consultant for Eli Lilly & Co., which funded the research.

—Michele G. Sullivan

Narcolepsy Drug Is Safe, Effective for ADHD

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

TORONTO — Modafinil is safe and effective in treating pediatric attention-deficit hyperactivity disorder, decreasing symptom scores twice as much as placebo, according to two posters presented at the joint annual meeting of the American Academy of Child and Adolescent Psychiatry and the Canadian Academy of Child and Adolescent Psychiatry.

The posters, sponsored by Cephalon Inc., concluded that children tolerated the film-coated tablets well in dosages of up to 425 mg/day. Insomnia, headache, and decreased appetite were the most commonly reported adverse events. Those adverse events typically occurred during the first 2 weeks of therapy and decreased thereafter, said Dr. Christopher Kratochvil of the University of Nebraska.

The posters analyzed three multicenter, double-blind studies that included a total of 633 children aged 6-17 years. Two of the studies were identical 9-week flexible-dosing trials. The third was a 7-week fixed-dose placebo-controlled study (340 or 425 mg/day), followed by a 2-week period in which half the modafinil group was switched to placebo without tapering while the other half continued modafinil treatment.

Adverse events were more common in the active group than the placebo group and included insomnia (27% vs. 4%), headache (20% vs. 13%), and decreased appetite (16% vs. 3%).

The adverse events were all classified as mild to moderate. They peaked in the first 2 weeks of treatment and subsequently subsided. No apparent association was found between adverse events and dosage.

There were no significant changes in heart rate or blood pressure between the groups, and the abrupt discontinuation of the drug did not lead to acute withdrawal symptoms or rebound effects.

The drug effectively reduced the symptoms of ADHD, especially hyperactivity and inattention, reported Dr. Joseph Biederman of Massachusetts General Hospital. The effects were consistent whether assessed by physician, parent, or teacher.

Physicians assessed almost 50% of the active groups as much improved at the end of treatment, compared with 20% of the placebo group.

Parents and teachers rated symptom improvement of those in the active group at about twice that of the placebo group in all areas: oppositional behavior, inattention, and hyperactivity.

Symptom improvement differed significantly from placebo at week 2 of treatment and continued to diverge throughout the course of all three studies. ■

Conditioned Placebo Dose Reduction Tested for ADHD

BY DOUG BRUNK
San Diego Bureau

SAN DIEGO — Children with ADHD were effectively treated on 50% of their optimal stimulant dose by pairing placebo pills with their stimulant medication, Dr. Adrian Sandler reported at the annual meeting of the Society for Developmental and Behavioral Pediatrics.

The reduction technique could mark a new way to treat ADHD and other chronic conditions.

DR. SANDLER

The technique, known as conditioned placebo dose reduction, could mark a new way to treat attention-deficit hyperactivity disorder (ADHD) and other chronic conditions, said Dr. Sandler, medical director of the Olson Huff Center for Child Development at Mission Children's Hospital, Asheville, N.C.

He and his associates enrolled 137 children with ADHD aged 6-12 years.

The children were divided into 3 groups. Group 1's treatment was decreased from 100% of optimal stimulant dose plus placebo to 50% of stimulant dose plus placebo. Group 2's treatment decreased from 100% of stimulant to 50% of stimulant. Group 3 served as the control, which no reduction in stimulant treatment. Of the 137 children, 70 completed the dose reduction phase. Most children in group 1 remained stable or improved during dose reduction while most in group 2 deteriorated.

The investigators observed no differences in control of ADHD symptoms between groups 1 and 3, and both groups showed improved ADHD control compared with the children in group 2.

Treatment emergent side effects were lowest among children in group 1, while those in group 2 seemed to show an increase in side effects as dose reduction went on.

At the time of this meeting, only 22 children had completed the study's maintenance phase. But so far Dr. Sandler and his associates have detected no differences in ADHD control or in discontinuation rates between groups 1 and 3. ■

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