

# PEDIATRIC NEUROLOGY BRIEFS

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### ATTENTION DEFICIT DISORDERS

#### EXTENDED EFFICACY OF ONCE-DAILY ATOMOXETINE IN ADHD

The efficacy of atomoxetine administered once daily (final dose 1.3 +/- 0.3 mg/kg; mean 44.5 mg per day; range 10-80 mg per day) in the morning was assessed throughout the day, including evening and early morning, in a total of 197 children, 6 to 12 years of age (71% male), diagnosed with attention-deficit/hyperactivity disorder (ADHD) (69% had combined subtype ADHD, and 35% had comorbid oppositional defiant disorder). The randomized, multicenter, double-blind, placebo-controlled trial was conducted at 12 outpatient centers in the United States, and organized and funded at the Lilly Research Laboratories, Indianapolis, IN. Patients received 8 weeks of treatment with atomoxetine (n=133) or placebo (n=64), and ADHD symptoms were assessed with parent and investigator rating scales. An electronic data entry system was used to record the daily parent assessments of 11 children's home behaviors in the evening and early morning, including getting up, completing homework, and sitting through dinner.

Mean reductions in the total scores of ADHD Parent and Investigator-Administered Rating Scales were significantly greater for atomoxetine- than placebo-treated patients, and the benefits were noted at the first visit after initiating treatment and at all subsequent visits. Both inattentive and hyperactive/impulsive symptoms were significantly reduced by atomoxetine, and core symptoms continued to decrease throughout the 8-week study. Efficacy outcomes as determined by the Daily Parent Ratings of Evening and Morning Behavior-Revised (DPREMB-R) were significantly superior for atomoxetine cf placebo-treated, in both the evening and morning hours, on days 1, 2, 3, 6, and 7, and weeks 1, 4, and 8 follow-up. Decreased appetite in 18%, somnolence in 15%, and fatigue in 10% were significantly more frequent with atomoxetine than with placebo ( $p<0.05$ ). Vomiting occurred in 6.1% with atomoxetine and in 1.6% with placebo. Six atomoxetine-treated patients (4.5%) discontinued treatment because of adverse events (somnolence in 3; aggression 1;

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fatigue 1; and syncope 1), and 1 placebo-treated patient (1.6%) withdrew because of nausea. Eighty percent of atomoxetine-treated patients completed the study, compared to 73% of those receiving placebo. (Kelsey DK, Sumner CR, Casat CD, et al. Once-daily atomoxetine treatment for children with attention-deficit/hyperactivity disorder, including an assessment of evening and morning behavior: a double-blind, placebo-controlled trial. **Pediatrics** July 2004;114:e1-e8). (Reprints: Douglas K Kelsey MD, PhD, Lilly Technology Center South, DC4135, Indianapolis, IN 46285).

**COMMENT.** This is the third study showing superior efficacy of once-daily atomoxetine (Strattera<sup>®</sup>) versus placebo in children with ADHD. Compared to previous studies (Heiligenstein et al. 2000; Michelson et al. 2001, 2002; and Newcorn 2002), this report extends the demonstration of efficacy, persisting not only into the evening but also the next morning, after a single morning dose. Contrary to some reports warning of a delayed onset of benefit with atomoxetine compared to methylphenidate, an effect is also measured on the first day of treatment. This study does not address school behavior, but teacher-rating scales completed in previous trials have shown significant benefits. Short-term studies point to some initial adverse events (decreased appetite, abdominal pain, drowsiness, and fatigue), but none life threatening and few resulting in discontinuance of therapy. In one long-term study (Wernicke et al, 2002), adverse events, including slight increases in blood pressure and heart rate, declined in frequency with continued therapy. Since atomoxetine is not considered a stimulant, it may be recommended as first-line therapy for ADHD in patients who present with comorbid tics, seizure susceptibility, and/or sleep disorders. Patients who fail to respond or develop persistent adverse events with stimulant therapy (methylphenidate, amphetamines) may be considered for treatment with atomoxetine. Those who have the hyperactive/impulsive subtype or combined type of ADHD, with behaviors that persist in the evening and early morning hours, may benefit more from the extended efficacy of atomoxetine compared to shorter acting stimulants. Notwithstanding the encouraging early reports of efficacy and safety of atomoxetine, it is a relatively new addition to the ADHD treatment regimen. My personal preference is to rely initially on well-tried and proven remedies. (Millichap JG. *Attention Deficit Hyperactivity and Learning Disorders*. Chicago, PNB Publishers, 1998).

**Alternative/complementary therapy for ADHD.** Zinc sulfate supplements (55 mg/~~day~~), as adjunctive therapy with methylphenidate (MPH 1 mg/kg/day) in a double-blind, placebo-controlled trial in 40 children with combined subtype of ADHD, provided significantly greater improvement than MPH/placebo treatment, in a study at Teheran University of Medical Sciences, Iran (Akhondzadeh S, et al. **BMC Psychiatry** 2004;4:9; biomedcentral.com/1471-244X/4/9). Zinc levels and further evaluation of zinc supplements for ADHD are indicated.

## MOTOR INCOORDINATION IN ADHD

The relationship between motor performance, attention deficit, impulsiveness, and hyperactivity in 42 school-aged children with ADHD (36 males, 6 females; mean age 8 years 2 months; range 6-11 years) was studied at National Taiwan University, Taipei, Taiwan.