Youths aged 6 to 16 years with any subtype of ADHD participated in the study. Comorbid bipolar disorder, pervasive developmental disorder, psychotic illness, anxiety disorders, and tic disorders were exclusionary criteria. Patients with other comorbid psychiatric disorders, including major depressive disorder, were allowed to participate if ADHD was the primary diagnosis.

The American Academy of Child and Adolescent Psychiatry Practic Parameter for the Assessment and Treatment of Children and Adolescents with Attention-Deficit/Hyperactivity Disorder1 (ADHD) recommends that initial psychopharmacological treatment consist of an FDA-approved medication. Agents in this category include stimulants (dextroamphetamine, methylphenidate, mixed salts amphetamine) and atomoxetine.

The clinician and the patient’s family must decide whether to initiate pharmacological treatment with a stimulant or atomoxetine. The largest study to date compared responses to atomoxetine and osmotic-release oral methylphenidate and may help to guide medication selection.2 Youths aged 6 to 16 years with any subtype of ADHD participated in the study. Comorbid bipolar disorder, pervasive developmental disorder, psychotic illness, anxiety disorders, and tic disorders were exclusionary criteria. Patients with other comorbid psychiatric disorders, including major depressive disorder, were allowed to participate if ADHD was the primary diagnosis.

The acute phase of the study was a double-blind, placebo-controlled, 6-week trial. Patients were randomized to receive 0.8 to 1.8 mg/kg/d of atomoxetine (n = 222), 18 to 54 mg/kg/d of osmotic-release methylphenidate (n = 220), or placebo (n = 74). The mean final dosage of atomoxetine was 1.45 mg/kg/d, or 53 mg/d; the mean final dosage of osmotic-release methylphenidate was 1.16 mg/kg/d, or 39.9 mg/d.

Response was defined as at least a 40% decrease in the ADHD Rating Scale-IV total score. After 6 weeks, 56% of patients responded to osmotic-release methylphenidate and 45% responded to atomoxetine; both responses were significantly superior to the 25% who responded to placebo. The number needed to treat was 3 for osmotic-release methylphenidate and 5 for atomoxetine. Osmotic-release methylphenidate was significantly superior to atomoxetine. Effect size was higher for osmotic-release methylphenidate (0.8) than for atomoxetine (0.6).

Completion rates were similar across treatment groups, as were discontinuation rates from adverse events. Adverse effects were higher in the medication treatment groups than in the placebo group. Decreased appetite occurred significantly more in the medicated patients. Insomnia was more common in methylphenidate-treated patients than in atomoxetine-treated patients, and somnolence was more common in atomoxetine recipients than in methylphenidate recipients.

After patients completed the initial 6-week comparison trial, those treated with methylphenidate were switched to atomoxetine under double-blind conditions for 6 weeks. The aim of this portion of the study was to determine whether there was a differential response to the 2 treatments. Of the 220 patients who were initially assigned to receive osmotically released methylphenidate, 178 patients participated in the treatment switch to atomoxetine. Response rates were as follows: 34% of patients responded to atomoxetine or to osmotic-release methylphenidate but not to both, 44% of patients responded to both treatments, and 22% of patients did not respond to either medication. Of those patients who did not respond to methylphenidate in the initial trial, 43% later responded to atomoxetine. Of those who did not respond to atomoxetine, 42% had previously responded to osmotic-release methylphenidate.

In summary, this large, controlled study provides evidence that the efficacy of osmotic-release methylphenidate is superior to atomoxetine. The study also suggests that there is a differential response to the 2 treatments because one-third of the patients responded to methylphenidate or atomoxetine—but not to both. These findings support the Texas Children’s Medication Algorithm Project for the pharmacotherapy of ADHD, which recommends initial treatment with stimulants. If there is no response to 2 stimulant trials, patients should be switched to atomoxetine.3 ECG before treatment?
There has been considerable controversy regarding the initial American Heart Association (AHA) recommendation that an ECG be obtained before initiating stimulant medication for children and adolescents with ADHD. This recommendation has been clarified in a Joint Advisory Statement of the American Academy of Pediatrics (AAP) and the AHA. This new statement has been endorsed by the American Academy of Child and Adolescent Psychiatry, the American College of Cardiology, Children and Adults with ADHD, National Initiative for Children’s Healthcare Quality, and the Society for Developmental and Behavioral Pediatrics. The AAP and AHA believe it is important to assess for heart conditions in children who will be receiving medication treatment for ADHD. A patient and family health history as well as a physical examination, with focus on cardiovascular disease risk factors, are recommended before pharmacotherapy begins. The AAP and AHA stated that it is “reasonable for a physician to consider obtaining an ECG as part of the evaluation of children being considered for stimulant drug therapy, but this should be at the physician’s judgment, and it is not mandatory to obtain one.” The groups also noted that treatment should not be withheld because an ECG is not obtained. The AAP and AHA stated that drugs used to treat ADHD can cause changes in heart rate and blood pressure but that these agents have not been shown to cause heart conditions or to cause sudden cardiac death.

**Comorbid substance abuse**

A recent study provides additional information about stimulant use and substance abuse disorders. Mannuzza and colleagues assessed whether the age at which methylphenidate treatment is initiated in children with ADHD is related to the subsequent development of substance abuse disorders. A total of 176 boys aged 6 to 12 years with ADHD and without a comorbid conduct disorder participated in this prospective, longitudinal study. A comparison group of 178 non-ADHD participants was also included. The study participants were evaluated at 2 time points: late adolescence (mean age, 18.4 years) and adulthood (mean age, 25.3 years). Early age at initiation of methylphenidate treatment did not increase the risk of substance abuse disorders. Rather, later initiation of stimulant therapy was associated with an increased risk of developing nonalcohol substance abuse disorder. The authors speculated that early initiation of treatment with methylphenidate for children with ADHD may have long-term benefits.

Although stimulant medication is very effective, there is some interest in herbal treatments for children with ADHD. A recent study examined the efficacy and safety of St John’s wort (Hypericum perforatum) for children with ADHD. In an 8-week, randomized, double-blind, placebo-controlled trial, 54 children and adolescents aged 6 to 17 years with ADHD were randomized to receive 300 mg of St John’s wort, standardized to 0.3% hypericin (n = 27) or placebo (n = 27), 3 times daily. No significant difference was found between the treatment and placebo groups on change in ADHD Rating Scale-IV scores from baseline to week 8. Similarly, there was no significant difference in Clinical Global Improvement Scale scores (2 or less; much or very much improved) between the treatment group (44.4%) and the placebo group (51.9%). There was no difference in the number of adverse effects between the 2 treatment groups.


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