

Is Atomoxetine as Effective as Methylphenidate in Controlling Behavioral Problems in Children with Attention-Deficit/Hyperactivity Disorder?

D. Benning and A. Griffin

Department of Physician Assistant, Wichita State University, Wichita, KS 67260, U.S.A.

Introduction: Attention-deficit /hyperactivity disorder (ADHD) is among the most prevalent psychiatric disorders seen in children, affecting 3% to 7% of school-aged children [1]. Boys are nine times more likely to have a diagnosis of ADHD than girls [2]. The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [DSM-IV] now allows sub-typing as predominantly inattentive type, predominantly hyperactive type or combined type. Treatment of ADHD primarily consists of pharmacological interventions, particularly stimulants [3]. For decades stimulants, especially methylphenidate (Ritalin[®]), have been used in ADHD management [4]. Methylphenidate accounts for over 90% of the pharmacological treatment provided for ADHD and 2.8% of youth in the United States between the ages of 7 and 15 are taking some form of this medication. A new pharmacologic intervention, atomoxetine (Strattera[®]), is a nonstimulant that was approved for use in treatment of ADHD by the U.S. Food and Drug Administration in November 2002. Literature has documented improvement in behavioral problems with the use of methylphenidate. However, atomoxetine has a body of evidence documenting efficacy in improving the same problems. The purpose of this study is to assess, using current evidence-based literature, whether atomoxetine is as effective as methylphenidate in controlling behavioral problems in children with attention-deficit/hyperactivity disorder.

Methodology: *Study design:* This study is a systematic review of the body of evidence concerning the use of atomoxetine and methylphenidate in the treatment of children diagnosed with ADHD. Articles included met the following parameters: all were from peer-reviewed professional journals, all were published in the year 2000-present, and all used evidence-based data. *Study population:* Children aged 7 to 15 who had been diagnosed with attention-deficit/hyperactivity disorder utilizing the criteria set forth in the DSM-IV and who are receiving pharmacotherapy of either atomoxetine or methylphenidate. *Measures:* Comparison was conducted of the studies findings regarding symptom resolution using atomoxetine or methylphenidate and the side effects and compliance of both therapeutic agents. Symptom reduction was assessed by reduction in mean ADHD RS scores [5].

Discussion: In the treatment of children diagnosed with attention-deficit/hyperactivity disorder, various studies have provided evidence of the efficacy and safety of the use of stimulants. A trial, conducted by Kratochvil and colleagues, comparing atomoxetine and methylphenidate concluded the therapeutic effects to be comparable and, as a nonstimulant, atomoxetine is unlikely to have significant abuse liability or cardiac safety concerns and therefore could become an attractive option in the treatment of ADHD [1]. An open-label trial of atomoxetine and methylphenidate was conducted in which subjects were randomized to treatment with either atomoxetine or methylphenidate for a 10-week period. At the end of the trial, it was concluded that symptom reduction was similar between groups for both hyperactivity/impulsivity and inattention subscales of the parent-rated ADHD RS [6]. Atomoxetine, the first non-stimulant approved by the FDA for treatment of ADHD, has been reported to be efficacious and well-tolerated in children with ADHD [5]. Both atomoxetine and methylphenidate were well-tolerated and no statistically significant differences in discontinuations were noted due to adverse side effects [6]. In a multicenter, double-blind, parallel-group study of atomoxetine, placebo, and methylphenidate, which was recently presented, both atomoxetine and methylphenidate produced significant reductions in ADHD behavior problems relative to placebo and were found to be comparable to each other [7]. In a study conducted by Kratochvil et al., 2002, comparing the efficacy of methylphenidate with that of atomoxetine, there were found to be similar reductions in ADHD symptoms in both treatment groups [1]. These results were measured using the ADHD RS, an 18-item scale in which one item corresponds with one of the 18 DSM-IV symptom criteria for ADHD based on interviews with the parents. The results are as follows:

Symptom Severity Outcomes (ADHD RS total score)

	<i>n</i>	<u>Baseline</u>	<u>Endpoint</u>	<u>Change</u>
Atomoxetine	178	39.43	19.99	-19.44
Methylphenidate Kratochvil et al.	40	37.60	19.83	-17.78

Controlled trials have proven that atomoxetine is more effective than placebo in the treatment of children with ADHD and provides an efficacious alternative for patients who do not respond to stimulant therapy [8]. In an open-label study comparing atomoxetine with methylphenidate, it was concluded that symptom reduction was similar between both groups for both hyperactivity/impulsivity and inattention subscales of the parent-rated ADHD RS [6]. Both medications were well-tolerated with no significant differences in discontinuations due to adverse drug reactions. Most studies found atomoxetine to be safe and well tolerated [5]. While prescribers treating patients with ADHD have both stimulant and nonstimulant options available, current evidence base strongly supports the use of stimulant medications as first-line agents [9]. The relative newness of atomoxetine (2002) warrants further study as to the therapeutic effects on a long-term basis. The studies available show that atomoxetine has promising initial results as nonstimulant treatment of ADHD and could be beneficial for those at risk of stimulant abuse, those who cannot tolerate stimulant therapy, or those who have preexisting cardiac abnormalities [1,4,6,7,8,10,11].

Conclusion: Atomoxetine is the first non-stimulant drug approved for the treatment of attention-deficit/hyperactivity disorder. Evidence has proven it to be an efficacious and well-tolerated alternative to stimulant therapy in the management of patients with ADHD. One study showed that both atomoxetine and methylphenidate were associated with reductions in ADHD symptoms and improved global ratings in children aged 7 to 15. Atomoxetine initially has been found to be as effective in controlling behavioral problems in children with ADHD and is an efficacious alternative for patients who do not respond to stimulant therapy or do not tolerate them. It offers prescribers another option for patients who cannot tolerate stimulants or for those patients whose parents hesitate to use a stimulant to treat ADHD in their children. Although studies reviewed to date suggest considerable promise, more clinically relevant treatment studies are needed to address the long-term efficacy and safety of these treatments.

- [1] Kratochvil C.J., Heiligenstein J.H., Dittmann R., Spencer T.J., Biederman J., Methylphenidate treatment in children with ADHD: A prospective, randomized, open-label trial. *J. Am. Academy Child & Adolescent Psychiatry*. 2002 July; 41(7):776-784.
- [2] Caballero, Joshua, PharmD, Mahata, Milap C., PharmD. Atomoxetine hydrochloride for the treatment of attention-deficit/hyperactivity disorder. *Clinical Therapeutics*. 2003: 3065-3083.
- [3] Stein, Mark A. PhD. Innovations in attention-deficit/hyperactivity disorder Goldman L.S., Genel M., Bezman R.J., Slanetz P.J. Diagnosis and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *JAMA*. 1998 April; 279(14): 1100-1107.
- [4] New approaches to the management and treatment of attention-deficit/hyperactivity disorder. *The American Journal of Managed Care*. 2004 July; 10(4) Supp.: S87-S88.
- [5] Michelson, Faries, Wernicke, Kelsey, Kendrick, Sallee, Spencer and the Atomoxetine ADHD Study Group. Atomoxetine in the treatment of children and adolescents with attention-deficit/hyperactivity disorder: a randomized, placebo-controlled, dose-response study. *Pediatrics*. 2001 November;108(5).
- [6] Kratochvil CJ, Vaughan B, Harrington M, and Burke W. Atomoxetine: a selective noradrenaline reuptake inhibitor for the treatment of attention-deficit/hyperactivity disorder. *Expert Opinion on Pharmacotherapy*. 2003:1165-1174.
- [7] Pliszka, Steven MD. Non-stimulant treatment of attention-deficit/hyperactivity disorder. *CNS Spectrums*. 2003 April;8(4): 253-258.
- [8] Olfson, M. M.D. MPH., New options in the pharmacological management of attention-deficit/hyperactivity disorder. *The American Journal of Managed Care*. 2004 July; 10(4) Supp.: S117-S124.
- [9] Reeves, Gloria, Schweitzer, Julie. Pharmacological management of attention-deficit hyperactivity disorder. *Expert Opinion on Pharmacotherapy*. 2004 5 (6):1313-1320.
- [10] Brown Thomas E. PhD. Atomoxetine and stimulants in combination for treatment of attention-deficit/hyperactivity disorder: four case reports. *Journal of Child and Adolescent Psychopharmacology*. 2004 Spring; 14(1): 129-136.
- [11] pharmacotherapy: long-acting stimulant and nonstimulant treatments. *The American Journal of Managed Care*. 2004 July; 10(4) Supp.: S89-S98.