Trend Watch

Short-acting versus Long-acting Medications for the Treatment of ADHD

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ABSTRACT: Primary care physicians, pediatricians, and psychiatrists account for approximately 80 percent of attention deficit hyperactivity disorder (ADHD) treatments prescribed in the United States. Selection of short-acting versus long-acting ADHD treatment varies by specialty with long-acting agents representing 56 percent of primary care prescriptions, 64 percent of psychiatrist prescriptions, and 79 percent of pediatric prescriptions. There appears to be a correlation between short-acting versus long-acting treatment selection and age, with long-acting agents accounting for 78 percent of prescriptions for pediatric patients (age 0–17) but only 49 percent of prescriptions for adults (patients aged 18+). A discussion of data is included.

KEY WORDS: ADHD medication, attention deficit hyperactivity disorder, long-acting formulation, short-acting formulation, stimulant, prescription

INTRODUCTION

In this article, we explore use of long-acting versus short-acting treatment for attention deficit hyperactivity disorder (ADHD) by primary care physicians, pediatricians, and psychiatrists. Variation in treatment selection by patient age is also investigated.

METHODS

We obtained data on total retail prescriptions for ADHD medications in March, April, and May 2008 from Verispan's Vector One National (VONA), which captures nearly half of all prescription activity in the US. Individual products were classified as short acting, medium acting, or long acting as follows:

- Short acting: amphetamine/dextroamphetamine (Adderall), dextroamphetamine

sulfate (Dexodrine, Dextrostat), dexmethylphenidate (Focalin), methamphetamine (Desoxyn), and methylphenidate or MPH (Methylin, Ritalin)
- Medium acting: methylphenidate sustained release (Metadate CD, Metadate ER, Methylin ER, Ritalin LA, Ritalin SR)
- Long acting: amphetamine/dextroamphetamine (Adderall XR), methylphenidate (Concerta), methylphenidate (Daytrana), d-amphetamine sulfate (Dexedrine Spansules), dexmethylphenidate (Focalin XR), atomoxetine (Strattera), and lisdexamfetamine dimesylate (Vyvanse).

RESULTS

In 2007, almost seven million Americans filled at least one prescription for an ADHD therapy. Approximately 80 percent of therapies prescribed were written by primary care physicians (21%), pediatricians (28%), or psychiatrists (30%). Figure 1 displays short-acting versus medium-acting versus long-acting ADHD treatments prescribed by physician specialty. As seen in Figure 1, selection of short-acting versus long-acting ADHD treatment varies by specialty with long-acting agents representing 56 percent of primary care prescriptions, 64 percent of psychiatrist prescriptions, and 79 percent of pediatric prescriptions.

We examined the data further to determine whether there were any differences in use of short-acting versus long-acting ADHD treatments by patient age. The data presented in Figure 2 show that there does appear to be a difference in long-acting therapy use among pediatric and adult patients. Long-acting agents account for 78 percent of ADHD prescriptions in pediatric patients ages 0 to 17 years, but only 49 percent of adult ADHD prescriptions.

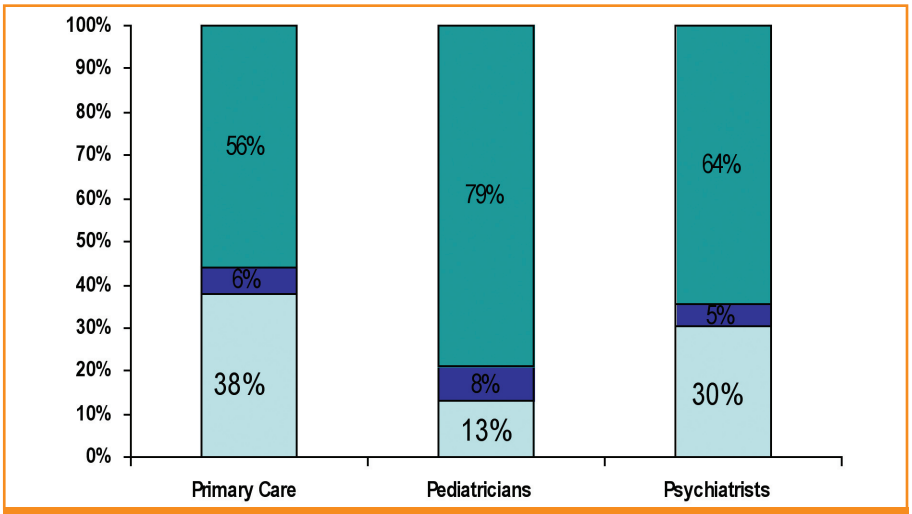

FIGURE 1. Short-acting vs. medium-acting vs. long-acting ADHD therapies prescribed by specialty
Source: Verispan VONA, ADHD Therapies, March, April, May 2008.

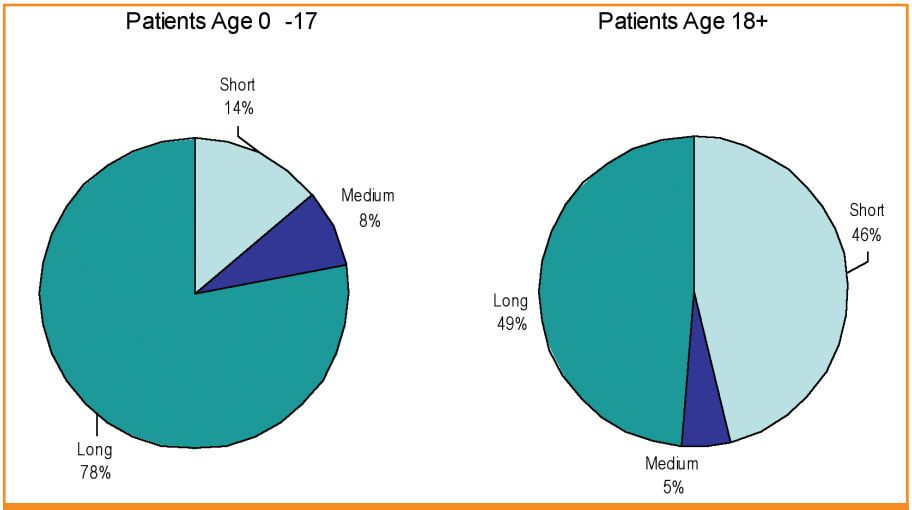

FIGURE 2. Short-acting vs. medium-acting vs. long-acting ADHD therapies prescribed by patient age
Source: Verispan VONA, ADHD Therapies, March, April, May 2008.

COMMENTARY

by Richard H. Weisler, MD

The data presented in this article suggest that pediatricians are ahead of the curve compared to many psychiatrists and primary care providers in regard to utilizing the clinical advantages of long-acting medications for ADHD. Children and adolescents given long-acting medications for ADHD generally are adequately treated for the entire day with once-daily morning dosing. The benefits of this once-daily dosing are that these children are not forced to go to a very busy school nurse or school office to receive their medications, nor are they singled out from their classmates in order to receive an additional dosage of immediate-release, short-acting ADHD medication. There is also less likelihood of diversion of long-acting agents because the giving and taking of medication is supervised at home

during the morning dosing.

The possibility of diversion or nonmedical use of stimulants is an issue clinicians should be aware of even though it is not a problem for the vast majority of patients. Johnston, et al.,[1] reported that lifetime nonmedical use of prescription MPH and amphetamines among secondary school students in 2007 was 6.5 (–1.0), 11.1 (–0.8) , and 11.4 (–3.6) in 8th, 10th , and 12th grade students, respectively. In 2005, college students were interviewed 1 to 4 years beyond high school. These young adults, whose modal age was 19 to 28 years, reported lifetime nonmedical use of MPH and amphetamines of 12.3 (–0.4) for college students and 14.6 (–1.3) for young adults.[2] In a study of college students reporting nonmedical stimulant use, most (75%) indicated immediate-release mixed amphetamine salts (Adderall) was the stimulant used.[3] Two other studies in adolescents and young adults reported that immediate-release MPH (Ritalin) was most frequently used (75% and 93%, respectively).[4,5]

Long-acting ADHD stimulant medications may also be less prone to contribute to the development of drug abuse or dependence. With extended-release stimulants, the slower rise and fall of MPH, amphetamine, and dexamphetamine levels in the brain may contribute to decreased drug abuse potential.[6] Two studies compared short-acting and long-acting MPH formulations to examine this hypothesis. The subjective effects of oral immediate-release (40mg) and osmotic-release (e.g., osmotic-controlled release oral delivery system [OROS®]) (90mg) MPH were studied in healthy volunteers.[7] These two formulations had almost similar average peak-drug concentrations and dopamine-transporter blockade, but the immediate-release formulation achieved these targets several hours earlier than did the osmotic-release formulation, suggesting a more rapid drug absorption and central drug activity with immediate-release MPH versus osmotic-release MPH. Importantly, the immediate-release formulation yielded significantly greater drug likeability ratings compared with the osmotic-release formulation.[8]

Lisdexamfetatine is a pro-drug that requires enzymatic cleavage of lysine before dexamphetamine, to which it is attached, becomes biologically active. Lisdexamfetamine's need for enzymatic cleavage may reduce the risks of intravenous and nasal abuse due to significantly decreased levels of the active compound seen in animal studies. Jasinski, et al.,[9] in a human study, also showed that 50mg of lisdexamfetamine given intravenously to known stimulant abusers showed a lower c_{max} and much longer t_{max} as well as decreased drug likeability scores that were not significantly different than placebo when compared to 20mg immediate-release dexamphetamine. In a recent review article, Kollins[10] concluded, "Patients with ADHD are at increased risk for SUD [substance use disorder]. Under certain conditions, psychostimulants may be a pharmacologic option in the treatment of patients with comorbid ADHD and [SUDs]. However, clinicians should be mindful of the risks and benefits of this treatment approach in a high-risk population and should also bear in mind the labeling guidelines when working with this comorbidity." In difficult cases like those patients with comorbid ADHD and SUD, long-acting ADHD medications are, in my opinion, almost always preferable to short-acting agents.

Medication adherence is also a well-known problem in a chronic disorder like ADHD, with only about 20 percent of patients remaining on the same medication 15 months after first being prescribed that medication.[11] The need for multiple daily dosing of immediate-release medications only further increases the risk of nonadherence in children, adolescents, and adults. As there is a significant likelihood that one of the parents of a child with ADHD will also have ADHD (often undiagnosed), or another psychiatric disorder, there is potentially a significant risk that the parent will forget to give the additional immediate-release doses of medication to the child every 4 to 6 hours.

In adults, the reported prescribing pattern data suggest that some psychiatrists and primary care providers have as yet failed to fully take advantage of long-acting ADHD medications. It is important to consider that often a day in the life of late adolescents and adults is full of activities and responsibilities. Work and/or educational daytime hours blur with parental/social activities in the evening. With long-acting medications, many patients report that their mental focus remains clearer for them throughout the full day and sometimes into the early evening due to minimizing the negative impacts of the peak-trough effects often seen with twice or thrice daily dosing of immediate-release ADHD medications. Hyperactive symptoms when present are better controlled in many cases with long-acting ADHD medications for the same reason. Long-acting agents vary in duration with atomoxetine, a nonstimulant norepinephrine reuptake inhibitor, providing 24-hour coverage after chronic dosing in those patients that respond. Long-acting stimulants vary in duration and peak effect, though the longest-acting marketed compounds work in some studies for up to 12 hours in the cases of lisdexamfetamine in adults, mixed amphetamine salts extended-release preparations, MPH extended-release preparations, or dexmethylphenidate extended-release preparations.[12]

Clinicians and patients also have to take into account the possible negative

impact of uncontrolled ADHD on driving performance. Poor driving records that include multiple speeding tickets, multiple accidents, and ignoring driving regulations at times resulting in points on one's drivers license or loss of license are seen in many young adults with ADHD.[13] Safe driving demands that one remain attentive. It is possible that minimizing peak-trough medication-related attention problems by using long-acting ADHD medications might also help boost driving performance and improve traffic safety as well, though additional research is needed in this area.

When deciding on which medication to prescribe a patient with ADHD, it is important to keep in mind that prescribing short-acting ADHD medications in some situations can also be advantageous. For example, a number of patients will benefit from the addition of a short-acting stimulant taken at 5 or 6 o'clock in the evening, sometimes to supplement a long- or another short-acting medication given earlier in the day. Attention and other ADHD symptoms then improve for a night class or important evening meeting, without keeping the patient awake all night. If a clinician is concerned about how a particular patient will respond to a dosage titration or whether he or she will be able to tolerate a stimulant, sometimes it is best to begin with short-acting agents. This may also be the case when ADHD is comorbid with other psychiatric or medical disorders that potentially could worsen with use of a stimulant. Some individuals even with significant ADHD manage to cope extremely well or they have structured their lives in such a way that taking an ADHD medication on an as-needed basis for special situations is all they really need. And in these cases, a short-acting formulation would be optimal.

In the end, it comes down to a judgment call by the clinician after consultation with each individual patient, his or her family, and other sources if needed. The clinician weighs the risks and benefits of the various ADHD medications and discusses these openly with the patient and his or her family. The safety and tolerability of long-acting medications are similar to those of short-acting medications, appear to have a somewhat lower risk of abuse and diversion, and may be associated with significant improvements in medication adherence, while short-acting medications may allow for more flexibility with the dosing frequency, titration, and determining drug tolerability and can be taken on an as-needed basis when coverage is only needed for a few hours.

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