OPINION

Abuse of Stimulant Medications for Attention-Deficit/Hyperactivity Disorder

A New Alternative

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Attention-Deficit/Hyperactivity Disorder (ADHD) is a treatable condition that affects more than four million children and nine million adults in the U.S.[1–3] We are fortunate that today many medication options are available that can relieve the symptoms of ADHD. Research continues to support the use of stimulant medications as the first-line therapy for ADHD, and stimulants have been a reliable option for the past 50 years.[4,5]

Hundreds of randomized controlled trials have shown unequivocally that stimulant medications effectively reduce hyperactivity, impulsivity, and inattentiveness. A large-scale study presented at the U.S. Psychiatric and Mental Health Congress in 2006 demonstrated that stimulant medications are significantly more effective than nonstimulant medications in the treatment of patients with ADHD.[6] Without these stimulant medications, untreated ADHD, in combination with conduct disorders, can acutely affect a child's life.

Stimulant drugs have proved helpful in managing the symptoms of ADHD, but they can also be abused and misused. The 2002 National Survey on Drug Use and Health (NSUDH) indicated that an estimated 21 million people 12 years of age or older in the U.S. (approximately 9% of the population) have used stimulants without a prescription at some point in their lifetimes.[7] Patients who have prescriptions for stimulant medications do not always follow their physician's directions. When patients take medications at the wrong time or in doses higher than those recommended, adverse events may occur. In addition to these types of non-medical uses, people sometimes also use stimulant medications for purposes other than those intended, such as getting "high" and as a study aid.

According to a 2005 survey conducted by the Partnership for a Drug-Free America, one in five teenagers abused prescription drugs, and more teenagers were getting high with prescribed medications than with cocaine, methamphetamines, and ecstasy combined.[8] The survey also noted that college students were abusing stimulants, mainly as a study aid. The Monitoring the Future Study found that 5.7% of college students reported higher rates of non-medical use of methylphenidate in the previous year than their same-age peers not attending college (2.5%).[9]

This abuse is not limited to children or adolescents; the prevalence of medication abuse by adults is also high.[10] Some adults use stimulants inappropriately to lose weight, to maintain concentration or focus at work, and to obtain the drug's euphoric effects. Unfortunately, most medications that relieve the symptoms of ADHD also satisfy the needs of drug abusers. Furthermore, a person who abuses stimulant drugs might not look like the stereotypical drug abuser. All too frequently, a drug abuser can be the mother next door, a sibling, or a straight-A student.

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Adverse events resulting from stimulant medications for ADHD send thousands of people to emergency departments each year, according to a 2006 study. The study examined data retrieved by the National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance Project (NEISS–CADES) from 2003 to 2005.[11] It was determined that 188 emergency visits resulted from adverse events associated with stimulant medications. The use of stimulant drugs was the primary cause of admissions in 84% of the emergency events, and 36% of those events were a result of stimulant misuse.[11]

Pivotal studies have indicated that a new drug, lisdexamfetamine dimesylate (Vyvanse [NRP 104], Shire/New River Pharmaceuticals), might be as efficacious for ADHD as other drugs in its class but with a lower potential for abuse. The Food and Drug Administration (FDA) approved Vyvanse in February 2007 as a once-daily, extended-release formulation indicated for treating ADHD in children six to 12 years of age.[12] In clinical studies designed to measure duration of effect, Vyvanse provided significant efficacy, compared with placebo, for a full treatment day, up to 6:00 p.m.

Furthermore, when Vyvanse was administered orally and intravenously in two clinical studies on human drug abuse, it produced subjective responses on a scale of "drug-liking effects" (DLEs) that were smaller in degree than *d*-amphetamine at equivalent doses. DLE is used in clinical abuse studies to measure relative preference among known substance abusers.[13]

One of these studies, presented in June 2006 at the College for Problems of Drug Dependence, was designed to evaluate the safety, tolerability, and abuse liability of intravenous (IV) lisdexamfetamine dimesylate in 12 healthy adult volunteers with a history of stimulant abuse. An IV dose of 50 mg produced a smaller degree of euphoria or amphetamine-like subjective effects, compared with an equivalent amount, on the basis of molar weight, of IV dextro (*d*)-amphetamine sulfate 20 mg.[14]

Vyvanse also produced a less euphoric effect when compared with *d*-amphetamine and diethyl propion.[15]

This amphetamine prodrug is administered in an inactive (or a significantly less active) form.[16,17] After the prodrug is given, it is metabolized *in vivo* into the active compound. Thus, the drug must travel through the digestive system before it becomes active. This novel aspect of the drug enables it to effectively deliver symptom relief on a continual basis[18] while de-

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creasing the risk of abuse, compared with other stimulant medications that are used to treat ADHD.[19]

Because medication is the cornerstone treatment for ADHD, an effective formulation that poses a lower risk of drug abuse is a welcome development. It is hoped that this new treatment will be able to reduce the negative stigma attached to stimulant medications and that it might provide an effective therapeutic option for managing the symptoms of ADHD.

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