Effects of AD/HD Medication on Future Substance Abuse

by Timothy Wilens, M.D.

When deciding on treatment options for youths with AD/HD, it is necessary to understand the risks and benefits of medication. While information from short-term trials has supported the use of medications in the treatment of AD/HD, there are fewer long-term results on their effects in youths and even less is known about the long-term risks of medication.

One area that has received considerable attention in both the mainstream press and scientific literature is the potential risk of medication in general, and stimulants in particular, on the development of substance abuse. Since stimulants and amphetamines are the most commonly prescribed agents for AD/HD, a number of sources have questioned whether exposure to this class of medication in youths with AD/HD could lead to either prescription abuse or serve as a gateway to the abuse of other drugs. These concerns are based on the known abuse potentials of the stimulants in both animal and human studies.

One way to explore this important issue is to evaluate what we know about the link between substance abuse and prior exposure to stimulants or other psychotropic medications by examining the literature that is available.

When assessing the literature, several points place the findings in a better context. First, is the nature of the study: those studies in which youths are followed over time (prospective) are typically more informative than those that evaluate only the past histories of the individuals (retrospective). Second, is the issue of who was chosen to be on the medication as compared to those who were managed without medication.

Presumably, medication is reserved for more problematic cases, whereas other types of treatment may be employed for children exhibiting less severe symptoms. The intensity of treatment often increases with a disorder's severity. As a result, untreated cases may be less severe than treated ones. This sometimes leads to the paradoxical result in which treatment is linked to poorer outcomes in these types of natural studies, even when the treatment is known to produce the desired results in well controlled trials. This is not only a problem for AD/HD, but also for a myriad of other conditions including cancer, high blood pressure and psychiatric conditions. In the following sections, a position of the relevant studies are described in which substance abuse was evaluated in adolescents and young adults with AD/HD in relation to previous medication treatment.

The positive influence of treatment on reducing substance abuse and the failure to show a worsening of substance abuse associated with stimulant medication should be comforting to the many parents who are worried that giving a child a stimulant might predispose them to drug addiction.

Substance Abuse in Adolescents

A follow-up study of adolescents with AD/HD who were previously treated with methylphenidate as school-aged children and youths without AD/HD who were not treated, Beck *et al.* reported a trend toward higher drug use in the unmedicated group as compared to the treated group. Similarly, using lifetime data, a greater proportion of the untreated group was reported to use drugs "habitually." Limitations include a lack of data on rates of drug abuse, no alcohol data, and no data on the severity of baseline illnesses.

Blouin *et al.* reported on substance use patterns in a controlled study of youths with AD/HD. A trend toward greater *use* (not abuse) of beer and wine was observed in the treated AD/HD group; however, the treated group had a baseline that reflected a higher degree of severity for AD/HD. In addition, treated youths with AD/HD reported to be 'responders' to methylphenidate, had significantly less substance abuse than those who did not respond well to treatment. Limitations in the study included the mismatched baseline severity of illness, lack of clinical characteristics, limited follow-up period (two years), and lack of substance abuse rates.

Biederman, Wilens, Mick *et al.* reported that medicated youths with AD/HD were at lower risk for subsequent substance abuse than their unmedicated peers with AD/HD. In the complete data of the four-year follow-up study of AD/HD, medication of AD/HD in children was strongly associated with *lower* rates of substance abuse in mid-adolescence, including alcohol, cocaine, stimulants and hallucinogens as compared to those youths with AD/HD who did not receive medication. Marijuana was the most common drug abused in the untreated group. Rates of substance abuse were similar between youths who were treated for their AD/HD and kids without AD/HD. Limitations to the study included the lack of information on specific medications used for AD/HD treatment (the vast majority were receiving stimulants), and the details of how long they received them.

As part of a prospective study of youths treated in a summer camp, Molina and Pelham observed lower rates of substance abuse in treated versus untreated youths with AD/HD in mid-adolescence. Lower rates of alcohol and drug use problems were noted in the treated group four years later. Treated and untreated groups had similar severity of AD/HD at baseline. Limitations include that the unmedicated group was one year older at follow-up assessment, no stimulant dosing was delineated, and little information was available on the untreated group.

While not giving specific rates of substance abuse, other studies have shed light on the nature of AD/HD and substance abuse. Loney showed that older adolescents whose AD/HD symptoms responded best to medication were less likely to have later irritable behavior and illegal drug use, similar to findings by Blouin *et al.* In another example of youths with AD/HD who were treated with medication compared to an unmatched group with AD/HD, stimulant medication decreased the risk of subsequent use of illegal drugs, although specific rates of disorders were not presented.

Follow-up in Adults

There were three studies available on adults with AD/HD who were treated with stimulants as children and followed up on in adulthood: two were prospective (patients followed over time) and one was retrospective (patient history reviewed). In a highly publicized study, Lambert *et al.* reported that adults previously treated with stimulant medications had significantly higher rates of cigarette and cocaine use as compared to AD/HD adults who were not treated with stimulants. The data from a long-term prospective study of youths with AD/HD followed into adulthood showed similar rates of alcohol, marijuana and stimulant abuse between groups. The authors reported a trend toward a higher risk of cigarette and cocaine abuse, with increased previous exposures to stimulant medications. The major limitation to the study includes apparent differences in the baseline severity of illness, with the stimulant treated group for more severe illnesses (i.e., conduct disorder), which may have distorted the findings.

In a prospective, 15-year follow-up study of youths with AD/HD into adulthood, a lower risk for alcohol abuse, but not drug abuse, was observed in adults treated with stimulant medications versus those who were untreated as youths. Adults who were considered responders to stimulant medications were found to have lower rates of substance abuse than those considered nonresponders. The treated and untreated groups were similar at baseline for AD/HD severity including symptoms, overactivity, aggression and oppositionality. Limitations include limited data on medication exposure, naturalistic design and the relatively small number of untreated adults with AD/HD.

Using a retrospective recall of past treatment in

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adults with AD/HD, Huss *et al.* recently reported a significantly reduced risk of substance abuse associated with treatment. In this German study of young adults, methylphenidate treatment of AD/HD was associated with a robust reduction in substance abuse. Limitations include limited details of the study, such as actual substance abuse rates, length of medication exposure or specific substances abused.

Discussion

The results of this evaluation of studies on the long-term effects of AD/HD medication, despite methodological limitations, support a protective effect of medication treatment of AD/HD concerning the development of later substance abuse. The literature does not support that stimulant treatment of AD/HD increases the risk for substance abuse. All studies in which baseline severity of AD/HD was similar between groups showed a reduced risk for substance abuse associated with treatment. (CHADD advocates a multimodal approach for the treatment of AD/HD, which often includes: parent training, behavioral intervention strategies, education, individual and family counseling, and medication when required.)

Clarification of the critical influence of AD/HD treatment in youths on later substance abuse remains hampered by the few studies completed which evaluate this and limitations in the designs of the studies. Since these studies in youths with AD/HD followed the natural course of the AD/HD and were not long-term intervention studies, attempts to decipher positive or negative effects of treatment from the severity of the AD/HD is difficult. In all of the studies in which the groups of treated and untreated children with AD/HD had a baseline similarity, the medications used for AD/HD helped reduce the risk of later substance use disorders. In contrast, the studies in which the treated and untreated children with AD/HD were not similar, the stimulants were related to increased substance abuse.

The findings from these studies reject the idea that stimulant treatment of AD/HD increases the risk for substance abuse—either general substance abuse or specific types of drug use disorder. Although some animal models suggest that substance abuse related behaviors are associated with earlier stimulant administration, the route and dose administration of stimulants used may not be applicable to humans. For example, in certain rat studies, the dose of methylphenidate far exceeded the upper limit of recommended guidelines for stimulants.

Why medication treatment of AD/HD may lead to reduced substance abuse remains unclear and under study at our site. AD/HD may lead to less impairing symptoms and overall improvement in self-esteem, academic and social success, which are direct and indirect risk factors for substance abuse. It may also be that the close monitoring of youths receiving medications by their parents may have had a protective effect on the development of substance abuse, independent of the actual medication effect.

The findings that the treatment of AD/HD results in a lowered risk for later substance abuse is of major interest. The positive influence of treatment on reducing substance abuse, coupled with the failure to show a worsening of substance abuse associated with stimulant medication, should be comforting to the many parents who are worried that giving a child a stimulant might predispose them to drug addiction. These findings will also provide information to clinicians when discussing the risks and benefits of medication intervention. Research on AD/HD medication treatment and its reduction of substance abuse is of great interest. It is among the strongest literature available in pediatric mental health indicating a protective effect of treatment on preventing substance abuse. Hence, the mechanism of medication protecting against substance abuse in these youths with AD/HD could serve as a template for other mental health disorders. From the public health perspective, given the high prevalence of AD/HD in youths and their high risk of developing substance abuse over their lifespan, the identification and treatment of youths with AD/HD may affect a large group of adolescents and young adults susceptible to substance abuse.

Despite the many limitations of literature in this area, current data supports the medication treatment of AD/HD, almost invariably with stimulants. It does not increase, but appears to decrease the risk for substance abuse. Further studies investigating the longer-term outcome of youths with AD/HD who are pharmacologically treated and later abuse substances, and the possible ways in which medication treatment of AD/HD reduces substance abuse are currently underway. ■

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