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Treatment Strategies for Co-Occurring ADHD and Substance Use Disorders

John J. Mariani, MD and **Frances R. Levin, MD**
New York State Psychiatric Institute, New York, New York

Division on Substance Abuse, Columbia University College of Physicians and Surgeons, New York, New York

Abstract

Attention-deficit hyperactivity disorder (ADHD) is a common co-occurring mental disorder among patients with substance use disorders (SUD). Clinicians must be cognizant of the complicated nature of diagnosis and treatment of ADHD when comorbid with SUD. Pharmacotherapy remains the mainstay of treatment for ADHD, although complementary psychotherapeutic approaches have been developed. Psychostimulant medications are the most commonly used medications to treat ADHD, but many clinicians are reluctant to prescribe stimulants to patients with SUD. Recommendations for treatment planning and clinical management for patients with co-occurring ADHD and SUD are discussed.

LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

- Identify typical challenges in clinical diagnosis of ADHD in adults with co-occurring SUD.

- Explain how different types of ADHD pharmacotherapies affect the risks of SUD in specific patient types.

- Distinguish between primary symptoms and substance-induced symptoms in ADHD patients with SUD.

- Discuss the advantages and disadvantages of non-stimulant medications in patients with ADHD and co-occurring SUD, including second-line medications.

- Describe treatment scenarios in ADHD that are most likely to lead to SUD, exacerbate ongoing SUD, or minimize risks of SUD.

Address correspondence to Dr. Mariani, 1051 Riverside Drive, Unit 66, New York, New York 10032. E-mail: E-mail: jm2330@columbia.edu.

- Provide an overview of psychosocial treatments for ADHD and co-occurring SUD that can help optimize long-term treatment effectiveness.

INTRODUCTION

Attention-deficit hyperactivity disorder (ADHD) is a syndrome characterized by persistent patterns of inattention and/or impulsivity and hyperactivity that is inappropriate for a given age or developmental stage. ADHD is the most common mental disorder in childhood,[1] with an estimated prevalence in the United States of 5–10%.[2,3] It is estimated that up to 60% of childhood cases of ADHD will continue to have clinically significant symptoms of ADHD as adults,[4-7] and the prevalence of adult ADHD in the United States is estimated to be 2–5%. [8-11] ADHD symptoms result in a large individual and public burden; it is estimated that consequences of ADHD result in the loss of 120 million days of annual lost work in the U.S. labor force, which is equivalent to $19.5 billion lost human capital.[12]

Large-scale epidemiologic surveys in the United States have reported that substance use disorders are associated with increased rates of comorbid psychiatric disorders,[9,13-16] including mood, psychotic, anxiety, personality, and other classes of disorders. While it is clear that substance use disorders are associated with increased rates of comorbid psychiatric disorders as compared to the general population, the converse is true as well: individuals with substance-independent psychiatric disorders are at an increased risk of having a substance use disorder. The Epidemiologic Catchment Area Survey[13] reported that among individuals with any lifetime mental disorder diagnosis, 28.9% had a lifetime substance use disorder, as compared to a rate of 13.2% for those respondents who had no history of a mental disorder. The ECA found that having a lifetime history of any mental disorder was associated with more than twice the risk of having an alcohol disorder and more than four times the risk of having a drug use disorder.

The association of ADHD and SUD has become an increasing focus of investigation over the past decade. Studies of clinical samples of individuals with SUD seeking treatment have demonstrated that ADHD is a common co-occurring mental disorder,[17-19] although historically, community-based studies have not included adult ADHD among the disorders surveyed.[13,14,16] However, the recently published National Comorbidity Survey Replication (NCS-R) included ADHD in its survey and estimated the prevalence of adult ADHD to be 4.4%.[8] With regards to the rate of co-occurrence of ADHD and SUD, the NCS-R found that 15.2% of individuals with adult ADHD met DSM-IV criteria for a SUD, as compared to 5.6% of individuals without ADHD, resulting in a significant odds ratio of 3.0.[8] Complimentary to these findings, the NCS-R found that among individuals with SUD, 10.8% met criteria for adult ADHD, as compared to a prevalence of 3.8% in individuals without SUD.

The rates of ADHD co-occurrence in studies of treatment-seeking clinical samples of individuals with SUD are higher than the community-based NCS-R, with the reported prevalence of adult ADHD ranging from 10–24%.[17-19] In addition, it is estimated that more than 25% of substance-abusing adolescents meet diagnostic criteria for ADHD.[20-22] This disparity in rates of co-occurring ADHD and substance use disorders between community-based and clinical studies is likely due to Berkson's bias,[23] which is the phenomenon that patients in clinical treatment settings are more likely to exhibit a higher degree of association between two disorders. A practical outcome of this phenomenon is that clinicians in SUD treatment settings will frequently encounter co-occurring ADHD.

While the exact cause of ADHD is unknown, the available evidence supports the theory that dopamine neurotransmission dysfunction is at least partly responsible for the characteristic

symptoms of ADHD. Evidence supporting dopamine involvement in ADHD symptomatology includes pharmacotherapy studies, which show that stimulant medications that increase dopamine levels effectively treat ADHD symptoms,[24-27] genetic studies, which have linked dopamine genes to ADHD,[28-30] and imaging studies, which have shown abnormalities of dopamine function and structural abnormalities in regions of the brain with concentrations of dopamine-producing neurons.[31-33] The therapeutic effects of psychostimulants on ADHD symptoms are thought to be due to their ability to increase extracellular dopamine,[34,35] particularly in the striatum.[36] Volkow and Swanson[37] have postulated that psychostimulant-induced extracellular dopamine release in the striatum improves attention by the enhancement of task-related neuronal cell firing.

As the development of SUD is also linked to dopamine,[38] there may be common factors that lead to the development of ADHD and co-occurring SUD. By definition, ADHD is present before the age of 7, and SUDs often develop during adolescence and early adulthood, so it is likely that the increased association of ADHD and SUD is the product of a developmental interaction with ADHD symptoms (eg, impulsivity or behavior dysregulation) and the consequences of ADHD (eg, poor academic performance), creating an increased opportunity for the development of a SUD. Emerging evidence suggests that psychostimulant treatment of ADHD during childhood reduces the likelihood of developing a SUD,[39] although the exact mechanism of this risk reduction is not known. The risk of initiation of substance use in adolescents is related more to symptom severity (eg, aggression or impulsivity) than the status of meeting criteria for ADHD,[40] suggesting that the risk of SUD development in adolescents with ADHD is dimensional, rather than categorical. In adolescents, the severity of attentional symptoms may be a more important risk factor than behavioral symptoms.[41]

Given the common co-occurrence of ADHD with SUD, clinicians working with patients with SUD must be proficient in the identification and treatment of ADHD. Due to the evolving understanding of the clinical manifestations of adult ADHD[42] and the relatively recent recognition of the elevated risk of ADHD among adults with SUD,[8] clinicians working with SUD patients are often unfamiliar with the assessment and management of ADHD. Further, because the primary treatment for ADHD is stimulant pharmacotherapy, which has an inherent abuse potential, the treatment of ADHD in patients with SUD is both complex and controversial. This article discusses treatment planning and clinical management of patients with co-occurring ADHD and SUD.

DIAGNOSING ADHD IN PATIENTS WITH SUD

The diagnosis of ADHD in children and adults remains a clinical diagnosis—there are no neuropsychiatric or laboratory tests that alone have been shown to have clinical utility in diagnosing ADHD. In adults, the clinical diagnosis of ADHD remains challenging, particularly in patients with co-occurring SUD, as there is a lack of consensus on diagnostic criteria,[42] symptoms overlap with other psychiatric disorders, and there is a need for a retrospective diagnosis of childhood ADHD. The criteria for ADHD in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR)[43] were developed for diagnosing ADHD in children and are currently used for adults as well, although the validity of the criteria set is debated.[42]

Diagnosing ADHD in patients who are actively using substances or who recently initiated abstinence is challenging. Substances of abuse have many acute and chronic effects that mimic the symptoms of psychiatric disorders, including ADHD. For example, the use of stimulants can lead to changes in attentional capacity and activity level both during intoxication and recovery, and chronic marijuana use may lead to deficits in attention. In addition, many patients are unable to describe recent periods of abstinence from substance use, making the distinction between primary and substance-induced symptoms difficult.

While some authorities recommend evaluating patients after a period of prolonged abstinence, [44] this is not possible in many cases. Often a careful clinical history of symptoms during past periods of abstinence or prior to the onset of substance use problems is the best available method to assess whether inattention and hyperactivity symptoms represent a primary disorder or are substance-induced. Symptoms that occur during periods of active substance use are difficult to interpret, because if they occur exclusively in the context of active substance use, a diagnosis of ADHD is inappropriate. Furthermore, in adults, the clinical diagnosis of ADHD remains challenging, because there is a lack of consensus on diagnostic criteria, particularly regarding the requirement that symptoms be present prior to the age of 7.[42] However, because retrospective diagnoses of childhood ADHD in adults made on the basis of self-report tend to overdiagnosis ADHD,[45] a conservative approach must be maintained. A practical approach when working with adults with a SUD might be to consider ADHD likely if symptoms can be recalled as having been present since early adolescence, but unlikely if the symptoms appeared simultaneously or subsequently to the development of the SUD. Collateral information from family or review of objective data (eg, school performance reports) can be very useful in determining whether symptoms were present during childhood.

While the diagnosis of ADHD is ultimately clinically-based, there are structured instruments and interviews that can assist in the evaluation of a patient for ADHD. A comprehensive diagnostic battery, such as might be employed in a research setting, would include, in addition to a comprehensive psychiatric interview, the Structured Clinical Interview for DSM-IV (SCID)[46] and the Conners Adult ADHD Diagnostic Interview for DSM-IV (CAADID),[47] which systematically assesses adults for both childhood and adult symptoms. However, in many clinical settings, performing a SCID and CAADID is not feasible. A more practical approach is to use a semi-structured clinical interview using the DSM-IV TR criteria for ADHD as a guide (ie, review symptoms in criteria set with patient). The ADHD Rating Scale-IV[48] and the DSM-IV SNAP checklist[49] can also be useful in screening for ADHD symptoms. In any setting, it is essential to gather data from other informants (eg, partner, parent, or close friend) to better understand the nature and severity of the symptoms and their impact on the patient's functioning.

IMPACT OF ADHD ON SUD TREATMENT

Given the ongoing controversy over the diagnostic criteria for ADHD in adults and the complicated clinical issue of using ADHD pharmacotherapy in patients with SUD, a reasonable starting point in discussing treatment strategies is to ask, How important is it to treat ADHD in patients with SUD? An initial approach this question is to consider the impact of ADHD on individuals who do not have SUD. Adults with ADHD have less educational attainment, increased dismissals from their jobs, more traffic accidents and car license suspensions, more psychosocial problems with social deficits, and a greater frequency of divorce.[12,50] The next step is to consider the evidence that ADHD affects the development and course of substance use disorders: individuals with substance use disorders and ADHD have an earlier onset of substance abuse than those without ADHD, a greater likelihood of having continuous problem if they develop substance dependence, a reduced likelihood of going into remission, and a tendency to take longer to reach remission.[51] Despite having more treatment exposure, individuals who have ADHD seem to do less well with SUD treatment,[51,52] although this may reflect that individuals with more severe symptoms are more likely to receive SUD treatment. Also, both adolescents and adults are less likely to progress well in treatment or remain in treatment.[53-55] Therefore, the diagnosis and treatment of ADHD in patients with SUD seems to be essential to achieve the best possible clinical outcome.

PHARMACOTHERAPY FOR ADHD IN PATIENTS WITH SUDs

The most commonly used pharmacotherapies for childhood ADHD are two psychostimulants, methylphenidate and analogs of amphetamine. In turn, methylphenidate and amphetamine analogs have been the most widely studied pharmacotherapies in adult ADHD, although non-stimulant medications, including tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), bupropion, monoamine oxidase inhibitors, atypical antipsychotics, clonidine, atomoxetine, and venlafaxine have been studied as well. Modafinil, a novel wake-promoting agent that is chemically and pharmacologically distinct from other psychostimulants, has also been investigated as a potential treatment for ADHD.

Stimulant Medications

Amphetamine is a potent CNS stimulant of which the effects are thought to be due to the stimulation of the cortex and the reticular activating system.[56] Amphetamine's mechanism of action is primarily due to promoting dopamine release, although it blocks dopamine reuptake as well. Amphetamine analogs, a first-line treatment for childhood ADHD, have also been shown to be effective for the treatment of ADHD in adults.[57] In the United States, amphetamine analogs are used primarily for ADHD and also for narcolepsy. Commercially available amphetamine analogs include methamphetamine, dextroamphetamine, and mixed amphetamine salts (MAS). Methamphetamine is available only as an immediate release preparation and is rarely used due to abuse and diversion concerns. Dextroamphetamine is available in immediate and sustained release preparations. MAS is a fixed-combination amphetamine composed of equal amounts of dextroamphetamine saccharate, dextroamphetamine sulfate, racemic amphetamine aspartate monohydrate, and racemic amphetamine sulfate. It is available in immediate and sustained release preparations. Side effects most commonly associated with amphetamine administration include insomnia, emotional lability, nausea/vomiting, nervousness, palpitations, elevated blood pressure, and rapid heart rate. Rare, but serious adverse effects include severe hypertension, seizures, psychosis, and myocardial infarction.

Methylphenidate is a classical psychostimulant widely used in the United States for the treatment of ADHD. Methylphenidate is a piperidine derivative that is structurally related to amphetamine.[56] The mechanism of action of methylphenidate is primarily due to blocking dopamine reuptake in the striatum. Methylphenidate has been one of the first-line treatments for ADHD in children for decades and has been demonstrated to be effective for the treatment of ADHD in adults.[58] Methylphenidate is available in multiple immediate and sustained release preparations, using a variety of strategies for delaying absorption. The most common side effects of methylphenidate are insomnia, nervousness, tachycardia, and hypertension. As with amphetamines, rare but serious adverse effects include severe hypertension, seizures, psychosis, and myocardial infraction.

Abuse Potential of Psychostimulants—Methylphenidate and amphetamine analogs are widely used in the treatment of ADHD; however, concern exists with respect to their abuse potential, particularly in patients with SUD. The phenomenon of nonmedical use of stimulant medications has been documented in large-scale survey studies; according to the National Survey on Drug Use and Health (NSDUH), 8.8% of Americans aged 12 years or older reported having used prescription-type stimulants non-medically at least once in their lifetime.[59] Therefore, the risks of using these potentially abusable medications in a vulnerable population must be considered carefully.

There is a limited body of laboratory and clinical evidence to consider when assessing the risks of using stimulant medications in patients with SUD. In a laboratory double-blind choice procedure, individuals with ADHD significantly chose methylphenidate over placebo,[60] while

other measures of abuse potential were not elevated. In laboratory studies of patients with[61] and without[62] SUD, both methylphenidate and amphetamine analogs demonstrate characteristics associated with abuse potential. Methamphetamine, which is a commonly abused substance,[59] has been shown to be a positive reinforcer (ie, individuals exposed to the substance are likely to choose to be exposed again) in humans,[63] providing further evidence for its abuse potential. In contrast to the data described above, a laboratory study of methylphenidate in cocaine-dependent patients receiving treatment did not increase cocaine craving nor ratings associated with abuse potential,[64] suggesting that the context of use, in this case therapeutic, may influence subjective effects and abuse potential.[37] Because the reinforcing effects of stimulants are associated with rapid changes in serum concentrations[37] and sustained-release preparations of methylphenidate (which slow the rate of onset of the drug's effect) are associated with less stimulant-like drug effects (eg, increased ratings of "good effects") in healthy volunteers,[65,66] it is likely that delayed-release stimulant preparations have lower abuse potential than immediate-release stimulant preparations. An additional characteristic of delayed-release preparations that make diversion and abuse less likely is that they are more difficult to use via a non-oral route (eg, injected or insufflated intranasally).

The use of stimulants and non-stimulant medications has been studied in patients with co-occurring adult ADHD and SUD. Methylphenidate has been shown to be effective in uncontrolled trials in reducing ADHD symptoms and cocaine use.[67,68] A three-arm double-blind placebo-controlled trial of bupropion and methylphenidate for the treatment of ADHD in cocaine-dependent patients receiving methadone maintenance treatment for opioid dependence found no benefit of bupropion or methylphenidate on ADHD symptoms or cocaine use outcomes.[69] A double-blind placebo-controlled trial of methylphenidate in the treatment of adult ADHD patients with comorbid cocaine dependence found that methylphenidate improved ADHD symptoms on some measures but not others, and it did not show a reduction in cocaine use.[26] Consistent with this, Levin et al.[70] found that sustained-release methylphenidate did not demonstrate an improvement in cocaine use in cocaine-dependent individuals with ADHD. An uncontrolled trial of bupropion for the treatment of cocaine dependence and adult ADHD in 11 patients reported that ADHD and cocaine use symptoms decreased significantly.[71] In none of the trials using stimulants was abuse of prescribed stimulant medication reported.

Additionally, psychostimulants, including amphetamine analogs, methylphenidate, and modafinil, have been studied for the treatment of cocaine dependence. The results of these studies have been mixed with regard to the effects on cocaine use outcomes, with the most consistent effects reported for dextroamphetamine.[72,73] Dextroamphetamine has also been studied for the substitution treatment of amphetamine dependence[74,75] and this approach has been found to be feasible. Despite concerns that psychostimulants use may lead to increased craving and cocaine use, this has not been reported in controlled clinical trials.[26,69,70,72,73,76]

In summary, while stimulants are clearly diverted for nonmedical use, clinical data suggest that the use of delayed-release preparation and the context of therapeutic risk may reduce the potential for abuse.

Nonstimulant Medications

Nonstimulant pharmacotherapies for ADHD include a heterogeneous group of medications, which with the exception of atomoxetine are off-label and typically considered second line treatments. However, there are certain instances where non-stimulant medications would be considered first line, such as if a motor tic disorder is present or in the case of cardiovascular disease.

Atomoxetine is a recently FDA-approved nonstimulant agent for the treatment of ADHD in children, adolescents, and adults. Atomoxetine is a noradrenergic reuptake inhibitor with efficacy for treating the symptoms of ADHD.[77,78] The effects of atomoxetine are more gradual than those experienced with stimulant medications. Common side effects of atomoxetine include sedations, appetite suppression, nausea, vomiting, and headache. Rare but serious side effects reported in children and adolescents include increased suicidal ideation and hepatotoxicity. Atomoxetine has no known abuse potential, so it is an attractive candidate medication for study in the treatment of ADHD in patients with substance use disorders, though published studies are presently lacking.

The antidepressants are off-label and considered second-line treatments for ADHD. Tricyclic antidepressants, which block the reuptake of norepinephrine in addition to other neurotransmitters, have some efficacy in reducing ADHD symptoms, but are considered less effective than the stimulant medications.[79] The dopaminergic antidepressant bupropion has been reported to be effective in the treatment of ADHD,[80-82] although when studied in patients with SUD, it offered no benefit over placebo.[69] Venlafaxine, a norepinephrine-serotonin reuptake inhibitor antidepressant medication, has limited evidence of efficacy in ADHD in uncontrolled clinical trials.[83,84] Monoamine oxidase inhibitors have been shown to have efficacy for ADHD, but the potential for hypertensive crises associated with tyramine-containing foods and medications (both illicit and prescribed) limit their utility, and should be considered contraindicated in patients with SUD.

Clonidine, a noradrenergic alpha-2 agonist antihypertensive agent, is effective for the treatment of ADHD, particularly among adolescents with hyperactivity and aggressiveness.[85] Side effects includes sedation, dry mouth, depression, confusion, electrocardiographic changes, and hypertension with abrupt withdrawal. Guanfacine, also a norepinephrine alpha-2 agonist, has limited evidence supporting its efficacy as a treatment for ADHD.[86]

Modafinil, a novel wake-promoting agent that is FDA-approved for narcolepsy and shift work sleep, has recently been shown to be effective for the treatment of ADHD in children and adolescents,[87-89] and more limited evidence suggests that it may be effective for adult ADHD as well.[90] Because there is limited evidence that modafinil may have potential as a treatment for cocaine dependence,[91] it is deserving of further study in the treatment of co-occurring ADHD and SUD. Although modafinil has some stimulant-like properties (eg, promoting wakefulness), it has minimal abuse potential, so for the purposes of discussion it is being grouped with non-stimulants.

Choice of Pharmacotherapy for Co-Occurring ADHD and SUD

The treatment of adult ADHD in patients with SUD has been controversial, as the primary pharmacotherapy for ADHD is psychostimulants and, historically, there has been reluctance on the part of clinicians to use these medications in patients with addictive disorders. However, although non-stimulant medications have been shown to have efficacy for ADHD, these agents have not been demonstrated to have comparable efficacy to the psychostimulants.[92] Some authorities[93,94] have proposed approaches that emphasize medications with a lower risk of abuse, such as antidepressants or clonidine, before using traditional stimulant medications such as methylphenidate or amphetamine analogs. However, clinical trials of methylphenidate[26,67,70,95] and dextroamphetamine[72-74,76] for the treatment of either cocaine dependence or ADHD in patients with co-occurring SUD have shown that stimulant medications can be used safely in patients with SUD and have a relatively low risk of abuse under monitored conditions.

While the treatment literature for ADHD in patients with SUD is not well developed, the emerging trend is that medications effective for adult ADHD may be effective for adults with

ADHD and co-occurring SUD, but the therapeutic benefit may be less or non-existent if substance use is ongoing.[82] Several possible causes of this phenomenon include the following:

- patients with ongoing SUD do not reliably take their medication,

- patients with SUD may require higher doses (ie, higher tolerance) than administered in clinical trials, and

- ongoing SUD makes detection of a therapeutic effect less likely.[70]

As in children, the available evidence supports the use of stimulant medications over non-stimulant medications for adult ADHD, although direct comparisons are lacking. While stimulant medications, such as methylphenidate and amphetamine analogs, have the potential for abuse, which is a heightened clinical concern in patients with comorbid SUD, the available evidence suggests that this risk is relatively low under monitored conditions, such as in clinical trials. However, it should be expected that a proportion of patients with ADHD comorbid with SUD will misuse, abuse, or divert stimulant medications,[96-98] particularly in less structured treatment settings. A related clinical concern, that stimulant treatment would worsen SUD outcomes, has not been observed in clinical trials, and in children, stimulant treatment of ADHD has been associated with reduced risk of developing SUD.[39]

The primary approach to the treatment of ADHD remains pharmacotherapy; thus, a rational treatment plan for a patient with ADHD co-occurring with ADHD will most likely include pharmacotherapy. For patients without SUD, stimulant medications are the first line treatment choice; however, given the risk of misuse and diversion of stimulant pharmacotherapy, which may be heightened in patients with SUD, the decision to use stimulant medications must be undertaken carefully. In some cases, nonstimulant pharmacotherapy would be more a more desirable alternative. The decision to use stimulant pharmacotherapy in a patient with ADHD and co-occurring SUD requires an individualized risk-benefit assessment.

The assessment of risk in using stimulant pharmacotherapy in a patient with SUD is a broad consideration of the patient's clinical condition, past history, and overall functional status. A conservative approach for treating co-occurring ADHD and SUD would be to begin treatment with a non-stimulant pharmacotherapy, but if an adequate response is not obtained, stimulant pharmacotherapy should be considered. While this approach would minimize the risk of diversion and the misuse of stimulants, given that nonstimulants do not appear to have equivalent efficacy to stimulants, this increased assurance in terms of misuse may come at the expense of ADHD symptom response. The available evidence does not support differing degrees of risk based on type of SUD (eg, cannabis dependence vs. cocaine dependence) or even current substance use, because, as discussed previously, stimulant pharmacotherapy has been used successfully in patients with active cocaine dependence.[26,67,69,70,72-74,76,95] Perhaps the only absolute contraindication to stimulant pharmacotherapy in a patient with SUD would be current abuse of prescription stimulants or a clear indication that the patient would sell or divert their medication.

While it would be desirable to provide clear-cut recommendations or an algorithm (eg, when patient has characteristic X, give drug Y), the data are lacking to provide such guidance. Instead, clinicians must consider all of the available clinical information and make the best initial decision, with the understanding that the treatment plan may need to be modified over time. The known efficacy of psychostimulants must be balanced against the risk of diversion or misuse, and although this risk is likely heightened in patients with SUD, it likely varies considerably between patients, and needs to be assessed clinically rather than be defined categorically. Factors such as ongoing substance use, prior history of misuse of stimulant medication, other co-occurring psychiatric disorders, and overall clinical stability should be taken into account. For a patient who is abstinent from substance use and has good social

functioning, a trial of stimulant medication probably represents a low risk intervention, whereas if a patient is using substances or is otherwise clinically compromised, the use of stimulant pharmacotherapy must be approached more cautiously. The individualized risk assessment should also dictate other elements of clinical management, such as the frequency of office visits or urine toxicology testing.

When the decision to use stimulant pharmacotherapy is made, the choice of formulation should be considered carefully. Most clinicians experienced in the treatment of ADHD in patients with SUD would likely recommend the use of sustained-release preparations of stimulants to reduce the potential for misuse, although clinical data are lacking to support this approach. Novel delivery systems such as the crush-resistant shell of Concerta (Alza Corporation, Fort Washington, Pennsylvania, USA)[99] or the recently FDA-approved methylphenidate skin patch, are more resistant to abuse and may be desirable alternatives in patients with co-occurring ADHD and SUD.

A final consideration regarding choice of medication is that of combination pharmacotherapy. While there is very minimal data to guide choices with regard to combinations of ADHD pharmacotherapies, nonetheless, clinicians will often be faced with clinical situations that call for the consideration of combination pharmacotherapy. These clinical situations can broadly be categorized into four groups: partial response, dose-limiting side effects, associated disorders, and comorbid diagnoses. Potential approaches to these clinical situations include combinations of stimulants and non-stimulant medications, combinations of non-stimulant medications, and combinations of immediate- and delayed-action stimulants.

PSYCHOSOCIAL TREATMENTS FOR ADHD AND CO-OCCURRING SUD

Although pharmacotherapy is the cornerstone of treatment for ADHD, a variety of psychosocial treatments can be employed in combination with medication to optimize the long-term management of this chronic disorder. Unfortunately, little controlled research has been undertaken on psychosocial treatments for adults with ADHD. Data on treatments for children are not likely to be directly relevant, given that those interventions typically emphasize parent training[100] and, in some cases, show no additive benefit of psychosocial treatment to patients receiving stimulant pharmacotherapy.[101]

An important element of the treatment of ADHD is psychoeducation. Having the patient learn about the disorder and its pervasive effects on their functioning can help to set the stage for developing an effective therapeutic alliance. Providing educational literature or referrals to community education/support groups, such as Children and Adults with Attention Deficit Disorder (CHADD; http://www.chadd.org) or the Attention Deficit Disorder Association (ADDA; http://www.add.org), can be very useful for patients and families in gaining understanding about the disorder.

Cognitive behavioral therapy (CBT) has been shown to be effective in reducing symptoms of adult ADHD.[102] Modifications of CBT such as structured skills training[103] or cognitive remediation[104] have also been shown to be effective. However, in patients receiving CBT for SUD, there is evidence that cognitive deficits, such as those associated with ADHD, are associated with low treatment retention,[105] suggesting that retaining patients with cognitive deficits in CBT-based SUD treatment is difficult, and that individualized treatment strategies may need to be developed.

Additional behavioral strategies for ADHD that are used clinically but not studied in controlled trials in adults include coaching and behavior modification. Coaching is a collaborative relationship between the patient and a professional to develop strategies for managing problems such as procrastination, time-management, and organization. Behavior modification is a

technique used mainly for children where desired behaviors are positively reinforced to increase their frequency.

CLINICAL MANAGEMENT OF ADHD CO-OCCURRING WITH SUD

The management of patients with co-occurring ADHD and SUD requires a comprehensive approach to assessing symptom burden and functional impairment. The simultaneous treatment of both conditions is likely to be the optimal approach because ADHD symptoms (eg, impulsivity, poor planning) will interfere with SUD treatment, and substance use will limit the benefit of ADHD treatment.

When using psychostimulant pharmacotherapy for ADHD in patients with SUD, careful attention to the clinical frame and boundaries of treatment needs to be made. It should be discussed explicitly with the patient that the use of stimulant medication carries an inherent risk of misuse or abuse, and that if evidence of such develops, the appropriateness of stimulant use will be reconsidered. Emphasis should be placed on the adherence to the prescribed medication regimen, and that medication should not be taken on an "as needed" basis. It should be made clear to the patient, and ideally the family, that if it becomes apparent that prescribed stimulant medication is being misused, abused, or diverted, that there is no obligation on the part of the physician to continue treatment. Fortunately, stimulant medications can be discontinued abruptly without dangerous sequelae.

The use of psychostimulants in patients with substance use disorders requires careful monitoring, including urine toxicology testing. Relapse or worsening of substance use may necessitate re-assessing the appropriateness of stimulant pharmacotherapy. Careful documentation of all prescriptions must be maintained in order to monitor the amount and frequency of the drug being prescribed. Repetitive requests to replace "missing," "lost," or "stolen" medication should be cause for concern, as should similar requests for dose increases when not clinically supported. Delayed-release preparations are preferred to reduce the rate of change of drug blood levels, which is less reinforcing, as well as to discourage non-oral use. Patient visits should be frequent. Despite all mechanisms in place to reduce the risk of diversion, misuse, or abuse of stimulants, it should be expected that a small percentage of patients with ADHD comorbid with substance use disorders will do so, and that careful clinical monitoring will detect such nontherapeutic use early and minimize its adverse effects.

Rating scales, such as the Conners Adults Attention-Deficit Rating Scale,[106] can be useful for monitoring symptom severity over time in response to prolonged abstinence or ADHD pharmacotherapy. One important caveat is that ADHD rating scales administered to patients who have not yet achieved a prolonged period of abstinence will capture substance-induced symptoms of inattention and hyperactivity in addition to possible symptoms due to ADHD. In such cases, sequential rating scale administration over time can help resolve the diagnosis; substance-induced symptoms should improve with abstinence, whereas symptoms due to ADHD will be stable in the absence of treatment. Rating scales help provide benchmarks from which the efficacy of therapy can be measured, particularly if multiple trials of medications are required to achieve a clinical response.

Assessment for malingering is an important component of managing a patient with co-occurring ADHD and SUD, given that the mainstay of treatment for ADHD are stimulants that are potentially abusable. Because inattention symptoms tend to predominate in adults with ADHD and symptom assessment is almost entirely based on self-report, the potential for patients with substance use disorders attempting to mislead clinicians in an effort to obtain stimulants is always present. Efforts to obtain collateral data from family and other sources should be made, including childhood school records.

SUMMARY

ADHD and SUDs frequently co-occur, particularly in SUD treatment settings. The etiology of the increased association of ADHD and SUD is unknown, although one possible cause is that substance use represents an attempt to "self-medicate" ADHD symptoms. Untreated ADHD leads to significant consequences and may impair a patient's ability to benefit from SUD treatment. Pharmacotherapy remains the mainstay for the treatment of ADHD, and psychostimulants continue to be first-line treatments. Several non-stimulant medications have shown promise for the treatment of ADHD, but their role for patients with co-occurring SUDs has not yet been determined. While stimulant medications have the potential for abuse and must be used cautiously in patients with substance use disorders, the available evidence suggests that stimulant medications administered under monitored conditions can be safe and effective in patients with substance use disorders. However, ongoing substance use can limit the efficacy of stimulant pharmacotherapy, and there is an irreducible risk of misuse, abuse, and diversion of stimulant medications when used to treat ADHD comorbid with substance use disorders. A conservative approach for treating co-occurring ADHD and SUD would be to begin treatment with a non-stimulant pharmacotherapy, but if an adequate response is not obtained, consider stimulant pharmacotherapy. The decision regarding the use of stimulant medications for a patient with ADHD and a co-occurring substance use disorder should be made on the basis of a broad clinical assessment and an individual risk-benefit analysis. For many patients, psychostimulants can be used safely and effectively; however, careful monitoring during treatment is essential to ensure prescribed stimulants are being used in a therapeutic manner, and in the case of worsening substance use or when faced with evidence of the diversion of prescribed medication, treatment should be discontinued.

Acknowledgements

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