REVIEW

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Universal precautions to reduce stimulant misuse in treating adult ADHD

ABSTRACT

In the United States, stimulants remain the approved pharmacotherapy of choice for adults with attention-deficit/hyperactivity disorder (ADHD). Many patients respond to these drugs, but stimulants also have a significant potential for misuse. This article suggests the "universal precautions" approach to reducing these risks while promoting appropriate medication use.

KEY POINTS

Untreated adult ADHD is associated with negative outcomes that include unemployment, arrests, divorce, and psychiatric comorbidities.

Available ADHD guidelines suggest that children and adults who respond to pharmacotherapy should continue it for as long as it remains effective. In this context, there is increasing recognition of adult ADHD as a valid and treatable disorder.

Following the guidelines of universal precautions in the diagnosis and treatment of adult ADHD can alleviate clinicians' concerns when diagnosing and treating this disorder.

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Children are not the only people affected by attention-deficit/hyperactivity disorder (ADHD). Characterized by high levels of inattention, overactivity, and impulsivity, ADHD affects 5% of school-aged children, but also 4% of adults.[1–3] Adults with untreated ADHD are likely to develop serious psychosocial problems that manifest as unemployment, arrests, divorce, underachievement, and psychiatric comorbidities.[4,5]

However, many clinicians are reluctant to manage adults with ADHD, partly because of concerns about misuse of the stimulant drugs they must prescribe to treat it.

Here, we outline an approach whereby clinicians can diagnose and treat adult ADHD while taking "universal precautions" to discourage misuse of the medications involved.

RECOGNIZING ADHD IN ADULTS

ADHD is characterized by developmentally inappropriate levels of inattention, impulsiveness, and hyperactivity that arise in childhood and result in impairments that often persist.

The presentation of ADHD in adults may be influenced by the longevity of their ADHD, associated sequelae (eg, low self-esteem and interpersonal, educational, and occupational difficulties), and comorbid disorders.[6] There are neither reliable biomarkers nor neuropsychological tests for diagnosis, and persons with ADHD typically have a complex presentation with at least one comorbidity.[6,7]

In patients diagnosed in childhood, difficulties with organization as well as initiating, maintaining, and completing tasks become more prominent in adulthood and hyperac-

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tivity tends to subside. Adult impulsivity may present as edginess, shopping sprees, quitting jobs, and risky behaviors.[6]

Overall, the clinical manifestations of ADHD in adolescents and adults include inattention, difficulties with task completion, disorganization, and executive dysfunction—all skills critical to managing the various roles of adult life.

OBSTACLES TO EFFECTIVE TREATMENT

In the past, ADHD treatment was routinely discontinued during adolescence, as it was unclear whether adults still had significant symptoms or benefited from treatment.[8,9] Now, available ADHD guidelines suggest that children and adults who respond to pharmacotherapy should continue it for as long as it remains effective. In this context, there is increasing recognition of adult ADHD as a valid and treatable disorder.[10]

One of the challenges clinicians face is the reliability of adult recall of childhood ADHD. A controlled, prospective 16-year follow-up study found that of all adults retrospectively given a diagnosis of childhood ADHD, only 27% actually had the disorder.[11] This study suggests that retrospective diagnoses of childhood ADHD made solely on the basis of self-reports are unlikely to be valid.

Another obstacle is that traditional medical education has seldom included training in adult ADHD.[8,12] In a UK study, clinicians felt that they lacked training and knowledge to assess and manage adult ADHD patients.[9]

Even if adult ADHD is recognized, diagnosis is just the first step of care.[13] These patients require ongoing management and follow-up assessments.

Although practice patterns vary, efforts to encourage doctors to provide adult ADHD care may be hindered by the fact that the gold standard of treatment is stimulant medication.[4,10] Medications approved by the US Food and Drug Administration for adult ADHD include the stimulants lisdexamfetamine, osmotic-release methylphenidate, mixed amphetamine salts extended release, dexmethylphenidate extended release, and the nonstimulant atomoxetine.[6] While stimulants are generally more efficacious for ADHD symptoms than nonstimulants, they are associated with misuse and diversion.[14]

TABLE 1

Psychiatric comorbidities in patients with attention-deficit/hyperactivity disorder

Associated comorbidity	Prevalence (%)
Social phobia	29.3
Impulse control disorder	19.6
Bipolar affective disorder	19.4
Major depressive disorder	18.6
Substance use disorder	15.0
Dysthymic anxiety disorder	12.8
Posttraumatic stress disorder	11.9
Panic disorder	8.9
Generalized anxiety disorder	8.0
Alcohol use disorder	6.0

Data from Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am J Psychiatry 2006; 163:716–723.

UNIVERSAL PRECAUTIONS: A SIMPLIFIED APPROACH

The universal-precautions approach to prescribing stimulants aims to allay physician concerns and promote appropriate medication use to allow for proper management of this disorder.[15] These precautions, to be applied to all adult ADHD patients for whom stimulants are being considered, include careful diagnosis and consideration of comorbidities, baseline risk stratification, informed consent processes, treatment agreements, periodic reassessments of treatment response, and meticulous documentation.

Adults with ADHD tend to lack critical skills to manage the various roles of adult life

DIAGNOSIS

A frequently used screening assessment for adult ADHD is the ADHD Rating Scale (ADHD RS), which consists of two subscales for assessing hyperactivity/impulsivity and inattentiveness.[16] ADHD can be classified into one of three subtypes based on symptoms:

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inattentive, hyperactive, or combined type. Symptoms must persist for at least 6 months for a diagnosis to be made. Other ADHD scales include the Conners Adult ADHD Rating Scales and the Brown Attention-Deficit Disorder Scales.[4]

High scores on screening scales must be interpreted within the clinical context. Clinicians need to ask about ADHD symptoms, establish their presence in various settings, and determine if these symptoms interfere with functioning. A diagnosis of adult ADHD also requires evidence of symptoms beginning in childhood.[17] According to the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, inattentive or hyperactive-impulsive symptoms must be present before age 12 in two or more settings and interfere with function and development.

Although self-reporting screening tools are helpful, these tests are not reliable for diagnostic purposes, and collateral information is also required.

Neuropsychological testing may detect impairments in persons with ADHD. The most consistently employed neuropsychological tests to evaluate ADHD include the Conners Continuous Performance Test, Stroop Color and Word Test, Trail-making Test, verbal fluency tests, Controlled Oral Word Association Test, and the Weschler Adult Intelligence Scale.[6]

After diagnosing adult ADHD, assess the risk for misuse of stimulant medications

COMORBIDITY

Epidemiologic studies suggest that adults with ADHD develop many psychiatric problems including anxiety, depression, and substance use disorders.[7,16] **Table 1** illustrates common comorbidities and their associated prevalence in the ADHD patient.[7]

Comorbid psychiatric disorders may affect the presentation of adult ADHD. For instance, adults with comorbid depression and ADHD are more likely to present with heightened irritability and difficulties concentrating on tasks than those with either condition alone.[18] Similarly, antisocial personality disorder is more common in adults with ADHD.[19] Such patients exhibit stable antisocial behavior (lying, stealing, and aggression) as well as medication misuse.[5,14,19]

While these comorbid disorders may obscure the ADHD diagnosis, their recognition is essential to effectively manage adult ADHD. In sum, a careful evaluation of the adult, including elucidating both ADHD and comorbid symptoms, functionality in several domains, and the degree of impairment, should precede initiating pharmacotherapy for adult ADHD.

BASELINE RISK STRATIFICATION: RISK FACTORS FOR STIMULANT MISUSE

After diagnosing ADHD, the prescriber must assess the risk for misuse of stimulant medications.[20]

One study revealed that nonmedical use of stimulant medications occurred in only 2% of the 4,300 people surveyed.[21] Among the misusers, 66% had obtained medication from family or friends. Another 34% had stolen medication, and 20% had obtained prescriptions from a physician by falsely reporting symptoms. The study also assessed motivation for misuse. In this sample, 40% of misuse was to enhance performance, 34% was for recreation, and 23% was to stay awake.[21]

Other studies show that misuse of stimulant medications is common among youth in the United States, reporting that 18% of college students use some formulation of prescription stimulants.[22]

Still more research suggests that childhood conduct disorder or illicit drug use results in a higher risk of stimulant medication misuse.[20] Additional risk factors for misuse include male sex, white ethnicity, upper-class background, Jewish or no religious affiliation, affiliation with a sorority or fraternity, off-campus housing, and a low grade-point average.[23]

Table 2 illustrates clinical interventions providers can use, once they have risk-stratified their patients, to monitor for stimulant misuse.

HOW SHOULD THESE RISK FACTORS AFFECT TREATMENT?

Although no formal scoring system exists to help clinicians risk-stratify these patients, the presence of multiple risk factors suggests the need for vigilance.[14] Physicians should prescribe agents with less potential for abuse and

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monitor these patients more intensely.

Short-acting stimulant medications are the most likely to be abused, as phasic dopamine increase is more reinforcing than therapeutic dopamine release.[24] Longer-acting stimulant medications are less likely to be abused, and they provide better symptom relief, as tonic dopamine release maintains a steady state and increases the therapeutic efficacy of these medications.[25] For example, methylphenidate extended-release tablets have an osmotic oral controlled-release system and are less likely to be crushed for recreational inhalation.[6,14]

Lisdexamfetamine is a prodrug therapeutically inert until converted to D-amphetamine when lysine is cleaved from the molecule. This medication may be a good option for patients at high risk of misuse because it is tamper-resistant. However, it still may be subject to misuse for performance enhancement.[26,27]

The nonstimulant atomoxetine is also approved for ADHD, has no abuse potential, and may be particularly useful when anxiety, mood, and substance use disorders co-occur with ADHD.[6] Rarely, atomoxetine can damage the liver, and liver function tests should be monitored if right upper quadrant pain develops.[4,10]

Other nonapproved agents such as bupropion and desipramine also have been used empirically and off-label for ADHD.[4,10]

Overall, treatment should be selected according to the risk of misuse of stimulant medication and the patient's comorbidities.

TABLE 2

Interventions to minimize drug misuse based on patient risk stratification

If at low risk for misuse
Education, including: Abuse potential Consequences of sharing or selling Interactions with illicit substances Safe storage
Check a prescription monitoring program, if available
If at high risk for misuse
Education
Check prescription monitoring program
Use delayed-release preparations
Prescribe small quantities at a time
If showing red-flag behavior[a]
Education
Check prescription monitoring program
Pill counts at each visit
Urine drug screens

[a] Red-flag behavior: missed appointments, early refill requests, appearing intoxicated at visit, requesting dose increase.

INFORMED CONSENT

Informed consent may help patients appreciate the risks and benefits of the treatment options and develop realistic expectations about treatment.[26] Patients are instructed to take their stimulant medications as prescribed and are informed of the risks of combining stimulants with other substances, particularly those that may interact with stimulants (eg, cocaine) and raise the risk of seizures and cardiovascular complications.

Stimulant medications lead to elevations in blood pressure and heart rate, although large-scale studies have shown no increase in the rate of serious cardiovascular events when these drugs are used appropriately.[6] Less serious side effects associated with stimulant medications include insomnia, weight loss, decreased appetite, dry mouth, headache, and rarely, depression and anxiety.[6]

Patients need to be warned about diversion and abuse liability of stimulant medications, as well as alternative treatments.

The nonstimulant atomoxetine has no reinforcing properties but also raises the blood pressure and heart rate.[6] As with stimulants, these elevations are generally minimal, time-limited, and of minor clinical significance.[4,10] Frequent reasons to prescribe atomoxetine include poor tolerability of stimulants and a history of substance abuse. In addition, women with ADHD and high levels of emotional dysregulation or social anxiety appear to be particularly responsive to atomoxetine.[6]

Another consideration is cognitive behavioral therapy, which can augment the effects

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of pharmacotherapy.[4] Cognitive behavioral therapy focuses on time management, prioritization, organization, problem-solving, motivation, and emotional regulation.[4]

Finally, patients also need to understand the possible consequences of nontreatment.[5] Adults with untreated ADHD have high rates of academic and occupational difficulties, antisocial behaviors, and other forms of psychosocial adversity.[4,5]

Overall, this process should involve discussing risks and benefits of treatment options with the patient and promoting joint decision-making.

TREATMENT AGREEMENTS

Stimulant medications are classified by the US Drug Enforcement Administration as schedule II substances due to their abuse potential.[20]

It is important to inform patients of the addictive nature of the medication and to instruct them on how to store stimulants safely.[27] Patients need to know that giving away or selling these medications is illegal.[27]

Treatment agreements establish rules for prescribing and are signed by the patient before initiating therapy.[28,29] Patients are expected to attend all of their appointments, receive their prescriptions from one doctor, and obtain their medication from one pharmacy. These agreements may also require patients to submit to monitoring with random urine drug screens.[29] Overall, they underscore the need for patients to follow a treatment plan in order to continue therapy with controlled substances.[29]

Short-acting stimulant medications are the most likely to be abused

Manning[27] recommends using agreements for high-risk college students prescribed stimulant medications. Red flags for misuse include signs of active substance use (eg, intoxication, a pattern of "lost" prescriptions, and doctor-shopping).[27]

The effectiveness in reducing risk of misuse in the adult ADHD population has not yet been investigated. Nonetheless, a method of communicating the seriousness of stimulant misuse to adult patients is essential to ADHD care.

STAYING ON TRACK

In the clinical setting, treatment response is measured not just by symptom reduction, but also by functional improvement. Thus, clinicians and patients must set functional goals whenever possible.[27] Successful progress toward these goals justifies continuation of therapy, whereas lack of improvement signals the need to reconsider stimulant therapy.[27]

MONITORING AND DOCUMENTATION

Adults with ADHD present with varying levels of functional impairment and comorbidities, which may require different levels of monitoring.[30] Not all patients with ADHD respond optimally to stimulant medications or tolerate them well.[31,32] Hence, monitoring parameters for therapeutic change and adverse outcomes are important in that they guide the alteration or even discontinuation of pharmacotherapy.[4,6,14]

Documenting the decision-making process to continue stimulant medications under certain circumstances is also essential. Documentation should include discussion of goals and expectations, risks and benefits, and alternatives to stimulant use.

In adults, risk of stimulant medication misuse adds a new layer of complexity to monitoring.[13,14] Adults may get multiple prescriptions from multiple providers, seek early refills, fill prescriptions at different pharmacies, or alter formulations. Many states track stimulant prescription use, and prescribers can use this information to determine if patients are refilling their prescriptions appropriately or obtaining stimulants from more than one provider.

Although these monitoring strategies are useful,[6] it is prudent to structure the level of monitoring according to the patient's risk of adverse events or medication misuse.[14,27] Gourlay and Heit[15] proposed the following "four-A" mnemonic for four domains to be explored at each visit in patients receiving pain medicine. This mnemonic can be applied to adult ADHD patients to more accurately monitor the patient throughout treatment.

THE 'FOUR-A' MNEMONIC

ADHD symptoms

Several ADHD scales can be used to track symptom changes over time.[33] However, these self-report scales may be subject to positive illusory bias, a phenomenon observed in in-

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dividuals with ADHD in which they tend to overrate their functioning,[34] which may limit the accuracy of self-report scales.[35]

Activities of daily living

Since patients with ADHD tend to overrate their functioning in various aspects of living, collateral information should be gathered to corroborate patient self-reports whenever possible.

Adverse events

Blood pressure, heart rate, and weight should be assessed at baseline and monitored during stimulant treatment. Other symptoms to monitor include gastrointestinal distress, headache, aggression, depression, appetite, and sleeping habits.[4,6] More intensive monitoring (eg, electrocardiography) may be indicated for those with hypertension and cardiovascular risk factors.

Aberrant behavior

Monitoring for misuse and diversion of stimulant medications is essential, as ADHD itself is a risk factor for addiction.[20,21] Pill counts, prescription monitoring programs, urine drug screens, and collateral informants have all been proposed but not studied in monitoring for the misuse of stimulant medications.[27] Before prescribing, it is prudent to check the prescription monitoring program, get a urine drug screen, and discuss any positive findings with the patient.[36,37]

Treatment agreements ensure that patients are aware of the consequences of misuse and allow the clinician to reference prior discussion when terminating treatment with stimulants.

LIVES CAN BE ENHANCED

ADHD is a common disorder that arises in childhood and can persist throughout life. Adults with untreated ADHD are at risk of severe impairments in various domains of functioning. Stimulant medications are an effective treatment but may be diverted into the street market. Using the universal-precautions model may reduce the risks of both nontreatment of ADHD and misuse of stimulants.

Accordingly, clinicians need to confirm the ADHD diagnosis, assess comorbidities, estimate risk of misuse, and provide informed consent prior to prescribing. Subsequent monitoring should involve the use of treatment agreements and evaluating treatment response, paying particular attention to ADHD symptom control but also to level of function, adverse effects, and aberrant behavior.

With these principles in mind, clinicians can address the risks of misuse and potentially enhance the lives of people who may have been suffering substantially due to lack of appropriate care.

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