

Abuse of Prescription Stimulant Drugs

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This knowledge-based activity is targeted for all pharmacists and is acceptable for 1.0 hour (0.1 CEU) of continuing education credit. This course requires completion of the program evaluation and at least a 70 percent grade on the program assessment questions.

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Objectives

At the conclusion of this article, the participant should be able to:

- Explain the current extent of prescription stimulant abuse.
- Describe the mechanism of action for common stimulants and the addictive properties.
- Identify which populations are the most affected and who is at the highest risk of abusing prescription stimulants.
- Explain treatment options for acute overdose and withdrawal symptoms of prescribed stimulants.
- Identify what pharmacists can do to help reduce the abuse potential in high risk populations.

Background

Prescription stimulants such as dextroamphetamine/amphetamine combination (Adderall®), methylphenidate (Concerta®), and lisdexamfetamine (Vyvanse®) are schedule II medications and are the most commonly prescribed drugs to children and adults for the treatment of attention deficit hyperactivity disorder (ADHD). ADHD is one of the most common childhood disorders and can continue into adolescence and even into adulthood. The common symptoms include difficulty staying focused and paying attention, difficulty controlling behavior, and over activity. Symptoms usually improve as the patient grows older. It is estimated that about 8 percent of children 4-17 years old are diagnosed with ADHD.¹ These drugs are very effective in the treatment of ADHD but also have the potential for both abuse and addiction.

There are many reasons reported for the potential abuse of prescription stimulants. Some of the reasons include: to achieve a euphoric state or "high", increase mental alertness or energy level, to improve grades, and to aid in weight loss. When these stimulants are taken at higher than prescribed doses, or used in ways other than orally, (intravenously or snorted) they pose many health risks that may include dangerously high body temperature, seizures, and

cardiovascular events.² A 2009 investigational study tracked calls to the American Association of Poison Control Centers from 1998 to 2005. Calls related to teenagers abusing stimulant drugs rose by 76% over that eight-year span.³ The FDA has issued black box warnings (BBW) for these drugs due to their addictive properties and potential cardiovascular events.⁴

It is important, as healthcare professionals, for us to recognize the current problem with prescription stimulants because many people may not be aware of the risks associated with these drugs. Making more people aware of the concerns with these medications may help to lower the amount of people willing to abuse them. To potentially help lower abuse risk, patients should be informed that using these medications for the proper indication and taking them as prescribed will decrease their risk of forming addiction or dependence.

Mechanism of Action

Amphetamines are noncatecholamine, sympathomimetic amines that promote release of catecholamines {dopamine (DA) and norepinephrine (NE)} from their storage sites in the presynaptic nerve terminals. Amphetamines may also have the ability to prevent reuptake of catecholamines due to competitive inhibition. Dopamine is a neurotransmitter that is associated with pleasure in the reward pathway of the brain. When stimulants are used therapeutically for ADHD, they cause slow and steady increases in DA. They should be prescribed starting at a low dose and titrated up until therapeutic effect is achieved. When abusers take high doses or use the intravenous route, the stimulants cause a very rapid increase in dopamine. This is what causes the feeling of euphoria or high. This also increases the risk of addiction dramatically.⁴ The rapid increase in DA is very similar to the way that illegal drugs such as cocaine can cause the feeling of euphoria.

Tolerance is defined as requiring higher doses of a drug to produce the same euphoric state as previously achieved with a lower dose. Tolerance to amphetamines is related to the way the drug is being taken. Tolerance is unlikely when being taken as prescribed to treat ADHD. When abusers begin to use higher doses to achieve the euphoria, they are increasing their risk for dangerous adverse events such as seizures or cardiovascular events.⁵

Populations Most at Risk

The most commonly assumed populations at risk for misuse include school age children and college students. This is most likely due to factors such as an increase in the amount of stimulants being prescribed to students, increasing the access of other students to obtain them without a prescription. A study done by the University of Michigan asked 12th grade students, who admitted to using stimulant drugs within the last year, how they were able to obtain these prescription drugs.^{6,7}

The results of this study, shown in the table above, show that the most common way that students were able to obtain the prescription stimulants is through their peers, either

purchased or received for free. The study also showed that over 40% of 12th grade students stated that it is “fairly easy” or “very easy” to obtain prescription stimulants.^{6,8}

A 2005 web survey based study of a randomly selected group of 9161 undergraduates reported an 8.1% lifetime prescription stimulant abuse rate among college students, including 5.4% over the past year. The most common reasons for the illicit use included improve alertness, help with concentration, and to get high.^{2,9}

Table 1: How Prescription Stimulants Were Obtained

| How they were obtained | % of Students |
|-------------------------------------|---------------|
| Purchased Online | 4.5 |
| Took from a friend without asking | 4.9 |
| Given for free from a friend | 56.5 |
| Purchased from a friend | 45.9 |
| Bought from a stranger/ drug dealer | 21.8 |
| From a Prescription | 18.1 |
| Other | 13.8 |

Chart adapted from The Monitoring the Future Study, University of Michigan. Results were taken from 2009-2011. Included 394 students in the 12th grade that admitted to having used stimulants within the

Many professionals believe that stimulants are being overprescribed today. This may be attributable to the fact that many parents believe these medications will improve their child's grades in school. There is now more pressure from parents and children on family physicians to provide these prescriptions. Patients and their parents need to be informed on the potential complications of long term stimulant use such as addiction or dependency. Parents need to know that stimulants should only be used in patients that have ADHD and are not an appropriate way of improving their child's grades in school if they do not have ADHD.¹⁰ Also, the patients receiving these prescriptions need to be informed of the risks associated with allowing their peers to abuse their medication, both legally and medically.

Diagnosing ADHD should be done using specific criteria. The patient must present with symptoms in multiple settings such as home, work, or school. The patient must present with at least six symptoms of hyperactivity, and these symptoms must be present for a minimum of six months. These symptoms must be serious enough to the patient that they are detrimental in multiple areas such as grades or work productivity. Before a physician makes a diagnosis of ADHD in a patient, he or she should conduct interviews with the patient or parents, look at family history, and provide the patient with a standardized questionnaire related to his or her symptoms.¹¹ ADHD is not easy to diagnose, but using guidelines similar to these will help lower the risk of over prescribing medications.

Identifying Abuse

It is important to be able to identify at risk populations and be able to identify patients who may be abusing the medications. It is crucial for early detection of patients who may be misusing medications before long term complications such as dependence develop. The Substance Abuse and Mental Health Services Administration recommends using the “**CAGE**” screening tool with patients that are at high risk for abusing stimulants. These are questions that healthcare professionals should ask patients while making sure to remain nonjudgmental.¹²

- Have you ever felt the need to **cut** down on your use of prescription drugs?
- Have you ever felt **annoyed** by remarks your friends or loved ones make about your use of prescription drugs?
- Have you ever felt **guilty** or remorseful about your use of prescription drugs?
- Have you **ever** used prescription drugs as a way to get going or study better?

Answering yes to any of these questions may indicate medication abuse or misuse. After the brief assessment, ask the patient for a few minutes to talk about the results to the screening tool. As appropriate, refer patients to further assessment or treatment.

Pharmacists play a vital role in providing information to their patients. Pharmacists have the ability to educate patients about the importance of using their medications the way they were prescribed and even inform patients on the proper way of disposing of medications they no longer take. Disposing of medications the correct way, such as going to drug take-back programs offered by local pharmacies, will prevent someone else from taking their medications for abuse purposes. It is also important that pharmacists increase the public’s awareness of prescription abuse. It may be beneficial to provide pamphlets or flyers at the pharmacy to help spread information regarding prescription abuse.

Observing trends in patient profiles such as repeatedly early attempts to fill prescriptions each month may indicate potential abuse. The Ohio Automated Rx Reporting System (OARRS) is a tool that can be utilized by health care professionals to identify drug seeking behavior. Pharmacists, physicians, and law enforcement agents may register for an OARRS account. This tool is used to look into patient medication history and should be utilized to understand patient’s medication refill tendencies.

Treatment of an Acute Over Dose and Withdrawal Symptoms

Pre-Hospital Care:

Patients with a major amphetamine overdose will most likely present with extreme agitation that usually requires chemical or physical restraint. IV access needs to be established immediately. Patients may also present with serious complications such as seizures that require

immediate treatment and control with benzodiazepines. The overdose victim may also require intervention to maintain an established airway. Another complication that may present is cardiac arrhythmias.¹³

Emergency Room Treatment:

Monitoring vital signs is key. Patients will present with hyperthermia, potentially severe (>104°F), elevated pulse, elevated blood pressure, and an increased breathing rate. Monitoring all these signs will help to determine the extent of the overdose.

Blood or urine tests should be used to identify renal function. An EKG should be used to identify potential heart damage.

| Complication of Acute OD | 1st Line Treatment Option |
|--|---|
| Oral overdose requiring GI decontamination | Activated charcoal (Max effect seen if used within 30 minutes of the oral ingestion). Not effective beyond 4 hours of oral ingestion. |
| Hyperthermia | Aggressive cooling with an ice bath (body fully emerged). Goal for temperature control is 15-20 mins |
| Dehydration | IV 0.9% NaCl (3-5 liters in first few hours) May be cooled to assist in treatment of severe hyperthermia |
| Convulsions | Diazepam is first line therapy at 5-10 mg IV every 10-20 minutes. Lorazepam 4 mg/dose slow IV at a rate of 2 mg/min is also a potential option |
| Hypertension | Nitroglycerin IV initial rate 5 mcg/min and titrate every 3-5 minutes up to maximum of 400 mcg/min |
| Tachycardia | Esmolol initial rate 50 mcg/kg/min and titrate no more frequently than q 4 min up to 200 mcg/kg/min |
| Very Severe Agitation | Diazepam 10 mg IV as a single dose, repeat 5 mg doses if necessary |
| Dysrhythmias | Cardioversion, Defibrillation, or Amiodarone 300 mg IV over a period of not less than 3 minutes initially, then followed by continuous infusion of 15-20 mg/kg over the next 24 hours |

Hyperthermia may be a common presentation with an acute overdose of amphetamines. The treatment options for hyperthermia induced by amphetamine toxicity include ice packs to the groin and axilla or the use of an ice-bath with the patient's full body totally immersed in the ice. Patients with severe hyperthermia (body temperature >104°F) may require neuromuscular paralysis to help rapidly decrease their body temperature. The goal to

achieve control of the body temperature should be within 20 minutes of presentation. This goal is set to help prevent multi-system failure and death.

If the overdose occurred orally, activated charcoal is the first line treatment. The charcoal will help to prevent up to 60% of the drug absorption. Charcoal's peak effect is seen if used within 30 minutes of ingestion and it loses most of its efficacy after four hours. This is because most of the drug has been absorbed from the stomach at this point. Some experts believe it loses efficacy quicker than four hours, so the general rule is to administer activated charcoal as soon as possible following ingestion of the drug.^{13,14}

Monitoring after initial admission:

After the patient is treated in the ED, it is important to continue to monitor all vital signs, because they may become unstable. Continue to monitor the patient's blood pressure, body temperature, heart rate, and continue to monitor the EKG for potential dysrhythmias. The patient may also have chest pain if there was myocardial damage. Monitor for any respiratory distress because this may potentially be a sign of pulmonary edema. The patient is still at risk for neurological complications such as seizures or strokes, so these need to be assessed regularly. It is also necessary to involve drug abuse social services with the case to help monitor for complications and properly advise the patient on drug addiction treatment centers.¹³

Treating withdrawal symptoms:

Amphetamine withdrawal is not easily treated, and symptoms will vary on a patient to patient basis. Common symptoms include severe fatigue, anxiety, depression including suicidal ideation, and hallucinations. Due to the possibility of severe withdrawal complications, the detoxification should take place in a rehabilitation facility where the staff is fully trained to deal with these complications.

It is important for the patient not to discontinue the amphetamines suddenly because that is when the withdrawal symptoms are the most severe, leading to the highest chance of relapse. The best approach to treating amphetamine withdrawal is a combination of pharmacologic therapy and psychosocial therapy. Although no specific pharmacological therapy has been established as the treatment of choice for withdrawal, but some options exist with the potential to decrease symptoms. Short term use of fluoxetine 40mg per day was shown to decrease drug cravings and imipramine 150mg per day was shown to improve overall adherence to the withdrawal therapy.¹⁵ Many experts disagree on the benefits of any agents to therapeutically treat amphetamine withdrawal. Symptoms of withdrawal will be less severe if the patient is slowly taken off of the medication. Addiction treatment centers offer the best care for treatment of withdrawal and prevention of relapse.¹³

The Ways Pharmacists Can Help

Pharmacists are in a unique position to be able to help with the problem of stimulant misuse. Very often, pharmacists are the most approachable health care professionals. It is the duty of a pharmacist to make patients more aware of the problem of prescription medication abuse. One potentially significant cause of people misusing amphetamines is that they do not know of all the dangers associated with the medications. Pharmacists need to discuss with patients the seriousness of not sharing their prescription with anyone, especially students sharing with their peers.

When a child is prescribed these ADHD medications, it may be beneficial to talk with his or her parents about the common problem of illicit use of the amphetamines. Parents may not be aware that students report that the most common way they access prescription drugs is through their peers and friends. Advice for parents may be to keep the medication locked up and always keep track of how much medication is left. It is also very important for parents to talk to their children about the serious consequences of allowing anyone else to have their medication, including close friends or family members.

Identifying abuse or misuse is also imperative in preventing an overdose or addiction. It may be tough for pharmacists to identify risk factors such as changes in behavior, depression, problems in school, or legal problems. A warning sign for a high risk patient that may be misusing their prescription is if he or she repeatedly tries to have it filled early every month. Another warning sign may be if the patient has provided prescriptions from multiple doctors or uses multiple pharmacies. Using the CAGE screening technique as recommended by the Substance Abuse and Mental Health Services Administration may be difficult because it will be challenging to identify the high risk patients. The best practice is to inform the child's parents of these risk factors because many parents may be unable to identify any of these abuse risk factors. It is beneficial to talk to the parents about what they should be looking for and also to provide them with a handout or pamphlet. The handout should contain information such as risk factors for addiction, how to identify signs of addiction, and what to do if they believe their child is abusing or addicted to prescription drugs. It may even be appropriate to teach the parents the CAGE screening tool, and how to interpret the results to the questions.¹⁶

Prescription amphetamine abuse is a problem in today's society but pharmacists can make a difference. Communication with the patients or the patient's parents is a key to success in preventing misuse of prescription medications. As front line health care professionals, pharmacists have the ability to reach a large number of patients and have the opportunity to help improve knowledge and awareness of amphetamine abuse.

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