TOXICITY OF CNS STIMULANT DRUGS FIVE STAGE 2021-2022

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The term stimulants cover a broad class of drugs that increase the activity of the central nervous system. These drugs are used by a very high percentage of the general population for various reasons, including performance enhancement, medical benefits, and recreational purposes. Depending on the stimulant and jurisdiction, the drug may be legal or illegal.

Caffeine is the most commonly used stimulant in the world, used for a combination of dietary and recreational purposes as well as performance enhancement. Other legal stimulants are generally used for performance enhancement but may also find utility for specific symptoms depending on the drug. Illegal and/or prescription stimulants carry medical purposes but are also heavily used for recreational reason

Medical Indications

- Attention deficit hyperactivity disorder (ADHD)
- Narcolepsy
- Asthma
- Obesity
- Nasal and sinus congestion
- Hypotension due to anesthesia

As the most commonly used stimulant, caffeine is found in various drinks and foods such as tea, coffee, and chocolate. It is consumed habitually in many countries worldwide, given its mild to moderate stimulant effects, which promote alertness. Its general properties have also made it rampant among students and athletes who seek a cognitive or physical edge, respectively.

The amphetamine class of drugs is used for medical and recreational purposes. They carry a multitude of effects that include general and cognitive performance enhancement along with euphoric effects. They also induce aphrodisiac effects in many users. Methamphetamine is a widely trafficked and illegal drug used for recreational purposes. Athletes use many drugs that are related to the amphetamine class of drugs for physical performance enhancement. These drugs fall under bans by the world

Administration

The primary method of administration for stimulants is oral intake. Recreational administration of stimulants also occurs by intramuscular and/or intravascular injection, smoking, and intranasal administration.

Adverse Effects

Stimulants can induce a broad range of short-term and long-term adverse effects. The side effect profile is dependent on numerous variables. The user's body weight, the specific stimulant used, the dose of the agent taken, and tolerance are the major factors that influence adverse effect outcomes. Other factors include the use of other drugs and stimulants and oral intake on an empty stomach.

Toxicity

Treatment of a stimulant overdose depends on the specific agent used, the ongoing adverse effects, and the potential risk for further adverse effects. The generally available options for treating stimulant toxicity are benzodiazepines, beta-blockers, antiarrhythmics medications, and antihypertensive medications. Certain medications under these classes of drugs may be contraindicated depending on the specific drug used. Benzodiazepines lower the associated anxiety of stimulant toxicity and may improve the patient's vital signs. They are also the primary option if the patient is experiencing seizures.

Beta-blockers are useful for lowering the patient's heart rate, given that tachycardia is a very common symptom of stimulant overdose. As well, they can improve the patient's hypertensive state. Antiarrhythmic medications are generally reserved for ventricular arrhythmias that result from stimulant toxicity.

It is critical to confirm the specific drug that induces the stimulant toxicity given the potential treatment contraindications. For example, cocaine overdoses are a frequent cause of stimulant toxicity. While they induce tachycardia, chest pain, and hypertension, the use of beta-blockers may potentially be cardiotoxic to a patient who has overdosed on cocaine.

Treatment / Management

Patient acutely intoxicated on amphetamines will require chemical and physical restraints to prevent self-harm or harm to others, as these patients can be hostile with severe paranoia. Some life-threatening signs and symptoms need to be addressed on an emergent basis such as trauma, compromised airway, seizures, and any cardiac dysrhythmias. A patient can be treated with supportive therapy with sedation and observation if there are no life-threatening signs and symptoms. The medications that provide supportive treatment include benzodiazepines for sedation and to control seizures, activated charcoal in some cases if the patient is conscious and able to take it orally as this may help reduce amphetamine absorption in the digestive tract, and fluids to treat dehydration. Death related to amphetamine toxicity is rare; however, the risk of death is higher when a patient uses amphetamines while using or overdosing on other drugs.

Introduction

Caffeine is a stimulant that has been utilized globally for centuries secondary to its ability to improve mental alertness. As many as 85% of Americans consume caffeine daily with the average cup of coffee containing anywhere from 40 to 150 mg of caffeine.[1] Caffeine can be found in many over-the-counter preparations (energy drinks, appetite suppressants, stimulants, exercise supplements, decongestants, bronchodilators, and mental stimulants), increasing the risk of toxicity with inadvertent overuse or severe toxicity with an intentional overdose.[2] Lethal doses of caffeine have been reported at blood concentrations of 80 to 100 micrograms/ml which can be reached with ingestion of approximately 10 grams or greater

Etiology

Lethal overdoses of caffeine in adults are rare but when encountered are commonly caused by an intentional overdose of medications Conversely, caffeine toxicity in children is typically caused by accidental ingestion.[11] Toxic ingestions can be seen after ingestion of energy drinks but are rarely seen from ingestion of coffee or tea secondary to the excessive amount of fluid that would have to be ingested to reach toxic levels.[12] Over-the-counter drugs containing large doses of caffeine purchased for their stimulant properties can also complicate caffeine exposure. Some examples include health food products, diet aids decongestants, bronchodilators, or stay-awake pills

Pathophysiology

Due to caffeine's ability to affect a variety of different receptors, the side effects of caffeine overdose can be profound. Caffeine is a natural alkaloid methylxanthine that acts as a nonselective antagonist of adenosine receptors, with A1 antagonism triggering seizures and A2 antagonism triggering cerebral and coronary vasoconstriction. Caffeine also inhibits phosphodiesterase, resulting in increased intracellular cyclic AMP and intracellular calcium levels. Caffeine can stimulate the release of catecholamines, especially noradrenaline, with beta 1 agonist activity resulting in tachycardia and beta 2 agonist activity resulting in peripheral vasodilation and hypotension. [14][10][4][15] Caffeine also sensitizes dopamine receptors and is a competitive antagonist of benzodiazepine receptors. Furthermore, caffeine increases renin excretion, resulting in initial hypertension, sodium retention, and water retention

Toxicokinetics

Caffeine is rapidly and nearly completely (up to 90%) absorbed by the stomach with peak plasma concentrations occurring within 20 to 40 minutes.[18] As a result, toxic levels can be reached quickly and last for prolonged periods of time secondary to caffeine's 3- to 10-hour half-life. The liver metabolizes caffeine via N-demethylation, acetylation, and oxidation. Other substances that use these same pathways, such as alcohol or medications, can prolong the half-life of caffeine.

Evaluation

Routine serum laboratory evaluations can be useful in drug overdose cases, especially in the setting of unstable vital signs, seizures, or altered sensorium. Serum caffeine levels can guide prognosis and therapy. Although not available in all hospitals, serum caffeine levels are generally obtained with an immunoassay.[21][22] Lethal blood levels are typically above 80 to 100 mg/L, although one case occurred at 15 mg/L.[6] A venous blood gas may demonstrate anion gap metabolic acidosis which can be severe. Lactate levels are commonly elevated. Caffeine toxicity can result in hypokalemia, hypocalcemia, hyponatremia, and hyperglycemia. It is also important to obtain serum myoglobin and creatine kinase levels to monitor for rhabdomyolysis. An electrocardiogram may demonstrate tachycardia, ST-segment depressions, or T-wave inversions. Cardiac monitoring allows evaluation of heart rate and early recognition of dysrhythmias such as ventricular ectopy or fibrillation

Treatment / Management

Fatal caffeine overdose is relatively uncommon, and treatment data is limited to case reports. The primary treatment for minor caffeine ingestion is supportive. Hydration may be oral in minor cases, yet severe cases benefit from intravenous (IV) hydration. Beta-blockade with esmolol is useful for tachycardia. Procainamide, lidocaine, or bicarbonate have also been utilized for the treatment of tachydysrhythmias.[23] Vasopressors, such as vasopressin or phenylephrine, can be used to maintain blood pressure (goal mean arterial pressure greater than 65 mm Hg) without worsening tachycardia.[15]

Activated charcoal can bind caffeine if the ingestion is recent, and repeated doses can help diminish serum levels via the enterohepatic circulation. Hemodialysis has been effective in severe, life-threatening caffeine ingestions. Caffeine exhibits ideal characteristics to be dialyzed, including low protein binding (36%), low molecular size (194), and a small volume of distribution (0.6 to 0.8 L/kg). Imminent cardiac arrest in caffeine toxicity should prompt intra-lipid therapy to scavenge the free serum caffeine

Prognosis

There are relatively few deaths reported from caffeine overdose; however, prognosis largely depends on how quickly treatment is implemented.[12] In cases of severe caffeine overdose, the prognosis is directly correlated with the timeliness of caffeine removal from the bloodstream using hemodialysis or intralipid emulsion therapy

Complications

Complications of caffeine overdose include seizure, neurologic changes, tachy-dysrhythmia, ECG changes, hypokalemia, hyperglycemia, and anion gap metabolic acidosis secondary to lactic acidosis. Severe cases can result in acute kidney injury, rhabdomyolysis, and even cardiac arrest

Outcomes

The outcomes after caffeine toxicity are excellent. Mortality is very rare for patients who seek treatment. Those who do not seek treatment or the treatment is delayed may develop seizures, arrhythmias, or even aspirate vomitus. Over the past decade, less than 3 dozen deaths have been reported. For those who survive, there are no residual sequela