

Treatment of Acute Intoxication and Withdrawal from Drugs of Abuse

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Stimulants (Cocaine and Amphetamines)

“The intoxicated person may show signs of hyperawareness, hypersexuality, hypervigilance, and psychomotor agitation. Often, the symptoms of stimulant-induced intoxication resemble mania. The intoxicated person should be monitored by the medical staff until the symptoms of intoxication diminish. If the intoxication does not return to baseline level within 24 hours, mania may be present, and treatment for manic disorder may be required.

With increased dosage and duration of administration, stimulants can also produce a state of mental confusion and excitement known as stimulant delirium. Delirium is associated with becoming disoriented and confused as well as anxious and fearful. Extreme medical caution is needed when treating delirium because such symptoms may indicate stimulant overdose. For instance, patients addicted to crack cocaine who over-dose need careful monitoring for seizures, cardiac arrhythmias, stroke, and pulmonary complication. Overdose management has been reviewed in detail (see Gay, 1982: *Ann Emerg Med* 11:562-572), but more recently a syndrome of hyperthermia and agitation has been described that resembles neuroleptic malignant syndrome. Standard pharmacological management of overdose includes neuroleptics, but high doses of benzodiazepines may be safer alternatives for controlling the delirium and agitation because neuroleptics will worsen the hyperthermia in some cases of overdose and lead to fatality. Acute use of benzodiazepines can also help minimize the need for physical restraints.

During high-dose stimulant use, often seen during binge episodes, individuals can experience stimulant-induced psychosis characterized by delusions, paranoid thinking and stereotyped compulsive behavior. Delusional patients require close clinical monitoring and may need short-term treatment with neuroleptics to ameliorate the psychosis. Psychosis is induced more commonly by amphetamine than by cocaine, perhaps because it is difficult to maintain high chronic levels of cocaine in the body. Also, stimulant-induced psychosis in humans is related to the dose and duration of administration of amphetamine and cocaine rather than psychiatric predisposition.

Stimulant withdrawal, which occurs following cessation of chronic cocaine or amphetamine use, can produce a wide range of dysphoric symptoms:

- Following binge use, individuals may initially experience a “crash” period, which is characterized by symptoms of depression, anxiety, agitation and intense drug craving.
- During the intermediate withdrawal phase, individuals may experience fatigue, a loss of physical and mental energy, and decreased interest in the surrounding environment.
- During the late withdrawal phase, individuals may experience brief periods of intense drug craving, such that objects and people in the addicted person’s life can become a conditioned trigger for craving and relapse.

These withdrawal symptoms may be a target for pharmacological agents.”

“Treatment Guidelines for Stimulant Abuse

Treatment of stimulant abuse requires a comprehensive assessment of the patient’s psychological, medical, forensic and drug use history. Moreover, because information obtained from chemically dependent persons may be incomplete or unreliable, it is important that patients receive a thorough physical examination, including blood and supervised urine samples for analysis. The clinician must be aware that polydrug

abuse in common. Patients may ingest large amounts of one or more drugs at potentially lethal doses; therefore, the physician must be aware of the dangers of possible drug combinations, such as cocaine and alcohol or heroin.

Pharmacological intervention may be necessary during stimulant-induced drug states. For example, neuroleptics may be useful in controlling stimulant-induced psychosis or delirium, and anticraving agents with a fast onset of action may be helpful during the early withdrawal period. During the late withdrawal phase, when depression may be present, antidepressants may be an appropriate choice for treatment. Treatment medications can be given on an inpatient or outpatient basis. However, if medications are used for outpatient treatment the clinician must warn the patient of the potential adverse interactions between cocaine and the prescribed medication. For instance, high blood pressure can result from the release of epinephrine by cocaine combined with the reuptake blockade by the tricyclic, although later in the course of treatment, tricyclics decrease the sensitivity of the post-synaptic adrenergic receptors.

Opioids

In general, 2-3 weeks of daily administration of opioids are required to produce a clinically relevant withdrawal syndrome; this period is shorter in individuals who were previously addicted. The nature and severity of withdrawal symptoms upon abstinence from drug use are related to a variety of factors:

Specific drug used – The longer the duration of action of the opioid, the less intense, but longer lasting are the withdrawal symptoms.

Total daily amount used - The larger the amount used daily, the more severe the withdrawal symptoms.

Duration and regularity of use – Although some withdrawal can be observed with even a single dose of opioids, clinically significant withdrawal is usually not seen until a patient has used an opioid daily for 2-3 weeks. Over short periods of time, the severity of withdrawal will increase with the length of time the opioid has been regularly used. After 2-3 months of use, the severity of withdrawal no longer increases. Intermittent use will produce less severe withdrawal.

Psychological Factors – Personality, state of mind and anticipatory anxiety can all affect withdrawal severity.

Signs and symptoms of opioid withdrawal:

Early to moderate symptoms:

Anorexia, anxiety, craving, dysphoria, fatigue, headache, increased respiratory rate, irritability, lacrimation, mydriasis, perspiration, piloerection, restlessness, rhinorrhea, yawning

Moderate to advanced:

Abdominal cramps, broken sleep, hot or cold flashes, increased blood pressure, increased pulse, low-grade fever, muscle and bone pain, muscle spasm, nausea and vomiting.

Detoxification treatments:

Methadone/Buprenorphine treatment – Patients undergoing opioid withdrawal may be stabilized and detoxed using any opioid. To lessen the severity of withdrawal symptoms, a longer acting opioid is generally used to taper patients off of opioid dependence. Methadone is the most commonly used opioid for detoxification, as it has a long half-life, is orally active, and well tested. The partial agonist buprenorphine, which is also a weak kappa opioid receptor antagonist, has also been shown to work well. Being a partial agonist, it has a relatively large margin of safety; drug effects plateau making overdose very unlikely.

Clonidine/lofexidine – Alpha 2 adrenergic receptor agonists have been shown to reduce the severity of some opioid withdrawal symptoms, most likely by decreasing neuronal activity in the locus ceruleus. Thus the general alpha-2 adrenergic receptor agonist clonidine and the A subtype specific alpha-2 adrenergic receptor agonist lofexidine have both been used to help lessen the severity of opioid withdrawal symptoms in patients undergoing detox. They are generally used on their own, after opioid administration has been stopped, rather than in combination with a methadone taper.

Ultra-rapid detox

Detoxification from opioids can be accomplished much more rapidly by precipitating withdrawal with an opioid receptor antagonist such as naloxone or naltrexone. This will induce an immediate and severe withdrawal syndrome. To offset the withdrawal symptoms and make precipitated withdrawal a viable alternative, several techniques for managing withdrawal symptoms have been developed. The first of these uses the alpha-2 adrenergic agonist clonidine to lessen withdrawal symptoms, usually in combination with oxazepam to reduce muscle spasms and insomnia and antiemetics for nausea and vomiting. Using these agents, detoxification can be completed in 2-3 days, and because of the short time period there is a very good completion rate. Alternatively precipitated withdrawal may be done even more rapidly under anesthesia or sedation. Generally, this will be done using naltrexone in combination with propofol anesthetic, the antiemetic ondansetron, the antidiarrheal octreotide, and clonidine and benzodiazepines for the other symptoms. Heavy sedation via midazolam may be used instead of anesthesia. Though this procedure allows one to detoxify rapidly, it is expensive and the use of anesthesia makes it significantly more dangerous than natural withdrawal. Like other detox procedures, both methods have not been shown to produce high rates of long-term abstinence and relapse is likely.

Hallucinogens

Hallucinogens such as LSD produce significant autonomic activity. They can dilate the pupils, increase the heart rate, and produce slight hypertension and hyperthermia. While under the influence, the face may flush, and the deep tendon reflexes quicken. On occasion, piloerection, salivation, nausea, a fine tremor and lacrimation may be noted. In addition, a minor degree of incoordination, restlessness, and visual blurring can occur. A stress response with elevation of 17-hydroxy-corticoids may be present.

Dimethyltryptamine (DMT) also increases heart rate, pupil diameter and body temperature, and DMT and MDMA elevate plasma levels of adrenocorticotropic hormone, cortisol and prolactin. Some of the autonomic effects of the hallucinogens are variable and may be due in part, to the anxiety state of the user. LSD also can cause nausea; nausea and sometimes vomiting are especially noteworthy after the ingestion of mescaline.

In terms of adverse physiological effects, LSD has a very high therapeutic index. The lethal dose in humans has not been determined, and fatalities that have been reported usually are secondary to perceptual distortions with resultant accidental death. Overdose with the psychotomimetic drugs is rare. Instances are known of people surviving 10,000 mg of LSD, 100 times the average dose. Hemiplegia has been reported after taking LSD, possibly a result of the production of vasospasm. There is no generally accepted evidence of brain cell damage, chromosomal abnormalities, or teratogenic effects after the use of the indole-type hallucinogens and mescaline.

Drug interactions involving the hallucinogens do not appear to be an important source of adverse reactions. In some reports, the effects of LSD are reduced after the chronic administration of monoamine oxidase inhibitors or selective serotonin reuptake inhibitor antidepressants such as fluoxetine, whereas the effects of LSD are increased after the chronic administration of lithium or tricyclic antidepressants.

Phencyclidine (PCP)

Diagnosis of PCP or similarly acting arylcyclohexylamine intoxication is based on behavioral changes that occur following ingestion, including belligerence, assaultiveness, impulsiveness, unpredictability, psychomotor agitation, impaired judgement, and impaired social and occupational functioning. Physical findings may include horizontal and/or vertical nystagmus, hypertension, tachycardia, diminished pain sensation, ataxia, dysarthria, muscle rigidity, seizures, and hyperacusis. Low-dose intoxication (5-10mg orally, by snorting or inhaling) induces agitation, excitement, catalepsy, and mutism. Patients with severe PCP intoxication are generally unresponsive and comatose yet their eyes are open. A diagnosis of PCP intoxication should be confirmed with toxicological analysis of blood or urine. Without this confirmation, the diagnosis can be only presumptive at best.

Although not discrete from one another, three stages for PCP intoxication have been described depending on the dosage taken: behavioral toxicity, stuporous stage, and comatose stage. The patient may fluctuate between the stuporous stage and behavioral toxicity in 1-2 hour periods. The comatose stage may last 1-4 days, depending on the dosage of PCP taken and the rate of excretion of the drug. The EEG shows delta wave activity followed by theta wave activity.

The differential diagnosis for PCP intoxication should include head trauma, schizophrenia or acute psychosis, organic brain syndrome, mania, cerebrovascular accident and stupor and/or coma

Management of PCP intoxication

A thorough physical and neurological examination should be performed. Vital signs need to be monitored for laryngeal stridor or respiratory depression and a respirator may be required. Restraints should be avoided; Lahmeyer and Stock reported that the use of restraints may cause rhabdomyolysis with resultant acute renal failure, and Mercy et al identified PCP as a major factor associated with the death of prisoners who were restrained by police. If required, the preferred method of physical restraint for combative patients is total body immobilization by rolling the patient in a sheet. Although the talking down technique has been used to treat acute hallucinogen reactions, this approach should be avoided in PCP intoxicated patients because it may intensify agitation.

Most patients who have mild to moderate symptoms of acute PCP intoxication will improve rapidly. Intoxicated patients should be observed until their mental status has remained normal for several hours. If symptoms continue to diminish and no cognitive impairment is present after 12 hours the patient may be discharged from the ER.

PCP excretion is very pH dependent and acidification of the urine increases the clearance rate of PCP by about 100 fold. Thus, if urine acidification is thought to be safe for the patient, treatment with vitamin C or ammonium chloride may be helpful.

Club Drugs

MDMA is usually ingested orally at a dose of 100-150mg. The onset of effect begins about 20-40 min after ingestion and is experienced as a sudden, amphetamine-like "rush." Nausea, usually mild, but sometimes severe enough to cause vomiting, often accompanies this initial feeling.

The plateau stage of drug effects last 3-4 hours. The principal desired effect, according to most users, is a profound feeling of relatedness to the rest of the world. Most users experience this feeling as a powerful connection to those around them, but this may include the larger world. In general, people taking the drug appear to be less aggressive and less impulsive. Users also experience a drastically altered perception of time and a decreased inclination to perform mental and physical tasks. Although the desire for sex can increase, the ability to achieve arousal and orgasm is greatly diminished in both men and women. MDMA has thus been termed a sensual, not a sexual, drug. In addition, people taking the drug experience mild psychomotor restlessness, bruxism, trismus, anorexia, diaphoresis, hot flashes, tremor and piloerection. The array of physical effects and behaviors produced by MDMA is remarkably similar across mammalian species.

Common after effects can be pronounced, sometimes lasting 24 hours or more. The most dramatic hangover effect is a sometimes severe anhedonia. The hangover effects of MDMA share many similarities with amphetamine withdrawal. MDMA users can experience lethargy, anorexia, decreased motivation, sleepiness, depressed mood and fatigue, occasionally lasting for days. In a few instances, more severe effects have been reported, including altered mental status, convulsions, hypo or hyperthermia, severe changes in blood pressure, tachycardia, coagulopathy, acute renal failure, hepatotoxicity, and death.

Treatment of MDMA intoxication

Generally, keep patient hydrated. Acute MDMA reactions resemble a combination of the serotonin syndrome and neuroleptic malignant syndrome. This is an uncommon but potentially fatal occurrence. Clinicians should be alert to the possibility of these syndromes in any patient who exhibits confusion or impaired sensorium, hyperthermia, muscle rigidity and fever. IV fluids, and measures to lower the patient's body temperature should be taken. Dantrolene sodium is a skeletal muscle relaxant that lessens rigidity and hyperthermia. This medication is given to the patient in a dose of 2-3 mg/kg iv three times/day.