MANAGING THE PATIENT WITH A COCAINE OVERDOSE

2.0 Contact Hours

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MANAGING THE PATIENT WITH A COCAINE OVERDOSE

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OBJECTIVES

When you complete this module, you will be able to:

1. Explain the basic mechanism of action of cocaine.
2. Explain the pathophysiology of cocaine intoxication
3. Identify one sign/symptom each of cardiac, neurologic, pulmonary and musculoskeletal cocaine intoxication
4. Discuss the basic treatment of a patient with cocaine intoxication

BACKGROUND

Cocaine is an alkaloid that is found in the leaves of the coca plant, *Erythroxylon coca*. The plant grows (and is cultivated) extensively in Mexico, South America and the West Indies. It has a long history of use by the indigenous people of the mountainous areas of South America for the prevention of fatigue. It has been used medically since the late 1800s (as a treatment for asthma, syphilis, menstrual pain and alcohol and morphine addiction) and was once an ingredient of Coca Cola. Cocaine is available, but seldom used, as a local anesthetic. As a drug of abuse, it is available as a powder or as small solid pieces ("rocks") of "crack" cocaine (this form of cocaine is called crack because of the cracking and popping sound produced when it is smoked.)[1]

Cocaine is one of the most commonly abused drugs. According to the National Institute on Drug Abuse (NIDA), in 2002, there were more than 2 million current (within one month) users of cocaine; the Drug Abuse Warning Network (DAWN) reported over 125,000 Emergency Department visits associated with cocaine use. In 1999, DAWN reported that cocaine was the number one drug reported in medical examiner reports in 13 metropolitan areas, and was directly responsible for 4864 deaths. The Youth Risk Behavior Surveillance of 2003 reported that 8.7% of the nation's high school students had used some form of cocaine one or more times during their lifetime.[2]

PHARMACOLOGY

Cocaine can be insufflated ("snorted"), injected, smoked or absorbed through mucous membranes. Smoking cocaine is particularly dangerous. When cocaine is snorted (the most common form of use), there is local vasoconstriction that limits its absorption, however cocaine that is smoked is absorbed almost completely. The intravenous route and smoking crack seem to have higher risk for drug dependence. The onset of action is very rapid (almost immediate when it is smoked), and the effects of intoxication last, depending on the route, from 30 minutes to approximately 2 hours. A standard dose of insufflated cocaine is approximately 25-100 mg (although given the purity of the preparation, this can vary widely. A fatal dose via the IV route can be as low as 20 mg and the median fatal dose via insufflation is 500 mg.

Most of a dose of cocaine is metabolized by liver and plasma enzymes while a smaller amount (approximately 20%) is metabolized nonenzymatically. The metabolites produced by enzymatic action are benzoylecgonine and ecgonine methylester. They are both metabolically active (benzoylecgonine has a half-life of 7.5 hours and can cause seizures hours or days after the last use of cocaine.) People with a genetic deficiency in, or a low level of, the enzyme that metabolizes cocaine, plasma pseudocholinesterase, will not metabolize cocaine as quickly or completely and these people are more susceptible to cocaine intoxication (Because organophosphate and carbamate insecticides are potent inhibitors of plasma pseudocholinesterase, cocaine users have occasionally used them in conjunction with cocaine to prolong intoxication.) The half-life of cocaine is 0.5-1.5 hours; the half-lives of benzoylecgonine and ecgonine methyl ester are, respectively, 5-8 hours and 3.5-6 hours. These metabolites are excreted in the urine, and benzoylecgonine can be detected in the urine for 48-72 hours after cocaine use.[3]

Cocaine has many complex pharmacologic effects on the body.[4]

1. Release of norepinephrine

2. Prevention of reuptake of norepinephrine and epinephrine

3. Sensitization of adrenergic receptors to norepinephrine and epinephrine

4. Direct stimulation of the adrenergic nerve terminals

5. Inhibition of dopamine reuptake in the central nervous system

6. Inhibition of reuptake of serotonin

7. Increase in the concentration of the excitatory neurotransmitters aspartate and glutamate

8. Ion channel effects: Cocaine interrupts the movement of sodium through the fast sodium ion channels. This increases membrane stability and prevents depolarization.

9. Vagal nerve stimulation (initially) then reduction of vagal activity

All of these effects play an important part in the clinical picture of cocaine intoxication, *but it is the stimulation of the alpha-adrenergic and beta-adrenergic receptors by catecholamines and cocaine itself that produce the cardiovascular effects that are a prominent ~~a~~ part of the clinical picture of cocaine intoxication.*

Instant feedback: Name three neurotransmitters affected by cocaine.
Answer: Aspartate, dopamine, epinephrine, glutamate, norepinephrine, and serotonin

Instant feedback: What pharmacological property of cocaine makes it useful as an anesthetic?
Answer: Cocaine interrupts the movement of sodium through fast sodium in channels and prevents cell depolarization.

CLINICAL EFFECTS

Cocaine is a dangerous drug. The list of deleterious effects caused by cocaine is seemingly endless and involves almost every organ system. Serious morbidity can happen to the experienced user as well as the first-time user. Cocaine is also tremendously addicting and tolerance develops with long-term use.

Cardiovascular

The cardiac effects of acute cocaine intoxication include:[5]

Tachycardia
Hypertension
Positive inotropic effect
Chest pain: This may be – but not always – caused by myocardial ischemia
Vasoconstriction (the coronary arteries appear particularly susceptible)
Myocardial infarction
Thrombus formation
Aortic dissection and aortic rupture

Note that as a result of the tachycardia and the positive inotropic effect, there is an increased **myocardial oxygen demand** (the tachycardia and positive inotropic effects are due to stimulation adrenergic receptors) and that as a result of the vasoconstriction (also caused by adrenergic stimulation) there is a **decreased oxygen supply.** As the coronary arteries appear to be especially susceptible to the vasoconstrictive effects of cocaine, this imbalance between oxygen demand and oxygen supply, along with other factors, make the patient with cocaine intoxication vulnerable to myocardial ischemia and/or infarction.

Cocaine also causes vagal nerve stimulation, and it affects membrane potential. These effects would result in:

Bradycardia (this is usually of very brief duration)
QT and QRS prolongation
Arrhythmias: both atrial and ventricular arrhythmias have been reported

There are also changes in cardiac function that are the result of *chronic* cocaine use.

Cardiomyopathy caused by high circulating levels of catecholamines
Increased platelet aggregation
Left ventricular hypertrophy
Accelerated atherosclerosis
Endocarditis (seen in intravenous drug users)

Instant feedback: Why are myocardial ischemia and/or infarction likely in the patient acutely intoxicated with cocaine?
Answer: There is an increased demand for oxygen, but there is a decreased supply of oxygen. Also, acute cocaine intoxication can cause thrombus formation.

Instant feedback: Why does cocaine cause tachycardia and hypertension?
Answer: Alpha and beta-adrenergic receptors are stimulated, are sensitized to, and stimulated by, catecholamines.

Myocardial infarction

Myocardial infarction is a well-known and well-described complication of cocaine use. It occurs in approximately 6% of all patients with cocaine-related chest pain.[6] However, the presentation of a patient with a cocaine-related myocardial infarction can be confusing and complex. The standard assessment tools – ECG, laboratory markers and clinical history – that are used to confirm a diagnosis of myocardial infarction appear to be less useful and specific in the patient with a cocaine-related myocardial infarction.

The patients are often young, they do not have a history of atherosclerosis, and a significant percentage do not have coronary artery disease detectable by angiography. Myocardial infarction can happen to the first-time user or to someone who has been using cocaine for years. It can happen shortly after use or days after use. Patients with an infarction cannot be distinguished from patients without infarction based on the onset, severity, location and duration of pain. The one variable that appears to be constant is cigarette smoking; most patients who suffer a cocaine-related myocardial infarction smoke.

The baseline ECG is abnormal in many chronic cocaine users, (the ECG will have ST segment elevation. This is relatively common and is called **early repolarization**) and many patients with cocaine intoxication who are *not* having a

myocardial infarction will present with an ECG that indicates a need for reperfusion therapy (eg, ST-segment elevation of at least 0.1 mV in two or more contiguous leads.) Also, the sensitivity of the ECG in these situations is only 36% and the positive predictive value is only 18%.

Serum creatine kinase concentrations are elevated in approximately 50% of all patients with cocaine intoxication who do *not* have myocardial infarction. This is thought to be due the rhabdomyolysis that is a relatively common feature of cocaine intoxication.

Instant feedback: Why is it difficult to use the ECG to diagnose a cocaine-related myocardial infarction?
Answer: Many patients with cocaine-associated chest pain have an abnormal baseline ECG with changes that would indicate a need for reperfusion therapy, but they are not having a myocardial infarction.

Neurological

Cocaine is a central nervous system stimulant – that is part of its attraction as a drug of abuse – and the typical patient with cocaine intoxication presents with anxiety, agitation, tremors and headache. These effects are distressing and uncomfortable for the patient, but they are transitory and do not cause permanent harm. They are thought to be caused, in part, by inhibition of reuptake of dopamine in the central nervous system.

Unfortunately, cocaine intoxication *can* cause serious, potentially lethal neurological complications. **Seizures** are common; they have been reported in as many as 9% of patients with cocaine intoxication, and their presence increases the risk of morbidity and mortality. They are usually generalized, they are single events, and there are no sequelae. Multiple seizures are uncommon and are often due to intracerebral hemorrhage, a history of seizures, or the effects of a coingestant.

Other neurological effects of cocaine intoxication include **transient ischemic events**, **cerebral infarction, cerebral hemorrhage**, and **subarachnoid hemorrhage**.[7] Some patients who suffer the serious cerebrovascular effects of cocaine have underlying vascular disease, but most do not. Vasospasm and vasoconstriction of the cerebral vasculature are thought to be the causes of these neurologic disasters. Occasionally, patients with cocaine intoxication may present with a depressed level of consciousness and lethargy. This is called the cocaine "wash out" syndrome, and it is thought to be due to depletion of catecholamines. An unusual neurologic effect of cocaine intoxication is dystonic reaction; this has been called "crack dancing."[8]

Instant feedback: Name three characteristics of seizures caused by cocaine.
Answer: They are usually single events, they are generalized and there are no sequelae.

Pulmonary

Pulmonary morbidity is not usually a prominent feature of cocaine intoxication. However, there have been reports of **asthma exacerbations, acute lung injury, alveolar hemorrhage, pneumothorax, pneumomediastinum, and noncardiogenic pulmonary edema.** Smoking crack cocaine can cause **bronchoconstriction.** A specific clinical syndrome associated with smoking cocaine is **crack lung.**[9] **Dyspnea, bronchospasm, pulmonary infiltrates, fever, and hemoptysis** are seen. It is not known if this is due to the cocaine itself, thermal injury, or irritating adulterants.

Hyperthermia

Hyperthermia is caused by the seizure activity and/or increased motor activity (heat generation) and the vasoconstriction (decreased loss) that are common with cocaine intoxication. It may also occur in the absence of seizures; it is postulated that cocaine may affect the thermoregulatory center and may stimulate the liver to convert glycogen to glucose. Hyperthermia is a serious complication. Patients with an elevated temperature often develop seizures, rhabdomyolysis, renal failure and occasionally disseminated intravascular coagulation. Also, there is clinical data that suggests that among the many effects of cocaine intoxication – tachycardia, hypertension, seizures and hyperthermia – hyperthermia is most associated with serious complications and death.[10]

Rhabodmyolysis and renal failure

There are obvious reasons for **rhabdomylolysis** (seizures, increased motor activity, hyperthermia), but rhabdomyloysis *can* occur in the absence of these precipitating factors and in the absence of hypotension or a prolonged loss of consciousness.[11] Approximately one third of patients with rhabdomyolysis caused by cocaine will develop renal failure. (Note: this can be precipitated by rhabdomyloysis, but renal ischemia due to vasoconstriction may contribute.)

Instant feedback: Name three causes of rhabdomyolysis.
Answer: Seizures, hyperthermia, and increased motor activity.

Adulterants/Substitutes

It is common practice to add adulterants to cocaine (this is called “cutting.) This is done to increase profits and at times to simulate the action of cocaine. Common adulterants are local anesthetics, stimulants (amphetamine, caffeine, phencyclidine, methylphenidate), quinine, talc, boric acid, plaster of paris, or cornstarch. Some of these can cause systemic effects and can add to the clinical picture.

Cocaine has many other effects – ophthalmic, hepatic, gastrointestinal, hematologic, reproductive, psychological – but a complete list of all the complications associated with cocaine would be very long and many of these problems are unusual and seldom seen. **It is more important to be familiar with the typical clinical presentation of someone with cocaine poisoning.** Notice that most of the signs and symptoms are the result of a *hyperadrenergic state.*

The patient is typically young and in good health.
The patient is anxious, agitated, tremulous and restless.
Tachycardia and hypertension (usually mild) are common.
Chest pain is common.
Dyspnea is common.
The temperature is elevated.

This clinical picture also can be caused by amphetamine and phencyclidine, drug or alcohol withdrawal, or hallucinogens. However, each of these has distinguishing characteristics that can be used to identify them.

TREATMENT

Most patients with cocaine intoxication do not suffer serious sequelae. However, there is the potential for disaster, and good supportive care is essential to help avoid and treat the more dangerous complications of cocaine poisoning.

Treatment should start with a basic assessment and this should pay particular attention to the vital signs – especially the temperature. Assuming these are stable, do a systems assessment and focus on the cardiovascular, neurologic and pulmonary systems. If the patient is stable, ie, there is no severe hypertension, a normal temperature, there are no serious arrhythmias or severe dyspnea, begin taking a history. Determine how long ago the cocaine was taken and in what form. Determine the pattern of use; do they use cocaine everyday, sporadically, etc. Find out if there were any other drugs taken, and find out what prescription medications the patient uses. Cocaine and ethanol form a metabolite called **cocaethylene** that has effects similar to cocaine but is more toxic. Concurrent use of cocaine and ethanol may increase the risk of sudden death compared to the use of cocaine alone.[12] Drugs that affect the metabolism of epinephrine and norepinephrine – monoamine oxidase inhibitors and tricyclic antidepressants – can aggravate the adrenergic effects of cocaine, and selective serotonin reuptake inhibitors (eg, fluoxetine, paroxetine) and cocaine taken together may result in serotonin syndrome. Nicotine aggravates the toxic effects of cocaine. It causes hypertension and tachycardia, coronary artery vasoconstriction and can contribute to the platelet aggregability caused by cocaine. If the patient is female, find out the date of her last menstrual period.

There is no antidote for cocaine; the treatment is symptomatic and supportive.[13]

Tachycardia: Mild tachycardia does not need treatment unless the patient is hemodynamically compromised, but the patient will be more comfortable – and you can avoid cardiovascular complications – if a rapid heartbeat is controlled. The best treatment is **intravenous benzodiazepines.** The exact mechanism by which these drugs control tachycardia in a patient with cocaine poisoning is not clear (it may be due to a reduction of the central effects of cocaine), but clinical experience has shown that they work. Diazepam 5-10 mg or lorazepam 1-2 mg, repeated as necessary is the standard therapy. Adenosine can also be used.

Hypertension: Mild hypertension can be treated with diazepam or lorazepam. If the patient's blood pressure is severely elevated, phentolamine (an alpha-adrenergic antagonist) or nitroprusside (a peripheral vasodilator) can be used (these are drugs with short half-lives and a short duration of action; this is useful in patients that may become hemodynamically unstable.)

Note: **Beta-blockers should not be used to control tachycardia and/or hypertension caused by cocaine.**[14] Cocaine stimulates beta receptors and alpha receptors. Beta blockade could result in unopposed alpha receptor stimulation and severe hypertension and coronary artery vasoconstriction. Some researchers and clinicians have recommended **esmolol** (a short-acting beta-blocker) and **labetalol** (a drug that is an alpha and beta-blocker), but these should not be used. Esmolol has been shown, regardless of its short duration of action, to cause hypertension in cocaine-toxic patients, and the beta blocking effects of labetalol are much stronger than the alpha blocking effects.

Hyperthermia: This should be treated with conductive and evaporative cooling methods. Agitation and excess motor behavior that contribute to heat production can be treated with benzodiazepines.
Chest pain: Chest pain usually responds well to oxygen and intravenous benzodiazepines; most chest pain due to cocaine is probably musculoskeletal.
Dysrhythmias: Atrial tachyarrhythmias that do not respond to intravenous benzodiazepines can be treated with **verapamil** or **diltiazem**. Ventricular arrhythmias can be treated with **sodium bicarbonate** or **lidocaine**. Sodium bicarbonate can overcome the membrane stabilization cased by the blockade of the fat sodium channels. Lidocaine has a membrane stabilizing effect, as does cocaine, but clinical experience has shown it is safe to use for a patient experiencing ventricular arrhythmias due to cocaine.
Myocardial infarction: Cocaine-associated myocardial infarction is treated with 1) **oxygen**, 2) **benzodiazepines**, 3) **aspirin**, 4) **nitroglycerin** (sublingual and intravenous), 5) **phentolamine** (stimulation of the alpha receptors in the coronary arteries causes vasoconstriction; phentolamine is an alpha-adrenergic antagonist), and 6) **verapamil** (this decreases heart rate and is a negative inotrope.

Thrombolytic therapy has been used for patients with cocaine-associated myocardial infarction, but its use is not universally accepted. The risks (eg, cerebrovascular hemorrhage) are greater for these patients than patients with a non-cocaine related myocardial infarction, it is difficult to make a reliable diagnosis of myocardial infarction in the patient with cocaine intoxication, and patients with a cocaine-associated myocardial infarction have a lower mortality rate. Angioplasty and stenting have also been used successfully. However, although there is evidence that these approaches are safe, neither thrombolytic therapy nor angioplasty have been proven to be efficacious.[15]
Seizures: Seizures are treated with **oxygen** and intravenous **benzodiazepines**. Rhabdomylolysis, fever are treated with standard supportive care.

Instant feedback: Name three common signs/symptoms of cocaine intoxication.
Answer: Anxiety, agitation, tremors, restlessness, chest pain, hypertension, tachycardia, dyspnea, and fever.

Instant feedback: Which is the preferred treatment for a patient with a cocaine-related myocardial infarction, thrombolytics or angioplasty and stenting?
Answer: Both have been used, but there is no data that supports the use of one as opposed to the other.

Body packers/body stuffers

Body packers deliberately ingest tightly wrapped packages of cocaine with the intent to smuggle them. **Body stuffers** ingest packages of cocaine, but this is done hurriedly in an attempt to avoid arrest for possession. These patients are at a tremendous risk; rupture of a sealed package (body packers) or leakage of a poorly sealed package (body stuffers) can release large amounts of cocaine in a short period of time.[16] Asymptomatic patients should have a contrast study to determine how many packages were swallowed and where they are. Activated charcoal and whole bowel irrigation can be used to adsorb drug that is leaking from the packages and to hasten their passage. The patient should be monitored until all the packages have been eliminated. If the patient is symptomatic, emergency surgery may be needed to remove the packages.

Instant feedback: Name three basic treatments for the patient experiencing a cocaine-related myocardial infarction.
Answer: Oxygen, benzodiazepines, aspirin, nitroglycerin, phentolamine, and verapamil

TREATMENT SUMMARY

The “average” clinical presentation of a patient with cocaine intoxication includes central nervous system stimulation, hypertension, tachycardia, fever, dyspnea and chest pain. These effects are due to cocaine’s properties as a central nervous system stimulant and the hyperadrenergic state it produces. There is no antidote. Standard, supportive care is sufficient for most cases, and *basic* care of the patient with cocaine intoxication should include: oxygen, intravenous fluids, benzodiazepines and external cooling. Although there is a definite risk for serious morbidity and mortality, with good supportive care, the patient should recover with no sequelae.

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