Cocaine Intoxication and Hypertension

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Cocaine toxicity has been reported in virtually all organ systems. Many of the adverse effects of cocaine are similar to adverse events that can result from either acute hypertensive crisis or chronic effects of hypertension. Recognizing when the specific disease requires treatment separate from cocaine toxicity is paramount to the treatment of patients with cocaine intoxication.

The initial physiologic effect of cocaine on the cardiovascular system is a transient bradycardia as a result of stimulation of the vagal nuclei. Tachycardia typically ensues, predominantly from increased central sympathetic stimulation. Cocaine has a cardiostimulatory effect through sensitization to epinephrine and norepinephrine. It prevents neuronal reuptake of these catecholamines and increases the release of norepinephrine from adrenergic nerve terminals,[1] which leads to enhanced sympathetic effects. The vasopressor effects of cocaine are mostly mediated by norepinephrine of sympathetic neural origin, and the tachycardic effects of cocaine are mostly mediated by epinephrine of adrenal medullary origin.[2] Cocaine also blocks fast sodium channels, stabilizing the axonal membrane (a local anesthetic-type effect), causing cocaine to have type I antidysrhythmic properties.[3]

Chronic use of cocaine can result in accelerated atherosclerosis and coronary artery disease, and cocaine use is associated with a 7-fold increase of strokes in women and increased risk of myocardial infarction.[4-8] Cocaine use can mimic a hypertensive cardiomyopathy both in terms of acute effects and long-term effects. Cocaine also has a direct myocardial-depressant effect.[9-11] Chronic cocaine use leads to a dilated cardiomyopathy, possibly from recurrent or diffuse ischemia, with subsequent "stunned" myocardium,[11] as well as left ventricular hypertrophy similar to hypertensive heart disease. Cocaine causes aortic dissection and rupture.[12] Most patients with cocaine-induced aortic dissection are chronic cocaine users and have a history of hypertension.

Evaluation of the Patient With Cocaine Toxicity

Patients manifesting cocaine toxicity should receive a complete evaluation, including a history of cocaine use, recognition of signs and symptoms consistent with sympathetic nervous system excess, and evaluation of organ-specific complaints. The emergency department approach to the patient with cocaine intoxication is analogous to that of the patient with hypertension: the treatment should be geared toward the patient's presenting complaint.

When the medical history is clear and symptoms are mild, laboratory evaluation is usually unnecessary. In contrast, if the patient has severe toxicity, evaluation should be geared toward the presenting complaint. Laboratory evaluation may include a CBC count; determination of electrolyte, glucose, blood urea nitrogen, creatine kinase, and creatinine levels; arterial blood gas analysis; urinalysis; and cardiac marker determinations. Increased creatine kinase level occurs with rhabdomyolysis. Cardiac markers are increased in myocardial infarction. Cardiac troponin I is preferred to identify acute myocardial infarction.[13] A chest radiograph should be obtained in patients with cardiopulmonary complaints. An ECG should be obtained in patients with chest pain or cardiovascular complaints. Patients with headache or other neurologic manifestations may require a head computed tomographic scan and lumbar puncture.

Treatment of Cocaine Intoxication

The treatment of the hypertensive patient with cocaine intoxication differs from the approach to other patients who are symptomatic, with acute increases of blood pressure. Major differences stem from the α-adrenergic effects of cocaine, in combination with the relationship between the neuropsychiatric and other systemic complications. Acutely, cocaine results in coronary artery vasoconstriction, tachycardia, hypertension, increased myocardial oxygen demand, platelet aggregation, and thrombus formation.[1,4]

Hypertension and tachycardia caused by cocaine rarely require specific treatment. Resolution of anxiety, agitation, and ischemia will often lead to resolution of the hypertension and tachycardia. When necessary, treatment directed toward the central effects of cocaine, such as benzodiazepines, usually reduce blood pressure and pulse rate. When sedation is unsuccessful, hypertension can be managed with sublingual or intravenous nitroglycerin or intravenous phentolamine.[1,4,7,14-16] One study compared the effects of hypertension and tachycardia, pH, acidosis, seizures, and hyperthermia on cocaine lethality. Only agents that corrected hyperthermia improved survival.[17] Thus, isolated treatment directed toward hypertension did not improve outcomes.

Studies in the cardiac catheterization laboratory have provided the evidence-based approach to patients with cocaine-

Table. Treatment summary for cardiovascular effects of cocaine.

Medical Condition	Treatments
Acute coronary syndrome	Oxygen
	Diazepam 5–10 mg IV or lorazepam 2–4 mg IV
	Aspirin 325 mg
	Nitroglycerin 1/150 sublingual ×3 every 5 min, followed by an infusion titrated to a mean arterial pressure reduction of 10% or relief of chest pain.
	Phentolamine 1 mg IV; repeat in 5 min
	Verapamil 5–10 mg IV
	Heparin 60 units/kg bolus, followed by 12 units/kg/h
	Percutaneous intervention (angioplasty and stent placement) or fibrinolytic therapy for STEMI
	Glycoprotein IIb/IIIa inhibitors
Hypertension	Observation
	Diazepam 5–10 mg IV or lorazepam 2–4 mg IV titrated to effect
	Phentolamine 1 mg IV; repeat in 5 min
	Nitroglycerin or nitroprusside continuous infusion titrated to effect
Pulmonary edema	Lasix 20–40 mg IV
	Nitroglycerin infusion titrated to blood pressure
	Consider phentolamine or nitroprusside
Neuropsychiatric Symptoms	
Anxiety and agitation	Diazepam 5–10 mg IV or lorazepam 2–4 mg IV titrated to effect
Seizures	Diazepam 5–10 mg IV or lorazepam 2–4 mg IV titrated to effect
	Phenobarbital 25–50 mg/min up to 10–20 mg/kg
Intracranial hemorrhage	Neurosurgery consultation, avoid β-blockers for blood pressure control

STEMI, ST-segment-elevation myocardial infarction.
Adapted from Hollander JE, Hoffman RS. Cocaine. In: Goldfrank LR, Flomenbaum NE, Lewin NA, et al, eds. *Goldfrank's Toxicologic Emergency*. 7th ed. McGraw Hill; 2002:1011.

induced coronary vasoconstriction. These studies can be extrapolated to the patient with cocaine-induced hypertension. Phentolamine vasodilated constricted coronary arteries back to baseline.[18] According to these data, case reports, and anecdotal experience, most guidelines recommend α-adrenergic antagonists (phentolamine) for the treatment of cocaine-associated acute coronary syndrome.[1,4,7,14] It makes sense to use this agent for treatment of cocaine-induced hypertension, when necessary.

Nitroglycerin has been shown to also reverse coronary artery spasm while it relieves cocaine-induced chest pain.[16,19] Benzodiazepines, which have a salutary effect on the hyperdynamic effects of cocaine, also relieve chest pain.[19] Benzodiazepines are similar to nitroglycerin with respect to effects on cardiac dynamics and left ventricular function.[19]

The precise role of calcium channel blockers for the treatment of cocaine toxicity is unclear. Cocaine-intoxicated animals pretreated with calcium channel blockers have had favorable effects with respect to survival, seizures, and cardiac dysrhythmias in some studies but not in others. Studies in the cardiac catheterization laboratory show that verapamil reverses cocaine-induced coronary artery vasoconstriction; hence, calcium blockers can likely be used safely to treat blood pressure when necessary.[20]

Beta blockade results in an unopposed α-adrenergic effect, which leads to vasoconstriction and an increased blood pressure.[21,22] Therefore, the use of β-adrenergic antagonists for the treatment of cocaine toxicity is contraindicated.[1,4,7,23] Labetalol does not reverse coronary artery vasoconstriction in humans.[24] Nitroglycerin or phentolamine is a better option to achieve vasodilation.

The other cardiovascular end-organ manifestations of cocaine toxicity may necessitate specific intervention. The general strategies for managing catecholamine excess, myocardial ischemia, and hypertension are summarized in the Table and allow for case-specific approaches to individual medical complications of cocaine.

SUMMARY RECOMMENDATIONS

Asymptomatic hypertension associated with acute cocaine intoxication rarely requires treatment.

When treatment is necessary, benzodiazepines are the first-line treatment for hypertension and tachycardia associated with acute cocaine intoxication.

Persistent severe hypertension in the presence of chest pain associated with acute cocaine intoxication requires treatment with sublingual nitroglycerin or intravenous phentolamine.

β-Blockers and labetalol are contraindicated in the treatment of hypertension associated with cocaine toxicity.

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