Mini-Review Article

Cocaine, Marijuana, Hypertension and Cardiovascular Effects

Mohammad Hassan Ghadiani*

Department of Nephrology, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Abstract

Cocaine is used by more than 14 million people worldwide, about 0.3 percent of the global population age is 15 to 64 years. After alcohol, cocaine is the most common cause of acute drug-related emergency department visits in the United States. Cocaine consumption is more frequently associated with acute cardiovascular illness. Cocaine stimulates α_1, α_2, β_1 and β_2 adrenergic receptors through increased levels of norepinephrine and a lesser extent epinephrine. The cardiovascular effects of cocaine are thought to be similar and regardless to the route of consumption. An acute coronary syndrome is the most common cardiac problem including myocardial ischemia and infarction even in young persons without atherosclerosis, aortic dissection and rupture, arrhythmias, ventricular tachycardia and fibrillation, asystole and finally sudden death. Other cardiovascular effects that caused by cocaine include coronary artery aneurysm, palpitation, sinus tachycardia, increased systemic vascular resistance and hypertension crisis, left ventricular hypertrophy, myocarditis, cardiomyopathy, myocardial fibrosis, bundle branch block, heart block, supraventricular arrhythmia, accelerated atherosclerosis, hypotension, bradycardia and infective endocarditis among intravenous users.

Cocaine by three mechanisms cause ischemia: 1. increased myocardial oxygen demand, 2. decreased coronary blood flow due to coronary artery vasoconstriction and spasm and 3. Coronary artery thrombosis via activation of platelets, stimulation of platelet aggregation and potentiation of thromboxane production.

Keywords: Cocaine, Cardiovascular ischemia, Hypertension, Arrthythmia

***Corresponding Author:** Mohammad Hassan Ghadiani, Department of Nephrology, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: mhghadiani1346@gmail.com

Please cite this article as: Ghadiani MH. Cocaine, Marijuana, Hypertension and Cardiovascular Effects. Novel Biomed. 2015;3(3):155-9.

Introduction

Cocaine is the most common cause of acute drug related emergency department visits after alcohol, and is currently the most frequent cause of drug related deaths reported by medical examiners in the United States[1].

Cocaine related disorders remain an important public health concern today, with continued high rates of legal, psychiatric, medical and social problems[2]. Drug use disorders are believed to result from the complex interplay of cultural, environmental, familial and neurobiological influences[2]. Its widespread use is attributable to the following[1]: Its ease of administration, ready availability of relatively pure drug, its relatively low cost and misperception that its recreational use is safe.

Individuals with cocaine abuse have higher rates of major depressive and antisocial personality disorders[2]. Males are about 1.5 to 2 times more than females have report cocaine abuse in any form[2].

Cocaine (benzoyl methyl ecgonine) is a natural alkaloid and in all its forms is a product of the leaves of the plant Erythroxylon coca[1,3,4]. It is well established that cocaine directly produces changes in dopaminergic neurotransmission[2,5]. By binding to

monoamine transporters, cocaine inhibits reuptake of serotonin and norepinephrine as well as dopamine[2,5]. It is available in two forms, the hydrochloride salt and the freebase[1]. Cocaine hydrochloride is prepared by dissolving the alkaloid in hydrochloric acid to form a water soluble powder or granule, with can be taken orally, intravenously or intranasally[1]. The freebase form is manufactured by processing the cocaine with ammonia or sodium bicarbonate[1]. Unlike the hydrochloride form, freebase cocaine is heat-stable so that it can be smoked (crack)[1]. Cocaine hydrochloride is well absorbed through all mucous membranes; therefore users may achieve a high blood concentration with intranasal, sublingual, vaginal or rectal administration[1].

The route of administration determines the rapidity of onset and duration of action[1]. Smoking and intravenous use of cocaine produce the most rapid pharmacologic and subjective onset of action[2]. The euphoria associated with smoking crack cocaine occurs within seconds and is short-lived and is more strongly correlated with rate of increase in serum levels than with absolute amount of cocaine ingested[1,2]. Crack cocaine is the most potent and addictive form of the drug[1].

Cocaine metabolites can be detected in blood, hair, sweat, saliva and urine. In clinical practice, urine and blood cocaine testing are most useful[2,3]. Cocaine is metabolized by serum and liver cholinesterase to water-soluble metabolites, primarily benzoyl ecgonine and ecgonine methyl ester which are excreted in the urine[1]. Because cocaine serum half-life is only 45 to 90 minutes, it is detectable in blood or urine only for several hours after its use[1]. However its metabolites persist in blood or urine for 24 to 36 hours after its administration[1].

In individuals who use cocaine in temporal proximity to the ingestion of ethanol, hepatic transesterification leads to the production of a unique metabolite, cocaethylene[1]. Similar to cocaine, cocaethylene blocks the reuptake of dopamine at the synaptic cleft, thereby possibly potentiating the systemic toxic effects of cocaine[1]. In experimental animals, cocaethylene is more lethal than cocaine[1]. In humans, the combination of cocaine and ethanol causes a substantial increase in myocardial oxygen demand[1]. The concomitant use of cocaine and ethanol is associated with a higher incidence of disability and death than either agent alone[1]. Individuals presumably dying of a combined cocaine-ethanol overdose have much lower blood cocaine concentrations than those presumably dying of a cocaine overdose alone, thereby suggesting an additive or synergistic effect of ethanol on the catastrophic cardiovascular events that are induced by cocaine[1].

When applied locally, cocaine acts as an anesthetic by virtue of its inhibition of membrane permeability to sodium during depolarization, thereby blocking the initiation and transmission of electrical signals[1]. When given systemically, it blocks the presynaptic reuptake of norepinephrine and dopamine, thereby producing an excess of these neurotransmitters at the site of the postsynaptic receptor.

Discussion

Consumption of cocaine is more frequently associated with acute rather than chronic cardiovascular illness[1]. As cocaine abuse has increased in frequency, the number of cocaine related cardiovascular complications, including angina pectoris, myocardial infarction, cardiomyopathy and sudden death has increased[1].

Cocaine may cause transient but significant hypertension that may cause strokes and serious cardiac damage[1]. Most cocaine related deaths are associated with myocardial injury similar to that seen from catecholamine excess and aggravated by acute hypertension[1]. Chronic cocaine use does not appear to induce hypertension but may be associated with chronic renal disease[1].

Cocaine stimulates α1, α2, β1 and β2 adrenergic receptors through increased levels of norepinephrine and to a lesser extent epinephrine[1]. The cardiovascular effects of cocaine are thought to be similar and regardless to the route of consumption[1].

An acute coronary syndrome is the most common cardiac problem including myocardial ischemia and infarction even in young persons without underlying heart disease and atherosclerosis, aortic dissection and rupture, arrhythmias, ventricular tachycardia and fibrillation, asystole and finally sudden death[1].

Chest pain is the most common cardiovascular complaint of patients seeking medical assistance following an hour of cocaine abuse[1]. Occasionally

some individuals note the onset of symptoms several hours after the administration of the drug when the blood cocaine concentration is low or even undetectable (due to increasing the concentrations of the cocaine major metabolites)[1]. Approximately 6% of those who come to the emergency department with cocaine associated chest pain have enzymatic evidence of myocardial necrosis[1]. In subjects who are considered to be at low risk for myocardial infarction (MI), the risk of infarction increases 24-fold during the first 60 minutes after cocaine use[1]. About 50% of patients with cocaine related MI has no angiographic evidence of atherosclerotic coronary artery disease[1].

Cocaine by three mechanisms cause ischemia: 1. increased myocardial oxygen demand, 2. decreased coronary blood flow due to coronary artery vasoconstriction and spasm and 3. coronary artery thrombosis via activation of platelets, stimulation of platelet aggregation and potentiation of thromboxane production and increase concentrations of plasminogen activator inhibitor.

The presence of premature atherosclerotic coronary artery disease may provide a nidus for thrombosis[1]. In vitro studies have shown that cocaine causes structural abnormalities in the endothelial cell barrier, increase the expression of endothelial adhesion molecules, thereby favoring leukocyte migration, all of which are associated with atherogenesis (1).

By virtue of its sympathomimetic effects, cocaine increases the three major determinants of myocardial oxygen demand: heart rate, left ventricular wall tension and left ventricular contractility[1]. At the same time, ingestion of even small amounts of the drug causes vasoconstriction of the epicardial coronary arteries (so-called inappropriate vasoconstriction), in that myocardial oxygen supply decreases as demand increases[1]. Cocaine induces vasoconstriction in normal coronary arteries but exerts a particularly marked vasoconstrictive effect in diseased segments[1]. As a result, cocaine users with atherosclerotic coronary artery disease probably have an especially high risk for an ischemic event after cocaine use[1]. In addition, cocaine causes increased endothelial production of endothelin (a potent vasoconstrictor) and decreased production of nitric oxide (a potent vasodilator) which also may promote vasoconstriction[1].

Other cardiovascular effects of cocaine include coronary artery aneurysm , palpitation, increased systemic vascular resistance and hypertension crisis, left ventricular hypertrophy, myocarditis, left ventricular diastolic and/or systolic dysfunction, congestive heart failure, dilated cardiomyopathy, myocardial fibrosis, accelerated atherosclerosis, hypotension and infective endocarditis among intravenous users[1,6].

Cocaine abuse accounts for less than 1% of aortic dissection and is associated with crack cocaine use[1]. Cocaine related dissection is most typical in young, African, American and hypertensive men who smoke cigarettes. In one study, 38 patients with acute aortic dissection, 14 (37%) were related to cocaine use with an average interval from cocaine use to the onset of symptoms of 12 hours (range 0 to 24 hours)[1].

The intravenous use of cocaine appears to be accompanied by a greater risk of bacterial endocarditis than the intravenous administration of other drugs[1]. The reason for this matter is unknown, but several hypotheses have been proposed[1]: The increases in heart rate and systemic arterial pressure may induce valvular injury that predisposes to bacterial invasion, Cocaine immunosuppressive effects may increase the risk of infection, The manner in which cocaine is manufactured may increase the risk of endocarditis.

In contradistinction to the endocarditis associated with other drugs, the endocarditis of cocaine users more often involves the left sided cardiac valves[1].

Cocaine may adversely affect left ventricular systolic function by several mechanisms[1]: myocardial ischemia or infarction, microscopic changes of subendocardial contraction band necrosis and cardiomyopathy following the profound repetitive sympathetic stimulation similar to that observed in patients with pheochromocytoma, myocarditis due to concomitant infectious or other agents which has been seen on occasion in intravenous cocaine users, cocaine increases the production of reactive oxygen species, alters cytokine production in the endothelium and in circulating leukocytes, induces the transcription of genes responsible for changes in the composition of myocardial collagen and myosin and induces myocyte apoptosis in experimental animals.

Aside from the effects of long-term cocaine use on

myocardial performance, it may cause an acute deterioration of left ventricular systolic and/or diastolic function or transient apical ballooning (also called takotsubo cardiomyopathy or broken heart syndrome)[1]. In some subjects, this deterioration results from neurohormonal, metabolic and/or acid-base disturbances that accompany cocaine intoxication, whereas in others it may be caused by a direct toxic effect of the drug[1].

Cocaine may affect the generation and conduction of cardiac impulses by several mechanisms[1]:

Its sympathomimetic properties may increase ventricular irritability and lower the threshold for fibrillation. It inhibits action potential generation and conduction similar to class 1 antiarrhythmic agents (i.e. it prolongs the QRS and QT intervals) as a result of its sodium channel-blocking effects. Cocaine increases the intracellular calcium concentration which may result in ventricular arrhythmias. It reduces vagal activity, thereby potentiating its sympathomimetic effects.

In many cases, the dysrhythmias ascribed to cocaine occur in the setting of profound hemodynamic or metabolic derangements, such as hypotension, hypoxemia, seizures or myocardial ischemia or infarction[1]. Long-term cocaine use is associated with increased left ventricular mass and wall thickness which are known risk factors for ventricular arrhythmias[1]. Cardiac dysrhythmias and conduction disturbances reported with cocaine use include[1]:

Sinus tachy or bradycardia, Supraventricular tachycardia, Bundle branch block, Complete heart block, Accelerated idioventricular rhythm, Ventricular tachycardia or fibrillation, Torsades de pointes, Brugada pattern (right bundle branch block with ST-segment elevation in leads V1-3 and Asystole.

Pulmonary edema may develop abruptly after an individual smokes the free alkaloid form of cocaine (free base) or its heated bicarbonate precipitant (crack)[7].

Similar to cocaine, cigarette smoking induces coronary arterial vasoconstriction[1]. The deleterious effects of cocaine on myocardial oxygen supply and demand are exacerbated substantially by concomitant cigarette smoking[1]. Following concomitant cocaine use and smoking , heart rate and systemic arterial pressure increased markedly and coronary arterial vasoconstriction is more intense than with either alone[1].

Cannabis is the most widely used illegal drug in the world and is the fourth most commonly used psychoactive drug among adults in the United States, after caffeine, alcohol and nicotine[2,8]. Cannabis preparations are obtained from the plant cannabis sativa[2,8]. The most common cannabis preparations are marijuana and hashish[2]. The primary psychoactive constituent in cannabis is tetrahydrocannabinol (THC)[9-11].

The acute toxicity of cannabis and cannabinoids is very low[2]. Within 3 to 15 minutes after cannabis is smoked or swallowed, THC increases heart rate by 20 to 50 percent for up to 3 hours[2]. Blood pressure also increases while the person is sitting and decreases on standing[2]. In healthy young users these cardiovascular effects are unlikely to be of any clinical significance because tolerance develops to the effects of THC, and young, healthy hearts will only be mildly stressed[2]. These changes in heart rate and blood pressure may be less benign in older adults with hypertension, cerebrovascular disease, and coronary atherosclerosis[2]. Cannabinoids can be detected in the head hair, pubic hair, urine, sweat, saliva, and blood of users[3]. Cannabinoids are stored in the fat cells of the body and so can remain in the body for an extended period compared to other drugs[2]. In some cases, it may be detectable in urine for up to 11 weeks after use[2].

Conclusion

Cocaine, Marijuana and other street drugs cause multiple medical, legal, psychiatric and social problems and related disorders remain an important public health concern today, therefore prevention of these drug abuses is necessary.

References

1.Bonow RO, Mann DL, Zip D, et al. Braunwald,s Heart disease. Ninth ed., Elsevier Saunders. 2012;1254:1631-4.

2. Sadock BJ, Sadock VA, Ruiz P, Kaplan, Sadock S. Comprehensive text book of psychiatry. Ninth ed., Lippincott Williams and Wilkins. 2009;1309-30.

3. Sadock BJ, Sadock VA. Kaplan and Sadock Synopsis of psychiatry. Tenth ed., Lippincott Williams and Wilkins. 2007;1294:421-7.

4. Cannabis use disorder: Epidemiology, comorbidity and

pathogenesis. Uptodate, Version 19.3
5. Shannon MW, Borron SW, Burns MJ. Clinical management of poisoning and drug overdose.4th ed., Elsevier Saunders. 2007;747-65.
6. Irwin RS, Rippe JM. Intensive care medicine. Fifth ed., Lippincott Williams and Wilkins. 2003;1429-31.
7. Cooper DH, Krainik AJ, Lubner SJ, et al. The Washington manual of medical therapeutics. 32nd ed., Lippincott Williams and Wilkins. 2007:753.
8. Hoffman RS, Nelson LS, Howland MA, et al. Goldfrank,s manual of toxicologic emergencies.Mc Graw Hill. 2007;633-9,675-8.
9. Longo DL, Fausi AS, Kasper DL. Harrison,s principles of internal medicine.18th ed., Mc Graw Hill. 2012;3556-8.
10. Andreoli TE, Benjamin I, Criggs RC., et al. Cecil essentials of medicine.8th ed., Elsevier Saunders. 2010;1230-1.
11. Kaplan NM, Flynn JT. Clinical hypertension. Ninth ed., Lippincott Williams and Wilkins. 2006;455-76.