Effect of cocaine on the cardiovascular system

Summary

- Chest pain, the most common complaint of cocaine users presenting to the Accident and Emergency (A&E) Department, could be caused by many cocaine-induced cardiovascular complications
- Cocaine-induced myocardial infarction is the most common cardiovascular complication of cocaine use and can occur even in first-time users
- Cocaine has contrasting effects: an indirect stimulating effect on the autonomic nervous system whilst simultaneously having a local anaesthetic effect, which causes problems such as dysfunction of the left ventricle
- Cocaine indirectly causes enhanced stimulation of adrenergic receptors which interferes with the electrical stability of the heart
- Intravenous drug use can cause infection of the heart valves which can lead to systemic problems

Introduction

The most common presenting complaint from cocaine users when they go to A&E is chest pain. Underlying this pain could be many possible cocaine-related cardiovascular complications. Cocaine can cause sudden death even in first-time users. Of all the drug-related deaths in the UK in 2008, 235 of these were due to cocaine, which increased by 20% from 2007. 2 As deaths from cocaine are increasing, it is important to consider the physiological changes that cocaine causes. This will have implications in a clinical context; investigations and initial treatments in the A&E department can be improved, as can the management of cocaine-induced heart diseases.

Method

For this review, MetaLib (an electronic journal database) and Google Scholar were used to search first for the cardiovascular effects of cocaine use. Key words included cocaine, cardiovascular complications, coronary arteries, intravenous drug use and the heart. From these reviews, specific topics for further study were selected. The most reliable articles were those that have been cited many times, so this was taken into account when selecting articles for this review.

Pharmacology

Cocaine is extracted from the leaves of the Erythroxylon coca plant. 1 Cocaine comes in two main forms; cocaine hydrochloride is a powder that is formed by dissolving the extract in hydrochloric acid, and freebase or ‘ crack’ cocaine is produced by using ammonia or sodium bicarbonate to remove the hydrochloride.

Cocaine can be inhaled (crack cocaine can be melted so it can be smoked) or administered by nasal, sublingual, intravenous (IV), rectal, and vaginal routes. 1 This is because cocaine is easily absorbed through almost all body mucous membranes. The peak effect, onset and duration of action of the drug vary with route of administration. Compared with IV injection, the other routes of administration, i. e. those absorbed through mucous membranes, result in a slower onset of action and a later peak effect, but a longer duration of action (see Appendix, table 1).

Clinical presentation

The most common cocaine-related symptoms in the A&E department are chest pain, dyspnea (shortness of breath), palpitations (unusually strong heart beat) and syncope (transient loss of consciousness, i. e. fainting). 1 There are many possible explanations for this chest pain, some of which are explained by complications in the lungs and musculoskeletal system, but for this review I will focus only on the cardiovascular complications.

Myocardial ischemia and infarction

Myocardial ischemia, also known as angina, occurs when blood flow to the heart is reduced. 3 Myocardial infarction (MI) occurs when blood supply to an area of heart muscle is suddenly lost; causing damage that leads to a heart attack. 4 MI is the most common cardiac complication of cocaine use and first-time users are just as likely to be affected as addicts. Most patients will develop chest pain almost straight after administration, but MI has been reported up to 15 hours after cocaine use. 5

There are many mechanisms that have been proposed to explain cocaine-induced MI. Firstly, it is thought that coronary thrombosis is caused by alteration to platelet and endothelial cell functions during vascular spasm. 6 Clots in the coronary arteries will reduce or even stop blood flow to the heart. Another way that blood flow to the heart is reduced is coronary artery vasoconstriction. In a study7 of 45 patients, cocaine hydrochloride was administered intra-nasally in an experimental group, compared with a control group where saline was administered. They found that the diameter of the left coronary artery decreased by 8% to 12% in the experimental group, compared to no change in coronary artery diameter in the control. A

reduction in coronary artery diameter means that oxygen supply to the heart is decreased. Oxygen supply can also be decreased by atherosclerosis – damage and inflammation in the vessels leads to the build-up of lipids, cholesterol, calcium, and cellular debris (collectively known as a plaque) within the vessel wall. 8 Plaque formation in the coronary arteries leads to obstruction of the lumen, causing disrupted blood flow and therefore less oxygen supply to the heart. Cocaine-induced coronary artery vasoconstriction and accelerated atherosclerosis reduce oxygen supply to the heart, whilst simultaneously oxygen demand is increased because cocaine increases heart rate and systemic arterial pressure. 5 Therefore, the supply and demand of oxygen to the heart are unbalanced, leading to myocardial ischemia and infarction.

It is also thought that cocaine can induce a programmed cell death called apoptosis in myocardial cells. Cocaine-induced apoptosis has been demonstrated in human coronary artery cells. 9 This could disrupt blood flow to the heart, leading to myocardial infarction. A study of MI in rats found that during the first 6 hours after the occlusion of a coronary artery, apoptosis accounted for more than 90% of the dying cells. 10 Apoptosis occurring after MI can leave scarring, acting as a predisposing factor for cardiovascular complications. The use of animal studies predicts the response in humans, but further investigation needs to be carried out to confirm these mechanisms. Apoptosis is a highly controlled process, therefore a better understanding of its role in MI could lead to better management and preventative measures for cardiovascular complications.

Cardiomyopathy and myocarditis

In terms of damage to heart muscle (cardiomyopathy), a study in Florida diagnosed left ventricular (LV) dysfunction in 6 out of 84 asymptomatic apparently healthy cocaine users after 2 weeks of abstinence from cocaine. 11 In the 6 cases identified in the study, the dysfunction was unsuspected after routine evaluation. Even though there were not many cases (only 7% of the patients studied had LV dysfunction), the significance of this matter in clinical diagnosis still needs to be studied further.

Ventricular dysfunction may result from the toxic effect of cocaine on cardiac muscle or myocarditis. Myocarditis is an inflammation of the heart muscle, 12 which in this case is caused by the introduction of infections to the body when cocaine is used intravenously. Cocaine blocks the re-uptake of catecholamines (hormones produced by the adrenal glands, including norepinephrine and dopamine)13 at the synapses of the central and peripheral nervous systems. 14 The synaptic concentration of catecholamines is increased, enhancing stimulation of Î²-adrenergic receptors in the heart muscle and vascular smooth muscle. 14 This leads to a series of enzyme-controlled reactions that result in an excess of calcium in the myocardial cells14 which can damage the heart cells.

Arrhythmias

Non-IV, recreational use of cocaine has been found to affect the normal rhythm of the heart. 15 Cocaine-induced adrenergic stimulation interferes with the electrical stability of the heart. An abundance of catecholamines leads to enhanced stimulation of the Î±-adrenergic receptors in the heart. A series of enzyme-controlled reactions lead to increased levels of calcium in

the heart muscle. 5 Increased levels of calcium can cause oscillations of membrane voltage – leading to contraction of the heart even in diastole (when it should be resting). 16

Evidence shows that any intervention that causes an increase in cardiac nerve activity makes cardiac arrhythmias more likely. For example, exercise or psychological stress decrease the ventricular fibrillation (VF) threshold (i. e. the current necessary to induce VF) and increase the likelihood that cardiac arrhythmias will occur. 17 A study on mongrel dogs18 found that cocaine does cause arrhythmias when under stress. In the control, ischemia was induced in the dogs by occluding one of the left coronary arteries, then the dogs underwent an exercise stress test – this failed to elicit ventricular arrhythmias. Conversely, 12 of the 13 animals developed ventricular arrhythmias when the test was repeated after administration of cocaine. This has important implications in the clinical setting – history taking is important when dealing with a cocaine user as exercise before onset of pain could suggest a cardiac arrhythmia.

Infective endocarditis

Endocarditis is an infection that affects the endocardium (the tissue that lines the inside of the heart chambers). The infection usually involves one or more of the heart valves. 19 Infective endocarditis (IE) occurs in 2% to 5% of IV drug users each year; far more often than it occurs in patients with other cardiovascular risk factors. 20 Staphylococcus aureus (S. aureus) is the bacteria responsible in more than 50% of cases. 20 It is still unknown how S. aureus infects structurally normal valves with no previous damage. It is thought that repeated injections of foreign or infective material may damage

the valves or cause non-specific valvulitis (inflammation of a valve). 21 Risk factors for IE in IV drug users include immunosuppression, HIV infection and frequent injection (at least daily). 22

The clinical presentation of IE in IV drug users depends on the infected valve or the organism causing the infection. A heart murmur is usually present in adults with IE, but may not be present when the cause is IV drug use. The symptoms include fever, dyspnea, pleuritic chest pain, and cough. 22 Complications of IE can include congestive heart failure because of infection-induced valvular damage, and embolism of fragments of bacterial growths can cause MI. 23 A more common complication of IE is systemic embolism (obstructions in multiple blood vessels). The emboli associated with IV drug use are fragments of the bacterial growths from the valves which break off and are spread throughout the body in the blood. Systemic embolism commonly involves the spleen, causing splenic abscess. The kidney, the liver, and the iliac or mesenteric arteries can also be affected. 23

Aortic rupture

Cocaine-induced aortic rupture, also known as aortic dissection, is caused by a large increase in systemic arterial pressure. 5 As previously discussed, cocaine causes arterial vasoconstriction and an excess of catecholamines in the blood, resulting in intense stimulation of the muscle of the heart and blood vessels. This, combined with an increased heart rate and increased contractility of the heart, causes a great deal of stress on the walls of the aorta. 24 These high pressures lead to rupture of the aorta, which is far more likely to occur in a patient who already has weakened vessels, e. g. someone with other cardiovascular risk factors present (chronic hypertension, obesity,

etc). However, aortic rupture can also occur in a previously healthy patient, as cocaine-induced hypertension can weaken the walls of the aorta and cause an aortic rupture later on, perhaps with chronic use of cocaine. An example demonstrating the complications of long-term use of cocaine is a case study25 of a 58-year old man who had been injecting cocaine subcutaneously (under the skin) for several years was diagnosed with aortic rupture after presenting with an onset of abdominal pain five minutes after injection, and hypertension. The implications of this study are that management of cocaine-induced heart disorders must include regular monitoring of the heart, paying particular attention to the aorta.

Conclusion

Cocaine is a dangerous drug that causes many lethal cardiac complications. The presentation of chest pain indicates the possibility of many underlying complications, each of which is multifactorial. This results in a very broad differential diagnosis, stressing the importance of a detailed drug history in this situation – long-term use of cocaine needs to be identified. The effects of cocaine need to be seriously considered in young patients with minimal risk factors for heart disease presenting with chest pain.

A few of the mechanisms referred to in this review are not yet confirmed; further research is being carried out to discover how exactly S. aureus associated with IE damages the structurally normal and undamaged heart valves, and why apoptosis of heart cells is important in MI. Further studies will provide conclusive evidence of the mechanisms involved in the cardiac complications of cocaine.