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REVIEW

The emergency care of cocaine intoxications

M.P. Vroegop[1], E.J. Franssen[2], P.H.J. van der Voort[3], T.N.A. van den Berg[4], R.J. Langeweg[4], C. Kramers[5*]

[1]Emergency Department and [5]Department of Pharmacology-Toxicology (233), Radboud University Medical Centre, Nijmegen, the Netherlands, Departments of [2]Pharmacology, [3]Intensive Care and [4]Medicine, Onze Lieve Vrouw Gasthuis, Amsterdam, the Netherlands,
[*]corresponding author: e-mail: c.kramers@pharmtox.umcn.nl

ABSTRACT

Cocaine is frequently used, especially among adolescents and by men between the age of 25 and 44. Many of them are able to use cocaine in normal day-to-day life, without any problems.[1] Reduced prices of cocaine and other recreational drugs such as MDMA (ecstasy) and gamma hydroxybutyrate (GHB) has led to an increased incidence of intoxications with these drugs.[2] Since the production of cocaine is illegal, it may be impure and mixtures with other drugs such as atropine may occur. The treatment of patients with an acute cocaine intoxication can be complicated. Combination of cocaine with other drugs results in clinical pictures which are difficult to discriminate and that may have important consequences for treatment.

KEYWORDS

Cocaine, cocaine intoxication, emergency room

INTRODUCTION

Intoxications with drugs of abuse are part of day-to-day care at the emergency department (ED). Among these, intoxications with cocaine are especially challenging. Firstly, cocaine in itself may lead to life-threatening complications and is secondly frequently used in combination with other drugs, which may lead to a wide variety of clinical pictures with important consequences for treatment. In this review we describe four cases of patients who visit the ED because of a cocaine intoxication, with several different complications and co-intoxications. After some background information and a review of the literature about cocaine, we advise on the do's and don'ts in case of an acute cocaine intoxication.

CASE REPORTS

Patient A

A 39-year-old man with a history of alcohol abuse arrived at the ED with haematemesis after he had been found by a friend. He was very agitated, had a sinus rhythm of 126 beats/min and a blood pressure of 220/117 mmHg. Physical examination showed no abnormalities except for mydriasis. Electrocardiography (ECG) showed left ventricular hypertrophy, ST depression in the inferior (II, III and aVF), lateral (I, aVL, V_5 and V_6) and anterior leads (V_1 to V_4). Laboratory analysis showed a decreased haemoglobin level (3.6 mmol/l), and elevated troponin I (3.16 µg/l). Coagulation tests, arterial blood gas analyses, electrolytes, liver enzymes and creatinine were within the normal range. Urine tox-screen for cocaine was positive. Gastroscopy revealed a bleeding ulcer in the proximal duodenum, which was treated by local injection of adrenaline. Further initial management consisted of supplementary oxygen, acetylsalicylic acid, labetolol, nitroglycerin, diazepam and pantoprazole. The clinical course was uneventful and the patient could be discharged after one week in a good clinical condition.

Patient B

A 39-year-old man was found subcomatose in the lavatory of a care centre for drug addicts. He reported he had used cocaine and heroine, two bottles of strong liquor, five tablets of 5 mg diazepam and five tablets of 25 mg levopromazine. He complained of chest pain, pain in the epigastrium and in his left jaw region. He was taking naltrexone 1 x 50 mg, loperamide 8 x 2 mg, diazepam 2 x 5 mg, levomepromazine 3 x 25 mg, pantoprazole 1 x 40 mg and mirtazepine 1 x 30 mg. The physical examination showed a blood pressure of 93/50 mmHg and a heart rate of 110 beats/min. The ECG showed a sinus rhythm without signs of ischaemia, infarction, or left ventricular hypertrophy. Arterial blood gas analysis, while receiving oxygen (5 litres/min), showed

a respiratory acidosis: pH 7.25, pO_2 30.5 kPa, pCO_2 7.2 kPa, HCO_3 22.8 mmol/l. Further laboratory results showed an alcohol concentration of 1.2‰, but no other abnormalities. He lost consciousness in the emergency room and was intubated and mechanically ventilated. Neither naloxone nor flumazenil were administered. The patient was admitted to the intensive care unit (ICU). His vital functions were supported and treatment with acetylsalicylic acid and nitroglycerine was initiated. The next day his physical condition had improved and he was discharged after consultation of a psychiatrist.

Patient C

A 27-year-old man presented to the ED in the early morning. He was sweating, his hands were shaking, he complained of a sore throat and was agitated. During the last week he had had a flu-like illness. The evening before presentation he had snorted cocaine and consumed 15 alcoholic beverages. He used escitalopram because of depression. The physical examination showed a temperature of 40.3°C, heart rate of 130 to 160 beats/min, a blood pressure of 200/110 mmHg and a breathing frequency of 25/min. He had mydriasis, an inflamed throat and inspiratory wheezing. Blood analysis revealed an increased white blood count, elevated CRP and mildly elevated liver enzymes. Blood alcohol concentration was 2.2‰. The ECG showed sinus tachycardia, without further abnormalities. The patient was treated with oxazepam and metoprolol. He was seen by the ear, nose and throat specialist who concluded that the patient had a bacterial pharyngitis and prescribed amoxicillin/clavulanic acid. After five hours of observation his temperature decreased and the heart rate and blood pressure normalised. He was allowed to leave the ED and was further evaluated at the outpatient clinic.

Patient D

A 35-year-old man became unconscious and in shock under obscure circumstances in a hotel room in the centre of Amsterdam. His friend phoned 112. At arrival of the ambulance the patient was in ventilatory and circulatory arrest and cardiac arrest without heart action on the ECG. After resuscitation in the ambulance the circulation was restored and the patient was brought to the ED. He was treated with naloxone and flumazenil, since a mixed intoxication with drugs of abuse was suspected. After intubation, the patient was admitted to the ICU for mechanical ventilation and for medical support to improve the circulation. For 24 hours, the patient was kept at 32 to 34°C to reduce post-anoxic cerebral damage. Urine tox-screen was positive for cocaine and heroin. In addition a toxic diazepam serum level was found (1200 µg/l; therapeutic level 125 to 750) and the blood ethanol concentration was 0.8‰.

The patient remained in a comatose state after normothermia. In addition, no cerebral activity was observed, including absence of activity on the electroencephalography (EEG) at several readings. Therefore the treatment was discontinued and the patient died the fourth day after he was admitted.

EPIDEMIOLOGY

Cocaine is a widely used drug, especially in North America (6.35 million people, 2% of the population >14 years), South America (2.74 million people, 1% of the population) and Western Europe (3.4 million people, 1% of the population.[3] Also in the Netherlands cocaine is used throughout society. In Amsterdam cocaine use is about four times higher than in the rest of the country.[1] The prevalence of people who had ever used cocaine has increased from 2001 to 2005, but first-time use of cocaine is decreasing. The percentage of recent and actual users was stable in this period.[1] The percentage usage in 12 to 18 year olds was also stable between 1996 and 2003. Between 2001 and 2005 the average age of recent users increased. Use of cocaine is most prevalent in 25- to 44-year-old men. It is especially used in trendy clubs and pubs.[1] Cocaine is also popular among users of heroin. About 70 to 90% of heroin addicts also smoke cocaine ('crack').[1]

PHARMACOLOGY

Cocaine, benzoylmethylecgonine ($C_{17}H_{21}NO_4$) is an alkaloid, extracted from the leaves of Erythroxylon coca.[4] Cocaine increases the activity of monoamine neurotransmitters in the central and peripheral nervous system by blocking reuptake pumps (transporters) of dopamine, norepinephrine and serotonin.[3] The concentration of these neurotransmitters in the presynaptic cleft is enhanced. In addition cocaine modulates preprodynorphin and the µ-, en κ-receptors of the endogenous opiate system.[5] All this leads to a feeling of increased energy, alertness, intense euphoria and decrease of tiredness, appetite and sleep.[3] Unwanted effects such as fear, irritation, panic attacks, paranoia, impaired judgement, delusions, disturbance of sleep, weight loss and hallucinations occur with increased doses, or a more efficient route of administration.[3] It also leads to an increase in heart rate and blood pressure, to mydriasis and diaphoresis as a consequence of stimulation of the sympathetic nervous system. Cocaine causes arrhythmias.[6] It acts as a local anaesthetic by inhibition of the membrane permeability of sodium ions during depolarisation. This leads to blocking of both initiation and transmission of electric signals.[5] Cocaine can be smoked, snorted or used

intravenously.[3,4] It is absorbed readily through all mucosae. The peak effect occurs between 1 to 90 minutes, depending of the route of administration. The initial half-life varies between seconds and 20 minutes after inhalation, intravenous administration or snorting respectively. After oral use the half-life is three hours. There are two forms of cocaine. Cocaine base ('crack', 'freebase') may be smoked. Because of its relatively low melting temperature (98°C), it evaporates before degradation takes place. It is relatively insoluble and therefore it cannot be used intravenously. The cocaine salt cannot be smoked, for it does not melt until 195°C. Therefore the molecule already degrades before evaporation takes place. The cocaine salt is well soluble and it may be administered intravenously or it may be snorted.[3,4] After intravenous administration the effect lasts for about 15 to 30 minutes, after snorting one hour and after oral use three hours.[7] Cocaine is hydrolysed in the liver by carboxyesterases. This results in the formation of the inactive benzoylecgonine.[3] The majority of metabolites are excreted in the urine.[3]

LIFE-THREATENING COMPLICATIONS OF A COCAINE INTOXICATION

Cocaine and the heart

Cocaine induces tachycardia, hypertension and an increased systemic vascular resistance due to an increase of sympathetic activity both directly on the heart and indirectly via the central nervous system.[3,4] This leads to an increased cardiac oxygen consumption, whereas oxygen supply decreases because of coronary vasoconstriction, eventually leading to cardiac ischaemia as was seen in patient A.[8] In addition activation of platelets results in thrombus formation.[9-11] The most frequently occurring cardiac complications of cocaine are angina pectoris, myocardial infarction, acute cardiac death, complicated acute arterial hypertension, myocarditis, cardiomyopathy, aortic rupture or dissection and left ventricular hypertrophy as was seen in patient B.[8] Blocking of sodium channels of myocytes results in decreased electric conduction and arrhythmias. Also without myocardial infarction, syncope or acute heart death may occur (patient D).[12] The typical patient with cocaine-related myocardial infarction is a young man, without cardiovascular risk factors other than smoking.[4] The relative risk of myocardial infarction is 23.7 times (95% CI 8.5 to 66.3) within 60 minutes after cocaine use and does not appear to be related to amount, route of administration or frequency of use.[13] At the ED most cocaine users complain about chest pain.[4,14] The incidence of myocardial infarction in these patients is about 6%. This suggests that these symptoms are not usually related to myocardial necrosis.[11,15]

In patient A the myocardial necrosis is also facilitated by the severe anaemia caused by a bleeding duodenal ulcer. This is infrequently seen after cocaine use and is caused by severe gastrointestinal vasoconstriction leading to mucosal ulceration.

Cocaine and hyperthermia

The autonomic adaptation of elevated body temperature consists of skin vasodilation and perspiration.[16] Normal behavioural adaptation results in evading heat and refraining from physical activities.[17] Cocaine results in an increase of the core temperature, decrease of heat perception and decrease of perspiration and skin circulation. Moreover the agitation hampers the normal behavioural response. All of these may lead to fatal hyperthermia.[16] Patient C had an elevated body temperature caused by an infection. However, cocaine-induced hyperthermia should always be considered in a patient with fever in the context of cocaine use. These patients should be aggressively cooled and one should be aware of complications such as rhabdomyolysis and diffuse intravascular coagulation.

CLINICALLY RELEVANT COMBINATIONS WITH COCAINE

Cocaine and alcohol

Most cocaine users also drink alcohol (patients B and C).[18] Cocaine has a sobering effect after ingestion of alcohol, leading to use of cocaine in the context of excessive alcohol consumption. Transesterification of cocaine and alcohol, catalysed by carboxyesterase 1, leads to the formation of the active metabolite cocaethylene, instead of the inactive hydrolysis product benzoylecgonine.[18] As cocaine, cocaethylene has a central stimulating effect. So co-ingestion of alcohol leads to an increase and longer duration of the effect of cocaine.[19] The combination leads to a further increase in heart rate and blood pressure and increased myocardial oxygen consumption.[20] Cocaethylene is associated with a 40-fold increase in the risk of cardiac events and 25-fold the risk of acute cardiac death.[21,22] Patients who die as a consequence of the combined use of cocaine and alcohol have lower blood cocaine concentrations than patients dying after the use of cocaine alone. This suggests that there is an additive or synergistic effect of alcohol on the severe cardiovascular effects of cocaine.[21,23] Lastly, the combination decreases the feeling of drunkenness and increases cocaine-induced euphoria.

Cocaine and heroin

Combined cocaine/heroin intoxications are not uncommon at the ED (patient B and D). In about 50% of the cases heroin is used in combination with cocaine,

alcohol or other drugs (usually benzodiazepines).[24,25] The combination of cocaine and heroin leads to clinical pictures which are difficult to interpret and have important consequences for treatment. Naloxone is an effective and potentially lifesaving antidote for opiate intoxications. However, it is not without side effects.[26] The administration of naloxone to a patient with a co-intoxication of an indirect sympathicomimetic, such as cocaine, can lead to severe complications. Firstly, it may lead to potentially life-threatening sympathicomimetic toxicity because the inhibiting effect of the opiate is suddenly reversed.[27] Secondly, the arrhythmogenic effect of naloxone may be synergistic with cocaine.[28] So, in the context of a co-intoxication with cocaine, the potential benefit of naloxone should be weighed against its possible harm. In many cases of comatose patients after heroin/cocaine overdose it is better to observe the patient and if necessary support the ventilation. The same is true for co-ingestion of cocaine with a benzodiazepine. Administration of flumazenil may precipitate seizures, agitation, sympathetic activity and thus cardiac complications.

THE TREATMENT OF AN ACUTE COCAINE INTOXICATION

In most instances treatment of a cocaine intoxication is supportive. The challenge for the physician in the ED is to identify patients at risk who would benefit from a specific intervention. All patients with an acute coronary syndrome, but especially young man without other risk factors than smoking, should be asked about cocaine usage. First-line treatment of a patient with cocaine-related chest pain compatible with myocardial ischaemia and ST-segment elevation consists of administration of oxygen, and sublingual nitroglycerin or verapamil. If there is no response, immediate coronary angiography should be performed. Both nitroglycerin and verapamil have been shown to reverse cocaine-induced hypertension, coronary arterial vasoconstriction, and tachycardia.[29] Beta-blockers (especially non-selective β-blockers) are relatively contraindicated in cocaine-associated acute coronary syndrome. However, in clinical practice they are frequently used in this situation as was the case in patients A (labetalol) and C (metoprolol). Beta-receptor blockade causes unopposed α-receptor stimulation which may lead to aggravation of coronary arterial vasoconstriction and systemic hypertension.[30] Some authors advise labetalol, a combined α- and β-blocker. However, labetalol is a non-selective β-blocker with only modest α-blocking properties. Thrombolysis should only be given when a thrombus has been shown on angiography or if pharmacological treatment has failed and angiography is not possible.[3] Administration of naloxone and flumazenil should be avoided, since they may lead to severe complications.

CONCLUSION

The emergency care of cocaine intoxications may be challenging. Cocaine is frequently used and its use is not always readily apparent, since users may deny cocaine usage. Moreover, it is frequently combined with other substances such as heroin and benzodiazepines, which may mask some of the cocaine effects. An acute cocaine intoxication may be lethal due to cardiovascular complications or hyperthermia. Alcohol increases the cardiovascular toxicity of cocaine. In the treatment of an acute cocaine intoxication administration of a benzodiazepine has a prominent place, whereas β-blockers are contraindicated. In the case of combined use of cocaine with heroin or benzodiazepine administration of naloxone or flumazenil may be dangerous.

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