Open Access Maced J Med Sci **electronic publication ahead of print,**
published on March 22, 2017 as https://doi.org/10.3889/oamjms.2017.046

ID Design 2012/DOOEL Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences.
https://doi.org/10.3889/oamjms.2017.046
eISSN: 1857-9655
Case Report

Multi–System Complications after Intravenous Cocaine Abuse

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Citation: Petkovska L, Chibishev A, Stevcevska A, Smokovski I, Petkovski D, Antova E. Multi–System Complications after Intravenous Cocaine Abuse. Open Access Maced J Med Sci. https://doi.org/10.3889/oamjms.2017.046

Keywords: cocaine toxicity; intravenous application; hyperthermia; seizures; acute renal insufficiency; hepatotoxicity.

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Received: 25-Dec-2016; **Revised:** 25-Feb-2017; **Accepted:** 26-Feb-2017; **Online first:** 22-Mar-2017

Funding: This research did not receive any financial support.

Competing Interests: The authors have declared that no competing interests exist.

Abstract

BACKGROUND: Use and abuse of cocaine are associated with numerous adverse effects, independent of the route of administration. More severe conditions of poisoning, however, are observed after cocaine intravenous administration.

AIM: We present a case of severe poisoning after violent intravenous injection of cocaine, but with a good outcome.

CASE PRESENTATION: Cocaine was intravenously (i.v.) administered in 16-years old female patient as a homicide attempt. Shortly after that, patient experienced series of generalised tonic-clonic seizures, was highly febrile (40^0C), somnolent, agitated, presenting with tachycardia, tachypnea and with increased blood pressure 150/90 mmHg. Neurologic status, lumbar puncture and computerised tomography (CT) of the brain were without remarks. Electroencephalogram (EEG) was characterised with signs of diffuse encephalopathy, and acid-base analyses resulted in metabolic acidosis. Urine screening revealed the presence of cocaine and benzodiazepines. The patient presented with signs of the hepatic lesion, acute renal insufficiency (ARI), and increased D-dimers resulting from activated fibrinolysis. The patient was discharged in stable general condition after being hospitalised for 23 days.

CONCLUSION: Intravenous abuse of cocaine results in overdose and serous multi-system complications requiring multidisciplinary diagnostic and intensive therapeutic approach.

Introduction

Cocaine abuse is one of the most frequent reasons for visits to emergency centres. Patients are usually complaining of nausea, vomiting, chest pain, tachycardia, tremor, fever, dyspnea, seizures. Most of the overdosed patients are recovering fast and are responding well to medical interventions, due to short cocaine half-life [1]. Cocaine abuse in older patients or patients with other chronic diseases such as hypertension, chronic renal insufficiency, and pulmonary or heart diseases, results in deterioration of the background disease and prolonged hospital treatment [2]. Cocaine overdose can occur independently of administration route. However, the risk of overdose and the fatal outcome is higher after intravenous administration of cocaine. Smoking and intranasal administration are coming next regarding risk of overdose and fatal outcome [1].

Fatal cocaine overdose is most frequently associated with seizures, cardiac arrhythmia, respiratory insufficiency, stroke, hyperthermia and renal insufficiency [1-3]. Cocaine toxicity may not be dose-specific, particularly in regular cocaine use [1]. Despite cocaine tolerance, users may be cocaine sensitised and even lower doses may cause anaesthetic effects, anxiety, seizures and other toxic effects [4, 5].

The aim of this study was to present a case of severe poisoning after violent intravenous injection of cocaine, but with a good outcome.

Case report

The sixteen-year-old female patient suddenly lost consciousness under undetermined conditions and felt in the school yard, presenting with series of tonic-clonic seizures, and was hospitalised in the nearest hospital shortly after that. At admission, the

patient was highly febrile (40^0C), experienced series of tonic-clonic seizures, presented with an altered mental status that led to a coma. The family provided information the girl was suffering from epilepsy after a childhood trauma. The patient was transferred to neurology department on day 3. At admission at neurology department, she was somnolent, afebrile, presenting with tachycardia and blood pressure of 150/90 mmHg, with absent lateralization and meningeal signs.

Laboratory analyses resulted in normal glycaemia, complete blood count, electrolytes and proteins. Degradation products were increased: BUN 44.9 mmol/l and creatinine 272 μmol/l. Lumbar puncture excluded the presence of meningo-encephalitis - clear cerebrospinal liquor with cells 5, albumin 0.23 g/l, glucose 4.1 mmol/l, lactates 1.92 mmol/l. Chest radiography depicted bronchopneumonia on the right side. Computer tomography of the brain was without remarks. EEG was pathologically altered with continuously diffuse and bilateral presence of high voltage slow delta waves.

Toxicological urine analyses (high-performance liquid chromatography–HLC) were positive for cocaine and benzodiazepines. On day 6, the patient was transferred to the University clinic of toxicology. At admission at toxicology clinic, the patient was still somnolent, confused, agitated and disoriented, afebrile, tachypneic (28 respirations per minute) and without seizures. ECG was characterised with sinus rhythm, the rate of 105 per minute, normal axis. Echocardiography was normal. She still had injection marks in the left cubital vein. Blood assays showed leukocytosis, haemoglobin values from 121 to100 g/l, while the platelets increased from 149 x 10^9 to 667 x 10^9 in few days. Hemostatic analyses revealed thrombocytosis with strongly activated secondary fibrinolysis. Prothrombin time (PT) was 13 seconds, activated Partial Thromboplastin time was 31 seconds, Thrombin time was 16 seconds, and D-dimers were higher than 4500, and anticoagulant treatment was prescribed. Highest values of hepatic enzymes were: AST 190 U/l, ALT 482 U/l, demonstrating a hepatic lesion. Virus marker analyses excluded hepatitis A, B or C virus, and HIV infection. Creatinine kinase (CK) value on day 6 of intoxication (day 1 of admission at toxicology clinic) was 640, CK-MB 45, LDH 1344, and myoglobin 125 ng/ml, confirming a rhabdomyolysis. Signs of hepatic lesion and rhabdomyolysis are shown in Table 1.

Table 1: Laboratory findings - signs of hepatic lesion and rhabdomyolysis

Parameters	Day 1	Day 3	Day 6	Day12
ALP (U/L)	125	90	77	79
AST (U/L)	190	54	35	31
ALT (U/L)	482	290	135	31
CPK (U/L)	640	196	238	168
CK-MB (U/L)	45	36	22	18
LDH (U/L)	1344	705	778	401
Myoglobin (ng/ml)		120		65

The patient was diagnosed with acute renal insufficiency (ARI). Highest values of degradation products were: BUN 49.6 mmol/l, creatinine 757 mmol/l, uric acid 733 mmol/l. Two hemodialyses were performed with polyuric phase afterwards, followed by stabile electrolytes levels and gradual normalisation of BUN and creatinine values. Signs of renal failure are shown in Table 2.

Table 2: Laboratory findings – signs of renal failure

Parameters	Day 1	Day 2	Day 3	Day 4	Day 6	Day 8	Day 12
Na (mmol/L)	131	135	137	138	147	141	146
K (mmol/L)	4.2	3.2	3.3	3.2	3.8	3.7	3.8
Urea (mmol/L)	49.6	45	20	9.4	8.0	7.5	2.0
Kreatinin (mmol/L)	757	752*	380*	273	184	90	60
Ac. Uricum (mmol/L)	733		402	268			
Diuresis (ml/day)	2000	1350	2500	3900	4500	3500	3000

* hemodialysis.

Urine analysis demonstrated the presence of proteins, blood, and lots of erythrocytes in the urine sediment, 6-7 leucocytes, 1-2 hyaline cylinders, epithelial cells and urate crystals. Ultrasonography of abdomen demonstrated cholelithiasis, increased kidneys (130 x 70 mm tight, 135 x 72 mm left) with edematous parenchyma up to 38 mm in diameter, without signs of calculus or obstruction in urodynamics, reflecting the ARI. Control ultrasonography revealed kidneys with normal dimensions and parenchyma up to 25 mm.

Acid-base analysis at admission at toxicology clinic demonstrated normosaturation, hypoxemia and hypocapnia. Metabolic acidosis was present, compensated with respiratory alkalosis (pH 7.37, pCO_2 2.92 kPa, pO_2 11.30 kPa, sO_2 96.5%, HCO_3 13.1 mmol/l, BE -9.9, BE ecf -1.2). Control acid-base analysis demonstrated normosaturation, hypoxemia and hypocapnia accompanied by non-compensated respiratory alkalosis (pH 7.46, pCO_2 4.01 kPa, pO_2 10.17 kPa, SO_2 96.1%, HCO_3 21.8 mmol/l, BE -0.5, BE ecf -2.2).

Control chest radiography revealed recovering bronchopneumonia on the right side. No pathogen bacteria were found in the sputum. Pneumoslide confirmed the presence of Influenza A IgG antibodies. Blood culture was sterile. Psychiatric examination revealed the presence of stress reaction.

The patient was treated with benzodiazepines, crystalloid infusions, a third-generation cephalosporin, fluoroquinolone, electrolytes, anticoagulant treatment, oxygen therapy, hemodialysis, hepatoprotective treatment, iron-substituting treatment, Ca channel blockers, vitamins, isogroup plasma and erythrocytes. The patient was discharged in stable general condition after being hospitalised for 23 days, with normal blood pressure, normal renal function and normal transaminase activity.

Discussion

Cocaine, also known as benzoylmethylecgonine, is a potent central nervous system stimulant inhibiting the catecholamine reuptake, increasing the sympathetic activity of central nervous system and stimulating the activity of adrenergic nerve endings to norepinephrine. It is the most widely used recreational drug after cannabis [6]. Cocaine is used by insulation, injection and smoking of so-called crack cocaine. Numerous cocaine associated complications are described, both dependent and independent of the route of administration. Some complications are dose–independent and can be life-threatening, such as acute myocardial infarction with or without atheromatous coronary disease, ventricular dysrhythmia, renal infarction, bowel infarctions, pulmonary dysfunctions, subarachnoidal haemorrhages, hepatic insufficiency, renal insufficiency, etc. [5].

Most fatal cases associated with recreational use of cocaine are observed after intravenous administration. Sixty-eight fatal cases were reported after cocaine use, although 29 of them also used other drugs, such as heroin, and 24 subjects died as a result of the toxic effects of cocaine, shortly after its intravenous application [7].

Cocaine overdose caused hyperthermia and increased blood pressure that could be life-threatening [8]. Arrhythmia and lethal outcome from acute myocardial infarction are due to the blocking effect of cocaine on myocardial sodium channels [9].

Cocaine often causes seizures in non-epileptic patients and causes deterioration in patients with previous history of seizures. Alvaro Pascual-Leone (1990) reported 474 patients with medical complications associated with acute cocaine intoxication. Out of 403 patients without a previous history, seizures occurred in 32 (7.9%) patients. Most patients had single generalised seizures caused by crack-cocaine or after intravenous administration, unrelated to other neurologic deficit. Out of 71 patient with a history of non-cocaine related seizures, 12 (16.9%) presented with cocaine-induced seizures, most of them multiple and of the same type as in the previous history. Forty-four patients with cocaine-induced seizures presented with brain atrophy as confirmed by CT and EEG [10, 11]. Seizures are considered to be caused by certain cocaine metabolites: Thirty to fifty percent of cocaine is metabolised through hepatic esterases and plasma pseudocholinesterases, resulting in the formation of ecgonine methyl ester. Spontaneous non-enzymatic hydrolysis of remaining 30-40% results in the formation of benzoylecgonine. Both metabolites are hydrosoluble, metabolically active and may increase blood pressure. Benzoylecgonine, with a half-life of 7.5 hours, can induce seizures several hours to several days after its last use [12]. On the other hand, increased motor activity with a concomitant vasoconstriction that decreases heat loss may result in hyperpyrexia.

Authors studying EEG alterations in patients with toxic cocaine levels, reported non-specific changes of generalised deceleration of theta and delta activity [13]. Since EEG is a test of brain function, diffuse abnormal patterns are indicative of diffuse brain dysfunction, i.e. encephalopathy [14]. Electroencephalogram of our patient demonstrated diffuse and bilateral high voltage slow delta waves.

Hepatic lesions occur several hours to several days after an acute cocaine overdose, most frequently associated with other medical complications. In self-limiting cases, recovery is fast, and transaminases are normalised within 1-2 weeks [15, 16]. Cases of acute fulminant hepatitis with lethal outcome are also reported. Silva MD et al. (1991) reported 39 patients with acute intoxication and rhabdomyolysis. In 23 (59%) patients, biochemical signs of hepatic dysfunction were reported. In 16 of those, ALT values were above 400 U/l, associated with hyperpyrexia, hypotension, Disseminated Intravascular Coagulation (DIC) and ARI. Fatal outcome occurred in seven of those patients. Authors concluded that reasons for hepatic dysfunction are multi-factorial, and its presence identifies patients with significant morbidity and mortality. Histopathological analyses demonstrate central-lobular and mid-zonal coagulation necrosis with marked fatty infiltration of periportal hepatocytes without cholestasis, fibrosis or damage of biliary channels [17, 18].

Cocaine-induced ARI is most frequently associated with rhabdomyolysis. Reasons for rhabdomyolysis are sympathetic hyperactivity, trauma, seizures and hyperpyrexia [19-21]. David Roth (1988) reported 39 patients with rhabdomyolysis after cocaine abuse. Thirteen (33%) of them developed ARI, and six of this group have died. Patients with ARI presented with hyperpyrexia, seven of them developed DIC, and 11 presented with hepatic lesion [21]. Acute renal insufficiency after cocaine intoxication can also occur without rhabdomyolysis. Authors reporting such cases are elucidating ARI by cocaine-induced ischemia through intensive intra-renal vasoconstriction [22-25]. Cocaine-induced vasoconstriction is associated with blocking of norepinephrine reuptake and release of adrenal catecholamines [23, 26]. Ischemia caused by intensive intra-renal vasoconstriction results in medullar hypoxia and tubular dysfunction [23]. In our case, ARI was induced by rhabdomyolysis. Initial increased CK values at admission in our institution, i.e. on day 6 of the intoxication, were recorded. It is well known that CK reaches its peak value after two-three days, and then falls by 50% every 48 hours, indicating that CK values were much higher on day 2. Nevertheless, ischemia and renal vasoconstriction could not be

excluded as additional reasons for acute renal insufficiency.

Metabolic and respiratory acid-base abnormalities are common in cocaine intoxication. Stevens et al. (1994) evaluated acid-base analyses in 156 cocaine intoxications: most of them (52%) were with normal pH 7.35-7.45, 33% had metabolic acidosis with HCO_3 14 ± 6 mmol/l. Respiratory alkalosis was reported in 15% of patients, resulting from tachypnea and low $_PCO_2$. Both acidosis and alkalosis were associated with various clinical presentations: chest pain, shortness of breath, altered mental status, trauma, seizures, unrelated to the route of cocaine administration [27]. Other authors reported severe lactic acidosis in a patient with acute cocaine intoxication and excessive muscular activity, successfully sedated, with muscle paralysis and mechanical ventilation. Lactic acidosis could cause life-threatening arrhythmia, autonomous instability and cardiac arrest [28, 29].

Nutt D et al. (2007) studies substances that are abused and concluded that cocaine is second in causing dependence and adverse effects, right after heroin [29].

Presented case of severe intoxication after intravenous administration of cocaine is first in our institution and our country. It confirms that almost every organ or system can be affected by the cocaine toxicity and suggests the need of complex diagnostic and therapeutic approach. This is especially important because there is still no available specific antidote for cocaine. The medical community should be aware of the potential complications of cocaine use, in particular about the high morbidity after intravenous administration, and of the minor difference between the recreational and toxic cocaine dose.

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