Forensic Science International 227 (2013) 52–59

Contents lists available at SciVerse ScienceDirect

Forensic Science International

journal homepage: www.elsevier.com/locate/forsciint

Cocaine in sudden and unexpected death: A review of 49 post-mortem cases☆

Jennifer L. Pilgrim [a,*], Noel Woodford [a,b], Olaf H. Drummer [a,b]

[a] Department of Forensic Medicine, Monash University, Victoria, Australia
[b] Victorian Institute of Forensic Medicine, 57-83 Kavanagh Street, Southbank 3006, Victoria, Australia

ARTICLE INFO

Article history:
Available online 13 September 2012

Keywords:
Cocaine
Fatality
Cardiotoxicity
Comorbidities
Concomitant drug use

ABSTRACT

Cocaine is a potent sympathomimetic drug that is associated with cardiotoxicity, including ventricular arrhythmia, systemic hypertension, acute myocardial infarction and left ventricular hypertrophy. The use of cocaine in Australia has risen steadily since the late 1990s. What remains unclear in the literature is whether cocaine-associated death can occur in the absence of other contributing factors, such as concomitant drug use or natural disease. A search was conducted on the National Coroners Information System database, to identify all deaths occurring in Victoria, Australia, between January 2000 and December 2011, where cocaine or its metabolites were detected by post-mortem toxicological analysis. All cases were closed by the Coroner. These cases were examined with regards to case circumstances, pathology and toxicology results, and coronial findings, to determine the prevalence of cardiotoxicity and the involvement of cocaine in the deaths compared with other contributing factors. There were 49 cases where cocaine, benzoylecgonine, ecgonine methyl ester, methylecgonine or cocaethylene, were detected in the 11-year period. The individuals ranged in age from 16 to 70 years (median 30). There were 36 males. In 22 cases the cause of death was determined to be drug toxicity, 22 were external injury and 5 were attributed to natural disease. The concentration of cocaine in the cases was relatively low (range 0.01–3 mg/L, median 0.1 mg/L). Cocaine metabolites were detected frequently in blood and urine: benzoylecgonine (46 cases); ecgonine methyl ester (12 cases); cocaethylene (8 cases); and methylecgonine (9 cases). Opioids were commonly detected (23 cases), in addition to amphetamines (15 cases), ethanol (17 cases) and benzodiazepines (12 cases). Of the 43 cases receiving a full autopsy, there were 14 cases involving significant heart disease. This included coronary artery disease (11 cases), an enlarged heart (5 cases), myocarditis and contraction band necrosis. Cocaine is detected relatively infrequently in Victorian coronial cases. However it appears to be associated with a significant degree of cardiotoxicity, particularly coronary artery disease and ventricular hypertrophy, independent of cocaine concentration.

1. Introduction

Cocaine is a potent sympathomimetic drug deriving from the leaves of the *Erythroxylon coca* plant, which grows primarily in South America. It is available as the hydrochloride salt used in nasal insufflation (most common in Australia), or the free-base 'crack' used in smoking, with street purity ranging from 1% to over 90% [1,2]. Cocaine possesses a half-life of between 0.5 and 1.5 h and is metabolized to partially active metabolites benzoylecgonine and ecgonine methyl ester [2]. Cocaethylene is also found as metabolite in cocaine users consuming alcohol. This metabolite is associated with more toxic effects than alcohol or cocaine used alone [3].

The most serious consequences of cocaine use are the cardiac and cerebrovascular complications. The increase in adrenergic activity along with the local anesthetic effect caused by sodium inhibition results in an increase in myocardial contractility, heart rate (up to 34%), systemic arterial pressure (up to 15%), and myocardial oxygen demand due to vasoconstriction, with only a limited or fixed supply. The transient flux of calcium across the cell membrane also may be independently altered by cocaine [4]. Cocaine-related fatalities have been linked to a number of cardiac events including ventricular arrhythmias, tachycardia, systemic hypertension, acute myocardial infarction, left ventricular hypertrophy and/or acute coronary syndrome (ACS) [5]. These effects are independent of the cocaine dose or administration route [6]. Pre-existing coronary atherosclerosis, particularly of the left anterior descending coronary artery, is also associated with an increased risk of death in cocaine users [7].

☆ This paper is part of the special issue entitled "The 50th Annual Meeting of the International Association of Forensic Toxicologists (TIAFT)". June 3–8, 2012, Hamamatsu, Japan. Guest edited by Adjunct Professor Einosuke Tanaka and Associate Professor Masaru Terada.

* Corresponding author at: Department of Forensic Medicine, Monash University, 57-83 Kavanagh Street, Southbank 3006, Victoria, Australia. Tel.: +61 3 9684 4444.
E-mail address: jennifer.pilgrim@monash.edu (J.L. Pilgrim).

0379-0738/$ – see front matter © 2012 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.forsciint.2012.08.037

The use of cocaine in Australia has risen steadily since the early 2000s [8]. It was reported that in 2010, 2.1% of the population had recently used the drug, compared with 1.6% in 2007. Cocaine users are predominantly male, aged between 20 and 29 years, residing in the state of New South Wales. However the proportion of females also using the drug has risen significantly in recent years [9].

Given its increasing use and the number of cocaine-associated deaths in Australia, it is important to examine the toxicity of this drug and discern whether cocaine-associated death can occur in the absence of other contributing factors, such as use of other drugs or natural disease. This study examines a cohort of individuals where cocaine or its primary metabolite benzylecgonine was detected by post-mortem toxicological analysis, to determine the involvement of this potent stimulant drug in sudden and unexpected death.

2. Methods

2.1. Case collection

The National Coroners Information System is an internet-based storage and retrieval system containing information pertaining to every death reported to an Australian Coroner since July 2000 (2001 for Queensland). Data stored on the system include demographics about the deceased person, details about the circumstances and the incident that led to the death, the medical cause of death, and the object and mechanism involved in the death.

The NCIS was used to retrieve all closed coroners' cases from the state of Victoria, Australia, that occurred between January 2000 and December 2011, where the object or substance involved in the death was coded as "Cocaine/Crack" or where the drug and/or its metabolites were identified in the autopsy or police reports, or in coroners' findings. This includes cases where benzylecgonine was detected without cocaine, indicating the parent compound had been recently consumed but predominantly metabolized by the time of death.

The cohort of cases comprised deaths from various causes, including natural disease, external injury, and cases of accidental or intentional drug toxicity. Extracted data included demographics (age, gender, socio-economic background), co-morbidities (e.g. cardiac disease), circumstances of death (e.g. trauma, external injuries), and, where present, drug exposure (pharmaceutical versus illicit drug use, acute versus chronic use) and information from medical records. These cases had been referred to the Victorian Institute of Forensic Medicine (VIFM) for a medico-legal death investigation due to the perceived unexpected or suspicious nature of the death.

2.2. Data analysis

A detailed analysis of the cohort was undertaken to examine the following:

1. *Basic characteristics*. This included the prevalence of deaths attributed to the drug, the ratio of male to female users, age of users and other relevant demographic data.
2. *Toxicology*. This included the concentration of cocaine and metabolites and the presence of other drugs that may have exacerbated drug toxicity through interactions. In cases where more detailed information was provided, the route of administration and duration of cocaine use was examined, i.e. whether the individual was a recreational user or a chronic intravenous drug user.
3. *Pathology*. This included the presence of disease that may have exacerbated drug toxicity, including primarily cardiac disease, in addition to others such as renal and liver disease (due to interference with drug metabolism and excretion). Additionally, the potential involvement of cocaine in the death compared with other contributing factors, such as natural disease or external injury, was investigated.

2.3. Ethical review

This research study was approved by the Victorian Institute of Forensic Medicine Research Advisory committee and the Department of Justice Human Research Ethics Committee.

3. Results

3.1. Basic characteristics

There were 49 cases that had been closed by the Coroner, where cocaine, benzoylecgonine, ecgonine methyl ester, methylecgonine or cocaethylene, were detected in this 11-year period. The individuals ranged in age from 16 to 70 years (median 30), of which most were males ($n = 36$). 22 cases were caused by drug toxicity, 22 were external injury cases and 5 were attributed to natural disease. Summary details of these cases are given in Table 1.

3.2. Toxicology findings

The concentration of cocaine in the cases was relatively low (range 0.01–3 mg/L, median 0.1 mg/L). Cocaine metabolites were detected frequently in blood and urine: benzoylecgonine (46 cases); ecgonine methyl ester (12 cases); cocaethylene (8 cases) and; methylecgonine (9 cases) (see Table 2 for details). The average concentration of cocaine varied according to manner of death, with drug toxicity cases showing the highest average concentration (0.46 mg/L), followed by external injury (0.2 mg/L) and natural disease (0.1 mg/L), respectively. The average cocaine concentration for cases with heart disease or acute changes (i.e. myocarditis) was 0.55 mg/L. For those not involving heart disease it was much lower: 0.24 mg/L.

All cases involved the concomitant use of other drugs. Opioids were commonly detected (23 cases), in addition to amphetamines (15 cases), benzodiazepines (12 cases) and cannabinoids (11 cases). Alcohol was detected in 17 cases (range 0.01–0.24 g/100 mL, median 0.1 g/100 mL), of which cocaethylene was detected concurrently in 7 cases. Three of these cases also involved significant heart disease (Cases 11, 28 and 29).

There was evidence of intravenous drug use in 17 cases (35%). This was indicated by intravenous access scarring on the inner elbow (reported by the pathologist), or by information provided in the coroners' findings. The majority of these were drug toxicity deaths attributed primarily to heroin. Cocaine was believed to be administered via nasal insufflation in all cases.

3.3. Pathology findings

Of the 43 cases receiving a full autopsy, there were 15 cases involving significant heart disease (31%).

There were 11 cases involving coronary artery atherosclerosis and five cases involving an enlarged heart. Other cardiac pathologies included myocarditis (Cases 48 and Case 49), and contraction band necrosis (Case 4). The youngest of these individuals was 17 years of age (range 17–70 years, median 39 years). Four of these cases also involved the use of amphetamines (Case 8, 9, 16, 4). The cause of death was attributed exclusively to heart disease in the presence of cocaine in four cases (Case 45, 46,