Non-fatal cocaine overdose among injecting and non-injecting cocaine users in Sydney, Australia

Sharlene Kaye & Shane Darke
National Drug and Alcohol Research Centre, University of New South Wales, Australia

ABSTRACT

Aim To investigate the frequency of non-fatal cocaine overdose, and responses to overdoses, among injecting and non-injecting cocaine users.

Design Cross-sectional study.

Setting Sydney, Australia.

Participants Two hundred current cocaine users.

Measurements Structured interview.

Findings Thirteen per cent of the sample had overdosed on cocaine, 7% in the preceding 12 months. Cocaine injectors were more likely to have overdosed, both ever (17/6%) and in the preceding 12 months (9/3%). The most common symptoms of overdose were palpitations (68%), intense sweating (44%) and seizures (40%). The use of other drugs in combination with cocaine prior to the most recent overdose was prevalent (64%), most commonly opioids (40%), alcohol (24%) and cannabis (24%). Those who had overdosed were more likely to be female, had longer cocaine use careers, had used more cocaine in the preceding month and preceding 6 months, had higher levels of cocaine dependence and more extensive polydrug use. Twenty-four per cent had witnessed a cocaine overdose, 13% in the preceding 12 months. Injectors were more likely to have witnessed overdoses, both ever (35/8%) and in the preceding 12 months (20/3%).

Conclusions Experience of, and exposure to, overdose were not rare events. Cocaine users need to be aware of the possibility and nature of overdose, and that cocaine overdose can occur irrespective of method of use. There is a need to emphasise the potential danger of combining cocaine with other drugs.

KEYWORDS Cocaine, harm, overdose.

INTRODUCTION

Cocaine has been implicated in the majority of fatal accidental drug overdoses in the United States [1–3]. Tardiff et al. [3] found that almost three-quarters of drug overdose deaths in New York between 1990 and 1992 were caused by cocaine, often in combination with opiates and alcohol. Coffin et al. [1] reported that 70% of accidental drug overdose deaths in New York from 1990 to 1998 were due to cocaine, with cocaine/opiates the most frequently observed combination. Cocaine overdose has arisen in recent years as a significant problem in Australia. A recent Australian study reported that 146 cocaine-related deaths occurred between 1993 and 2002 in New South Wales, the state that is the focal point for Australian cocaine use [4]. Most deaths occurred among injectors, and in combination with opiates and/or alcohol.

Cocaine-related deaths are typically caused by seizures, cardiac arrhythmias or respiratory failure [5–7], with cardiovascular complications accounting for the majority of cocaine-related deaths [7]. Fatal cocaine overdose has also occurred due to brain haemorrhage, stroke and kidney failure [5,6]. Hyperthermia may also contribute to cocaine-related mortality, with previous research...
demonstrating an increase in cocaine overdose fatalities during hot weather [8]. Cocaine toxicity, or overdose, is not dose-specific. Although deaths have been reported after a single dose of a few hundred milligrams, there are cases in which a dose of several grams has not proved fatal [9–11]. Moreover, overdose can occur regardless of route of administration, although the risk of overdosing, as well as the likelihood that an overdose will be fatal, increases when cocaine is administered in a way that causes a rapid increase in brain levels of the drug [6,12]. Thus, injecting cocaine is likely to pose the greatest risk of overdose, followed by smoking and intranasal use [12].

The risk of cocaine overdose is also influenced by the concomitant use of other drugs. After the combination of cocaine and alcohol, cocaine and heroin was the second most prevalent drug combination among those admitted to emergency rooms in the United States during 2001 [13]. As mentioned above, heroin has been present in a substantial proportion of cocaine-positive deaths in the United States and Australia [1,3,4]. A common pattern of use among polydrug injectors is to inject a combination of cocaine and heroin, known as a ‘speedball’ [14]. The injection of speedballs has been associated with a greater risk of overdose. A recent study found speedball injectors were 2.6 times more likely than other injecting drug users (IDU) to report having overdosed [15]. The increased risk associated with speedballing may be due to cocaine exacerbating the respiratory depression caused by heroin [14]. In addition, the concomitant ingestion of cocaine and alcohol produces cocaethylene, an active metabolite of cocaine that enhances and extends the effects of cocaine [16,17].

Whereas heroin overdose is indicated by a specific diagnostic triad of signs (reduced level of consciousness, miosis, respiratory depression) [18], cocaine overdose is defined less clearly. Cocaine toxicity may manifest as a variety of acute physical and psychological symptoms. The presentation of a cocaine overdose can vary among individuals and does not necessarily entail loss of consciousness. Indeed, overdose signs such as excited delirium, which may result in cardiac arrest and death, by definition preclude loss of consciousness. Physical symptoms of cocaine overdose include nausea and vomiting, chest pain, tremors, increased body temperature, increased heart rate, breathing irregularities and seizures. Psychological symptoms such as extreme anxiety, panic, extreme agitation, extreme paranoia, hallucinations and excited delirium are also indicative of cocaine overdose [5,6]. The acute effects of cocaine, albeit intense, are generally short-lived, due to the short half-life of cocaine (45–90 minutes) [10,11,14]. As such, many cocaine overdose victims recover spontaneously or respond successfully to medical intervention, although chronic use may accelerate the development of serious cardiac pathology, such as coronary artery atherosclerosis and ventricular hypertrophy, which can increase the risk of cocaine-induced myocardial infarction, ischaemia and/or arrhythmia [4,6,11,19,20].

There has been little research on the prevalence and correlates of non-fatal cocaine overdose, and no research in Australia. In a study of cocaine/crack users in Miami, 40% had overdosed on cocaine at least once [12]. Those who had injected cocaine had more extensive overdose histories than those who used cocaine intranasally or smoked crack cocaine. A more recent study in Brazil found that 20% of cocaine users had experienced an overdose and 50% reported knowing other cocaine users who had died of an overdose [21]. Given, however, that Mesquita and colleagues [21] defined overdose as losing consciousness following the use of a drug, these figures may be conservative.

Cocaine use in Australia differs from that in the United States, United Kingdom and Europe, in that cocaine powder (cocaine hydrochloride) is overwhelmingly the predominant form used, with crack use rare [22]. Cocaine injecting in Australia occurs most commonly among regular heroin injectors, for whom polydrug use is the norm. Between 1996 and 2001, there was a progressive increase in both the prevalence and frequency of cocaine use among injecting and non-injecting drug users in Sydney [22,23].

Given that cocaine has become more widely used in Australia, the harms associated with its use warrant investigation. A recent Australian study of cocaine-related harm found that serious physical and psychological symptoms associated with cocaine use were commonly reported by both injecting and non-injecting cocaine users [24]. As noted above, a significant number of cocaine-related fatalities have also been identified recently [4]. Non-fatal cocaine overdose, however, has not been examined in Australia, nor studied widely elsewhere. In examining non-fatal cocaine overdose, it is necessary to examine the routes of cocaine administration. The few studies that have examined cocaine administration routes indicate that injectors may be at increased risk of fatal and non-fatal overdose [4,12,21]. Non-injecting routes, however, are not without risk: 16% of Australian cocaine fatalities resulted from non-injecting cocaine administration [4].

The present study aimed to:
1 Investigate the frequency and nature of non-fatal cocaine overdose among a sample of injecting and non-injecting cocaine users; and
2 Examine the presence at the cocaine overdoses of others, and responses to these overdoses.
METHOD

Procedure
All participants were volunteers who were paid A$ 30 for their participation in the study. Recruitment took place between July 2002 and February 2003, via advertisements placed in needle and syringe programmes, dance club magazines, rock magazines, local newspapers and by word of mouth. To be eligible for participation the respondent had to have used cocaine within the preceding 12 months. Among the injecting cocaine users (ICU) sample, it was a requirement that the primary route of cocaine administration during the preceding 12 months was by injection, and among non-injecting cocaine users (NICU) that the primary route of cocaine administration during this period was non-parenteral. Frequency of cocaine use was not an inclusion criterion as cocaine overdose associated with a range of use patterns was under investigation.

All participants were guaranteed, both at the time of screening and interview, that any information they provided would remain strictly anonymous and confidential. Interviews were conducted by a member of the research team and took approximately 30 minutes to complete.

Measures
A structured interview that addressed demographic characteristics, drug use history, cocaine use history, cocaine dependence and cocaine overdose was developed. Cocaine use in the preceding month was measured using the Opiate Treatment Index (OTI) [25]. It is important to note that the drug use section of the OTI is not specific to opiates. It measures drug use in the preceding month across 11 drug classes, and has good psychometric properties for all of these drug classes [25]. For the purpose of this study, only the questions on cocaine were asked. For all drug classes, OTI scores of 1 equate to one use episode a day, greater than 1 to more than daily use, and less than 1 to less than daily use. The number of days upon which each of the major drug classes had been used over the 6 months preceding interview was also recorded.

Cocaine dependence was measured using the Severity of Dependence Scale (SDS) [26]. A diagnostic cut-off score of 3 (i.e. a score of 3 or more) on the SDS has been determined previously to indicate cocaine dependence [27].

Specific questions were asked on experience of cocaine overdose. Participants were asked if they had ever overdosed on cocaine. If they responded in the affirmative, they were asked to nominate the symptoms they identified as indicators of their having overdosed. If the symptoms were consistent with known physical and psychological indicators of cocaine overdose (unprompted by the interviewer), they were classified as having overdosed. Signs and symptoms indicative of cocaine overdose were nausea and vomiting, chest pain, tremors, increased body temperature, increased heart rate, breathing irregularities and seizures. Psychological symptoms included extreme anxiety, panic, extreme agitation, paranoia and hallucinations. If the signs and symptoms reported by the person were not indicative of overdose, they were classified as not having overdosed. Subjects who were classified as having overdosed were asked how often they had overdosed, when they first and last overdosed, and whether medical intervention occurred. The circumstances of their most recent cocaine overdose were also ascertained.

Participants were asked how many times they had witnessed a cocaine overdose, time since most recent presence at an overdose, responses at cocaine overdoses, and how they knew the person had overdosed.

Analyses
For continuous variables t-tests were employed. Categorical variables were analysed using \( \chi^2 \) tests. All analyses were conducted using SPSS for Windows, version 11.0 [28].

RESULTS

Sample characteristics
The sample consisted of 200 illicit drug users who had used cocaine at least once in the 12 months preceding interview. Participants who had injected cocaine during the preceding 12 months (\( n = 120 \)) were classified as injecting cocaine users (ICU), while those who had employed non-injecting routes of cocaine administration (\( n = 80 \)) were classified as non-injecting users (NICU). Among ICU, 88% had injected cocaine on every use occasion in the preceding year, while the remainder reported occasional non-injecting cocaine use. No NICU had injected cocaine over the preceding 12 months. The mean age was 30.1 years (SD 7.9; range 18–54 years), with 65% being male. The mean length of school education was 10.4 years (SD 1.7; range 5–12 years), with 23% having completed a trade or technical course, and 19% a university course. Nearly two-thirds (60%) were unemployed at the time of interview. Nine per cent were currently engaged in sex work, and 3% had a prison history. Thirty-four per cent were in treatment for drug dependence at the time of interview and had been so for a median of 12 months (range 1–180 months). The majority of those in treatment (50/67) were enrolled in methadone maintenance. The remainder treatments...
were buprenorphine (n = 13), out-patient detoxification (n = 1), Narcotics Anonymous (n = 1) and drug counselling (n = 2).

ICU were significantly older (32.3 ± 26.7 years, \( t_{198} = 5.3, \ P < 0.001 \), had less education (9.6 ± 11.5 years, \( t_{198} = 8.8, \ P < 0.001 \), and were more likely to be male (72% ± 54%, \( \chi^2 = 6.7, \ P < 0.001 \)) than NICU. They were also more likely to be unemployed (84% ± 23%, \( \chi^2 = 75.7, \ P < 0.001 \), enrolled in drug treatment (54% ± 3%, \( \chi^2 = 57.5, \ P < 0.001 \)) and to have a prison history (53% ± 1%, \( \chi^2 = 59.4, \ P < 0.001 \)).

Cocaine and other drug use

The mean age of first cocaine use was 21.0 years (SD 5.4, range 13–45), with ICU having first used cocaine at a later age than NICU (21.8 ± 19.9, \( t_{198} = 2.7, \ P < 0.01 \)). The mean length of cocaine use career was 9.0 years (SD 11.5 years, \( t_{198} = 8.8, \ P < 0.001 \), and were more likely to be male (72% ± 54%, \( \chi^2 = 6.7, \ P < 0.001 \)) than NICU. They were also more likely to be unemployed (84% ± 23%, \( \chi^2 = 75.7, \ P < 0.001 \), enrolled in drug treatment (54% ± 3%, \( \chi^2 = 57.5, \ P < 0.001 \)) and to have a prison history (53% ± 1%, \( \chi^2 = 59.4, \ P < 0.001 \)).

The mean length of cocaine use career was 9.0 years (SD 11.5 years, \( t_{198} = 8.8, \ P < 0.001 \), and were more likely to be male (72% ± 54%, \( \chi^2 = 6.7, \ P < 0.001 \)) than NICU. They were also more likely to be unemployed (84% ± 23%, \( \chi^2 = 75.7, \ P < 0.001 \), enrolled in drug treatment (54% ± 3%, \( \chi^2 = 57.5, \ P < 0.001 \)) and to have a prison history (53% ± 1%, \( \chi^2 = 59.4, \ P < 0.001 \)).

### Table 1: Cocaine overdose histories of ICU and NICU.

<table>
<thead>
<tr>
<th></th>
<th>ICU (n = 20)</th>
<th>NICU (n = 80)</th>
<th>Total (n = 200)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Personal experience of overdose</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever overdosed on cocaine (%)</td>
<td>17</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Overdosed on cocaine in past year (%)</td>
<td>9</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>No. of past ODs (median)</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Time until first overdose (median months)</td>
<td>60</td>
<td>96</td>
<td>72</td>
</tr>
<tr>
<td>Time since last overdose (median months)</td>
<td>10</td>
<td>24</td>
<td>12</td>
</tr>
<tr>
<td><strong>Presence at overdose</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever present (%)</td>
<td>35</td>
<td>8</td>
<td>43</td>
</tr>
<tr>
<td>Present in past 12 months (%)</td>
<td>20</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>No. of times present (median)</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Time since present at an overdose (median months)</td>
<td>12</td>
<td>27</td>
<td>39</td>
</tr>
<tr>
<td>Witnessed fatal cocaine overdose (%)</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
</tbody>
</table>
Cocaine overdose

including 65% of ICU and 60% of NICU (Fig. 1). The most common other drugs used were opioids (36%), alcohol (24%) and cannabis (24%).

The most common location in which the most recent overdoses occurred was in a private home, either the person’s own or a friend’s home (48%). In 16% of cases the overdose occurred in a public location. Others were present at the time of overdose in 68% of cases. An ambulance was called, or the person taken to hospital, in 28% of most recent overdoses.

Factors associated with overdose

There was no difference between the ages of those who had overdosed and other cocaine users (Table 2). Overdoses, however, were significantly more likely to be female, with females comprising 56% of those who had overdosed, compared to 33% of non-overdoses. Stratified by gender, 20% of females had experienced a cocaine overdose compared to 9% of males. In addition, females were more likely to report a cocaine overdose in the preceding 12 months (11% v 4%, \( \chi^2 = 4.12, P < 0.05 \)).

There were a number of cocaine-related factors associated with a history of overdose. Those who had overdosed had longer cocaine use careers, had used more cocaine in the preceding month and preceding 6 months, had higher SDS scores and were more likely to be classified as cocaine dependent (Table 2). They had also used significantly more different drug classes in their lives. There were no differences, however, in current heroin or alcohol consumption.

Cocaine overdose in others

Twenty-four per cent had witnessed a cocaine overdose, and 13% had done so in the preceding 12 months.
likely to have done so (5% witnessed a fatal cocaine overdose, with ICU again more likely to have done so (5% v 0%, $\chi^2 = 4.12, P < 0.05$).

Among those who had witnessed a cocaine overdose, 48% had responded by calling an ambulance or taking the person to hospital. Mouth-to-mouth resuscitation and CPR had been performed by 13% of those who had been present at an overdose. Twenty-one per cent responded by giving the person another drug, typically one of the benzodiazepines or heroin. Fifteen per cent reported that they had taken no action at all at witnessed overdoses.

At the most recent overdose witnessed, the most common signs indicating that the person was overdosing were breathing difficulties (40%), seizures (33%), person turning a different colour (33%), physical collapse (25%), eyes rolling back in the head (19%), intense sweating (hyperthermia) (17%), extreme panic (15%) and frothing at the mouth (10%). An ambulance was called in 44% of cases, and in 8% of cases the person died as a result of the overdose.

**DISCUSSION**

The current study found clinically significant proportions of both ICU and NICU had overdosed on cocaine, with overdose more common among ICU. Thirteen per cent of the sample reported having overdosed, and 7% had done so in the preceding 12 months. The higher prevalence of cocaine overdose among ICU is consistent with previous studies [4,12,21], in which injecting cocaine use was more likely than snorting or crack smoking to be associated with overdose. The most commonly reported symptoms of overdose were palpitations, hyperthermia and seizures, all known sequelae of cocaine toxicity.

There were a number of factors relating to cocaine use that were associated with a history of cocaine overdose. As noted above, cocaine injectors were more likely to overdose, which is consistent with findings that the likelihood of an overdose increases when cocaine is administered in a way that causes a rapid increase in brain levels of the drug [6,12]. In addition, those who had overdosed had longer cocaine use careers. This may reflect prolonged risk exposure, in that the more times a drug is used, the greater the chance an overdose will eventually occur. Alternatively, it may reflect the cumulative cardiotoxic effects of cocaine, increasing the risk of a toxic reaction over time [4,6,11,19,20]. In our recent study of Australian cocaine fatalities, we reported that 57% had clinically significant cardiac pathology [4]. Those who had overdosed were also using cocaine more frequently and had higher levels of cocaine dependence. The general picture that emerged of those who reported cocaine overdoses was that of longer and more entrenched cocaine use.

More extensive polydrug use was associated with a history of overdose. Current alcohol and opioid use were not associated with a history of overdose. However, the use of another drug prior to a cocaine overdose was common in the present study, with two-thirds reporting polydrug use at the time of their most recent overdose. Thirty-six per cent had been using opioids, and a quarter had been using alcohol. These findings suggest that the depressant effects of opioids do not protect against cocaine overdose. Rather, these results are in accordance with the aforementioned literature in which heroin is implicated as a possible contributor to cocaine overdose [1,3,4,6,14,15]. As noted above, alcohol use has been proposed as a risk factor for cocaine overdose due to the production of cocaethylene, a metabolite resulting from the interaction of alcohol and cocaine which is not only more toxic than cocaine itself, but which has a synergistic effect in increasing the toxicity of cocaine [1,3,6,16,17].

Females were more likely to report having overdosed on cocaine. Mesquita et al. [21] also found that female gender was associated with cocaine overdose; however, it is unclear why this would be the case. Whether such findings reflect gender differences in the development of tolerance to cocaine or to the toxic effects of cocaine, or whether they are due to differences in the way males and females attribute causality, cannot be determined from the research to date. It should be noted, however, that there is no female dominance in self-reported non-fatal heroin overdose rates [29].

As discussed above, cocaine overdose is a less clearly defined and understood phenomenon than opioid overdose, and cocaine toxicity may manifest as a variety of acute physical and psychological symptoms. The overdose symptoms reported in the present study are consistent with the known indicators of cocaine toxicity, and an overdose was not classified as such unless the symptoms were indicative of overdose. The symptoms reported are cause for serious concern. This is particularly the case for cardiovascular and respiratory problems, seizures and those symptoms indicative of hyperthermia (i.e. intense sweating and high body temperature), which can be fatal. Overall, the results demonstrate that those who stated that they had overdosed on cocaine were describing a syndrome that has been well-documented as cocaine ‘toxicity’ or ‘overdose’, and not just a collection of benign or unrelated symptoms.

A quarter of the sample had witnessed a cocaine overdose. Consistent with their higher levels of personal overdose, ICU were more likely to have witnessed an overdose,
and to have done so recently. While the overdoses witnessed were typically non-fatal, one in 20 had witnessed a fatal cocaine overdose. Again, ICU were more likely to have been present at a fatality. In fact, no NICU reported having witnessed a fatality. This, in all probability, reflects the fact that most Australian cocaine-related deaths occur among the injecting population [4]. While half of those who had witnessed overdoses had responded by seeking medical attention, 15% reported that they had taken no action at all. Of serious concern, a fifth reported that they had attempted to intervene by administering another drug, typically heroin or benzodiazepines. Such interventions may well increase the risk of death, and reflect a poor knowledge of the phenomenon and of appropriate responses. Poor responses to heroin overdoses have been noted previously, but it has been demonstrated that intervention can improve these responses [30]. Increasing the knowledge of cocaine users about cocaine overdose and of appropriate responses would appear warranted.

Several caveats need to be raised at this point. First, how representative were the cocaine users in this study? To answer this, it must be borne in mind that it is not possible to obtain a random, stratified sample of a population of unknown parameters, such as illicit drug users. However, while a random, representative sample is impossible to obtain, the characteristics of the sample can be compared to those of other samples. Previous Australian research has indicated two distinct groups of cocaine users: lower SES injectors of the drug, with low levels of education and who are likely to be unemployed, and higher SES intranasal users with higher levels of education and employment [31,32]. Recent research on Australian cocaine fatalities demonstrated clearly these two groups being represented among deaths [4]. Indeed, the demographic characteristics of these cocaine-related fatalities was in sharp contrast to the pattern seen among heroin deaths, particularly in terms of professional employment [4]. The current sample is consistent with previous Australian research of both living cocaine users [31,32] and of fatal cases [4]. ICU were older, less educated, more likely to be unemployed, to have a prison history and to be enrolled in drug treatment. Overall, these samples appeared unremarkable, and similar to previous samples of these respective subgroups.

Secondly, the above findings were based on the reports and attributions of cocaine users themselves. Self-reported data have been found to be sufficiently reliable and valid to inform about drug use patterns and associated problems [33]. More specifically, drug users have been shown to be reliable in reporting on their general and drug-related health [34,35]. As such, it can be assumed that the participants in the present study were able to provide a reasonable estimate of the effects of cocaine on their physical and psychological health. In particular, as discussed above, the symptoms of overdose reported by the users, both of their own and others’ overdoses, were consistent with the documented sequelae of cocaine use.

Overall, the results of the present study highlight the importance of educating cocaine users about the possibility and nature of overdose. There is a need to emphasize the potential danger of combining cocaine with other drugs, such as heroin and alcohol. Importantly, while more common among injectors, overdoses occurred among both injectors and non-injectors of the drug, as has been demonstrated among fatalities in Australia [4]. Cocaine use is associated with serious sequelae. The current study illustrates the extent of this harm.

Acknowledgements

This study was funded by the Australian Government Department of Health and Ageing. We wish to thank Dr Ingrid van Beek and the staff at the Kirken Road Centre and K2, as well as Mr Fayyaz Laghari and the staff at REPIDU Canterbury, for assistance.

References


