Sudden death in cocaine abusers

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Online publish-ahead-of-print 12 January 2010

This editorial refers to ‘Cocaine-related sudden death: a prospective investigation in south-west Spain’, by J. Lucena et al. on page 318

Cocaine is the second most widely trafficked drug in the world, trailing only cannabis in this regard. Over the past decade, its recreational use has increased in most European countries (Figure 1). At present, it is estimated that ~1.2% of Europeans used cocaine in the last year, with the prevalence varying from 0.7% in Romania and Lithuania to 12.7% in the UK.1 However, due to the absence of standardized survey and reporting procedures, it is likely that the prevalence of cocaine abuse is under-reported in many European countries. Cocaine use is concentrated among young adults, aged 15–34 years: of the 4 million Europeans who used it in the last year, almost 90% were in this age group.1

Among European countries, Spain ranks second to the UK in the prevalence of cocaine abuse, with 7% of the population estimated to have used it at least once and 3% to have done so in the past year. Among those aged 15–34 years, 10% are estimated to have used it.1 The higher prevalence of recreational cocaine use in Spain when compared with most other European countries is due, at least in part, to the fact that it is a major European port of entry for the drug from South America.

Several factors account for the increasing abuse of cocaine, including its ease of administration [i.e. it can be administered intravenously, intranasally, or by inhalation (smoking)], its availability and purity, its relatively modest cost (i.e. ~€40–€80/g), and the misperception that recreational cocaine use is safe. In a recent survey conducted by the US Department of Health and Human Services, only 50% of young people expressed the belief that monthly cocaine ingestion carries a great risk of harm.2 Lucena and colleagues have now provided data to dispel the belief that cocaine use is safe by reporting that 3% of sudden deaths in southwestern Spain during their period of observation were cocaine related.3 From a consecutive series of 686 sudden death victims in the Seville region collected over a 32-month period, they obtained blood and urine samples for toxicological evaluation and performed extensive macroscopic and histological studies at post-mortem to obtain a reliable assessment of the prevalence and causes of cocaine-related fatalities. As such, their study is one of the larger and more extensively characterized analyses of drug-related sudden death in Europe.

In the USA, the lifetime prevalence of recreational cocaine use is currently estimated to be >14%. As its use has increased, the number of cocaine-related cardiovascular events, including angina pectoris, myocardial infarction, cardiomyopathy, and sudden death, has increased commensurately (Figure 2). As a result, it is not surprising that cardiac disease was the most frequent cause of cocaine-related sudden death in the study of Lucena et al., occurring in 62%. Importantly, the individuals in this study who experienced cardiac-related death following cocaine use were younger [21–45 (mean, 35) years of age] than those who characteristically came to medical attention with symptomatic but non-fatal cardiac disease. Although the authors do not inform us of the presence or absence of traditional risk factors for atherosclerosis in their subjects, other studies have shown that most individuals with cocaine-related cardiac disease have few of these risk factors. In such otherwise ‘low risk’ subjects, investigators have reported that the risk of myocardial infarction is increased ~24-fold over baseline in the 60 min after cocaine use.6 Other studies have demonstrated that a quarter of non-ST-segment elevation myocardial infarctions in young patients are cocaine related.5

The study of Lucena et al.,3 as well as previously published post-mortem analyses, demonstrated an extremely wide range of serum cocaine concentrations (from 0.1 to 24 mg/L) in individuals who died following its use, suggesting that no blood concentration is always safe.6,7 In fact, cocaine-related myocardial infarction has been reported following the first-time administration of as little as 0.1 g of cocaine as a topical, local anaesthetic. Although detailed information regarding the duration and amount of cocaine use is not provided by Lucena et al.,3 they report that nearly 50% of cocaine-related sudden deaths occurred during the weekends, suggesting that they were probably related to recreational use rather than chronic, daily use. This observation is in agreement with previously published studies, which showed that most cocaine-related myocardial infarctions occur in individuals who use the drug infrequently (e.g. less than once a month).8

The opinions expressed in this article are not necessarily those of the Editors of the European Heart Journal or of the European Society of Cardiology.

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In the cases reported by Lucena et al., myocardial infarction was the most common cardiac condition responsible for sudden death following cocaine use, with some patients having occlusive coronary thrombosis with acute infarction and others having organized, recanalized thrombus and remote infarction. The pathophysiology of cocaine-related myocardial ischaemia and infarction is multifactorial; it is due to one or a combination of (i) increased myocardial oxygen demand in the setting of limited or fixed supply, (ii) marked coronary arterial vasoconstriction, and (iii) enhanced platelet aggregation and thrombus formation. Cocaine use has been associated with accelerated coronary atherosclerosis in individuals devoid of the traditional atherosclerotic risk factors; in fact, it was present in 76% of the sudden death victims of Lucena et al. Aside from being a nidus for plaque rupture and subsequent platelet aggregation and thrombus formation, sites of atherosclerotic narrowing manifest enhanced coronary arterial vasoconstriction in response to cocaine.
Most subjects who abuse cocaine also smoke cigarettes; in the current study, 81% of the sudden death victims reportedly smoked cigarettes concomitant with cocaine use. This combination is not innocuous, as human studies conducted during cardiac catheterization showed that concomitant cigarette smoking substantially exacerbates the deleterious effects of cocaine on myocardial oxygen supply (e.g. it potentiates cocaine-induced coronary arterial vasoconstriction) and demand (e.g. it dramatically potentiates the cocaine-induced increase in rate–pressure product). 12

Cocaine users often ingest ethanol or other illicit drugs concurrently. In fact, among drug abusers seeking help in emergency departments, a combination of cocaine and ethanol is the most common finding. Such a combination is popular, since ethanol enhances the euphoria of cocaine and minimizes the dysphoria that often occurs during its withdrawal. Of the cocaine-related complications exacerbating the deleterious effects of cocaine on myocardial oxygen supply (e.g. it potentiates cocaine-induced coronary arterial vasoconstriction) and demand (e.g. it dramatically potentiates the cocaine-induced increase in rate–pressure product). 12

In most circumstances, the combination of cocaine and ethanol is considered to be more toxic and arrhythmogenic than either substance alone. 11 This combination is associated with myocardial depression, decreased coronary arterial blood flow, dysrhythmias, and sudden death, all of which may be due, in part, to cocaethanol, a pharmacologically active metabolite of cocaine that is synthesized by the liver if ethanol is present. In fact, in studies in experimental animals, cocaethanol is more toxic and arrhythmogenic than either substance alone, and it has a longer elimination half-life and larger volume of distribution.

Although coronary arterial thrombosis was the predominant cause of cocaine-related cardiac death in the study of Lucena et al., 3 left ventricular hypertrophy, small vessel coronary arterial disease, and myocardial fibrosis were often observed in those who did not have a myocardial infarction. In these individuals, a cardiac arrhythmia was presumed to be the cause of sudden death, as post-mortem examination identified no other aetiology. This is a reasonable conclusion, as cocaine is a sodium channel blocker, and its ingestion has been associated with QT interval prolongation, torsades des points, Brugada pattern electrocardiographic abnormalities, ventricular tachycardia, ventricular fibrillation, and asystole. 14 Pre-mortem imaging and histological studies have shown that left ventricular hypertrophy, myocardial fibrosis, and small vessel coronary arterial disease are common in cocaine users. 14, 15 These conditions probably predispose them to develop arrhythmias following cocaine ingestion, especially if a metabolic abnormality (e.g. acidosis or hypoxaemia) is also present.

As Lucena and colleagues point out, 3 cocaine use is a growing problem in Europe and a frequent cause of sudden death. As a result, it is important to implement procedures with which drug use can be monitored and reported systematically and consistently. This should include the use of uniform protocols when performing post-mortem examinations in victims of sudden death, to include toxicoclogical examination of the blood and urine for illicit drugs. Until these are accomplished, the prevalence of cocaine and other illicit drug use will be underestimated, and cocaine-related complications will not be recognized. Physicians should consider the possibility of cocaine abuse in a young individual with cardiovascular disease or sudden death, especially in those without traditional risk factors for atherosclerosis. Finally, the notion that recreational cocaine use is ‘safe’ should be dispelled, since even small amounts may have catastrophic consequences, including sudden death.

Conflict of interest: none declared.

References