Putting cocaine use and cocaine-associated cardiac arrhythmias into epidemiological and clinical perspective

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Keywords

arrhythmias, cocaine, drug use, epidemiology

Received

28 July 2009

Accepted

5 October 2009

This is the first article in a series of three articles on cocaine-related cardiac arrhythmias, following on from the 2008 British Pharmacological Society Winter Meeting Clinical Section Symposium entitled 'Cocaine induced cardiac arrhythmias – from ion channel to clinical treatment'. We will summarize the epidemiology of cocaine use across the world and in particular will focus on UK, Europe and US use prevalence data. We will discuss the acute cardiac and non-cardiac toxicity associated with cocaine and highlight the lack of data on the true UK prevalence of acute cocaine toxicity and on the incidence of cocaine-related cardiac arrhythmias.

Cocaine is an alkaloid present in the plant *Erythroxylon coca*, which is predominantly found growing in South America. In 2008 there was an estimated 845 metric tons of cocaine produced in Bolivia, Colombia and Peru, and these three countries were responsible for almost all of the world's production and processing of cocaine [1]. Although there has been a significant decline from peak estimated production of cocaine of 1008 metric tons in 2004, this has mainly been due to large reductions in production by Columbia (640–430 metric tons); there has actually been small year on year growth in the estimated production in both Bolivia (98 metric tons in 2004 to 113 metric tons in 2008) and Peru (270 metric tons in 2004 to 302 metric tons in 2008) [1]. Whilst the *Erythroxylon coca* plant can grow in other geographical regions, such as Africa, production of cocaine from these regions is negligible. Interestingly there has been a change in the route(s) that cocaine enters the European recreational drugs market. Previously, the majority of cocaine in Europe was trafficked indirectly through West Africa [2]. The proportion of drug traffickers/couriers detected in Europe whose flights originated from West Africa has fallen from a peak of 59% in 2007 to less than 10% in the last quarter of 2008 and the beginning of 2009 [2]. It is therefore likely that more cocaine is trafficked either directly into Europe, particularly through Spain and Portugal, or through other areas.

The published data on cocaine production, seizures and use is based on total cocaine, which includes both powder cocaine and crack cocaine; there is limited data on the relative use of these forms of cocaine although it is assumed that most cocaine is sold and used in powder form rather than as crack cocaine [1, 3]. Street and 'wholesale' prices of cocaine appear to have been falling in the last 10 years, which may have influenced the increase in use seen in many developed nations. However alongside this the purity of powder cocaine has been decreasing and therefore in relative terms the price per unit mass of cocaine has been increasing. The collection of data on the purity of cocaine, at both a 'wholesale' and 'street' level is, with the exception of the UK, not routinely collected throughout Europe. The effect of reduction in the purity of wholesale cocaine seized by HM Customs and Excise entering the UK is whilst the wholesale price per kilogram has increased only slightly (£24.5K in 2005 compared with £45K in 2009). When this is adjusted for purity, this increase is more dramatic (£36K in 2005 compared with £80K in 2009) [1]. In the UK, the purity of police seizures has fallen from approximately 50% in 2003/4 to around 23% in 2009. Additionally, in the first quarter of 2009, around one third of 'retail' seizures of cocaine by police have purity of less than 9%, and some purity levels are as low as 4–5%. This variation in the purity of cocaine, particularly on a regional basis in the UK, puts those who purchase cocaine from

Table 1

Estimated 2007 prevalence of cocaine use in those aged 15–64 years in the last year (adapted from data from the UN World Drugs Report 2009) [1]

Continent	Estimated users in the last year (millions)	Percentage of those aged 15–64 years (%)
Africa	1.2–3.6	0.2–0.7
Americas	9.4–9.6	1.6
Asia	0.4–2.6	<0.1–0.1
Europe	4.3–4.6	0.8
Oceania	0.3–0.4	1.5–1.7

‘street dealers’ in different areas (e.g. whilst on holiday or travelling) at significant risk of inadvertent overdose due to the differences in purity.

Cocaine is commonly used throughout the world. The estimated total number of people worldwide aged 15–64 years old who used cocaine in 2007 was 15.6–20.8 million (0.4–0.5% of those in this age group). There is no reliable data collected on cocaine use outside of these age ranges on an international basis to be able to comment on the prevalence of use in younger and/or older populations. However, a number of studies have demonstrated that recreational drug use is not confined to the younger/middle-age groups, and that it does occur in older age groups, although the prevalence is lower [4, 5]. There is the potential that cocaine use in older age groups may increase in the future, as those who have used recreational drugs in young/middle ages continue as they become older.

There is significant geographical variation in the prevalence of cocaine use on a continental basis (Table 1). These estimates are based on surveys and studies undertaken using variable methodologies in each country (including different age groups studied in different countries). In most countries these studies are reported to responsible national organizations – in the UK this is the UK Focal Point on Drugs which forms part of the European Information Network on Drugs and Drug Addiction (Reitox), along with similar Focal Points in other European countries. These national systems provide information collated from around the European Union to International bodies such as the the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and the United Nations Office on Drugs and Crime (UNODC). However, in certain regions of the world, particularly in developing nations within Africa and Asia, there are no mechanisms in place to collect data on a reliable basis nationally and estimates are based either on small studies or the perceptions of country experts. The reliability of data collected on treatment needs from these areas is also poor, since in many of these countries/regions, admission of drug use by an individual may be associated with the risk of long custodial sentences and/or death. Therefore, whilst the data may suggest that

recreational drug use is a ‘developed world’ phenomenon, this may reflect the basis on which the data are collected.

Not only are there significant differences in terms of cocaine use on a continental basis, there are also major differences in the prevalence of cocaine use within each continent. For example within Europe, the prevalence of use is much higher in Western Europe than in Eastern Europe (1.4% and 0.3% of those aged 15–64 years, respectively). This is similar for the Americas with higher prevalence rates in North America compared with the Caribbean and Central and South America (2.3%, 1%, 0.7% and 0.9% of those aged 15–64 years, respectively). The highest individual country prevalence rates are spread across different regions of the world, but typically are in developed countries (Figure 1) [1].

Although the USA remains the largest cocaine market (cocaine was used at least once in 2008 by 5.8 million people in the USA) recently there have been significant decreases in cocaine use in the USA and other areas of North America [1]. In Europe, there were increases in the prevalence of cocaine use in many Western and Central European countries in the 1990s. However, there has been stabilization in the last 1–3 years, particularly in the highest prevalence countries such as Spain and Italy, where annual prevalence rates have remained stable at 3% and 2.2%, respectively. There are some areas of Europe, where the prevalence of cocaine use is increasing, including France, the Czech Republic, Portugal and Ireland. It is thought that the increase in the prevalence of cocaine use in Portugal from 0.3% in 2001 to 0.6% in 2007 reflects the increasing use of Portugal as a transit/entry point of trafficked cocaine into Europe from South America and West Africa [1, 3].

There were significant increases in cocaine use in England and Wales in the 1990s, from 0.3% in 1992 to 2.0% of those aged 15–59 years in 2000 (Figure 2) [1, 3]. Since then rates have been relatively stable between 2.0 and 2.5%. The 2008 prevalence rate of 2.3% is equivalent to approximately 860 000 individuals having used cocaine in the preceding 12 months. The UK as a whole, including Scotland and Northern Ireland, has an estimated 1 million cocaine users per year and therefore the UK has the largest numbers of cocaine users in Europe, although the UK has the second highest cocaine population prevalence rate behind Spain [1, 3]. Within England and Wales, there are regional differences in the prevalence of cocaine use, with highest rates in London (4.1% in 2005/6) and lowest rates in Wales (1.6%) and Yorkshire (1.8%) [6, 7]. Cocaine is the second most prevalent recreational drug used (2.3% of those aged 15–59 years) behind cannabis (7.4% of those aged 15–59 years), and significantly more than amphetamines, MDMA (ecstasy) and opioids (1%, 1.5% and 0.93–1% of those aged 15–59 years, respectively). Although it is difficult to be certain, in our opinion and based on our clinical experience, this is likely to be predominantly recreational use in the UK as cocaine is listed at

Figure 1

Cocaine annual use prevalence – top 10 countries in the world, adapted from the UN World Drug Report 2009 [1]. Data are for those aged 16–59 years for Scotland and England and Wales; 15–64 years for Spain, USA, Canada, Italy, Northern Ireland and Australia; 12–65 years for Argentina and 18–66 years for Monaco. Data are reported from 2004 for Canada, 2006 for Scotland and Argentina, 2007 for Australia, Northern Ireland, Monaco, USA and Spain; 2008 for England and Wales and Italy

Figure 2

Annual prevalence rates of cocaine use in England and Wales for those aged 16–59 years. Adapted from the UN World Drug Reports 2007–09 [1, 7, 24]

the primary drug for those in UK drug treatment programmes in only 11.1% compared with opioids in 68.9% [1]. However, there are other factors which may influence an individual's entrance into drug treatment programmes which include socio-economic class, unwanted effects related to drug abuse and the types and availability of drug treatment programmes. These factors may explain some of the regional geographical differences in the prevalence of cocaine as the primary drug in drug treatment programmes; for example rates are much higher in Spain (46.9% cocaine as primary drug compared with 11.1% in the UK) [1].

The above data for use in the UK is largely from the British Crime Survey and other data sources reporting to the UK Focal Point, and estimate the underlying prevalence of those aged 15–59 years old. However, there are differences between the overall population prevalence and that in those who would define themselves as 'clubbers'. Surveys of clubbers directly, have shown that the prevalence rates of overall recreational drug use, and that of cocaine is much higher than that of the overall population prevalence of 2.3%. A survey of over 200 people attending a dance event in Scotland reported that 38.5% had used cocaine within the preceding 12 months [8]. Of those who had used within the last 12 months, nearly 40% reported that they used cocaine once a month or more frequently. Studies using user surveys in a UK dance-related magazine, *MixMag*, reported lifetime prevalence rates for powder cocaine were relatively stable over a 5 year period (1999–2003) of between 73.1 and 80.3% of those surveyed [9]. This study reported 'use prevalence rates' for the preceding month, rather than annual prevalence rates, which were also much higher than the general population annual prevalence rates (ranging between 28.3% and 41.1% compared with 2.3%). A study of club drug use in the men who have sex with men community from Los Angeles, USA, reported that 32% of those surveyed had used cocaine in the last 30 days [10]. In addition to higher use prevalence rates, those who report using cocaine within the last month, typically have done so on multiple occasions (roughly 3–4 times in the last month) [9, 10]. A study from New York, reported that 20% had used cocaine on more than five occasions within the last month [11]. These studies only record the number of days of cocaine use

rather than the number of times that cocaine is used; typically individuals may consume large amounts of cocaine within a short period of time, and therefore these rates are likely to under-represent significantly the actual rate of exposure to cocaine.

Acute cocaine toxicity is a common reason for presentation to the Emergency Department, although there is no national collection of data in the UK on the actual numbers of presentations. The NHS Information Centre for Health and Social Care collects data on the number of presentations/admissions to hospitals, including those that relate to cocaine, known as Hospital Episode Statistics (HES). The data collected uses ICD-10 codes, and the use of these codes as the basis for HES data has recently been criticized, although this is currently the best available data [12]. Furthermore inpatient HES data only captures individuals who are admitted from the Accident and Emergency Department; patients who are discharged directly from the Accident and Emergency Department will not be captured in HES. Currently there is a trial underway publishing Accident and Emergency HES data, although this does not include the individual drug(s) that were involved in poisoning related presentations. The hospital inpatient HES data, which reports on completed hospital admissions, has shown increases in the number of hospital admissions related to cocaine from 289 episodes in the 2002/3 financial year to 699 in the 2005/6 financial year [13]. We have shown in our local clinical toxicology unit that approximately 50% of those who present to the Emergency Department with cocaine and all recreational drug related toxicity are admitted to hospital; therefore, the hospital inpatient HES data are likely to be a gross underestimate of the overall prevalence of the acute toxicity related to cocaine.

The US Drug Abuse Warning Network (DAWN) is a public health surveillance system that monitors drug related ED visits across the US, including Alaska, Hawaii, and the District of Columbia. This is used to track the impact of drug use and problems associated with its use in the US. In 2006, the DAWN annual report estimated that there were 958 164 visits to the ED that potentially involved a controlled drug (95% confidence intervals 690 218, 1 226 110). In particular, cocaine was thought to be involved in just under a third (31%) of controlled drug related ED presentations (548 608, 95% confidence intervals 374 579, 722 636); this represents an estimated 182 ED visits per 100 000 population related to cocaine [14].

Common non-cardiac features of acute cocaine toxicity include agitation and aggression, seizures, hyperthermia and intra-cerebral haemorrhage/infarction. Acute cardiac effects of cocaine include arrhythmias, hypertension and acute coronary syndrome/myocardial infarction [15–18]. The greatest risk of developing acute coronary syndrome related to cocaine is within the first hour following use, although this risk remains elevated for several hours after use [19]. Studies from North America looking at both urine

cocaine and cocaine metabolites suggest that up to 17% of those presenting with suspected acute syndrome have 'recent' cocaine use [20]. However, as these studies looked at detection of both cocaine and cocaine metabolites, the detection of a positive result may result from cocaine use within a few days rather than necessarily within a few hours of presentation.

Cardiac arrhythmias related to cocaine use can be due to ion-channel effects of cocaine, increased sympathetic nervous system stimulation and/or myocardial ischaemia [21]. There is no published data on the frequency of cardiac arrhythmias related to recent cocaine use. Studies from our group have shown that although doctors are aware that cocaine is a risk factor for acute coronary syndrome they are less likely to ask about cocaine use than classical cardiovascular risk factors such as smoking, diabetes and hyper-cholesterolaemia [22]. Therefore it is likely that, similar to acute coronary syndrome, doctors are not likely to ask patients presenting with cardiac arrhythmias about recent cocaine use which may at least in part explain the lack of published data in this area.

There is considerable controversy amongst cardiologists, toxicologists and emergency physicians on the management of cocaine-related ion channel arrhythmias [23], in particular, the role of lidocaine and sodium bicarbonate. The focus of the following two articles is to discuss the mechanisms of cocaine-related ion-channel arrhythmias (O'Leary & Hancox [25]) and use this as the basis to discuss some of the controversies in their management (Hoffman [26]).

Competing interests

None declared.

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