

Cocaine in surface waters: a new evidence-based tool to monitor community drug abuse

Ettore Zuccato^{1*}, Chiara Chiabrando¹, Sara Castiglioni^{1,2}, Davide Calamari^{2§}, Renzo Bagnati¹, Silvia Schiarea¹ and Roberto Fanelli¹

¹Department of Environmental Health Sciences, Mario Negri Institute for Pharmacological Research, Via Eritrea 62, 20157 Milan, Italy

²Department of Biotechnology and Molecular Sciences, University of Insubria, Via Dunant 3, 21100 Varese, Italy

*Corresponding author

§Prof. Davide Calamari regrettably died before the paper was completed. We dedicate this paper to his memory.

Email addresses:

EZ: zuccato@marionegri.it
CC: chiabrando@marionegri.it
SC: castiglioni@marionegri.it
RB: bagnati@marionegri.it
SS: chiabrando@marionegri.it
RF: fanelli@marionegri.it

Abstract

Background

Cocaine use seems to be worryingly increasing in some urban areas worldwide, but it is not straightforward to determine the real extent of this phenomenon. Trends in drug abuse are currently estimated indirectly, mainly by large-scale social, medical, and crime statistics that may be biased or too generic. We thus sought a novel approach based on 'field' evidence of cocaine use by the general population.

Methods

Cocaine and its main urinary metabolite (benzoylecgonine, BE) were measured by mass spectrometry in water samples collected from the River Po and urban wastewater treatment plants of medium-size Italian cities. Drug concentration, water flow rate, and population at each site were used to estimate local cocaine consumption.

Results

We showed that cocaine and BE are present, and measurable, in surface waters of populated areas. The largest Italian river, the Po, with a five-million people catchment basin, steadily carried the equivalent of about 4 kg cocaine per day. This would imply an average daily use of at least 27 ± 5 doses (100 mg each) for every 1000 young adults, an estimate that greatly exceeds official national figures. Data from waste water treatment plants serving medium-size Italian cities were consistent with this figure.

Conclusions

This quantitative, evidence-based approach – in principle extendable to other illicit drugs – might become an additional tool to better estimate drug abuse, with the unique ability to monitor local drug abuse trends in real time.

Background

The use of cocaine, one of the most potent and addictive illicit drugs, appears to be worryingly increasing in some countries¹⁻³. International drug agencies suggest that this phenomenon should be closely monitored, in particular among young people in urban areas³.

The trends and magnitude of drug abuse are currently estimated indirectly from general statistics mainly based on population surveys, consumer interviews, medical records, and crime statistics^{3,4}. These general indicators, however, may not realistically estimate the phenomenon at the regional level, where specific socio-economic and cultural patterns can strongly influence drug abuse habits and trends. Moreover, since self-reporting of socially censured behavior is likely to be unreliable, the figures obtained by interviewing known or potential users may be underestimates. New methods are therefore needed not only to provide more realistic estimates of illicit drug consumption, but also to promptly detect changes in abuse trends in local populations⁵. This would help social scientists and the authorities to respond to changing habits with appropriate preventive countermeasures, in “real time”.

We describe here a novel approach based on “field” evidence of cocaine use by the general population in a given area. Excretion products of cocaine consumed in a given area could in principle be trackable in local waste waters (WW) and the receiving surface waters (SW), that can be viewed as a sort of transient “depository” for any

sufficiently stable compound excreted by the local population. As we have already shown for many widely prescribed pharmaceuticals^{6,7}, the total amount of a given drug consumed by the local population can be correctly estimated from measurements of its main excretion product(s) in WW and SW. Thus, if an excretion product of cocaine were found in WW and SW, it could be used to help estimate local consumption. Moreover, if monitored regularly, changing drug concentrations in WW or SW could reflect changes in drug use in real time.

In humans, only a small percentage of a cocaine dose is excreted in urine as the parent drug, while a large amount (about 50%) is excreted as benzoylecgonine (BE)⁸. We searched for cocaine and its metabolite in WW and SW, using BE concentrations to calculate cocaine consumption.

Our approach implies that consumption figures are very unlikely over-estimated. In principle, if a fraction of the excretion products of cocaine – entering the sewage system from a myriad scattered inlet points – were lost and/or degraded before they reach the common sampling site, this would result in under-estimates of the true consumption figures. If, again, we consider that cocaine metabolites that are sampled from WW and SW cannot come from sources other than human excretion, and that their concentration in flowing waters cannot reflect accumulation over time, we must conclude that our estimates of cocaine consumption could not over-estimate true values. We therefore tested our approach on the Italian territory (Figure 1), and compared our findings with official figures for cocaine use in Italy, obtained from surveys of the general population².

Methods

Sample collection

Composite water samples (pools of five 500-ml samples collected every 30 min) were collected on four different days from the River Po at Mezzano, Pavia (Figure 1). At this sampling site (flow rate $743 \text{ m}^3\text{sec}^{-1}$) the basin's population equivalent is 5.4×10^6 . Water samples were also taken from affluent WW at four treatment plants (WWTPs) serving medium-size Italian cities (Cagliari, Latina, Cuneo, and Varese; location shown in Figure 1). Flow rates of the WWTPs were 1.0, 0.36, 0.22 and $0.46 \text{ m}^3\text{sec}^{-1}$, and population equivalents 270, 140, 45 and 110×10^3 , respectively. For each plant, a 24-h, two-liter composite sample was obtained by pooling water collected every 20 min by an automatic sampling device. Water samples were stored at 4°C until analysis.

Drug analysis

Cocaine and BE were measured by adapting our method for pharmaceuticals in river water³. The reference standards of cocaine and BE were from MacFarlan-Smith Ltd (Edinburgh, UK), and LGC Promochem s.r.l. (Milan, Italy), respectively. Samples were filtered on a glass micro-fiber filter, extracted on Oasis MCX cartridges (Waters Corp, Milford, MA), and analyzed by HPLC-tandem mass spectrometry (MS/MS) using an API 3000 mass spectrometer (Applied Biosystems-Sciex, Thornhill, Ontario, Canada) with electrospray ionization. Quantitation was done by multiple reaction monitoring of selected fragmentation products of the protonated pseudo-molecular ions (m/z $304 \rightarrow 105$ and $304 \rightarrow 182$ for cocaine, m/z $290 \rightarrow 105$ and $290 \rightarrow m/z$ 168 for BE, and $243 \rightarrow 151$ and $243 \rightarrow 169$ for the internal standard, salbutamol-d3). Calibration curves showed excellent linearity ($r^2 > 0.998$). Recoveries were $>90\%$ for both compounds, and the limits of detection were 0.06 and 0.12 ng/liter, respectively,

for BE and cocaine. The identity of cocaine and BE, and the absence of interfering compounds, were further confirmed by full MS and MS/MS spectra obtained on a LCQ DecaXP Plus (Thermo Electron, Waltham, MA) ion trap mass spectrometer.

Calculations and assumptions

Given that about half a cocaine dose is excreted in urine as BE, and only a small fraction as the unchanged drug, we used the concentrations of BE in WW or SW to estimate the amounts of cocaine consumed locally. Concentrations of cocaine were useful to verify that the BE/cocaine ratio was as expected, thus giving confidence about their source being human consumption. If an unlikely accidental or intentional disposal of a significant amount of cocaine were to occur at any of these sites, the normal BE/cocaine ratio (see Results) would be altered in favor of cocaine.

BE loads (g/day) at each sampling site – calculated from the BE concentration (ng/liter) in water and water flow rate (m^3/sec) – were used to estimate the loads of parent cocaine, multiplying by a factor of 2.33. This takes into account the BE/cocaine molar mass ratio (0.954) and the known average molar fraction (45%) of a cocaine dose excreted as BE⁸. Cocaine loads were then related to the local population equivalents (i.e. the number of people served by a WWTP or living in the river's catchment basin), using data from the Italian 14th General Population and Housing Census (2001)⁹. The estimated consumption (g per day per 1000 people) at each site was referred both to the general population and to young adults, since this age group (15-34 y) reportedly includes almost all consumers². The data were also expressed as the number of doses per day per 1000 people, assuming 100 mg as an average dose¹ (four 25-mg lines of cocaine).

Results

Cocaine and BE were found in all WW and SW samples tested. Concentrations at the various sampling sites are shown in Table 1. As expected, the parent drug levels were much lower than the metabolite, their ratio in WW samples (0.15 ± 0.03 , mean \pm SD) being in accordance with the known metabolic fate of cocaine in humans. In the River Po, the cocaine/BE ratio was stable over time but lower than expected (0.05 ± 0.02), suggesting less stability in the environment for cocaine than BE.

On four different occasions, at the same sampling site, the River Po was found to steadily carry almost 4 kg of cocaine equivalents per day (Table 1). This suggests a total of about 40,000 doses per day, or about seven doses for every 1000 people living in the river's basin. However, considering only young adults, the estimated use reaches 27 doses per day per 1000 people (Table 2). In agreement with these findings, cocaine loads determined at WWTPs gave drug consumption estimates of about 2-7 doses per 1000 people, or 9-26 doses per day per 1000 young adults (Table 2).

Discussion

Our data suggest that actual cocaine consumption may be much greater than estimated by current methods. This is a striking finding, considering that the method employed and the assumptions made are very unlikely to lead to *overestimated* consumption figures. There is in fact no reasonable mechanism by which cocaine excretion products could accumulate in *flowing* surface waters, and we found steady concentrations in the River Po over time. Moreover, having chosen in our study to monitor an abundant metabolite in addition to the parent drug, any increase in cocaine

levels due to illicit disposal rather than human use would be promptly disclosed by an increased cocaine/metabolite ratio.

Official statistics² for the year 2001 indicate that in Italy about 1.1% of young adults (15-34 yr old) admit having used cocaine “at least once in the preceding month”, but the actual dosages and frequency of use are not known. Therefore, it is hard to estimate the amount of cocaine that is consumed by the population. If we consider that in the River Po basin there are about 1.4 million young adults, the official figures in this area would translate into at least 15,000 cocaine use events *per month*. We however found evidence of about 40,000 doses *per day*, a vastly larger estimate. The economic impact of trafficking such a large amount of cocaine would be remarkable. The 1500 kilograms of cocaine supposedly consumed per year in the River Po basin would amount, in fact, to about \$150 million in street value (based on average US street value, \$100 per gram^{10,11}).

The above estimates – obtained from the heavily populated basin of the largest Italian river – were confirmed by similar values found in a completely different setting, i.e. in urban WW of medium-sized cities, chosen in widespread geographical locations to estimate local cocaine consumption on a small scale. The fair correspondence of SW and WW findings, despite the different settings and assumptions, suggests that our approach is reliable, and our estimates realistic. The rather narrow variation of estimated consumption among WWTPs may reflect different local habits, as the urban areas chosen have significant socio-cultural differences.

Conclusions

Surveys of the general population are useful to describe patterns of drug abuse, but they are very expensive, and certainly too lengthy to detect changing trends promptly⁴. Continuous monitoring of illicit drug consumption would be very important for assessing the actual extent of this phenomenon, and detecting changes in trends. A more realistic picture of local use patterns for the most common illicit drugs would also be needed to identify priority problems and plan selective countermeasures. We propose our evidence-based approach, which is in principle extendable to other illicit drugs, as an additional, rapid method to help estimate drug abuse at the local level. This approach, with its unique ability to monitor changing habits in real time, could be helpful to social scientists and authorities for continuously updated appraisal of drug abuse.

Abbreviations

WW- waste waters

SW - surface water

WWTP - waste waters treatment plant

BE - benzoylecgonine

MS - mass spectrometry

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

EZ designed the study and wrote the paper.

CC analyzed the data and wrote the paper.

SC collected and analyzed the samples.

DC designed the study and analyzed the data.

RB developed the analytical method and supervised the analyses.

SS collected and analyzed the samples.

RF had the original idea, and critically reviewed the results and the manuscript.

Acknowledgements

The University and Scientific Research Ministry (MIUR) funded this study (project no. 2002098317, 2002). Silvia Schiarea was the recipient of a “COFIN 2002” fellowship from University of Insubria.

References

1. United Nations Office of Drug and Crime: *World Drug Report 2004. Volume 2. Statistics*. [http://www.unodc.org/pdf/WDR_2004/methodology.pdf]
2. Ministero del Lavoro e delle Politiche Sociali: *Italy drug situation 2001. Report to the EMCDDA by the Reitox National Focal Point*. [www.emcdda.eu.int/index.cfm?fuseaction=public.AttachmentDownload&nNodeID=1240&slanguageISO=EN]
3. European Monitoring Centre for Drugs and Drug Addiction: *The state of the drug problem in the European Union and Norway. Annual Report 2003*. EMCDDA, Lisbon; 2004. [<http://annualreport.emcdda.eu.int/en/home-en.html>]
4. European Monitoring Centre for Drugs and Drug Addiction: *Handbook for surveys on drug use among the general population. EMCDDA project CT.99EP.08B*. EMCDDA, Lisbon; 2002.

[<http://www.emcdda.eu.int/?fuseaction=public.AttachmentDownload&nNodeID=1390>]

5. Daughton CG: **Pharmaceuticals and Personal Care Products in the Environment: Scientific and Regulatory Issues**. In *Symposium Series 79*. Edited by Daughton CG & Jones-Lepp T. Washington, D.C.: American Chemical Society; 2001: 348-364.

[<http://www.epa.gov/nerlesd1/chemistry/pharma/book-conclude.htm>]

6. Zuccato E, Calamari D, Natangelo M, Fanelli R: **Presence of therapeutic drugs in the environment**. *Lancet* 2000, **355**:1789-1790.

7. Calamari D, Zuccato E, Castiglioni S, Bagnati R, Fanelli R. **Strategic survey of therapeutic drugs in the rivers Po and Lambro in northern Italy**. *Environ Sci Technol* 2003; **37**:1241-1248.

8. Baselt RC: *Disposition of toxic drugs and chemicals in man*. 2nd edition. Davis (CA): Biomedical Publications; 1982.

9. ISTAT: **14° Censimento Generale della Popolazione e delle Abitazioni**; 2001. [<http://www.istat.it/English/Population/index.htm>]

10. Drug Policy Information Clearinghouse (Office of National Drug Control Policy): *Fact Sheet*; November 2003.

[<http://www.whitehousedrugpolicy.gov/publications/factsht/cocaine/>]

11. United States Department of State, Foreign Press Center: **Drug Control: International Policy and Approaches**. *CRS Issue Brief for Congress*; May 14, 2004 [<http://fpc.state.gov/documents/organization/33744.pdf>]

Figures

Figure 1 - Sampling sites for cocaine measurement

Map of Italy showing the River Po basin with the site of sampling, and the locations of the urban waste water treatment plants.

Tables

Table 1. Levels and loads of cocaine and its metabolite in the River Po and WWTPs.

	Levels ^a		Loads
	Cocaine (ng/liter)	BE (ng/liter)	Cocaine equivalents ^b (g/day)
River Po	1.2±0.2 ^c	25±5 ^c	3792±723 ^c
WWTPs^d			
Cagliari	83	637	128
Cuneo	76	416	30
Latina	125	751	33
Varese	42	383	36

^aCocaine and BE were analyzed by HPLC-MS/MS

^bCocaine loads were estimated from BE concentrations (see Methods)

^cMean±SD

^dWaste water treatment plant locations

Table 2. Estimated local use of cocaine in the River Po basin and medium-size Italian cities.

	Estimated local cocaine use			
	per 1000 people		per 1000 young adults ^a	
	g/day	no. doses ^b /day	g/day	no. doses ^b /day
River Po	0.70±13 ^c	7.0±1.3 ^c	2.7±0.5 ^c	27±5 ^c
WWTPs^d				
Cagliari	0.47	4.7	1.73	17.3
Cuneo	0.21	2.1	0.94	9.4
Latina	0.73	7.4	2.58	25.8
Varese	0.32	3.2	1.41	14.1
	0.44±0.23 ^c	4.4±2.3 ^c	1.7±0.7 ^c	17±7 ^c

^a15-34 yr old

^b1 dose=100 mg

^cMean±SD

^dWaste water treatment plant locations



VARESE

SAMPLING SITE

PO RIVER

CUNEO

LATINA

CAGLIARI