Addictive Behaviors 38 (2013) 1601–1604

Contents lists available at SciVerse ScienceDirect

Addictive Behaviors

Short Communication

Mortality in a cohort of young primary cocaine users: Controlling the effect of the riskiest drug-use behaviors

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HIGHLIGHTS

- Mortality in young cocaine users was 4.7 times higher than in the general population.
- Cocaine sniffers with no opioid use or drug injection had 3.1 times higher mortality.
- Short-term excess mortality in this cohort could largely be explained by opioid use.

ARTICLE INFO

Keywords:
Cocaine abuse
Mortality
Cohort

ABSTRACT

Background: Published studies indicate that primary cocaine users (PCUs) have a mortality rate 4–8 times higher than their age–sex peers in the general population. Most PCUs are primary intranasal cocaine users, never-injectors and never-opioid users (PICUNINOs) and are usually underrepresented in cohort mortality studies. The aim is to estimate excess mortality in all PCUs and in the subgroups of never-opioid users and PICUNINOs in Spain.

Methods: 714 PCUs aged 18–30 were street-recruited in 2004–2006 in Spain and followed until 2010 to ascertain vital status. Drug use was self-reported at baseline and 1–2 years later. Mortality was compared with that of the general population using standardized mortality ratios (SMRs).

Results: SMRs were 4.7 (95% CI: 2.4–9.0), 2.5 (95%CI: 0.8–7.8) and 3.1 (95% CI: 1.0–9.6), respectively, among all participants, never-opioid users and PICUNINOS when using only baseline data on drug use, and 1.2 (95% CI: 0.2–8.5) and 1.4 (95% CI: 0.2–9.9) among the latter two subgroups, when using baseline plus follow-up data.

Conclusion: Short-term mortality in young Spanish PCUs is 5 times higher than in the general population. This excess mortality may largely be explained by a history of opioid use or the risk of starting such use.

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1. Introduction

Cocaine use has been associated with an increased risk of cardiovascular, neurological, and psychiatric disorders, as well as unintentional injuries, violent behaviors, and other health problems (EMCDDA, 2007; Kaye & Darke, 2004a; Kuhns, Wilson, Maguire, Ainsworth, & Clodfelter, 2009; Macdonald et al., 2003; Maraj, Figueredo, & Lynn, 2010; Marzuk et al., 1995; Qureshi, Suri, Guterman, & Hopkins, 2001; Ryb et al., 2009; Santos et al., 2012; Schnitzer et al., 2010). Therefore, primary cocaine users (PCUs) can be expected to have excess mortality compared to the general population, a risk estimated as 4–8 times greater (Degenhardt et al., 2011b). These estimates come from cohorts of PCUs who are either in drug treatment or which include a high or unknown proportion of participants with very risky drug use behaviors, such as heroin use, injecting drugs or smoking crack/cocaine (Kaye & Darke, 2004a, 2004b). However, most PCUs in developed countries had never used illicit opioids or injected drugs or smoked cocaine —

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0306-4603/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.addbeh.2012.10.007

hereinafter called "primary intranasal cocaine users never-injectors and never-opioid users" (PICUNINOs) (EMCDDA, 2007; EMCDDA, 2011; UNODC, 2011). As with non-fatal acute problems related to cocaine (Kaye & Darke, 2004a, 2004b), excess mortality is probably lower in PICUNINOs than in the previously studied PCU cohorts, so the available estimates cannot be generalized to PICUNINOs or all cocaine users.

The aim is to estimate excess mortality in a Spanish cohort of young PCUs, partially controlling the effect of the riskiest drug-use patterns, such as heroin use, drug injection and crack/cocaine smoking.

2. Methods

A cohort of 714 cocaine users was recruited in 2004–2006 from drug scenes and non-treatment settings using incentive-driven chain-referral methods in Madrid, Barcelona and Seville, Spain (Heckathorn, 1997; Heckathorn, 2011). Recruitment criteria were: regular cocaine use (≥52 days/last year), age 18–30, and no regular heroin use (≤12 days/last year). Two personal interviews were conducted, at baseline and 1–2 years later. Questions were included on socio-demographic variables, history and patterns of drug use, and other subjects. Most questions concerned the last year or the time between the two interviews. Determination of HIV and HCV (hepatitis C virus) antibodies in a dried blood spot was made by enzyme immunoanalysis (Pulido et al., 2009).

Both vital status and cause of death were obtained through record linkage with the National Mortality Register. Follow-up ended on July 2010. In the analysis, several subgroups of PCUs were considered according to risky drug-use patterns. PCUs were classified first using only drug use patterns from the baseline interview, and again after incorporating such patterns from the follow-up interview. Crude mortality rates (CMRs) per thousand person-years of follow-up (py) were determined for age–sex groups, using the dynamic method of allocation of person-years and deaths to the age group (Cleves, Gould, Gutiérrez, & Marchenko, 2010). Excess mortality compared to their age–sex peers in the general population was estimated with standardized mortality ratios (SMRs), using mortality rates of the Spanish population in 2008 (INE, 2011). Stratification methods were used to partially control the possible confounding effect of opioid use, drug injection or smoking cocaine. It was not possible to control for other variables. Causes of death were coded according to the International Classification of Diseases (ICD-10). Statistical analyses were conducted with STATA (Cleves et al., 2010).

3. Results

At baseline PCUs were young (mean age: 23.0), mostly men and had used cocaine for 6.2 years on average. In the year before baseline they had used cocaine 135 days on average, mainly by sniffing (91.6%). Some 62.5% (446) had never used illicit opioids, 94.3% had never injected drugs, 64.4% had never smoked cocaine, and 50.7% (362) were PICUNINOs. Lifetime opioid users were older, with higher probability of unemployment, imprisonment, arrests, or accommodation in precarious housing or institutions than never-opioid users. Moreover, they had used cocaine for longer, currently used it more often, were more likely to be drug injectors, cocaine smokers or polydrug users, and had a higher prevalence of HCV infection (Table 1).

The vast majority of lifetime opioid users had used these drugs very sporadically in the year before baseline. Only 1.1%, 0.7% and 4.3% of total participants, respectively, had used heroin, street methadone or other opioids monthly or more frequently, and only 1% had been treated for opioid abuse or dependence in that year.

PICUNINOs were very similar in their characteristics to never-opioid users, since they comprise a large percentage of the latter subgroup (Table 1).

Average follow-up time was 5.07 years per participant (SD: 0.86). Among all baseline PCUs there were 9 deaths in 3922 py, giving a CMR of 2.3/1000 py and a SMR of 4.7 (Table 2). The causes of death were: acute drug intoxication (3), HIV infection (2), suicide (1), pulmonary embolism (1), unspecified respiratory failure (1), and ill-defined and unspecified cause (1). The SMR tended to be higher in lifetime opioid users than never-opioid users (8.1 vs. 2.5), although the confidence intervals overlapped. Among PICUNINOs, the CMR (1.5/1000 py) and the SMR (3.1) were similar to never-opioid users. No relevant changes in CMR and SMR between the first and the second half of the follow-up period were found.

Of the baseline participants, 503 PCUs (70.4%), 333 (73.7%) never-opioid users, and 278 PICUNINOs (76.2%) could be interviewed 1–2 years after baseline. About 2.6% (95% CI: 1.1–4.1) of all PCUs, 3.6% (95% CI: 1.5–5.6) of never-opioid users, and 1.8% (95% CI: 0.5–4.6) of PICUNINOs ceased cocaine use, and among those who continued using cocaine the annual mean number of days of use decreased, respectively, from 131.0 days (95% CI: 125.4–136.6) to 69.3 (95% CI: 62.6–76.5), from 119.5 days (95% CI: 113.2–125.7) to 61.1 (95% CI: 53.8–68.3), and from 115.4 days (95% CI: 108.4–122.5) to 58.7 (50.8–66.5). The proportion of never-opioid users who started opioid use (9.0%; 95% CI: 5.8–12.2) was much lower than the proportion of last-year opioid users who ceased such use (31.3%; 21.7–41.0). Similarly, the proportion of "initiators" of any risky behaviors (opioid use, drug injection or cocaine smoking) (6.8%; 95% CI: 3.7–10.0) was much lower than the proportion of those who ceased all such behaviors (46.2%; 39.3–53.0). When including follow-up data on patterns of drug use, the SMRs were 1.2 among never-opioid users and 1.4 among PICUNINOs. However, the SMRs were 7.2 and 6.6, respectively, among lifetime opioid users and participants with opioid use or drug injection or cocaine smoking (Table 2).

4. Discussion

In this study we have explored the excess mortality compared to the general population in a Spanish street-recruited cohort of young primary cocaine users who at baseline had never used illicit opioids (62.5%) or did so only sporadically (≤12 days in the year before baseline). Participants had a mortality rate 4.7 times (95% CI: 2.4–9.0) higher than their age–sex peers in the general population during the 5 years following baseline (short term).

From this study it is very difficult to clearly identify explanatory factors for this excess mortality. However, mortality seems to be lower among never-opioid users at baseline than among lifetime opioid users (SMR = 2.5 vs. 8.1) and among those who at baseline neither used opioids nor injected drugs nor smoked cocaine (PICUNINOs) than among those with any of these risky behaviors (SMR = 3.1 vs. 6.2), although neither of the two differences reached statistical significance. The differences appear to be even larger after excluding those who started opioid use or other risky behaviors during follow-up. It might therefore be hypothesized that in Spain the excess mortality of young PCUs in the short term may largely be explained by a history of opioid use (or some strongly associated factor) or the risk of starting opioid use during follow-up, which was not negligible.

This study is perhaps the first to estimate excess mortality in young PCUs, controlling simultaneously for the effect of heroin use, drug injection and crack/cocaine smoking. This control is essential to obtain valid estimates because the mentioned behaviors are associated with a high risk of mortality (Degenhardt et al., 2011a; Dias et al., 2011; Muhuri & Gfroerer, 2011). To control the effect of opioid use, we excluded from the cohort those participants who had used such drugs more than 12 days in the year before baseline. Thus, during that year all participants had used cocaine much more frequently than heroin (≥52 days vs. ≤12 days), and it could be assumed that they were not primary opioid users. Moreover, stratification methods were also used to control the confounding, focusing on those subgroups that had never used opioids or other risky behaviors at baseline or follow-up interview. The results show that controlling for

Table 1
Baseline characteristics of different subgroups of a Spanish cohort of young primary cocaine users (%).

		Lifetime opioid use[a]			Very risky drug use behaviors in lifetime[b]		
	Total	Yes	No	p-value	Yes	No[c]	p-value
No. of participants	714	268	446		352	362	
Sociodemographic characteristics							
Males[d] (%)	66.0	66.4	65.7	NS	65.9	66.0	NS
Age[d] (mean [SE])	23.0 [0.1]	24.0 [0.2]	22.3 [0.2]	<0.001	23.9 [0.2]	22.0 [0.2]	<0.001
Secondary studies or higher completed[d] (%)	87.0	87.3	86.8	NS	86.1	87.9	NS
Unemployed[e] (%)	26.8	35.5	21.5	<0.001	35.2	18.5	<0.001
Living in institutions, squatter, homeless[e] (%)	11.6	25.0	3.6	<0.001	21.6	1.9	<0.001
Having been arrested[e] (%)	18.4	27.6	12.8	<0.001	26.7	10.2	<0.001
Ever in prison[d] (%)	3.8	7.5	1.6	<0.001	6.8	0.8	<0.001
Cocaine use							
Length of use[d] (mean no. of years [SE])	6.2 [0.1]	7.5 [0.2]	5.3 [0.1]	<0.001	7.3 [0.2]	5.0 [0.1]	<0.001
Frequency of use[e] (mean no. of days [SE])	131.0 [2.9]	150.3 [5.3]	119.5 [3.2]	<0.001	148.3 [4.7]	115.4 [3.6]	<0.001
Cocaine smoking[e]	22.4	44.4	9.3	<0.001	_	_	_
Sniffing as usual route of cocaine administration[e] (%)	91.6	81.3	97.8	<0.001	83.0	100.0	<0.001
Other drug use							
Using more than 3 different drugs[e,f] (%)	71.3	91.0	59.4	<0.001	84.7	58.3	<0.001
Regular excessive drinking[e,g] (%)	69.9	73.5	67.7	NS	71.9	68.0	NS
Drug injection[e]	4.0	10.5	0.2	<0.001	_	_	_
Infections							
HIV infection prevalence[d] (%)	0.7	1.5	0.2	NS	1.6	0.0	<0.05
HVC infection prevalence[d] (%)	3.3	7.5	1.0	<0.001	6.4	0.6	<0.001

NS: Not significant; SE: Standard error.
[a] The term "opioids" refers to heroin or other opioids for nonmedical purposes.
[b] These behaviors include opioid use, drug injection or cocaine smoking.
[c] This subgroup is also called "Primary intranasal cocaine users, never-injectors and never-opioid users" or PICUNINOs.
[d] At the time of the baseline visit.
[e] The variable measurement refers to the last 12 months before the baseline visit.
[f] Considering the main groups of commonly abused psychoactive substances excluding cocaine, alcohol and tobacco.
[g] Men: ≥280 g of pure alcohol a week; women: ≥168 g a week.

opioid use also controls fairly well for drug injection and cocaine smoking, because in Spain the latter two behaviors were still highly concentrated among opioid users; it was extremely rare, for example, to find drug injectors who had never used opioids. Another strength is that, since participants were recruited outside legal or care services they are probably more representative of all cocaine users than cohorts recruited into or through such services.

However, the study also has some limitations. The number of deaths and years of follow-up is rather small, leading to relatively imprecise estimates. There may be some misclassification by drug use patterns because of recall biases or socially desirable responses. Patterns of drug use were assessed only at baseline and 1–2 years later. However, they may change over time, affecting the risk of dying. Therefore, we cannot know for certain that those who were non-opioid users or PICUNINOS at first follow-up interview remained so at the time of death or end of follow-up. Finally, the excess mortality cannot be automatically attributed to cocaine use, because the participants and the reference population may differ in other factors that could partly explain the excess mortality.

As hypothesized, the estimate of excess mortality among young Spanish PCUs is in the lower range of published studies (SMRs = 4–8), in which the effect of opiates and other risky behaviors was barely controlled (Degenhardt, Singleton, et al., 2011b). Our results are closer to those of an Italian cohort of cocaine users attending a drug addiction center, which controlled for opioid use at baseline, but not drug injection or cocaine smoking (SMR = 4.9) (Pavarin, 2008).

Table 2
Mortality of different subgroups of a Spanish cohort of young primary cocaine users (%).

		Deaths (no.)	py (no.)	CMR (per 1000 py)	95% CI	SMR	95% CI
Total		9	3922	2.3	1.2–4.4	4.7	2.4–9.0
Drug use patterns at baseline interview							
Lifetime opioid use[a]	Yes	6	1456	4.1	0.8–7.4	8.1	3.7–18.1
	No[c]	3	2467	1.2	0.0–2.6	2.5	0.8–7.8
Very risky drug use behaviors in lifetime[b]	Yes	6	1922	3.1	1.4–6.9	6.2	2.8–13.9
	No[c,d]	3	2000	1.5	0.0–3.2	3.1	1.0–9.6
Drug use patterns at follow-up *interview*[e]							
Lifetime opioid use[a]	Yes	8	2261	3.5	1.1–6.0	7.2	3.6–14.3
	No[c]	1	1662	0.6	0.0–1.8	1.2	0.2–8.5
Very risky drug use behaviors in lifetime[b]	Yes	8	2487	3.2	1.6–6.4	6.6	3.3–13.1
	No[c,d]	1	1435	0.7	0.0–2.1	1.4	0.2–9.9

CMR: Crude mortality rate. SMR: Standardized mortality rate. 95% CI: 95% confidence interval.
[a] The term "opioids" refers to heroin or other opioids for nonmedical purposes.
[b] These behaviors include opioid use, drug injection or cocaine smoking.
[c] Some of the participants in this subgroup could actually have had the considered behavior between the time of the baseline interview and follow-up interview because 30% of all participants did not attend the latter interview.
[d] This subgroup is also called "Primary intranasal cocaine users, never-injectors and never-opioid users" or PICUNINOs.
[e] The follow-up interview was made 1–2 years after the baseline interview. py: Person-years of follow-up.

The results suggest that short-term excess mortality in young Spanish PCUs could be partially explained by a history of opioid use or the risk of starting such use. Although regular cocaine use has been associated with an increased risk of cardiovascular and other health problems (EMCDDA, 2007; Kaye & Darke, 2004a; Kuhns et al., 2009; Macdonald et al., 2003; Maraj et al., 2010; Marzuk et al., 1995; Qureshi et al., 2001; Ryb et al., 2009; Santos et al., 2012; Schnitzer et al., 2010), it is unlikely that the amount of cocaine-related damage to the body accumulated at such a young age would be enough to cause death.

Despite the limitations, our findings among young Spanish PCUs could perhaps be generalized to young PCUs from other developed countries with socio-economic conditions, drug use patterns and health care coverage similar to Spain, for example, most Western European countries.

These estimates allow a better approximation to the population-attributable risk of death from cocaine use. Given the difficulty of estimating excess mortality in cohorts that are representative of all cocaine users in the general population, valid estimates of this population-attributable risk could be obtained by previously obtaining SMRs and population prevalence for major patterns of cocaine use, and adding the partial contributions of these subgroups. It may be that regular cocaine sniffing contributes much more to the population-attributable risk than other patterns of cocaine use due to the much higher prevalence of cocaine sniffing in the general population.

New studies incorporating changes in drug use patterns during follow-up are needed in different geographical areas with sufficiently large sample sizes to allow estimation of excess mortality in different subgroups of cocaine users, especially those like PICUNINOs that are more frequently represented in the general population.

Role of funding sources

This work was funded by the Foundation for Research and Prevention of AIDS in Spain (FIPSE 36253/01) and the Spanish Network on Addictive Disorders (RD06/0001/1018). These organizations had no role in the study design, collection, analysis of the data, writing the manuscript, or the decision to submit the paper for publication.

Contributors

All of the authors have revised the paper critically and approved the final version to be published. Gregorio Barrio conceived and drafted the article, directed the data analysis, and participated in the implementation of the cohort study. Gemma Molist performed the statistical analysis, including the record linkage with the mortality register. Luis de la Fuente, María J. Bravo and M. Teresa Brugal conceived, directed and coordinated the implementation of the cohort study and collaborated in the conception and drafting of the article and in the interpretation of the data. Fermín Fernández and Anna Guitart were actively involved in data acquisition (recruiting participants and conducting interviews), as well as in the preparation and data cleaning.

Conflict of interest

None of the authors has any actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations within 3 years of beginning the submitted work that could inappropriately influence, or be perceived to influence, their work. The views expressed herein do not represent the official policies or perspectives of the funders.

Acknowledgments

Grateful thanks are due to the participants in this study as volunteers, as well as all individuals and institutions that have helped us in the recruitment and follow-up of participants, have lent us their facilities to carry out interviews and have helped us in the management of the project. These institutions have been mentioned in the basic publication describing the cohort (Pulido et al., 2009).

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