Drug and Alcohol Dependence 134 (2014) 12–21

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Review

Association between depression and non-fatal overdoses among drug users: A systematic review and meta-analysis☆

Francesco Bartoli[a], Giuseppe Carrà[b,*], Giulia Brambilla[a], Daniele Carretta[a], Cristina Crocamo[c], Julia Neufeind[d], Alex Baldacchino[e], Gerry Humphris[d], Massimo Clerici[a]

[a] Department of Surgery and Interdisciplinary Medicine, University of Milano Bicocca, Milano 20126, Italy
[b] Mental Health Sciences Unit, Faculty of Brain Sciences, University College London, W1W 7EJ, UK
[c] Department of Mental Health, San Gerardo Hospital, Monza 20900, MB, Italy
[d] Medical and Biological Sciences Building, University of St Andrews, North Haugh, St Andrews KY16 9TF, UK
[e] Division of Neuroscience, Medical Research Institute, University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK

ARTICLE INFO

Article history:
Received 22 July 2013
Received in revised form
23 September 2013
Accepted 13 October 2013
Available online 24 October 2013

Keywords:
Depression
Drug overdose
Meta-analysis

ABSTRACT

Background: Assessing factors associated with non-fatal overdose is important as these could be useful to identify individuals with substance use disorders at high risk of adverse outcomes and consequences. Depression may play an important role in terms of overdose risk. We aimed to test if drug users suffering from a depressive disorder might have significantly higher risk of non-fatal overdose as compared with drug users without depression.
Methods: We conducted a systematic review and meta-analysis. PubMed, Embase and Web of Knowledge were searched. The pooled analyses were based on prevalence rates, risk difference (RD) and odds ratio (OR), reporting 95% confidence intervals (CIs). The combined estimates were obtained weighting each study according to random effects model for meta-analysis.
Results: Seven articles, involving 12,019 individuals, and run in the US, Canada, Sweden, Norway, and Australia, were included. Pooled analyses comparing depressed with not depressed individuals highlighted a RD (95% CIs) for non-fatal overdose of 7.3% (4.8–9.7%) and an OR (95% CIs) of 1.45 (1.17–1.79). The subgroups analyses based on specific characteristics of included studies confirmed the association between depression and overdose.
Conclusions: Depressive disorders seem to be important factors associated to the risk of non-fatal overdose. Longitudinal studies might appropriately clarify causal inference issues. Future research should address the role of depressive disorders as predictors of subsequent non-fatal overdoses.

Contents

☆ Supplementary material can be found by accessing the online version of this paper. See Appendix A for more details.

* Corresponding author at: Mental Health Sciences Unit, Faculty of Brain Sciences, University College London, Charles Bell House, 67–73 Riding House Street, London W1W 7EJ, UK. Tel.: +44 20 7679 9428; fax: +44 20 7679 9426.
E-mail addresses: g.carra@ucl.ac.uk, g.carra@hsgerardo.org (G. Carrà).

0376-8716/$ – see front matter © 2013 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.drugalcdep.2013.10.007

1. Introduction

Substance use disorders are related to serious consequences, such as risk of overdose and early mortality (Cornelius et al., 2008; Kertesz et al., 2012). Heroin, cocaine, and amphetamine use disorders show standardized mortality ratios of 9.1 (CI: 8.5–9.8), 6.4 (CI: 3.9–10.0), and 6.0 (CI: 4.2–8.3), respectively (Arendt et al., 2011). The median estimated non-AIDS-related mortality rate among persons who inject drugs has been estimated 1.08% per annum (Degenhardt et al., 2006). Illicit drug overdose is a leading cause of premature death and morbidity among opioid users (Darke and Hall, 2003). Overdose-related mortality accounts for 0.65 (0.55–0.75) deaths per 100 person-years, followed by trauma and suicide related deaths, with values of 0.25 and 0.12, respectively (Degenhardt et al., 2011). People from Asia who inject drugs have the highest pooled overall crude mortality rate (5.25), followed by populations from North America (2.64) and Western Europe (2.31). An overall crude mortality is related to male gender, not being in treatment, and living in low- and middle-income countries (Mathers et al., 2013). A 2010 meta-analysis (Merrall et al., 2010) showed an increased risk of drug-related deaths during the first 2 weeks after release from prison. The risk remained high up to at least the fourth week. Furthermore, as HIV-serostatus may consistently affect outcomes of opiate dependents (Carrà et al., 2008a), HIV comorbidity seems to represent also an important factor associated with an increased risk of mortality for overdose (pooled risk ratio = 1.74; 95% CI: 1.45–2.09) (Green et al., 2012). Despite being clearly more common than fatal overdose, non-fatal overdose has received considerably less attention in the literature (Kerr et al., 2007), possibly because public health concerns have been focused on lethal consequences (Darke and Zador, 1996; Carrà et al., 2006). However, non-fatal overdose is an important cause of morbidity among illicit drug users and can result in a number of serious medical consequences, such as cardiovascular and pulmonary complications, peripheral neuropathy, anoxia-induced cognitive impairment, rhabdomyolysis, and renal failure (Warner-Smith et al., 2001). Evidence shows also that non-fatal overdoses consistently increase the risk of subsequent overdose mortality (Stoové et al., 2009). An improved assessment of non-fatal overdose rates and risk factors may help clinicians for preventing the excess of overdose fatalities (Darke et al., 2003). The prevalence rates of lifetime history of non-fatal overdose range between 13% and 69% among drug users (Bohnert et al., 2010). Evidence suggests that severity of dependence, polysubstance use, serious withdrawal symptoms, history of suicide attempt, length of drug using career, number of network members who inject drugs, homelessness, all are important risk factors for non-fatal overdoses (Backmund et al., 2009; Bohnert et al., 2010; Brugal et al., 2002; Coffin et al., 2007; Jenkins et al., 2011; Kerr et al., 2007).

Comorbidity for a mental disorder, involving more than half of drug-abusing individuals (Regier et al., 1990), may play an important role on the likelihood of nonfatal overdose. Drug users with co-occurring mental disorders report poorer prognosis, in terms of remission and relapse likelihood (Hasin et al., 2002), emergency department use (Curran et al., 2003), family/social relationships (Carrà and Clerici, 2006; Carrà and Johnson, 2009; Carrà et al., 2012), medical comorbidity (Rosenberg et al., 2001). Little is known on the potential influence of depression on non-fatal overdose (Conner et al., 2008). Depression among drug users in residential programs is related to lower adherence and higher drop-out rates (Ravndal and Vaglum, 1994). Depressed methadone patients may be more sensitive to negative opioid effects and withdrawal (Elkader et al., 2009), and such a comorbid disorder seems associated also to an increased risk of suicide attempt and ideation among drug and opioid users (Aharonovich et al., 2002; Darke and Ross, 2002; Phillips et al., 2004).

To the best of our knowledge this is the first meta-analysis that systematically analyzes the relationship between depression and non-fatal overdose. We tested the hypothesis that drug users suffering from a depressive disorder would have shown rates, and experienced risk, of non-fatal overdose significantly higher than non-depressed drug users.

2. Methods

The present systematic review and meta-analysis was conducted according to the Metaanalyses Of Observational Studies in Epidemiology (MOOSE) guidelines (Stroup et al., 2000).

2.1. Search strategy

We searched the Electronic databases PubMed, Embase and Web of Knowledge for papers published up to September 2012. Additionally, we explored the reference list of a relatively recent relevant systematic review (Bohnert et al., 2010) on the association between overdose and suicide attempts in samples of substance users. We searched for papers in English, Spanish, French, German, Portuguese or Italian. Search phrases combined thesaurus terms related to overdose, depression, and mental disorders. In addition, synonyms of thesaurus terms were used for free search in titles and abstracts. Full search strategies are detailed in Supplementary Material[1].

2.2. Eligibility criteria

We included any observational study that provided:

1. A target population composed by adults with at least one of the following characteristics. A) a problem drug use defined as intravenous drug use and/or long duration/regular use of illicit drugs, such as opiates, cocaine and/or amphetamines (Kraus et al., 2003); B) being in treatment in an addiction service

[1] Supplementary material can be found by accessing the online version of this paper. See Appendix A for more details.