Drug and Alcohol Dependence 176 (2017) 126–132

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

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

Full length article

Frequency and severity of non-fatal opioid overdoses among clients attending the Sydney Medically Supervised Injecting Centre

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ARTICLE INFO

Keywords:
Heroin
Oxycodone
Overdose rates
Overdose severity
Polydrug use
Prescription opioids
Supervised Injecting Centre

ABSTRACT

Background: Pharmaceutical opioid overdose rates have increased in recent years. The current study aimed to compare rates per 1000 injections of non-fatal overdose after heroin or oxycodone injection, and their comparative clinical severity.

Methods: Analysis of prospectively collected data from the Sydney Medically Supervised Injecting Centre (MSIC). Severity of overdose was measured using the Glasgow Coma Scale, oxygen saturation levels, and the administration of naloxone.

Results: Heroin overdoses occurred at three times the rate of oxycodone overdoses (12.7 v 4.1 per 1000 injections). Heroin overdoses appeared to be more severe than oxycodone overdoses, with higher levels of compromised consciousness (31 v 18%) and severe respiratory depression (67 v 48%), but there were no differences in naloxone doses (20 v 17%). Concurrent use of other depressants at the time of overdose was also associated with compromised consciousness, and the need for naloxone.

Conclusions: Heroin overdoses occurred at a greater rate than oxycodone overdoses, and had more severe clinical indicators.

1. Introduction

Fatal opioid overdose is the leading cause of mortality among people who inject drugs (PWID) (Degenhardt et al., 2013) and this group has a substantially elevated mortality rate (Degenhardt et al., 2010). Over the course of the past decade opioid consumption patterns have significantly altered, with an unprecedented increase in the prescribing and use of pharmaceutical opioids (Berterame et al., 2016; Bohnert et al., 2011; Dart et al., 2015; Girauden et al., 2013; Maxwell, 2011). Globally, between 2001 and 2013, the number of utilized opioid doses doubled (Berterame et al., 2016). This phenomenon has been most prominent in North America, but significant increases in consumption have also occurred in Western Europe and Australasia (Berterame et al., 2016). While these increases are predominantly of oral opioids, their injection by PWID has also increased markedly (Cicero et al., 2014; Darke et al., 2015; Maxwell, 2011).

The increases in the prescribing, use and abuse of pharmaceutical opioids have seen a paralleled increase in the prevalence of opioid overdose deaths (Bohnert et al., 2011; Dart et al., 2015; Hedegaard et al., 2015; Martins et al., 2015; Maxwell, 2011). Indeed, in the United States there was a marked change in the drug predominantly involved in overdose deaths from heroin and cocaine in the 1990s to pharmaceutical opioids by 2002 (Rudd et al., 2016). Large proportions of these overdose cases are people who inject drugs (PWID) (Darke et al., 2011; Hall et al., 2008; Ogle et al., 2012; Rintoul et al., 2011; Roxburgh et al., 2011). Despite changes in use patterns, deaths from heroin overdose have continued to occur in several countries (Dart et al., 2015; Degenhardt et al., 2013; European Monitoring Centre for Drugs and Drug Addiction, 2016; Hedegaard et al., 2015). Indeed, since 2010 heroin toxicity deaths in the United States have increased markedly (Dart et al., 2015; Hedegaard et al., 2015), and the use of pharmaceutical opioids appears to be a new entry point to heroin use (Cicero et al., 2014). Increases in heroin deaths in the United States also represent an increase in heroin use (Compton et al., 2016).

Despite increases in both pharmaceutical opioid use and overdose deaths among PWID, the relative risk of overdose following heroin injection compared to pharmaceutical opioid injection is unknown. Regardless of the opioid, overdose (and death) from opioid toxicity is due to the respiratory depressant effects of these drugs (Karch, 2009). Respiratory depression is seen more frequently amongst opioid users when severity is sufficient to constitute a medical emergency, even amongst those with high opioid tolerance (Lintzeris et al., 2007; Strang

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http://dx.doi.org/10.1016/j.drugalcdep.2017.02.027
Received 25 August 2016; Received in revised form 21 February 2017; Accepted 22 February 2017
Available online 17 May 2017

et al., 2015). This is thought to reflect the fact that the tolerance to the respiratory depression associated with opioids is less than complete, and slower to develop than tolerance to euphoric effects (White and Irvine, 1999).

Pharmaceutical opioids are, however, clearly different in composition to heroin, with the former being manufactured under regulation by dose and pharmacological action for licit use, compared to the unregulated manufacture of heroin with variable purity, for illicit use. Research shows however that purity alone does not explain overdose (Darke and Farrell, 2014). Heroin and oxycodone vary in both their half-lives post-injection (1.9 v 3.4 h) and time from injection to peak plasma concentration (10 v 25 min). In relation to the latter, these drugs have differing levels of liposolubility, which affects the rate at which they cross the blood brain barrier, with heroin liposolubility being 200 times higher than morphine (Trivedi et al., 2007; Poyhia and Seppala, 1994). Higher liposolubility produces more rapid respiratory depression. It is in this context that we investigate the potential differences between heroin and oxycodone overdose. We have chosen oxycodone as the comparative pharmaceutical opioid as oxycodone injections are more prevalent at the study site than any other pharmaceutical opioid.

The Sydney Medically Supervised Injecting Centre (MSIC) is the only facility of its kind in the Southern hemisphere. It is located within Sydney's Kings Cross area, which has a long history of street based illicit drug markets. The Centre has been operational since 2001, and provides a unique opportunity to examine opioid overdoses that occur on site among clients. Injections are observed by health professionals, and clients are observed post-injection for clinical signs of overdose. Notably, there have been no fatal overdoses onsite during the operation of this service.

In this study we investigated the comparative rates and severity of overdoses following heroin and oxycodone injection. Specifically, the paper aimed to:

- Determine the rates of non-fatal overdose per 1000 injections by opioid type (heroin and oxycodone) occurring at the MSIC 2007–2014; and
- Determine the comparative clinical severity of heroin and oxycodone overdoses in terms of reduced consciousness, oxygenation and the administration of the opioid antagonist naloxone;

2. Methods

2.1. Client data

Data presented in this paper are based on the total of 8382 individual clients who attended the MSIC to inject drugs during the period January 2007 to April 2014. We have chosen to analyse data from 2007 onwards as there were no oxycodone overdoses at the MSIC prior to this date. The eligibility criteria to use the service include being at least 18 years of age, and a history of injecting drug use. Data for non-fatal heroin and pharmaceutical opioid overdose are presented for clients overdosing while attending the MSIC to inject.

2.2. Measures

Upon arrival for the first time at the MSIC, all clients are required to complete a registration questionnaire that assesses client demographics, injection-related risk behaviour, drug use, drug treatment and drug overdose history. For each service occasion, data are collected on which drug the client intends to inject for that visit, and any other events that occur during the visit. Data are collected on the context of overdoses that occur on site (including drug injected, other drugs used prior to attending, reduced tolerance as reported by the client, and recent discharge from prison or drug treatment facility), as well as management of each overdose including interventions (including airway management, oxygenation and, where required, naloxone) administered.

2.3. Frequency and severity of overdose

We calculated rates of heroin overdose per 1000 heroin injections, and oxycodone overdose per 1000 oxycodone injections. We then calculated the comparative rate of heroin to oxycodone overdoses. We calculated 95% confidence intervals using Byar's method (Breslow and Day, 1987).

We use the following clinical outcome measures to indicate the severity of overdose:

- The Glasgow Coma Scale (GCS), a measure of consciousness, is used to determine responsiveness of clients at time of overdose. Scores of ≤ 8 indicate a severe reduction in consciousness, likely to require intervention (Teasdale and Jennett, 1974).
- Oxygen saturation levels are presented at the initial observation point. Oxygen saturation levels $\leq 85\%$ represent hypoxia and may compromise organ function.
- Naloxone administration, if deemed to be required by the attending clinician, occurs after airway management and oxygen administration has failed to improve consciousness.

2.4. Statistical analysis

We present data on opioid overdose at the MSIC for the period 2007–2014. Differences in severity (measured by GCS, oxygen saturation levels and naloxone administration) of heroin and oxycodone overdoses were analysed using logistic regression. Three models were built modelling the following outcomes; 1) a GCS score of ≤ 8; 2) oxygen saturation levels of $\leq$ 85%; and 3) naloxone administration. Variables included in the model were; substance (heroin or oxycodone), using a greater quantity than usual, reduced tolerance and concurrent use of other depressants. We included these variables due to extensive evidence of their involvement in opioid overdose (Darke and Farrell, 2014; Merrall et al., 2010). We identified further potential confounders by comparing client demographics, overdose and treatment history between users with a history of using 1) heroin; 2) oxycodone; and 3) both heroin and oxycodone at the MSIC (Supplementary Table S1). Factors that differed between the three groups and were adjusted for comprised: years registered at the MSIC at time of overdose, number of previous visits to the MSIC, indigenous status, having been in prison, a history of homelessness, public injecting, overdose prior to MSIC registration, and opioid substitution therapy. We also controlled for age at time of the overdose and gender. We retained all variables across the three outcomes of interest. We used analyses based on generalised estimating equations to account for the possibility of clients experiencing more than one on-site overdose using SAS v9.4 (SAS Institute Inc, 2015).

3. Results

3.1. Rates of overdose

Approximately two-thirds (62%) of all opioid overdoses (N = 2860) occurring onsite at the MSIC between May 2007 and April 2014 were due to heroin (N = 1784) and one third (37%) were due to pharmaceutical opioids (N = 1076). Oxycodone (N = 829) was the most predominant pharmaceutical opioid involved (Table 1). There were 688 clients who had overdosed on heroin and 305 who had overdosed on oxycodone (Table 1).

During the period 2007–2014, there were 12.7 heroin overdoses per 1000 injections compared to 4.1 oxycodone overdoses per 1000 injections. The rate of heroin overdoses was 3.1 (95% CI 3.0, 3.2) times higher than the rate of oxycodone overdoses (Table 2).