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Patterns and correlates of non-fatal heroin overdose at 11-year follow-up: Findings from the Australian Treatment Outcome Study

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ABSTRACT

Background: Overdose is a major cause of morbidity and mortality amongst opioid users. This paper reported recent non-fatal overdose amongst the Australian Treatment Outcome Study (ATOS) cohort at 11-year follow-up, and characteristics that predict recent overdose.
Methods: Longitudinal cohort, with 431 (70.1%) of the original 615 participants interviewed. Participants were administered the ATOS structured interview, addressing demographics, treatment history, drug use, heroin overdose, criminality, health and psychopathology.
Findings: Mean time since heroin initiation was 20.4 years. By 11-year follow-up, the proportion who had overdosed was 67.5%, and 24.4% had experienced five or more overdoses. In the 12 months preceding 11-year follow-up, 4.9% had overdosed (11.8% of those who had used heroin in that period). Of the 21 participants who had recently overdosed, 20 (95.2%) had overdosed previously, and 19 (90.5%) were not enrolled in a treatment programme at the time. Those who had recently overdosed reported higher levels of use of opiates other than heroin (57.1% vs 24.9%), benzodiazepines (61.9% vs 30.5%,), methamphetamine (38.1% vs 16.8%) and cocaine (19.0% vs 3.7%). They also had exhibited higher levels of heroin use and other drug use at baseline, 12 and 24 month follow-ups.
Conclusions: While the prevalence had declined, overdoses still occurred. A history of overdose and polydrug use patterns continued to provide strong markers for those at continued risk.

1. Introduction

Opioids make the largest contribution to illicit drug-related death, overdose being the leading cause (Bargagli et al., 2006b; Bird, 2010; Darke, 2011; Darke et al., 2011; Degenhardt et al., 2011; Stenbacka et al., 2010). Fatal outcomes, however, represent a minority of overdoses, with 25–50 non-fatal "near misses" for every fatality (Darke et al., 2003). The ubiquity of overdose amongst users is illustrated by lifetime prevalence, with studies consistently reporting a third to two thirds having overdosed (Backmunda et al., 2009; Bargagli et al., 2006b; Britton et al., 2010; Coffin et al., 2007; Darke et al., 2007; Kerr et al., 2007; Wines et al., 2007). Non-fatal overdose is of clinical significance, as it is associated with harms related to the event itself including anoxic brain damage (Warner-Smith et al., 2001, 2002), subsequent non-fatal overdose (Coffin et al., 2007; Darke et al., 2007) and subsequent death (Darke et al., 2011).

One of the major findings to emerge over the past few decades has been that overdose is *not* a random event and, hence, is preventable. A number of specific risk factors have been identified. Firstly, as noted above, a history of overdose strongly predicts future overdoses (Coffin et al., 2007; Darke et al., 2007). Heroin overdoses are also associated with more frequent use, higher levels of dependence and with the injection of the drug (Backmunda et al., 2009; Bargagli et al., 2006b; Britton et al., 2010; Coffin et al., 2007; Darke, 2011; Darke et al., 2007; Kerr et al., 2007; Wines et al., 2007). Overdoses, however, rarely involve only heroin, the overwhelming majority involving the concomitant consumption of other CNS depressants (Backmunda et al., 2009; Britton et al., 2010; Coffin et al., 2007; Kerr et al., 2007; Wines et al., 2007; Darke, 2014; Darke et al., 2010). There is also a substantially elevated risk during a relapse to use after a period of abstinence, such as having been in prison, detoxification or naltrexone maintenance (Davoli et al., 2007; Kerr et al., 2007; Wines et al., 2007; Darke et al., 2002;

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Farrell and Marsden, 2007; Strang et al., 2003). Finally, most overdoses occur when the person is not enrolled in a long-term, stable drug treatment (Davoli et al., 2007; Kerr et al., 2007; Darke et al., 2010).

There are little data on the long-term natural history of opioid overdose, with almost all research to date being cross-sectional. An exception to this has been the Australian Treatment Outcome Study (ATOS) cohort, recruited in 2001–2002, and interviewed at 12, 24 and 36-month follow-up (Teesson et al., 2008). Typical of such cohorts, at baseline 54% reported having a lifetime history of overdose, 22% having overdosed in the preceding year (Darke et al., 2005). Consistent with reductions in reported heroin use, past 12-month overdose declined across follow-up: 12% (12 months), 9% (24 months) and 8% (36 months; Darke et al., 2005, 2007). While there were marked declines in overdose, 20% had overdosed over the course of the first 36 months. By 2009, 31 (5%) of the cohort were deceased, predominately due to overdose (Darke et al., 2011). Indeed, the only significant predictor of mortality was a history of non-fatal overdose.

In this paper, we present new data on the natural history of overdose amongst the ATOS cohort, examining overdose at 11 years, approximately 20 years since the initiation of heroin use. A number of questions arise. Firstly, what are the levels of lifetime overdose exposure approximately 20 years after first heroin use? What is the prevalence of recent (12 month) overdose at 11-year follow-up, and what are the correlates? Specifically, the study aimed to: (1) determine lifetime and recent overdose prevalence amongst the ATOS cohort at 11-year follow-up; and (2) determine correlates of overdose in the year preceding 11-year interview.

2. Methods

2.1. Procedure

The data were collected from the New South Wales component of ATOS. Baseline interviews were conducted between February, 2001 and August, 2002. ATOS is a longitudinal study of heroin users, recruited from randomly selected treatment agencies delivering methadone/buprenorphine maintenance treatment (MT) ($n = 201$), drug free residential rehabilitation (RR) ($n = 133$) or detoxification (DTX) ($n = 201$). Subjects were recruited from 19 agencies treating heroin dependence in the greater Sydney region, randomly selected from within treatment modality. The agencies comprised 10 MT agencies, four RR agencies and nine DTX facilities. In addition, a comparison group of 80 heroin users not currently in treatment (NT) were recruited from needle and syringe programmes. Participants were interviewed at baseline, 3 months, 12 months, 24 months, 36 months and 11 years. The current study focuses on overdose data from the 11-year follow-up. Eligibility criteria at baseline were: (i) no treatment for heroin dependence in the preceding month, (ii) no imprisonment in the preceding month, (iii) agreed to give contact details for follow-up interviews, (iv) aged ≥18 years and (v) fluent in English. Subjects were paid A$40. Ethical approval was given by the University of New South Wales and all relevant area health services.

At the 3-month follow-up interview, hair sampling was conducted on 61 randomly selected participants (approximately 10% of the baseline sample) as a biomarker for heroin use over the month preceding interview (Ross et al., 2006). The overall agreement between self-reported heroin use and the presence of hair morphine was 75% (kappa = 0.49). In 15% of cases heroin use was reported, but morphine not detected and in 10% recent heroin use denied but morphine detected.

2.2. Structured interview

At baseline, participants were administered a structured interview that addressed demographics, treatment history, drug use, heroin overdose, criminal behaviours, health and psychopathology. As in previous studies (Darke et al., 2005, 2007), overdose was defined as any of the following symptoms occurring in conjunction with heroin use: difficulty in breathing, turning blue, collapsing, losing consciousness and being unable to be roused. It was emphasised that overdose did *not* mean acute heroin intoxication without these signs and symptoms. Participants were also asked about administration of the opioid antagonist naloxone hydrochloride, the principal drug used to treat overdoses. Drug use over the month preceding interview was measured using the Opiate Treatment Index (OTI; Darke et al., 1992). Drug classes measured were: heroin, other opioids, methamphetamine, cocaine, cannabis, hallucinogens, alcohol, tobacco, benzodiazepines, antidepressants and inhalants. Polydrug use, the number of drug classes used in the lifetime or preceding month, could thus range up to 11.

General mental and physical health were measured using the Short-Form 12 (SF12; Ware et al., 1996). DSM-IV diagnoses of current Major Depression were obtained using the Composite International Diagnostic Interview 2.1 (World Health Organization, 1998). ICD-10 screens for BPD were obtained using the International Personality Disorder Examination Questionnaire (Slade et al., 1998), and Diagnoses of ASPD were obtained from the Diagnostic Interview Schedule, modified to obtain DSM-IV diagnoses (Robins et al., 1981).

Follow-up interviews were abbreviated forms of the baseline interview. At 11 years, a life-chart technique was employed, using significant life events as anchor points over the follow-up period (Day et al., 2004; Hunt and Andrews, 1995). Participants were asked how many times they had commenced treatment, in any modality, for heroin dependence since the most recent interview, and the time spent in each treatment episode. Current drug use was measured by the OTI. Participants were asked about heroin overdoses since baseline. The SF-12 was re-administered to obtain a measure of general mental and physical health, and DSM-IV diagnoses of current Major Depression were obtained using the CIDI.

2.3. Statistical analyses

Means and standard deviations (SD) were reported for normally distributed continuous variables, otherwise medians were reported. For group comparisons of continuous variables, *t*-tests or Mann–Whitney *U*-tests were used. For categorical variables, odds ratios (OR) and 95% confidence intervals (CI) were calculated. All analyses were conducted using IBM SPSS Statistics 22.0 (IBM SPSS, 2013).

3. Results

3.1. Cohort characteristics

The initial cohort consisted of 615 current heroin users, full details of which may be found in Ross et al. (2005). At 11-year follow-up, 431 (70.1%) participants were interviewed, 63 (10.2%) were known to be deceased, 7 (1.1%) were incarcerated and 42 (6.8%) did not wish to participate. A further 21 (3.4%) were confirmed to be alive, but were not interviewed due to repeated cancellations. Overall, we could account for 91.6% of participants. The mean age at 11-year follow-up was 40.0 years (SD 7.6, range 28–66 years), and 64.5% were male. The main source of income was government benefits (64.5%), with wage/salary as the main source of 27.8%.

Comparisons between the cohort members interviewed and other living cohort members not interviewed at 11-year follow-up were conducted to determine if there were major differences between these groups, using *t* tests for continuous variables and chi square for categorical variables. There were no differences in the proportions enrolled in treatment at baseline entry (71.0% vs 63.7%), age at baseline (29.1 years vs 28.8 years), percent male (64.5% vs 73.6%), baseline daily heroin use (81.4% vs 78.5%), having ever overdosed prior to baseline (54.5% vs 46.3%) or overdose in the 12 months preceding baseline (24.1% vs 27.7%).

3.2. Drug use and treatment exposure at 11 years

The mean elapsed time since heroin initiation was 20.4 years (SD 7.2, range 10–41 years). Heroin had been used in the preceding year by 37.4% of the cohort, 24.8% in the month preceding interview, with 9.7% reporting daily use across that month. At baseline, the most commonly recently used substances, other than heroin, were nicotine (95.9%), alcohol (53.2%), cannabis (68.1%), benzodiazepines (47.8%) and cocaine (40.0%; Ross et al., 2005). At 11-year follow-up, the most commonly recently used substances, other than heroin, were nicotine (84.9%), alcohol (55.7%), cannabis (41.5%), benzodiazepines (32.0%) and opiates other than heroin (26.5%).

At the time of interview, 46.6% were currently enrolled in a drug treatment programme, overwhelming opioid maintenance (45.6%). Mean time enrolled in the current treatment programme was 59.4 months (SD 54.0, range 1–324 months). By 11-year follow-up, all