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Same-day use of opioids and other central nervous system depressants amongst people who tamper with pharmaceutical opioids: A retrospective 7-day diary study

Amy Peacock[a,b,*], Raimondo Bruno[a,b], Briony Larance[a], Nick Lintzeris[c,d], Suzanne Nielsen[a,d], Robert Ali[e], Timothy Dobbins[a], Louisa Degenhardt[a]

[a] National Drug and Alcohol Research Centre, University of New South Wales, Sydney, New South Wales, Australia
[b] School of Medicine, University of Tasmania, Tasmania, Australia
[c] Sydney Medical School, Sydney University, New South Wales, Australia
[d] Drug and Alcohol Services, South East Sydney Local Health District, New South Wales, Australia
[e] University of Adelaide, South Australia, Australia

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ABSTRACT

Objective: The aims were to determine: (i) quantity and frequency of same-day use of opioids with benzodiazepines and/or alcohol amongst people who regularly tamper with pharmaceutical opioids; and (ii) socio-demographic, mental health, harms and treatment profile associated with same-day use of high doses.
Method: The cohort (n = 437) completed a retrospective 7-day diary detailing opioid, benzodiazepine, and alcohol intake. Oral morphine equivalent (OME) units and diazepam equivalent units (DEU) were calculated, with >200 mg OME, >40 mg DEU and >4 standard alcoholic drinks (each 10 g alcohol) considered a "high dose".
Results: One-half (47%) exclusively consumed opioids without benzodiazepines/alcohol; 26% had days of opioid use with and without benzodiazepines/alcohol; and 26% always used opioids and benzodiazepines/alcohol. Same-day use of opioids with benzodiazepines/alcohol typically occurred on 1–3 days in the past week. Six in ten (61%) participants reported high dose opioid use on at least one day; one in five (20%) reported high dose opioid and high dose benzodiazepine/alcohol use on at least one day. The latter group were more likely to use prescribed opioid substitution therapy, often alongside diverted pharmaceutical opioids. Socio-demographic and clinical profiles did not vary according to high dose opioid, alcohol and benzodiazepine use, and there was no association with harms.
Conclusions: Same-day use of opioids with benzodiazepines/alcohol, and high dose combinations, are common amongst people who tamper with pharmaceutical opioids. Assessment of concomitant benzodiazepine/alcohol use during opioid therapy, implementation of real-time prescription monitoring systems, and research to clarify upper safe limits for polydrug depressant use, are potential implications.

1. Introduction

There has been an increase in opioid prescriptions, partly attributable to greater chronic non-cancer pain (CNCP) prevalence and a greater number of opioids registered for CNCP treatment (Berterame et al., 2016; Karanges et al., 2016). Increased pharmaceutical availability has seen greater prevalence of extra-medical use and tampering (i.e., manipulating a dosage form to change its drug delivery in a way not specified by the manufacturer, and may include dissolving, crushing, chewing, snorting and injecting; Katz et al., 2011, 2007), which in turn has led to greater rates of opioid-related harms (Hall et al., 2008; Manchikanti et al., 2012b).

Use of other central nervous system depressants, such as benzodiazepines and alcohol, with opioids may have an interactive or synergistic effect, increasing the risk of acute harms such as overdose (Warner-Smith et al., 2001; White and Irvine, 1999). An increasing proportion of unintentional overdoses have been observed involving the use of benzodiazepines, alcohol and other depressant drugs with opioids (Calcaterra et al., 2013; Jones et al.,

* Corresponding author at: Amy Peacock, National Drug and Alcohol Research Centre, University of New South Wales, New South Wales, 2052, Australia.
E-mail address: Amy.Peacock@unsw.edu.au (A. Peacock).

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2013), with death primarily attributed to respiratory depression (Gudin et al., 2013). As tolerance to the depressant effects of opioids is slower than tolerance to euphoric effects, consumers with a long history of opioid use are still often unknowingly at risk, although the underlying pathophysiology is complex and poorly understood (White and Irvine, 1999).

In addition, combined depressant use may contribute to increased sedation, greater motor impairment (e.g., falls or injuries) and enhanced abuse liability of these substances. Benzodiazepine or alcohol use enhances the euphoric effects of opioid analgesics (Chen et al., 2011; Lintzeris et al., 2007; Zacny and Gutierrez, 2011) and acute alcohol co-administration may increase maximum plasma concentrations and reduce time to maximum concentration for long-acting opioids (Fiske et al., 2012; Johnson et al., 2012; Sathyan et al., 2008).

Few studies have conducted in-depth investigation of concurrent use (specifically, same-day use) of opioids and benzodiazepines and/or alcohol among people who use opioids (e.g., Brands et al., 2008; Cropsey et al., 2015; Fleming et al., 2007; Lavie et al., 2009; Nielsen et al., 2007; Saunders et al., 2012). This is particularly the case for people regularly engaging in extra-medical pharmaceutical opioid use, a group at greater risk of opioid-related harms and among whom use of a range of substances is prevalent (Becker et al., 2008; Jones, 2013). As such, the aims of this study were to apply a novel methodology, a retrospective self-report daily drug diary, to determine:

1. Frequency of same-day opioid use with benzodiazepines/alcohol, and typical quantities consumed, by people who regularly tamper with prescription opioids; and
2. Demographic, mental/physical health, drug use, harms and treatment profile correlates of same-day use of opioids, benzodiazepines, and alcohol at high doses.

2. Material and methods

2.1. Participants and procedure

We used data from the National Opioid Medication Abuse Deterrence (NOMAD) study, a prospective cohort (n = 606) of people who reported regular extra-medical use and tampering with pharmaceutical opioids. Participants were recruited from metropolitan areas of New South Wales, Tasmania, and South Australia. Inclusion criteria required that participants: (i) were aged ≥18, (ii) reported monthly or more frequent extra-medical pharmaceutical opioid use in the preceding six months, and (iii) reported injecting, snorting, chewing or smoking pharmaceutical opioids on a monthly or more frequent basis in the preceding six months. Exclusion criteria comprised use of pharmaceutical opioids only in accordance with professional medical advice, or residing outside the metropolitan area/in prison for a month or longer in the preceding six months. Further details of the study are available from Degenhardt et al. (2015). The study was approved by the Human Research Ethics Committee of the University of New South Wales.

The current study utilised data from the third interview ('Wave 3') in April–June, 2015 (n = 499, 82% of the original cohort; 90% of those not in residential treatment or prison at the time of interview, and still alive at the time of follow-up). Only data collected in the 60-min computer-assisted interview from participants who completed the seven-day retrospective drug diary component (n = 5 excluded) and who reported at least one day of opioid use (n = 57 excluded) were included (final sample n = 437; see Supplementary Table 1 for comparison of final sample versus those excluded).

2.2. Key measures

2.2.1. Drug diary. Using a Timeline Followback approach (Sobell and Sobell, 1996), participants were asked to identify any alcohol, illicit drugs, and prescription medicines (including those not directly prescribed to them) which they had consumed in the past seven days. Participants reported intake on each day from the day prior to interview (Day 1) to Day 7. The approximate time of waking and sleeping (and time of drug consumption where reported) were obtained to facilitate recall. Participants reported the type/brand, quantity, unit (e.g., four 40 mg morphine tablets), route of administration, and source (e.g., own prescription, bought from dealer). Prompt cards with photographs of medications (full array of tablet sizes) were used to help identify the correct medicine/formulation.

2.2.2. Sample characteristics and mental/physical health. In addition to standard socio-demographic items, depression and generalised anxiety disorder were measured using the PHQ-9 and GAD-7 modules of the Patient Health Questionnaire (Kroenke et al., 2010). Likely presence of moderate to severe depression was defined as a PHQ-9 score of ≥10 (Kroenke et al., 2001); and likely symptoms of moderate to severe anxiety were defined as a GAD-7 score of ≥10 (Spitzer et al., 2006). Participants were also asked the first item of the Brief Pain Inventory; specifically, whether they had experienced pain (non-everyday) in the past month (Tan et al., 2004).

2.2.3. Drug use and behaviours. The Composite International Diagnostic Interview (World Health Organisation, 2001) assessed past-12 month pharmaceutical opioid use disorder based on the International Classification of Diseases (ICD-10) criteria. Participants reported whether they had used heroin, cannabis and methamphetamine in the past month. A short form of the Alcohol Use Disorders Identification Test (AUDIT-C) was included; a cut-off score of 5 was used to indicate alcohol-related problems (Bush et al., 1998). The Severity of Dependence Scale (SDS) was used to assess severity of benzodiazepine dependence; a cut-off score of 7 was used to indicate possible dependence (Cuevas et al., 2000).

2.2.4. Harms and treatment. Participants were asked about frequency of injecting any drug in the past month (with subsequent coding of binary 'any injection' and 'daily injection' variable), and whether they had overdosed in the past 12 months. Participants also reported past month engagement in opioid substitution treatment (OST) and past 12 month hospital and general practitioner visits (for any health-related reason).

2.3. Data analysis

2.3.1. Calculating oral morphine equivalent (OME) units and diazepam equivalent units (DEU). Opioid doses reported in the daily diary were converted into oral morphine equivalent (OME) units using conversion factors outlined by Nielsen et al. (2015). This conversion allows for comparison of opioid consumption across participants using different opioids based on the concept of equianalgesic dosing, where different doses of different opioids have similar analgesic effects. An OME unit is measured as being equivalent to 1 mg of orally-administered morphine. The conversion factors have been created such that the OME consumed on a particular day is calculated by multiplying the quantity of the particular opioid by the appropriate factor accounting for route of administration; for example, a participant who injected 80 mg of oxycodone on one day has consumed 240 mg OME (80 mg multiplied by conversion unit for oxycodone injection of 3).

A similar process was undertaken to calculate diazepam equivalent units (DEU) (National Prescribing Service, 1990; The Royal Australian College of General Practitioners, 2015; Therapeutic