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Research paper

Methods and predictors of tampering with a tamper-resistant controlled-release oxycodone formulation

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ABSTRACT

Background: In April 2014, a tamper-resistant controlled-release oxycodone formulation was introduced into the Australian market. This study aimed to identify the level and methods of tampering with reformulated oxycodone, demographic and clinical characteristics of those who reported tampering with reformulated oxycodone, and perceived attractiveness of original and reformulated oxycodone for misuse (via tampering).

Methods: A prospective cohort of 522 people who regularly tampered with pharmaceutical opioids and had tampered with the original oxycodone product in their lifetime completed two interviews before (January–March 2014: Wave 1) and after (May–August 2014: Wave 2) introduction of reformulated oxycodone.

Results: Four-fifths (81%) had tampered with the original oxycodone formulation in the month prior to Wave 1; use and attempted tampering with reformulated oxycodone amongst the sample was comparatively low at Wave 2 (29% and 19%, respectively). Reformulated oxycodone was primarily swallowed (15%), with low levels of recent successful injection (6%), chewing (2%), drinking/dissolving (1%), and smoking (<1%). Participants who tampered with original and reformulated oxycodone were socio-demographically and clinically similar to those who had only tampered with the original formulation, except the former were more likely to report prescribed oxycodone use and stealing pharmaceutical opioid, and less likely to report moderate/severe anxiety. There was significant diversity in the methods for tampering, with attempts predominantly prompted by self-experimentation (rather than informed by word-of-mouth or the internet). Participants rated reformulated oxycodone as more difficult to prepare and inject and less pleasant to use compared to the original formulation.

Conclusion: Current findings suggest that the introduction of the tamper-resistant product has been successful at reducing, although not necessarily eliminating, tampering with the controlled-release oxycodone formulation, with lower attractiveness for misuse. Appropriate, effective treatment options must be available with increasing availability of abuse-deterrent products, given the reduction of oxycodone tampering and use amongst a group with high rates of pharmaceutical opioid dependence.

Introduction

Although opioid medications play an important role in pain management, their use outside the bounds of a doctor's prescription (which we term here "extra-medical use"; Larance, Degenhardt, Lintzeris, Winstock, & Mattick, 2011) has been cause for concern because of the risk of serious adverse events including opioid overdose (Dhalla et al., 2009; Paulozzi, Budnitz, & Xi, 2006). Pharmaceutical opioids now comprise the majority of fatal and non-fatal drug overdoses in the US (Compton & Volkow, 2006; Paulozzi et al., 2006) and more recently in countries like Australia (Roxburgh, Burns, Hall, & Degenhardt, 2014).Opioids differ in the extent to which they are likely to be associated with hazardous patterns of use, due to different potencies, pharmacokinetic characteristics and propensities for dependence (differing 'abuse

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liability') (Grudzinskas et al., 2006; Quinn, Wodak, & Day, 1997; Schuster, 2006; Trescot, Datta, Lee, & Hansen, 2008). The past decade has seen pharmaceutical companies make significant investment in the development of formulations that are less prone to tampering (particularly via injection), dependence and diversion (Katz et al., 2011; Romach, Schoedel, & Sellers, 2013; US Department of Health and Human Services, Food and Drug Administration, & (CDER), C. f. D. E. a. R., 2013). The Food and Drug Administration in the US has developed labelling guidelines for 'abuse deterrent' formulations of pharmaceutical opioids, one form of which can involve tamper-resistant formulations (US Department of Health and Human Services et al., 2013).

In April 2014, a new formulation of oxycodone was introduced with public subsidy in Australia which was intended to have these tamper-resistant properties. This formulation of oxycodone is a controlled-release tablet, but its physicochemical properties make the tablets more difficult to tamper with and/or crush into a fine powder (Cone, Giordano, & Weingarten, 2013). Reformulated oxycodone is more resilient to chemical extraction and does not demonstrate an accelerated dissolution when placed in ethanol. The formulation comprises a polymer; a curing process takes place during manufacture whereby the controlled-release tablet is heated above the melting point of the polymer, which produces a hard plastic-like effect to the tablet upon cooling. If crushed, it produces large pieces (rather than fine powder), which turn into a glutinous gel-like mixture when combined with water, rendering the mixture difficult to use via intranasal or intravenous routes of administration (ROA; Sellers, Perrino, Colucci, & Harris, 2013). US studies suggest that reformulated oxycodone may be less attractive for misuse via tampering (Sellers et al., 2013), and much lower levels of diversion and use have been observed (Butler et al., 2013; Cassidy, DasMahapatra, Black, Wieman, & Butler, 2014; Severtson et al., 2013).

In Australia, the first national post-marketing surveillance study of the controlled-release oxycodone reformulation, called the National Opioid Medication Abuse Deterrence (NOMAD) study, is underway. Using data from a prospective cohort forming part of the NOMAD study, the aims of this paper are to:

(1) Examine the levels of tampering with the controlled-release oxycodone reformulation among people who regularly tamper with pharmaceutical opioids;
(2) Examine predictors of tampering with the controlled-release oxycodone reformulation in the cohort;
(3) Describe the methods of tampering attempts with the controlled-release oxycodone reformulation; and
(4) Identify potential differences in perceived attractiveness for misuse (via tampering) between the original and reformulated controlled-release oxycodone product (amongst those who tampered with both forms).

Methods

Participants and procedure

The complete methods of the broader NOMAD study and the cohort component are available elsewhere (Degenhardt et al., 2015; Larance et al., 2015; Peacock et al., 2015). Participants (n = 606) were recruited through a variety of settings and services in Sydney, New South Wales (NSW), Adelaide, South Australia (SA) and Hobart and Launceston, Tasmania (TAS) including Needle–Syringe Programs (NSPs), snowballing and word-of-mouth, opioid substitution therapy (OST) clinics/prescribers, community pharmacies, and advertisements in newspapers and street media and other health/outreach services.

Individuals were eligible to participate in the cohort if they were English language proficient, over 18 years of age, reported extra-medical pharmaceutical opioid use on a monthly or more frequent basis in the last six months, and reported injecting, snorting, chewing, smoking and/or dissolving and drinking a pharmaceutical opioid in the last month and on a monthly or more frequent basis in the past six months. Participants were excluded if they had not been a resident of the city/state for the six months prior to the interview, had been in prison for the past month, had only tampered with an OST medication, or if they reported only using their opioid medication as per a doctor's instructions. Participants completed two waves of structured computer-assisted interviews (Wave 1 January–March 2014 prior to the release of the reformulated oxycodone, and Wave 2 May–August 2014 following its release) and reimbursed $50AUD and $40AUD on the two occasions for time and out-of-pocket expenses.

Ethics

This study has approval from the Ethics Review Committee (Royal Prince Alfred Hospital Zone) of the Sydney Local Health District, AIDS Council of New South Wales, Tasmanian Health and Medical Human Research Ethics Committee, University of Adelaide Human Research Ethics Committee and Southern Adelaide Clinical Human Research Ethics Committee. Access and site approvals were obtained from the following local area health ethics committees governing clinic sites: Sydney Local Health District, South Eastern Sydney Local Health District, South Western Sydney Local Health District and Western Sydney Local Health District.

Key measures

Patterns of original and reformulated oxycodone use

Lifetime and past month prescribed and non-prescribed use of OxyContin® original (Wave 1 and 2 interviews) and reformulated (Wave 2 interview only) 10–80 mg tablets were assessed. Methods of tampering and ROA (including injection, snorting, chewing, smoking and dissolving/drinking) were also assessed. Medication prompt cards with photographs of opioid medications and tablet sizes were used to ensure correct identification of target drugs and formulation.

Wave 1 correlates of tampering with reformulated oxycodone (Wave 2)

Variables were selected based on previous research showing demographic (e.g., age, prison history), physical and mental health (e.g., history of trauma), and drug use history correlates of injecting drug use (e.g., Kerr et al., 2009; Strathdee et al., 2008) and non-medical use of pharmaceutical opioid use (e.g., Becker, Sullivan, Tetrault, Desai, & Fiellin, 2008). During the Wave 1 interview participants were asked a range of demographic questions. The chronic conditions section of the Composite International Diagnostic Interview (CIDI; Kessler & Üstün, 2004) was included to assess problematic physical conditions in the past 12 months. The Patient Health Questionnaire (PHQ-9) and the Generalised Anxiety Disorder (GAD-7) modules of the Patient Health Questionnaire (Kroenke, Spitzer, Williams, & Lowe, 2010) were included; symptoms indicating moderate to severe depression were defined as a PHQ-9 score $\geq$10 (Kroenke, Spitzer, & Williams, 2001), symptoms of moderate to severe anxiety were defined as a GAD-7 score $\geq$10 (Spitzer, Kroenke, Williams, & Löwe, 2006). The Primary Care PTSD screen (PC-PTSD) was used to measure post-traumatic stress disorder (PTSD), with a score greater than 3 indicating presence of PTSD (Prins et al., 2004).

Participants reported their past month use (prescribed and not prescribed) of all available forms of morphine, methadone,