

Title: Prevalence and correlates of prescription opioid residue injection

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Abstract

Background: There is growing evidence of intravenous administration of prescription opioids (POs) in several countries. Preparation of POs for injection may leave residues in containers and filters used by people who inject drugs and may lead to adverse health outcomes if they are injected.

Methods: This exploratory study used cross-sectional data from the COSMO study, a prospective cohort of out-of-treatment cocaine users carried out in Montréal (Canada) between October 2010 and August 2015. For this analysis, only one visit per participant was selected, that is, the first time the participant reported PO injection during the study. The outcome of interest, “injection of PO residues”, was defined as having injected PO residues from a filter and/or a container in the last month. Correlates of this outcome were identified using logistic regression analyses.

Results: Of the 122 participants who reported PO injection during the study period, 41.8% had injected PO residues. Reporting an unstable source of income (AOR=4.26; 95% CI: 1.03-17.69), a recent overdose (AOR=5.45; 95% CI: 1.50-19.88) and a preponderant use of opiates (mostly opiate use versus other drugs excluding alcohol and cannabis) (AOR=2.46; 95% CI: 1.08-5.63) increased the risk of PO residue injection. The odds of reporting PO residue injection rose by 7% per unit increase in the score of psychological distress (AOR=1.07 per unit increase; 95% CI: 1.01-1.12).

Conclusions: The findings of this study suggest that PO residue injection is associated with markers of vulnerability. Further investigation is needed in order to better understand this understudied drug injection practice.

Keywords: Injection drug use, drug residue injection, prescription opioids, injection risk behaviors

1. Introduction

Amidst the significant increase of prescription opioid (PO) misuse in recent years, there is growing evidence of intravenous PO administration in several countries. Reports of PO injection have risen worldwide, including in the United States (Davis and Johnson, 2008; Young et al., 2010; Surrat et al., 2011; Lankenau et al., 2012; Black et al., 2013; Mateu-Gelabert et al., 2015), Europe (Partanen et al., 2009; Keijzer and Imbert., 2011; Roux et al., 2011), South Asia (Larance et al., 2011) and Australia (Degenhardt et al., 2006). In Canada, over the past decade, PO injection has gained in popularity among drug users across the country (UHRI, 2013; Leclerc et al., 2013; Firestone and Fischer, 2008; Roy et al., 2011; Roy et al., 2013; Bruneau et al., 2012; Fischer et al., 2006; PHAC, 2014). Data from I-Track, a multisite surveillance system that monitors HIV and hepatitis C virus (HCV) infection rates and associated risk behaviors among persons who inject drugs (PWID) in Canada, revealed that hydromorphone, morphine and oxycodone, either in tablet or capsule form, were injected more often than heroin. These prescription drugs were respectively the second, third and fourth most commonly reported injection drugs used in the last six months (PHAC, 2014). Only cocaine surpassed them as it was the most reported injected drug.

While PO injection has been observed in several parts of the world, its specific injection practices are not well documented. Now, it is generally acknowledged that injection practices may vary depending on the types of substances injected, resulting in more or less serious consequences for the health of users (Gordon and Lowy, 2005). The ethnographic work we carried out in downtown Montréal has allowed us to examine the injection techniques used by PWID to prepare PO tablets or capsules that are designed for oral use

(Roy et al., 2011). The study findings showed that, due to the physical composition of the two most available forms of POs in the area (Dilaudid® and Hydromorph Contin®), dissolution was complex and required large amounts of water. This constrained many PO injectors to inject themselves repeatedly during a single injection episode, generally using the same material several times. Also, as opposed to powder cocaine and the white/beige powder heroin available in Montréal, which are easily dissolvable, these PO formulations tended to leave significant amounts of residue in the containers and filters used for injection. The containers and filters were often kept for further use, a practice referred to by users as “doing a wash”, as it implies rinsing the used equipment with water to extract the drug residues for injection. Washes were often shared among users who considered them valuable goods they could exchange or offer to other users (Roy et al., 2011).

Injection of drug residues has been previously described among heroin users in the western United States, where black tar was the most prevalent form of heroin (Bourgois, 1998; Koester et al., 2005; Bourgois and Schonberg, 2009). Ethnographers observed that similar to some PO formulations, black tar heroin was not easily dissolvable and left significant amounts of residues in filters used for injection. Overall, ethnographic studies highlighted the vulnerability of PWID who inject residues, showing that this behaviour was mainly practiced by individuals who had unsuccessful income-generating strategies and, consequently had to rely on their own or others’ drug residues to relieve opioid withdrawal symptoms (Bourgois, 1998; Bourgois and Schonberg, 2009; Roy et al., 2011).

Drug residue injection entails several serious medical complications including bacterial and fungal infections due to re-use of injection equipment (Gordon and Lowy, 2005; Hope et al., 2008; Kaushik et al., 2011). With respect to PO specifically, residue injection could

increase the risk of injecting insoluble particles found in pharmaceutical tablets or capsules destined for oral use. Injection of such particles can cause serious health consequences such as pulmonary emboli and ischaemic necrosis (Ng et al., 2015; Roberts, 2002). Finally, drug residue injection can be problematic due to the risks of HCV transmission when drug residues are shared with other users (Roy et al., 2012). It should be noted that PO residue injection was stated as a possible hypothesis explaining the association between PO injection and HCV transmission in a cohort study of PWID in Montréal (Bruneau et al., 2012). Thus, from a public health perspective, there is a need to document this injection practice and characterize residue injectors in order to better inform harm reduction strategies.

To date, only four studies have looked at the prevalence of drug residue injection, focusing on injecting someone else's drug residue (Koester et al., 2005; Evans et al., 2009; Roy et al., 2012; Le Marchand et al., 2013). To our knowledge, PO residue injection has never been measured or discussed explicitly in epidemiological studies. Yet, in addition to our ethnographic study, PO drug residue injection has been recently qualitatively reported in New York (Mateu-Gelabert et al., 2015), which suggests PO residue injection is not an isolated phenomenon.

The goal of this exploratory study was to estimate the prevalence and correlates of injection of PO residue (either one's own or someone else's) among PO injectors. Secondary analyses were carried out using data from a prospective cohort study on mental health, drug use and HIV/HCV among out-of-treatment (OOT) cocaine users. Informed by ethnographic studies suggesting higher degrees of social and health vulnerabilities among

residue injectors, we examined the relationship between PO residue injection and socio-demographic characteristics, psychological states and drug use patterns.

2. Material and methods

2.1 The COSMO study

The COSMO study is a prospective cohort study conducted among OOT cocaine users in Montréal, Canada, between October 2010 and August 2015 among OOT cocaine users. The methodology was described in detail elsewhere (Lévesque et al., 2014). Briefly, to be eligible for the COSMO study, participants had to have used cocaine in the last month, either by smoking crack or by injection. They also had to speak French or English, be able to provide informed consent and be at least 14 years old. Study participants were mainly recruited in community-based programs located in downtown Montréal. After providing informed consent and contact information, participants completed interviewer-administered questionnaires at baseline and during five consecutive follow-up visits, scheduled at three-month intervals. Detailed contact information was updated at each interview and thorough follow-up procedures were used. Participants were paid \$30 financial compensation for their time, at each interview. This research was approved by the ethical boards of the Faculty of Medicine and Health Sciences at Université de Sherbrooke and of Centre Hospitalier de l'Université de Montréal.

2.2 Study sample

The sample included in this analysis was drawn from the COSMO study. Questions about injection of PO residues among participants reporting PO injection in the month prior to

interviews were added to the baseline and follow-up questionnaires on May 1, 2012. COSMO participants who completed questionnaires at that date or thereafter during the study period were eligible for this analysis if they had injected PO in the month prior to interview. For this paper, only one visit per participant was selected, that is, the first time the participant answered yes to the question about PO injection during the study.

2.3 Measurements

The outcome of interest for this study was “injection of PO residues,” which was defined as having ever injected PO residues from a filter and/or a container in the last month. This included one’s own material and material already used by someone else. Based on the literature, correlates of injection of PO residues examined include age (younger than 25 years old vs. older), sex, ethnicity (born in Canada vs. outside), level of education (less than high school vs. higher level), unstable housing (defined as having lived or slept at least once in a shelter or in any place not intended for housing in the past 3 months), reporting a marginal or criminal source of income in the past 3 months (e.g. panhandling, theft, drug dealing), sex work (defined as having vaginal, oral or anal sexual relations with a client in the past month) and recent drug overdose (past 3 months). The preponderant use of opiates, defined as having POs or heroin as the most commonly used drug in the previous month as opposed to any other drug excluding alcohol and cannabis, was also assessed as a surrogate marker of opiate dependency. Additional information was collected to describe patterns of PO injection in the past month, including number of days of injection in a typical week, number of injections during a day and main PO injected. Finally, psychological distress, assessed using the K10 scale (Kessler, 2002), was used as a continuous variable. K10 consists of ten questions on non-specific psychological distress and measures the level of

anxiety and depressive symptoms a person may have experienced in the previous four-week period, the final score ranging between 10 and 50.

2.4 Analyses

Descriptive statistics including means, medians, standard deviations and interquartile ranges (IQR) for continuous variables and frequency distributions for categorical variables were used to characterize the study population. Logistic regression analyses were conducted to determine the correlates of PO residue injection among PO injectors. All variables with p -values <0.05 in bivariate analyses were included in the multivariate model. Following the purposeful selection procedure, significant variables with p -values <0.05 and those with confounding effects were kept in the final model. A variable was considered confounding if its removal from the model changed a significant coefficient by more than 20%. The advantage of the purposeful selection method comes when the analyst is interested in risk factor modeling and not just mere prediction (Bursac et al., 2008). The algorithm is used in such a way that, in addition to significant covariates, it retains important confounding variables, resulting in a possibly slightly richer model. Simulation studies demonstrate that the purposeful selection algorithm identifies and retains confounders correctly at a larger rate than other selection procedures. Adjusted odds ratios (AOR) and 95% confidence intervals (CI) were derived from the final models. SAS 9.3 software was used to perform the analysis.

3. Results

A total of 605 cocaine users were recruited in the COSMO study. Of the 491 cocaine users who completed at least one interview between May 1, 2012 and the end of the study, 122

participants reported injecting POs in the previous month at least once during the study period, and were therefore eligible for this analysis; the majority (101) did so at their first interview. Demographic characteristics and patterns of PO injection are shown in Table 1. Most of the 122 participants were male (82.8%) and mean age was 37.0 years. In the last month, more than half of participants consumed opiates (54.1%), namely Dilaudid[®] or Hydromorph Contin[®] (41.8%) and heroin (12.3%) as their preponderant drug, followed by cocaine, crack or freebase (38.5%). Less than a tenth of participants had another preponderant drug such as amphetamines, psychotherapeutics drugs or solvent. Concerning PO injection, Dilaudid[®] was the main PO injected (65.6%) followed by Hydromorph Contin[®] (29.5%), and approximately two-thirds of participants injected at least once a week. Multiple injections in a given injection day was common, with slightly more than a third of participants injecting at least 4 times a day.

About four out of ten participants (41.8%) injected PO residues. Ten factors were examined as correlates of injection of PO residues in bivariate analyses, namely age, sex, ethnicity, level of education, housing, income, sex work, overdose, preponderant use of opiates and psychological distress. Results showed that PO injectors who reported injecting PO residues were significantly more likely ($p<0.05$) to be under 25 years old, to report unstable housing, marginal or criminal sources of income, recent drug overdose and preponderant use of opiates (Table 2). Psychological distress was also positively and significantly ($p<0.05$) associated with residue injection whereas sex, ethnicity, level of education and sex work were not. The six factors with p -values <0.05 in bivariate analyses were then included in the multivariate analysis and four were retained in the final model (Table 3). Participants who had marginal or criminal sources of income (AOR=4.26; 95% CI: 1.03-

17.69), recent drug overdoses (AOR=5.45; 95% CI: 1.50-19.88) or consumed opiates as their preponderant drug (AOR=2.46; 95% CI: 1.08-5.63) were more likely to inject PO residues compared to those who did not. The odds of reporting PO residue injection rose by 7% per unit increase in the psychological distress score (AOR=1.07 per unit increase; 95% CI: 1.01-1.12). Despite the fact that age and unstable housing were initially included in multivariate analysis, they did not remain significantly associated with PO residues injection when controlling for other factors aforementioned. Furthermore, given that they did not constitute confounding factors, they were removed from final multivariate model presented in Table 3, following the purposeful selection procedure.

4. Discussion

To our knowledge, this is the first study to assess the prevalence of PO residue injection and identify its correlates among PWID. Our results indicate that 41.8% of study participants had injected PO residues between May 2012 and August 2015. While no point of comparison exists in the literature, this proportion seems high and is of major concern given the potential adverse health outcomes resulting from this practice. Another important finding is that this injection practice is associated with markers of vulnerability and specific drug use patterns. One marker is income, for which PO residue injectors had greater odds of reporting marginal or criminal activity (such as drug dealing, sex work, panhandling) as their main source of income. This result is consistent with other studies that showed significant associations between illegal or marginal income sources and injection risk behaviours or risky patterns of drug use (Richardson et al., 2010; DeBeck et

al., 2007; 2011). For instance, in Vancouver, such sources of income have been linked to daily heroin injection (Richardson et al., 2010; DeBeck et al., 2007; 2011), injecting in public places (Richardson et al., 2010; DeBeck et al., 2011), binge drug use and syringe sharing (DeBeck et al., 2011). For drug residue injection, it can be hypothesized that, compared to legal income sources, marginal or criminal sources of income likely produce more irregular or weak income streams, which could force PO injectors to fall back on PO residues. These results are consistent with prior ethnographic studies reporting that residue injection is mainly practiced by PWID with low-income sources or unsuccessful income-generating strategies (Bourgois, 1998; Bourgois and Schonberg, 2009; Roy et al., 2011).

PO residue injectors in this study were more likely to report preponderant use of opioid substances (heroin or POs) during the last month. In a study sample of PO injectors, this association may indicate that individuals who inject residues have more severe opioid dependency than other PO injectors. More severe dependency among these PO injectors may explain why they inject drug residues to stave off “dopesickness,” particularly when financial resources are scarce (Bourgois, 1998; Bourgois and Schonberg, 2009; Roy et al., 2011).

The observation that PO residue injectors were more likely to have overdosed than other participants suggests that they not only have more severe opioid dependency but also have more intense drug use patterns (Darke et al., 2014). In our sample, overdoses may have been caused by the use of several drugs, and not only opioids, since study participants were polysubstance users (minimally cocaine and POs). It is possible that the

occurrence of overdoses is a marker of high-risk intensive drug use involving high doses and/or hazardous mixtures of substances.

Finally, our results show that PO injectors who injected residues were more likely to suffer from psychological distress as measured by the K10. Several studies have shown that symptoms of anxiety or depression were associated with drug-equipment sharing behaviours among drug users (Lundgren et al., 2005; Golub et al., 2007; Reyes et al., 2007; Lemstra et al., 2011; German et al., 2012; Armstrong et al., 2013). The mechanisms underlying these relationships are not well understood. A possible explanation for our findings regarding drug residue injection is that PWID do it as a last resort because they are suffering from withdrawal symptoms and have no heroin or other opioids on hand. It has been shown that opioid withdrawal can produce symptoms of anxiety that can heighten levels of distress (American Psychiatric Association, 2013; West and Gossop, 1994). It is also plausible that the experience of suffering from withdrawal symptoms and craving, while feeling forced to relieve these symptoms with what is perceived as a suboptimal alternative to a full dose of opiate, is altogether sufficient to induce a significant rise in level of psychological distress.

Our study is subject to a number of limitations, the first being that this is an exploratory study based on a cross-sectional design. Therefore it is impossible to establish a causal link between the studied covariates and PO residue injection. Also, since the study was based on secondary analyses of the COSMO study, only people who used cocaine in the last month were eligible, thus excluding PO users who did not simultaneously use cocaine. While this might have biased the proportion of study participants who had injected PO residues, it is impossible to know whether that bias pointed to over- or under-

estimation of prevalence. Furthermore, similar to most studies involving illicit drug-using populations, participants were not randomly recruited, thereby limiting the generalizability of our findings. Finally, data for this study were collected through self-report, which could have led to recall and social desirability biases. However, the impact of such biases was possibly limited by the short referral period, and the open and non-judgmental attitudes of the highly experienced study interviewers. Also, it has been shown that self-reported data collected from drug-using populations is generally reliable and valid (Darke, 1998).

5. Conclusion

In light of these findings, development of interventions seems imperative to reduce PO residue injection and risk vulnerabilities among PWID in general. Our results highlight the need for better access to low-threshold opioid substitution treatment, which should be facilitated and maximized among PO injectors. This type of treatment has the potential to reduce opioid dependency to more manageable levels which, in turn, could reduce risky behaviors (Mateu-Gelabert et al., 2010). Pharmacological approaches should be complemented by mental health interventions to reduce distress on emotional, cognitive and physiological levels. Furthermore, it is imperative that injection paraphernalia distributed in harm reduction programs be revised to allow safer injection practices among PWID who inject “new” substances. In this regard, it should be noted that public health authorities in Québec have conducted studies to evaluate PO preparation techniques and new drug injection equipment that could produce less drug residue (Noël

et al., 2015; Leclerc et al., 2015). Prevention messages should also be tailored to inform PWID about the risks of drug residue injection and the methods to inject PO more safely.

In conclusion, residue injection has remained an understudied topic; it has rarely been measured or discussed explicitly in epidemiological studies. Thus it is important to conduct additional studies examining not only its prevalence and correlates, but also the socio-sanitary consequences associated with this injection practice. Such studies could further contribute to tailoring public health interventions aimed at vulnerable PWID.

Tables

Table 1: Demographic characteristics and patterns of PO injection among study participants (n=122)

Characteristics of study participants	N (%)
Age	37.0 (10.2) [†]
Sex	
Male	101 (82.8)
Female	21 (17.2)
Ethnicity	
Born in Canada	118 (96.7)
Born outside Canada	4 (3.3)
Level of education	
Less than high school	61 (50.0)
Higher than high school	61 (50.0)
Housing**	
Stable housing	33 (27.1)
Unstable housing	89 (73.0)
Source of income**	
Conventional	18 (14.8)
Marginal or criminal	104 (85.3)
Sex work*	
Yes	17 (13.9)
No	105 (86.1)
Overdose**	
No	107 (87.7)
Yes	15 (12.3)
Preponderant use of opiates*	
Prescription opioid or heroin	66 (54.1)
Others	56 (45.9)
Psychological distress (K10)*	27.2 (8.2) [†]
Number of days of PO injection in a typical week*	
≤1 day/week	43 (35.3)
>1 days/week	79 (64.8)
Number of PO injections during a day*	
1-3 times/day	79 (64.8)
≥4 times/day	43 (35.3)
Main PO injected*	
Dilaudid [®]	80 (65.6)
Hydromorph Contin [®]	36 (29.5)
Others [‡]	6 (4.9)

[†]Mean (SD). [‡]Fentanyl, oxycodone or oxycodone and morphine.

*Past month. **Past 3 months.

Table 2: Univariate logistic regression analyses of correlates of PO residue injection

	PO residue injection*		OR (95% CI)	P value
	No n (%)	Yes n (%)		
Age				
<25 years	5 (33.3)	10 (66.7)	1.00 (reference)	0.045
≥25 years	66 (61.7)	41 (38.3)	0.31 (0.10-0.97)	
Sex				
Male	58 (57.4)	43 (42.6)	1.00 (reference)	0.705
Female	13 (61.9)	8 (38.1)	0.83 (0.32-2.18)	
Ethnicity				
Born in Canada	68 (57.6)	50 (42.4)	1.00 (reference)	0.499
Born outside Canada	3 (75.0)	1 (25.0)	0.45 (0.05-4.49)	
Level of education				
Less than high school	36 (59.0)	25 (41.0)	1.00 (reference)	0.854
Higher than high school	35 (57.4)	26 (42.6)	0.93 (0.46-1.92)	
Housing**				
Stable housing	25 (75.8)	8 (24.2)	1.00 (reference)	0.019
Unstable housing	46 (51.7)	43 (48.3)	2.92 (1.19-7.17)	
Source of income**				
Conventional	15 (83.3)	3 (16.7)	1.00 (reference)	0.028
Marginal or criminal	56 (53.9)	48 (46.2)	4.29 (1.17-15.70)	
Sex work*				
Yes	11 (64.7)	6 (35.3)	1.00 (reference)	0.559
No	60 (57.1)	45 (42.9)	1.38 (0.47-4.00)	
Overdose**				
No	67 (62.6)	40 (37.4)	1.00 (reference)	0.013
Yes	4 (26.7)	11 (73.3)	4.61 (1.37-15.44)	
Preponderant use of opiates*				
Others	38 (67.9)	18 (32.1)	1.00 (reference)	0.048
Prescription opioid or heroin	33 (50.0)	33 (50.0)	2.11 (1.01-4.42)	
Psychological distress (K10)*	25.7 (9.0) [†]	29.3 (6.5) [†]	1.06 (1.01-1.11)	0.019

*Past month. **Past 3 months.

Table 3: Multivariate logistic regression analyses of correlates of PO residue injection

	Injection of PO residues*	
	AOR (95% CI)	P value
Marginal or criminal source of income**	4.26 (1.03-17.69)	0.046
Psychological distress (K10)*	1.07 (1.01-1.12)	0.019
Overdose**	5.45 (1.50-19.88)	0.010
Preponderant use of prescription opioid or heroin**	2.46 (1.08-5.63)	0.032

*Past month. **Past 3 months.

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