Alternate Routes of Administration and Risk for HIV among Prescription Opioid Abusers

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Abstract

Route of administration is an important contributor to the adverse health consequences of prescription medication abuse. The present study examines characteristics associated with non-oral routes of administration among a large sample of prescription opioid abusers, and explores needle related

HIV risk behaviors as well. 791 opioid abusers completed a one-time, structured interview including complete histories of illicit and prescription drug abuse, and route of drug administration. The most common method of pill use was oral (91%), followed by intranasal (53.1%), injection (23.8%), and smoking (14.5%). The youngest prescription opioid abusers, ages 18–24, displayed significantly higher odds of employing alternate route of administration, and also of re-using nonsterile needles for injection. HIV prevention programming should be developed for young prescription opioid injectors.

Keywords

prescription opioid abuse; route of administration; HIV

INTRODUCTION

As the well-documented epidemic of prescription drug abuse in the United States continues to evolve[1–3], route of drug administration is emerging as an important contributor to the adverse health consequences associated with prescription medication abuse.[4–6] In this regard, recent data indicate that non-oral routes of prescription drug ingestion are not uncommon in samples of high school and college students, rural drug abusers and urban street drug users[7–10], and are associated with greater drug problem severity, including dependence and overdose.[6]

Because altered routes of administration provide faster drug delivery and onset, the reinforcing effects are often intensified [11], thereby increasing the vulnerability to addiction. Although there are some early indications that young prescription drug abusers seeking treatment are more likely to use alternate routes of administration and to display greater problem severity than their older counterparts[12], very few studies have systematically examined route of administration among large, diverse samples of prescription drug abusers. Moreover, there is general recognition that prescription drug injection increases risk for HIV and hepatitis infection through the use of non-sterile equipment[2], yet studies examining risky needle use practices among prescription drug injectors are not apparent in the literature. The present study examines the characteristics associated with alternate routes of drug administration among large samples of treatment and street-based prescription opioid abusers in South Florida, and explores the scope of needle risk behaviors among a sub-

sample of prescription drug injectors to examine risk for HIV and other blood-borne infections.

METHODS

Participants

Eligible participants were individuals 18 years of age or older who reported abuse of psychoactive prescription drugs at least 5 times in the past 90 days (or 90 days prior to treatment entry, where applicable). In addition, participants met criteria for membership in one of five subpopulations: 1) *methadone* clients (n = 201) were enrolled in a methadone-maintenance treatment program; 2) *street drug users* (n = 106) who reported current illicit drug use; 3) *public treatment clients* (n = 147) were enrolled in a publicly funded or subsidized drug treatment facility for fewer than 45 days prior to interview; 4) *private treatment clients* (n = 188) were enrolled in a substance abuse treatment program, paid for with private insurance personal funds, for fewer than 45 days prior to interview; and, 5) men who have sex with men (MSM; n = 149) who reported current illicit stimulant use.

Procedures

A variety of purposive sampling strategies were used to locate study participants. Print media advertisements and the posting or manual distribution of cards and flyers were largely used to recruit street drug users and MSM. We also used chain-referral sampling to recruit participants in these subgroups, such that each participant received a $10 cash incentive per eligible referral that completed an interview, up to a maximum of 5 referrals per participant. Referrals from methadone clinic and drug treatment center staff served as the primary recruitment method for methadone maintenance clients and drug treatment enrollees, and these treatment facilities also provided space for interviews to be conducted. The study was conducted in the investigators' research field offices or in treatment centers located in Broward, Lee, Miami-Dade, and Palm Beach Counties.

All participants were screened for eligibility by trained research staff prior to participation in a single standardized face-to-face interview. Following informed consent, computer-assisted face-to-face interviews were conducted in private offices and lasted 1½ to 2 hours. Participants received a $30 monetary incentive for their participation. All study protocols and instruments were reviewed and approved by the University of Delaware's Institutional Review Board.

Measures

The Global Appraisal of Individual Needs (GAIN)[13] was the primary data collection instrument for the study. The GAIN has eight core sections, including demographics, health status, mental health, risk behaviors, and substance use, abuse and dependence measures based on DSM-IV criteria. Questions were added to the GAIN to increase the range of abused prescription drugs we queried, including hydrocodone, hydromorphone, immediate (IR) and extended (ER) release oxycodone, morphine, methadone, codeine, as well as alprazolam, diazepam and clonazepam. We also queried abuse of prescription stimulants, antidepressants, and antipsychotics. The assessment instrument captured a complete illicit and non-medical prescription drug history, including number of days using in the past 90 days. Route of administration for prescription medications was assessed through a series of dichotomous 90-day items querying oral/swallowing, snorting, smoking, injecting, rectal/vaginal, and other administration. Routes of administration were not mutually exclusive.

HIV testing was beyond the scope of the study, therefore HIV prevalence was captured by self-report, using the following item: What was the result of your last HIV test (for which

you received the results)? Past year needle risk behaviors were captured by a series of dichotomous items querying needle re-use, re-use of non-sterile needles, and sharing needles with other individuals.

Data Analysis

For the analyses presented here, only participants who reported at least one occasion of prescription opioid abuse in the past 90 days and those who had complete data on route of administration items were included (N=1,070). Because route of administration items were asked jointly for all abused prescription pills, we conducted the analyses in two waves: first, including all 1,070 prescription opioid abusers, *regardless of other prescription medication abuse*; and, second, excluding opioid abusers *who also reported any abuse of prescription stimulants, antidepressants, or antipsychotics* (N=791). We were unable to exclude opioid abusers who also reported benzodiazepine abuse, due to the very high prevalence of benzodiazepine use in the sample. Comparison of the two analyses revealed no substantive differences in the findings, therefore, we present only the findings from the smaller, more focused sample of prescription opioid abusers (N=791).

Data were analyzed using Predictive Analytics Software (PASW, formerly SPSS) version 18. Descriptive statistics were calculated to describe the sample in terms of demographics, health status, substance use and dependence, and route of prescription drug administration. Bivariate logistic regression models were developed to predict route of administration by demographics, sub-population, substance-specific abuse, and DSM IV dependence. Finally, we computed multivariate logistic regression models to examine patterns of past year risky needle use among the sub-sample of drug injectors, including age and injection patterns (prescription vs. illicit drug injection) as predictors.

RESULTS

Sample characteristics are displayed in Table 1. The overall sample was young, with a mean age of 34.5 years. Given study eligibility criteria, substantial proportions reported illicit drug use in the 90 days prior to interview. Past 90 day injection of any drug was reported by 29.7% of participants. The prevalence of prescription benzodiazepine abuse in the past 90 days was 78.1%. Among the most commonly abused prescription opioids were immediate release oxycodone (78.1%), OxyContin® (51.3%), hydrocodone (38.7%), and methadone (21.2%). Just under 95% of the sample met DSM-IV criteria for substance dependence.

Oral administration was the most common method of pill use (91%), however, substantial proportions reported alternate routes as well, including intranasal (53.1%), injection (23.8%), and smoking (14.5%). More than 10% of the sample reported being HIV positive.

Bivariate logistic regression models predicting route of pill administration are displayed in Table 2. The odds of **oral** administration were: significantly *lower* among younger opioid abusers (ages 18–24, 25–34) compared to older abusers; significantly *lower* among whites compared to African Americans; and, significantly *lower* among all treatment-based participants compared to street drug users. In terms of substance use, the odds of **oral** administration were: significantly *higher* among powder cocaine users, benzodiazepine abusers, and codeine abusers compared to non-users of these substances; *lower* odds of **oral** administration were observed among heroin users, OxyContin abusers, and hydromorphone abusers.

The odds of **intranasal** administration were: significantly *higher* among younger opioid abusers (ages 18–24, 25–34, 35–44) compared to older abusers; significantly *higher* among both whites and Latinos compared to African Americans; and, significantly *higher* among

all in-treatment participants compared to street drug users. In terms of substance use, the odds of **intranasal** pill administration were: significantly *higher* among heroin users, and abusers of OxyContin, IR oxycodone, methadone, hydromorphone and hydrocodone; *lower* odds of **intranasal** administration were observed among crack users and codeine abusers. Past year substance dependence was also associated with increased odds of **intranasal** pill use.

Smoking of prescription medications was associated with younger age (18–24), and, the odds of **smoking** were significantly *higher* among public and private treatment participants compared to street drug users. Methadone clients had *lower* odds of **smoking** as a route of administration compared to street drug users. The odds of **smoking** were significantly *higher* among abusers of OxyContin and IR oxycodone.

The odds of **injection** of prescription pills were: significantly *higher* among all younger opioid abusers (ages 18–24, 25–34, 35–44) compared to older abusers; significantly *higher* among both whites and Latinos compared to African Americans; and, significantly *higher* among all in-treatment participants compared to street drug users. In terms of substance use, the odds of **injection** were: significantly *higher* among heroin users, and abusers of OxyContin, IR oxycodone, methadone, hydromorphone and morphine; *lower* odds of pill **injection** were observed among cocaine users and codeine abusers. Past year substance dependence was associated with increased odds of pill injection. Benzodiazepine use was not associated with injection or any other non-oral routes of administration.

Multivariate logistic regression models examining past year injection practices are displayed in Table 3. The youngest age group (18–24) had significantly higher odds of several HIV risk behaviors, including re-using needles, re-using needles without cleaning them, and lending needles, compared to their older counterparts. Compared to injectors of illicit drugs, those also endorsing prescription pill injection were also observed to have significantly *higher* odds of re-using unsterile needles.

DISCUSSION

This study is among the first to examine alternative routes of administration in a large and diverse sample of prescription opioid abusers. The prevalence of non-oral routes of administration in our sample far exceeds that documented in several studies[6–8], but is in line with estimates from opioid dependent patients in treatment.[12] Our findings indicate that treatment-based individuals had higher odds of abusing prescription opioids through non-oral routes, as did individuals who met DSM-IVR criteria for past year substance dependence, regardless of treatment status. These results are consistent with prior research in suggesting that non-oral routes of drug administration are associated with the development of more serious drug problems.[4]

In the present study, we identified race/ethnic differences in the abuse of prescription medications through alternate routes of administration. Compared to African Americans, both Hispanic and non-Hispanic white participants had substantially higher odds of snorting and injecting as routes for medication abuse. Abuse by medication tampering would appear to represent a more serious degree of opioid involvement among white participants in our study, which resonates with previous research documenting higher prevalence of prescription opioid misuse among whites in the general population, college students, substance abuse treatment clients and illicit drug users. [1, 14–16]

Age appeared to play an important role in route of administration as well. The youngest group of opioid abusers, ages 18–24, uniformly displayed the highest odds of employing non-traditional routes of administration. This finding accords with prior research indicating

higher levels of risk taking among younger treatment-based opioid abusers.[12] Importantly, younger individuals are also less knowledgeable about the risks associated with abuse of prescription opioids by tampering[4], and therefore may be especially vulnerable to adverse health consequences. Our findings demonstrated that the youngest opioid abusers had higher odds of unsafe needle use behaviors, which presents a substantial risk for exposure to HIV, hepatitis, and other blood-borne infections.

Notably, our study documented that specific opioids were associated with alternate routes of administration, particularly snorting and injecting, while others were more typically associated with oral ingestion. Immediate release oxycodone, OxyContin®, methadone, morphine, and hydromorphone abuse were each independently associated with higher odds of injection, while codeine and hydrocodone were not. Our findings add to the existing literature on substance-specific route of administration.[10] Clearly, route of administration is closely tied to the specific characteristics of the abused medication, including its pharmacokinetic properties and the presence or absence of additional ingredients, such as acetaminophen, which can cause unpleasant and harmful effects if taken by injection.

As an additional point, past 90 day heroin use was also found to be strongly associated with prescription opioid injection among our sample. This appears to represent an additional piece of evidence in support of the notion that the epidemics of heroin and prescription opioid abuse are increasingly intertwined. For some time abusers have been observed to substitute heroin for prescription opioids and vice-versa, based on availability, affordability, and other considerations, and increasingly it has been noted that prescription opioid abusers are switching to heroin in areas where heroin is less costly or of higher purity.[17, 18] As this situation continues to evolve, proactive monitoring of early warning systems for adverse events related to heroin use will be critical.

Our findings should be considered within the context of the study limitations. First, reliance on self-report data carries the potential for bias in reporting that may have impacted our prevalence estimates. In addition, measurement of route of prescription drug administration was somewhat restricted, with items not asked at the drug level. This limited our ability to examine prescription opioid abuse exclusively. Nevertheless, we documented that benzodiazepine abuse was not associated with any non-oral routes of administration, and therefore the route of administration data are attributable to prescription opioids. Lastly, because this research was conducted in South Florida, an area noted for its high prevalence of prescription drug abuse and diversion, the findings may not be generalizable to other locations.

Overall, our findings on route of administration among prescription opioid abusers have important implications for forward-looking prevention and intervention strategies. First, the continued development of abuse-deterrent opioid formulations would appear to be warranted[19], particularly for younger individuals at high-risk for opioid abuse through tampering. From a public health perspective, it is essential that young prescription opioid injectors be targeted for appropriate HIV and hepatitis education and intervention programming, as well as harm reduction initiatives. Given their young age and underrepresentation in populations traditionally considered to be at high-risk for HIV, increased exposure to injection-related disease prevention measures should be emphasized.

Acknowledgments

References

1. Cicero TJ, Inciardi JA, Muñoz A. Trends in Abuse of OxyContin® and Other Opioid Analgesics in the United States: 2002–2004. Pain. 2005; 6:662–672.

2. National Institute on Drug Abuse. Topics in Brief: Prescription drug abuse, 2011. Bethesda, MD: National Insitutes of Health; 2010.

3. Substance Abuse and Mental Health Services Administration, Office of Applied Studies. Results from the 2008 National Survey on Drug Use and Health: National findings. (Office of Applied Studies, NSDUH Series H-36, HHS Publication No. SMA 09-4434). Vol. 2009. Rockville, MD: 2009.

4. Katz N, Dart R, Bailey E, Trudeau J, Osgood E, Paillard F. Tampering with prescription opioids: Nature and extent of the problem, health consequences, and solutions. The American Journal of Drug and Alcohol Abuse. 2011:1–13. [PubMed: 21247284]

5. DuPont RL, Coleman JJ, Bucher RH, Wilford BB. Characteristics and motives of college students who engage in nonmedical use of Methylphenidate. The American Journal on Addictions. 2008; 17:167–171. [PubMed: 18463991]

6. McCabe SE, Teter CJ. Drug use related problems among nonmedical users of prescription stimulants: A web-based survey of college students from a Midwestern university. Drug and Alcohol Dependence. 2007; 91:69–76. [PubMed: 17624690]

7. Davis WR, Johnson BD. Prescription opioid use, misuse, and diversion among street drug users in New York City. Drug and Alcohol Dependence. 2008; 92:1–17. [PubMed: 17826005]

8. McCabe SE, Boyd CJ, Cranford JA, Teter CJ. Motives for non-medical use of prescription opioids among high school seniors in the United States: Self treatment and beyond. Archives of Pediatric and Adolescent Medicine. 2009; 163:739–744.

9. McCabe SE, Cranford JA, Boyd CJ, Teter CJ. Motives, diversion and routes of administration associated with nonmedical use of prescription opioids. Addictive Behaviors. 2007; 32:1–16. [PubMed: 16644136]

10. Young AM, Havens JR, Leukefeld CG. Route of administration for illicit prescription opioids: a comparison of rural and urban drug users. Harm Reduction Journal. 2010; 7:1–7. [PubMed: 20047690]

11. Compton WM, Volkow ND. Abuse of prescription drugs and the risk of addiction. Drug and Alcohol Dependence. 2006; 83:S4–S7. [PubMed: 16563663]

12. Budman SH, Grimes Serrano JM, Butler SF. Can abuse deterrent formulations make a difference? Expectation and speculation Harm Reduction Journal. 2009; 6:1–7.

13. Dennis, ML.; Titus, JC.; White, MK.; Unsicker, JI.; Hodgkins, D. Global Appraisal of Individual Needs - Initial (GAIN-I). Bloomington, IL: Chestnut Health Systems; 2002.

14. Miller NS, Greenfeld A. Patient Characteristics and Risks Factors for Development of Dependence on Hydrocodone and Oxycodone. American Journal of Therapeutics. 2004; 11:26–32. [PubMed: 14704593]

15. McCabe SE, Teter CJ, Boyd C. Medical Use, Illicit Use, and Diversion of Abusable Prescription Drugs. Journal of American College Health. 2006; 54:269–278. [PubMed: 16539219]

16. Vivian J, Saleheen H, SInger M, Navarro J, Mirhej G. Under the Counter: The Diffusion of Narcotic Analgesics to the Inner City Street. Journal of Ethnicity in Substance Abuse. 2005; 4:97–114. [PubMed: 16275636]

17. High intensity drug trafficking area. Drug Market Analysis 2010. National Drug Intelligence Center; South Florida: U.S. Department of Justice; May. 2010

18. National Drug Intelligence Center. National Drug Threat Assessment 2010. Johnstown, PA: U.S. Department of Justice; 2010.

19. Katz NP, Adams EH, Chilcoat HD, Colucci RD, Comer SD, Goliber P, Grudzinskas C, Jasinski D, Lande SD, Passik SD, Schnoll SH, Sellers E, Travers D, Weiss R. Challenges in the development of prescription opioid abuse-deterrent formulations. The Clinical Journal of Pain. 2007; 23:648–660. [PubMed: 17885342]

Table 1

Characteristics of prescription opioid abusers in South Florida (N=791)

	N	%
Demographics		
Age:		
18–24	176	22.3
25–34	262	33.1
35–44	169	21.4
45+	184	23.3
(Mean)	*34.5*	
Gender (% male):	493	62.3
Ethnicity:		
Hispanic	125	15.8
African American/Black	146	18.5
White	494	62.5
Other	26	3.3
Subsample:		
Street drug users	106	13.4
Public treatment clients	147	18.6
Private treatment clients	188	23.8
Methadone maintenance clients	201	25.4
MSM	149	18.8
Substance Use (past 90 days):		
Any drug injection	235	29.7
Cocaine (powder)	445	56.3
Crack cocaine	355	44.9
Heroin	211	26.7
Rx benzodiazepines	618	78.1
Rx opioids:		
Oxycodone (excluding OxyContin)	618	78.1
OxyContin	406	51.3
Hydrocodone	306	38.7
Methadone	168	21.2
Codeine	119	15.0
Hydromorphone	78	9.9
Morphine	65	8.2
Other	81	10.2
Past Year Substance Dependence:	750	94.9
Routes of Prescription Pill Administration:		
Oral	720	91.0
Snorting	420	53.1
Injecting	188	23.8

	N	%
Smoking	115	14.5
HIV Status (% Positive)[1]	77	10.4

[1] N=738

Table 2

Bivariate logistic regressions predicting route of administration (South Florida opioid abusers N=791)

	Route of administration [Odds ratio (95% CI) *p* value]			
	Oral	**Snorting**	**Smoking**	**Injecting**
Demographics				
Age				
18–24	**.126 (.048, .331) .000**	**9.57 (5.91, 15.5) .000**	**5.38 (2.86, 10.11) .000**	**8.39 (4.34, 16.25) .000**
25–34	**.265 (.099, .705) .008**	**4.71 (3.11, 7.13) .000**	1.87 (.977, 3.59) .059	**5.53 (2.91, 10.55) .000**
35–44	.487 (.163, 1.51) .218	**2.70 (1.72, 4.23) .000**	.928 (.417, 2.07) .855	**4.16 (2.09, 8.270) .000**
45+	---Ref----	---Ref----	---Ref----	---Ref----
Male gender	1.17 (.712, 1.92) .534	.778 (.582, 1.04) .090	1.23 (.810, 1.88) .328	.776 (.556, 1.084) .137
Ethnicity				
Hispanic	.275 (.055, 1.39) .118	**2.02 (1.21, 3.35) .007**	1.19 (.582, 2.45) .628	**5.97 (1.96, 18, 12) .002**
White	**.102 (.025, .424) .002**	**4.47 (2.97, 6.71) .000**	1.30 (.737, 2.28) .370	**17.3 (6.30, 47.62) .000**
African American	---Ref----	---Ref----	---Ref----	---Ref----
Subsample				
Public treatment	**.084 (.011, .645) .017**	**3.82 (2.22, 6.57) .000**	**2.56 (1.20, 5.50) .015**	**3.69 (1.63, 8.34) .002**
Private treatment	**.039 (.005, .288) .001**	**7.48 (4.37, 12.82) .000**	**3.77 (1.83, 7.78) .000**	**6.63 (3.04, 14.46) .000**
Methadone maint.	**.103 (.014, .786) .028**	**4.58 (2.73, 7.69) .000**	**.295 (.104, .837) .022**	**6.55 (3.01, 14.24) .000**
MSM	1.41 (.87, 22.8) .809	1.21 (.692, 2.10) .510	1.08 (.463, 2.49) .867	.881 (.336, 2.31) .797
Street drug users	---Ref----	---Ref----	---Ref----	---Ref----
Substance Use- 90 days				
Cocaine (powder)	**2.11 (1.28, 3.48) .003**	.897 (.677, 1.19) .448	.972 (.653, 1.45) .887	**.660 (.475, .917) .013**
Crack cocaine	1.06 (.65, 1.73) .829	**.742 (.560, .984) .038**	1.20 (.805, 1.78) .374	1.17 (.844, 1.63) .345
Heroin	**.559 (.737, .929) .025**	**1.84 (1.33, 2.54) .000**	1.13 (.726, 1.75) .596	**5.55 (3.90, 7.92) .000**
Rx benzodiazepines	**1.96 (1.16, 3.30) .012**	1.19 (.849, 1.67) .313	1.39 (.830, 2.33) .210	1.42 (.933, 2.16) .102
Opioid use:				
Oxycodone	.492 (.239, 1.01) .054	**2.47 (1.74, 3.50) .000**	**2.03 (1.15, 3.60) .015**	**4.45 (2.50, 7.90) .000**
OxyContin	**.543 (.327, .924) .019**	**2.45 (1.84, 3.26) .000**	**1.64 (1.10, 2.46) .016**	**2.42 (1.71, 3.41) .000**
Hydrocodone	1.45 (.858, 2.45) .165	**1.37 (1.02, 1.82) .034**	.898 (.596, 1.35) .606	1.27 (.912, 1.77) .156
Methadone	.920 (.513, 1.65) .780	**2.26 (1.58, 3.25) .000**	.700 (.414, 1.18) .183	**2.00 (1.37, 2.90) .000**

Route of administration [Odds ratio (95% CI) *p* value]				
	Oral	Snorting	Smoking	Injecting
Codeine	**4.35 (1.35, 14.1) .014**	**.667 (.451, .988) .043**	.976 (.560, 1.70) .932	**.316 (.170, .588) .000**
Hydromorphone	**.496 (.254, .970) .040**	**2.28 (1.37, 3.79) .001**	1.08 (.562, 2.06) .823	**9.08 (5.44, 15.13) .000**
Morphine	1.20 (.466, 3.09) .706	1.46 (.866, 2.45) .157	.812 (.377, 1.75) .595	**2.87 (1.71, 4.83) .000**
Past Year Dependence	.000 (.000, -----) .998	**4.18 (1.96, 8.89) .000**	6.99 (.951, 51.4) .056	**4.04 (1.23, 13.3) .021**

Table 3

Multivariate logistic regressions predicting past year needle risk among drug injectors in South Florida (N=264)

	[Odds ratio (95% CI) *p* value]
Re-used a needle	
Age	
18–24	**3.118 (1.20, 8.11) .020**
25–34	1.020 (.442, 2.35) .964
35–44	**2.811 (1.06, 7.49) .039**
45+	------ref------
Past 90 day Rx Drug Injection[1]	1.844 (.992, 3.43) .053
Re-used a needle without cleaning it	
Age	
18–24	**3.204 (1.31, 7.83) .011**
25–34	1.450 (.622, 3.38) .389
35–44	1.792 (.723, 4.44) .208
45+	------ref------
Past 90 day Rx Drug Injection[1]	**2.302 (1.30, 4.09) .004**
Let someone else use your needle after you	
Age	
18–24	**2.869 (1.18, 6.99) .020**
25–34	1.617 (.690, 3.79) .269
35–44	1.938 (.780, 4.81) .154
45+	------ref------
Past 90 day Rx Drug Injection[1]	1.647 (.928, 2.92) .088
Used a needle someone else used	
Age	
18–24	1.860 (.735, 4.71) .190
25–34	1.329 (.539, 3.28) .537
35–44	1.314 (.500, 3.45) .580
45+	------ref------
Past 90 day Rx Drug Injection[1]	1.230 (.672, 2.25) .502

[1]Reference category is "illicit drug injection only".