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Prior prescription opioid misuse in a cohort of heroin users in a treatment study

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ABSTRACT

This study investigates prior prescription opioid misuse in a cohort of heroin users whose progress was tracked in a treatment study conducted in the US from 2006 to 2010. Half of the sample misused prescription opioids ("other opiates/analgesics") prior to their onset of heroin misuse (POBs). We found that POBs were demographically younger and more likely to be white than other heroin users (OHUs). There were differences between the two groups with respect to the reporting of at least one year of regular use of substances and age of onset of substance use. POBs were more likely to report regular use, and earlier onset of use of several substances, mostly of the type potentially obtained via prescription. POBs were more persistent in their opioid use and more likely to suffer near-term elevated depressive symptoms compared with OHUs. These findings suggest that heroin addiction treatment may need to be tailored according to opioid misuse history.

1. Introduction

There is a widely held perception that the current heroin overdose crisis was fueled by the growth in the misuse of prescription opioids (POs). Indeed, research suggests that many heroin users started with opioid-related pain medications and then, once they became dependent, transitioned to heroin, which is less expensive, more accessible, and more potent (Canfield et al., 2010; Cicero, Ellis, Surratt, & Kurtz, 2014; Harocopos, Allen, & Paone, 2016; Lankenau et al., 2012). This analysis attempts to understand the prevalence of PO misuse history in a sample of heroin users enrolled in a treatment study. Additionally, the analysis seeks to understand how heroin users who transition from POs (POBs) differ from other heroin users (OHUs) in terms of key background, substance abuse and risk characteristics. Finally, the analysis examines how POBs and OHUs differ in terms of substance use and depressive symptoms after treatment initiation.

2. Methods

This study is based on a secondary data analysis of a treatment study implemented in the US (Boston, MA) from 2006 to 2010, Project AHEAD (Addiction, Health Evaluation and Disease Management) (Saitz, Cheng, Winter, et al., 2013). This study recruited 563 participants with alcohol and/or other drug dependence from a residential detoxification unit, hospital referrals and advertisements. Participants were either randomly assigned to "chronic care management" (CCM) or usual primary care. The CCM intervention involved coordinated treatment between members of a health care team that included a nurse case manager, a social worker, an internist, and a psychiatrist with addiction expertise (Saitz et al., 2013). The research team followed up respondents for a year after the intervention, with assessments at baseline, 3, 6, and 12 months. Although the percentage of respondents assessed at each specific follow-up wave varied, 95% of all respondents completed a 12-month follow-up in the original study (Saitz et al., 2013). The timing of this study, which was initiated early in the current US opioid epidemic, and its recruitment of a large number of heroin and opioid dependent patients makes it particularly appropriate for secondary analyses focused on understanding the background, risk, and treatment trajectories of this important group.

For this secondary analysis, we identified 265 participants who self-reported heroin as their only, primary, or secondary substance problem at baseline, based on responses to the ASI (Mclellan, Kushner, Metzger, et al., 1992). This analysis includes members of the heroin user cohort who completed all three follow-up waves of the study. Accordingly, we excluded 63 participants who missed at least one follow-up assessment to ensure all analyses utilized a consistent sample, leaving us with a sample of 202 participants (35.9% of the AHEAD sample). For those who used both heroin and POs, sequencing from POs to heroin was determined by comparing self-reported age of onset for heroin misuse with age of onset for misuse of "other opiates/analgesics" (Saitz et al., 2013).

We compared our sample of 202 current heroin users to the 63

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current heroin users who missed a follow-up assessment to assess what biases were introduced by excluding these participants. Based on responses to the baseline interview, there were no differences in the two groups with respect to demographics (race/ethnicity, gender, or age), prior prescription opiate use (POB/OHU), likelihood of assignment to the intervention or control group, or past month substance use at baseline. There were no significant differences with respect to the probability of reporting at least one year of "regular use" of any substance (where "regular use," is defined by the ASI as use of a substance "3×/week or more"), with the exception of other opiates/analgesics. Heroin users who were retained in our study were less likely to report at least one year of regular use of other opiates/analgesics (OR = 0.26; 95% CI 0.11, 0.62; $p < 0.01$).

All analyses were performed using Stata version 15.0 software (StataCorp, 2017). We performed descriptive analyses as well as logistic regression to assess differences between the two groups at baseline. To examine differences in number of days of substance use for substances with > 15% prevalence in the sample and elevated depressive symptoms at 3, 6, and 12 months from baseline, we performed negative binomial and logistic regressions.

3. Results

Exactly half of all heroin users in the sample reported PO use before heroin initiation. We compared the two groups with respect to their reporting of at least one year of regular use of 10 substances (alcohol use was measured twice, with one measure focused on drinking to intoxication; see Table 1). POBs were significantly more likely to report at least one year of regular use of other opiates/analgesics (88.1% vs 33.7%; $p < 0.001$), sedatives/hypnotics/tranquilizers (57.4% vs 32.7%; $p < 0.001$), and hallucinogens (34.7% vs 19.8%; $p < 0.05$). OHUs were marginally significantly more likely to report at least one year of regular use of alcohol to intoxication (84.2% vs 73.3%; $p < 0.1$). There were no significant differences between the two groups with respect to their reporting at least one year of regular use of any alcohol, heroin, barbiturates, cocaine, amphetamines, marijuana, or inhalants.

Furthermore, we compared the mean age of first use of various drugs between POBs and OHUs. OHUs reported a significantly younger age of onset for heroin (mean age = 20.0 vs 23.2; $t_{df=200} = -3.31$; $p < 0.01$). POBs reported a significantly younger age of onset for barbiturates (mean age = 17.8 vs 23.0; $t_{df=39} = 2.09$; $p < 0.05$), sedatives/hypnotics/tranquilizers (mean age = 18.6 vs 21.9; $t_{df=161} = 2.92$; $p < 0.01$), and cocaine (mean age = 17.8 vs 19.4; $t_{df=198} = 2.47$; $p < 0.05$). Age of onset for any alcohol, alcohol to intoxication, other opiates/analgesics, amphetamines, marijuana, hallucinogens, and inhalants were not significantly different for POBs and OHUs (see Table 1).

Logistic regression analysis was used to evaluate key sociodemographic, symptom and substance use differences across the two groups at baseline. Analyses revealed that POBs were significantly younger and more likely to be white than OHUs. There were no significant differences in gender and education level between POBs and OHUs. POBs and OHUs also did not differ significantly on elevated PHQ-9 depression scores, likelihood of alcohol-dependence, likelihood of recent overdose, or number of days of use of multiple substances at baseline (see Table 2).

Negative binomial and logistic regressions assessed differences between POBs and OHUs at 3, 6, and 12-month follow-up. POBs had significantly fewer days of any alcohol use in the past month and alcohol to intoxication in the past month at 3-month follow-up. POBs also had significantly fewer days of any alcohol use in the past month and alcohol to intoxication in the past month at 6-month follow-up. These significant differences disappeared at 12 months. POBs had significantly more days of other opiate/analgesic use in the past month at 12-month follow-up, but not at 3 or 6 months. No significant differences were found for any other substance at any of the three follow-up intervals. POBs had significantly higher risk for elevated depression

Table 1
POBs[a] vs OHUs[b]: regular use[c] and age of onset for substances.

	Reported at least 1 year of regular use		Mean age of onset (years)[h]	
	POB (n = 101)	OHU (n = 101)	POB	OHU
Alcohol	76.2%	85.2%	12.6	13.3
Alcohol to intoxication	73.3%[d]	84.2%	13.8	14.5
Heroin	98.0%	100.0%	23.2[i]	20.0
Other opiates/ analgesics	88.1%[e]	33.7%	18.1	17.5
Barbiturates	7.9%	7.9%	17.8[j]	23.0
Sedatives/hypnotics/ tranquilizers	57.4%[f]	32.7%	18.6[k]	21.9
Cocaine	71.3%	77.2%	17.8[l]	19.4
Amphetamines	17.8%	10.9%	20.3	20.1
Marijuana	78.2%	76.2%	13.9	14.2
Hallucinogens	34.7%[g]	19.8%	17.2	17.6
Inhalants	3.0%	3.0%	17.0	16.5

[a] POBs = heroin users who used prescription opioids before heroin initiation.
[b] OHUs = all other heroin users (who did not use prescription opioids before heroin initiation).
[c] "Regular use" is defined by the ASI as use of a substance "3×/week or more" and subjects are asked to indicate "How many years in your life have you regularly used…."
[d] $\chi^2_{df=1} = 3.58$; $p < 0.1$.
[e] $\chi^2_{df=1} = 62.88$; $p < 0.001$.
[f] $\chi^2_{df=1} = 12.50$; $p < 0.001$.
[g] $\chi^2_{df=1} = 5.62$; $p < 0.05$.
[h] Total number of participants for "age of onset" varies by substance and comparison group because calculations exclude participants who report no use.
[i] $t_{df=200} = -3.31$; $p < 0.01$.
[j] $t_{df=39} = 2.09$; $p < 0.05$.
[k] $t_{df=161} = 2.92$; $p < 0.01$.
[l] $t_{df=198} = 2.47$; $p < 0.05$.

Table 2
POBs[a] vs OHUs[b]: baseline comparisons[c,d] (n = 202).

Independent variable	OR	95% CI
Race/ethnicity		
Non-Hispanic white vs other	6.36***	3.13, 12.92
Gender		
Male vs female	0.80	0.36, 1.78
Age		
18–29 vs older	2.83**	1.39, 5.77
Alcohol dependence		
Yes vs no	0.86	0.41, 1.82
Recent overdose (3 months)		
Yes vs no	2.13	0.79, 5.77
# Days in past 30 days used > 1 substance per day	0.98	0.95, 1.01
Randomization group		
Intervention vs control	0.81	0.34, 1.30

[a] POBs = heroin users who used prescription opioids before heroin initiation.
[b] OHUs = all other heroin users (who did not use prescription opioids before heroin initiation).
[c] Logistic regression predicts POB vs OHU status.
[d] Regressions control for race/ethnicity, age, gender, randomization group, alcohol dependence, recent overdose, and use of > 1 substance per day in the past 30 days.
** $p < 0.01$.
*** $p < 0.001$.

Table 3
POBs[a] vs OHUs[b]: Three, six, and twelve-month follow-up[c,d] (n = 202).

Dependent variable	3 months		6 months		12 months	
	IRR/OR	95% CI	IRR/OR	95% CI	IRR/OR	95% CI
PHQ-9: > 9	0.90	0.46, 1.73	3.11**	1.54, 6.30	1.33	0.69, 2.58
# days any alcohol use (PM[e])	0.47*	0.23, 0.95	0.39*	0.16, 0.93	0.59	0.23, 1.48
# days alcohol to intoxication (PM)	0.41*	0.19, 0.88	0.33*	0.12, 0.89	0.45	0.16, 1.25
# days heroin use (PM)	0.54	0.26, 1.15	0.96	0.44, 2.10	0.77	0.32, 1.83
# days other opiates/analgesics use (PM)	2.68	0.81, 8.88	1.27	0.37, 4.41	3.85*	1.19, 12.46
# days sedatives/hypnotics/tranquilizers use (PM)	0.40	0.08, 1.97	1.20	0.29, 4.92	2.13	0.53, 8.59
# days cocaine use (PM)	0.72	0.30, 1.70	0.49	0.14, 1.78	1.16	0.40, 3.37
# days marijuana use (PM)	0.90	0.34, 2.41	0.39	0.12, 1.29	0.72	0.17, 2.99
# days of use of > 1 substance per day (PM)	0.54	0.27, 1.10	0.70	0.27, 1.85	0.84	0.37, 1.90

[a] POBs = heroin users who used “other opioids/analgesics” before they first used heroin.
[b] OHUs = all other heroin users (i.e., those who did not use “other opioids/analgesics” before they first used heroin).
[c] Logistic regression was used for the PHQ-9 depression measure and negative binomial regressions were used for all other dependent variable measures.
[d] All models control for race/ethnicity, age, gender, and randomization group and compare POBs to OHUs on outcomes.
[e] PM = past month.
* $p < 0.05$.
** $p < 0.01$.

scores than OHUs at 6-month follow-up. PHQ-9 depression scores did not differ significantly at 3 or 12-month follow-up (see Table 3).

4. Discussion

Portending current demographic trends in overdose mortality, POBs, who comprised half the sample of current heroin users in the AHEAD study, were more likely to be younger (in their late 20's rather than late 30's) and overwhelming white. There were significant substance involvement differences, with POB's more likely to report regular use of several non-heroin substances, mostly of the type potentially obtained via prescription. They also tended to use these substances at earlier ages than OHU's. After treatment initiation, OHUs were more prone to alcohol involvement; POBs were more persistent in their opioid use and more likely to suffer near-term elevated depressive symptoms.

This study is limited to the extent that it focuses on one particular sample of heroin users recruited from one location (Boston, Massachusetts) at one time period (2006–2010). Further, we note that the sample selection strategy (the requirement of 3 complete follow-up interviews) may have resulted in an underrepresentation of heroin users with a prescription opioid misuse history. If this subgroup (which potentially was harder to track) was in some way more problematic than the POBs included in the study, our study may underestimate the level of problems (and negative treatment outcomes) that POBs may experience compared to OHUs. Additionally, we note that the findings reported here may not be completely generalizable to other settings and time periods. For example, as the opioid crisis has evolved, the co-occurrence of other substances (such as fentanyl and carfentanyl) (Cicero, Ellis, & Kasper, 2017) may change the nature of both prior drug use history and treatment consequences for heroin users.

The considerable substance involvement differences between the two groups may have important implications for treatment outcomes. These findings suggest that heroin addiction treatment may need to be tailored according to opioid misuse history. It is not clear, however, whether these findings are generalizable to other treatment settings and conditions. For example, it would be important to see whether these background differences are consequential for responsiveness to medication assisted treatment. Further research on these treatment implications is clearly warranted.

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