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Lifetime history of heroin use is associated with greater drug severity among prescription opioid abusers

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Abstract

Background—While research suggests primary prescription opioid (PO) abusers may exhibit less severe demographic and drug use characteristics than primary heroin abusers, less is known about whether a lifetime history of heroin use confers greater severity among PO abusers.

Objective—In this secondary analysis, we examined demographic and drug use characteristics as a function of lifetime heroin use among 89 PO-dependent adults screened for a trial evaluating the relative efficacy of buprenorphine taper durations. Exploratory analyses also examined contribution of lifetime heroin use to treatment response among a subset of participants who received a uniform set of study procedures.

Methods—Baseline characteristics were compared between participants reporting lifetime heroin use 5 (H⁺; n=41) vs. <5 (H⁻; n=48) times. Treatment response (i.e., illicit opioid abstinence and treatment retention at end of study) was examined in the subset of H⁺ and H⁻ participants randomized to receive the 4-week taper condition (N=22).

Results—H⁺ participants were significantly older and more likely to be male. They reported longer durations of illicit opioid use, greater alcohol-related problems, more past-month cocaine use, greater lifetime IV drug use, and greater lifetime use of cigarettes, amphetamines and hallucinogens. H⁺ participants also had lower scores on the Positive Symptom Distress and Depression subscales of the Brief Symptom Inventory. Finally, there was a trend toward poorer treatment outcomes among H⁺ participants.

Conclusion—A lifetime history of heroin use may be associated with elevated drug severity and unique treatment needs among treatment-seeking PO abusers.

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Contributors

All authors contributed to and have approved the final manuscript.

Conflict of Interest

Dr. Sigmon has received consulting payments from Alkermes and, through her university, has received research support from Titan Pharmaceuticals. All other authors declare no conflicts of interest.

Keywords

Opioid; prescription opioid; heroin; abuse; dependence

1. Introduction

Prescription opioid (PO) abuse is a serious public health issue in the United States. In 2011, 1.9 million individuals reported first time non-prescribed PO use, 4.5 million reported past year use, and approximately twice the number of patients received treatment for POs vs. heroin (1). Efforts to better understand the treatment needs of PO abusers are central to developing effective treatments for these patients. Studies suggest that primary PO abusers may possess a unique profile of demographic characteristics and treatment needs (2). When compared to heroin abusers, for example, primary PO abusers may present with less severe baseline characteristics including greater education, greater earned income, lower levels of daily opioid use, and less IV use (3-9).

Less is known about how PO abusers' opioid use history may influence their clinical severity at treatment intake and perhaps even their response to treatment. For example, while not their primary drug at the time they present for treatment, many PO abusers report a history of using heroin. Of interest is whether a lifetime history of heroin use may confer greater severity in these patients. Among the limited studies on this topic, results have been mixed. Brands and colleagues (10) found that PO+heroin users reported greater illicit non-opioid drug and IV use compared to PO-only users, though there were no differences in psychosocial stability. Wu and colleagues (11) reported that PO+heroin users had higher rates of substance use and serious psychiatric disorders compared to both PO-only and heroin-only users. Others have found that the clinical severity of PO+heroin users may fall between PO-only and heroin-only users (3,4). These prior studies, however, were generally conducted in populations of general illicit opioid users, rather than primary PO abusers per se. More recently, in an investigation of characteristics associated with buprenorphine treatment outcomes among PO abusers, lifetime heroin use was associated with less successful outcomes (12). However, further baseline differences between PO users with and without prior heroin use were not examined. Taken together, an improved understanding of the contribution of lifetime heroin use to clinical severity and treatment outcomes will inform efforts to treat the growing population of PO abusers.

We recently completed a double-blind, placebo-controlled randomized trial evaluating the efficacy of three outpatient buprenorphine taper durations and subsequent naltrexone for PO-dependent adults (13). While the primary focus was on opioid abstinence and treatment retention, this trial also provided a unique opportunity to evaluate the role of lifetime heroin use in this sample of treatment-seeking PO abusers. Thus, in this secondary analysis we compare the demographics and drug use characteristics of PO-dependent patients based on lifetime history of heroin use.

2. Methods

Participants were 89 PO-dependent adults screened for the above randomized controlled trial. Participants had to be 18 years old, meet DSM-IV criteria for opioid dependence, provide an opioid-positive urine, accept detoxification, report a PO as their primary drug of abuse and be using it illicitly. The IRB approved the study and participants provided informed consent prior to participating.

Participants completed a comprehensive intake assessment including a drug history, Addiction Severity Index (ASI; 14), Beck Anxiety Inventory (BAI; 15), Beck Depression Inventory (BDI; 16), Brief Symptom Inventory (BSI; 17) and Michigan Alcoholism Screening Test (MAST; 18). As the full description of study methods has been reported elsewhere (13), only a brief description is presented here. Following brief buprenorphine stabilization, PO-dependent adults were randomized to receive a double-blind 1-, 2- or 4-week buprenorphine taper followed by oral naltrexone therapy for those who successfully tapered. Participants received individual behavior therapy and urinalysis regularly throughout the 12-week trial.

2.1 Data analyses

Participants were dichotomized based upon whether they reported at intake using heroin 5 (H^+ ; $n=41$) or <5 (H^- ; $n=48$) times during their lifetime, consistent with SAMHSA recommended diagnostic criteria to identify potential substance use problems (19). H^+ and H^- subgroups were compared on their intake demographic, psychosocial and drug use characteristics. Comparisons between H^+ and H^- participants were performed using t -tests for continuous variables and Chi-square tests for categorical variables. As more exploratory analyses, we also examined the association between lifetime heroin use and treatment response, defined as illicit opioid abstinence and treatment retention at the end of the study. This was done for a subset of participants randomized to receive the 4-week taper condition ($N=22$), as that experimental condition produced the greatest abstinence and retention in the parent trial and thus provided the most complete data for analyses (13). Analyses were conducted using SPSS statistical software (IBM, Armonk, NY), with significance determined at $p<0.05$.

3. Results

3.1 Demographic and Psychosocial Characteristics

H^+ participants were older (29.9 ± 7.0 vs. 25.7 ± 5.6 years, $p=0.003$) and included a greater proportion of males (81% vs. 54%, $p=0.009$) than H^- participants, respectively. H^+ participants had lower scores on the Depression (0.82 ± 0.60 vs. 1.19 ± 0.98 , $p=0.04$) and Positive Symptom Distress Index (1.52 ± 0.43 vs. 1.75 ± 0.51 , $p=0.03$) subscales of the BSI. There were trends toward H^+ participants endorsing fewer symptoms on the Obsessive-Compulsive subscale of the BSI (0.94 ± 0.67 vs. 1.23 ± 0.85 , $p=0.09$) and on the BDI (16.9 ± 10.3 vs. 20.9 ± 11.1 , $p=0.09$) than H^- participants, respectively.

3.2 Opioid Use Characteristics

H⁺ and H⁻ participants were generally similar on variables related to their initiation of illicit opioid use (Table 1). However, H⁺ participants reported a longer duration of regular illicit opioid use (6.1 ± 4.1 vs. 3.9 ± 3.5 years, $p=0.009$), and a greater proportion of H⁺ participants reported IV as their primary route of administration during that time (24% vs. 6%, $p=0.02$). As expected, more H⁺ participants reported ever using heroin (even a single use) compared to H⁻ (100% vs. 23%, respectively, $p<0.001$) and, of those that had ever used heroin, H⁺ participants reported a longer duration of use (1.6 ± 2.5 vs. 0.01 ± 0.03 years, $p=0.05$). With regard to route of heroin administration, fewer H⁺ participants reported intranasal use (46% vs. 82%, $p=0.04$) and more reported IV use (54% vs. 18%, $p=0.04$). More H⁺ participants also reported ever using IV administration for any opioid use (prescription opioids or heroin) than H⁻ (76% vs. 15%, respectively, $p<0.001$). Finally, more H⁺ participants had received prior treatment for opioid dependence than H⁻ participants (49% vs. 23%, respectively, $p=0.01$).

When current opioid use was assessed at study intake, there were no differences between H⁺ and H⁻ participants in type of primary PO used during the prior month (Table 1). However, of those that reported oxycodone as their primary drug, H⁺ participants used a greater amount per day than H⁻ (148.4 ± 90.5 vs. 81.7 ± 44.6 mg/day, respectively, $p=0.006$). A larger proportion of H⁺ participants also reported greater past 30-day heroin use (10% vs. 0%, $p=0.03$). Finally, more H⁺ participants reported IV as their primary route of administration at intake than H⁻ (27% vs. 8%, respectively, $p=0.02$).

3.3 Other Drug Use Characteristics

H⁺ participants scored higher on the MAST (12.4 ± 12.3 vs. 5.6 ± 5.6 , respectively, $p=0.002$; data not shown), and more H⁺ participants reported lifetime use of cigarettes (98% vs. 85%, $p=0.05$). A greater proportion of H⁺ participants reported past-month cocaine use (29% vs. 13%, $p=0.05$), as well as lifetime amphetamine (46% vs. 25%, $p=0.04$) and hallucinogen (59% vs. 31%, $p=0.01$) use, than H⁻ participants, respectively.

3.4 Response to Treatment

Among those randomly assigned to the 4-week buprenorphine taper condition, there was a trend toward poorer treatment outcomes among H⁺ than H⁻ participants, with 25% vs. 64% opioid abstinent at end-of-treatment ($p=0.08$; Figure 1, upper panel). A similar pattern was observed with treatment retention, with 25% vs. 64% of participants retained at end-of-treatment ($p=0.08$; Figure 1, lower panel).

4. Discussion

We examined baseline characteristics among treatment-seeking PO abusers as a function of lifetime heroin use. Our data suggest that a history of heroin use may be associated with elevated drug use severity among PO abusers. Compared to H⁻ participants, H⁺ presented with more severe opioid abuse, greater lifetime intravenous use, and more prior opioid treatment episodes. They reported greater heroin and cocaine use in the month prior to

intake, as well as greater lifetime use of cigarettes, heroin, amphetamine, and hallucinogens. H^+ participants also reported greater alcohol-related problems.

Among a subset of participants who received a uniform set of study procedures, a history of heroin use was also associated with a trend toward poorer treatment outcomes. Specifically, we observed a trend toward H^+ participants achieving less opioid abstinence and poorer treatment retention. While this did not reach statistical significance, these relative success rates between H^+ and H^- participants (25% vs. 64%) may reflect a clinically meaningful difference, particularly when one considers that relapse to illicit opioid use and treatment dropout represent a resumption of extremely high-risk, possibly life-threatening, behaviors in this population. Also worth noting is that our treatment outcome analyses were likely limited by the modest sample size used, as they were restricted to the subset of patients randomly assigned to the 4-week buprenorphine taper.

Taken together, these data suggest that meaningful differences may exist among PO-dependent patients as a function of lifetime heroin use and are consistent with several prior studies on this topic (3,4,10-12). The present study also extends those prior reports by examining treatment response specifically in a sample of treatment-seeking primary PO abusers, as well as among patients receiving opioid detoxification rather than maintenance (12). Several differences between these results and prior studies should be noted. While H^+ participants were older than H^- in the present study, Brands and colleagues (10) found the opposite, and still others have reported no age differences (3,4). While we found no differences in legal severity between the two groups, one prior study suggested that a history of heroin use was associated with greater legal problems (3). Finally, in the present study the H^+ group consisted of a greater percentage of males, while prior reports have found no gender differences (3,4,10,11). Differences across studies may be attributable to differences in the patient populations being examined. Brands et al. (10), for example, examined patients presenting for methadone maintenance, while Moore and colleagues (4) examined patients receiving office-based buprenorphine treatment. How these may compare to our present sample of primary PO abusers entering buprenorphine detoxification is unclear, though overall the differences observed in the present study were generally more similar than dissimilar to those reported previously.

Several potential limitations should also be noted. First, this was a secondary analysis of data from a randomized clinical trial with a limited sample size, and particularly limited with regard to our examination of treatment outcome. While the sample size did not allow for multivariate analyses to determine predictors of treatment outcome, it did permit a relatively thorough comparison of H^+ and H^- participants' intake characteristics as well as an initial look at whether treatment response may be influenced by patients' history of heroin use. A second possible limitation is that, unlike several prior reports, we did not include a heroin-only group for comparison. However, given the striking recent increases in prevalence of and treatment admissions for PO dependence (1), our focus on primary PO abusers is consistent with efforts aimed specifically at this important and growing population. Finally, our definition of lifetime heroin use was based on self-report, and it is also impossible to disentangle whether lifetime history of heroin use may be a proxy for another mechanism underling the differences observed between H^+ and H^- participants. Nonetheless, this simple

self-report item may provide a straightforward, convenient and cost-effective method for identifying patients who may warrant more intensive services during treatment.

Taken together, differences may exist between PO users with and without a history of heroin abuse, with H⁺ participants exhibiting more severe drug use and possibly poorer treatment outcomes compared to H⁻ participants. Future prospective studies with larger samples are warranted to further investigate these differences, as well as to more clearly identify the unique treatment needs of each subgroup of PO abusers. Overall, these efforts will improve our efforts to effectively respond to the PO epidemic in this country.

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Dr. Sigmon obtained funding for this study and designed the parent trial in which the data was collected. Drs. Sigmon and Patrick were involved in data acquisition. Drs. Meyer and Sigmon directed the data analysis. Dr. Meyer wrote the first draft of the manuscript, managed the literature searches and conducted the statistical analysis.

References

1. Substance Abuse and Mental Health Services Administration. Results from the 2011 National Survey on Drug Use and Health: Summary of National Findings. Substance Abuse and Mental Health Services Administration; Rockville, MD: 2012. NSDUH Series H-44, HHS Publication No. (SMA) 12-4713
2. Zacny J, Bigelow G, Compton P, Foley K, Iguchi M, Sammerud C. College on Problems of Drug Dependence taskforce on prescription opioid non-medical use and abuse: Position statement. *Drug Alcohol Depend.* 2003; 69:215–232. [PubMed: 12633908]
3. Fischer B, Patra J, Cruz MF, Gittins J, Rehm J. Comparing heroin users and prescription opioid users in a Canadian multi-site population of illicit opioid users. *Drug Alcohol Rev.* 2008; 27:625–632. [PubMed: 19378446]
4. Moore BA, Fiellin DA, Barry DT, Sullivan LE, Chawarski MC, O'Conner PG, Schottenfeld RS. Primary care office-based buprenorphine treatment: Comparison of heroin and prescription opioid dependent patients. *J Gen Intern Med.* 2007; 22:527–530. [PubMed: 17372805]
5. Nielsen S, Hillhouse M, Thomas C, Hasson A, Ling W. A comparison of buprenorphine taper outcomes between prescription opioid and heroin users. *J Addict Med.* 2013; 7:33–38. [PubMed: 23222095]
6. Rosenblum A, Parrino M, Schnoll SH, Fong C, Maxwell C, Cleland CM, Haddox JD. Prescription opioid abuse among enrollees into methadone maintenance treatment. *Drug and Alcohol Depend.* 2007; 90:64–71.
7. Sigmon SC. Characterizing the emerging population of prescription opioid abusers. *Am J Addict.* 2006; 15:208–212. [PubMed: 16923666]
8. Subramaniam GA, Stitzer ML. Clinical characteristics of treatment-seeking prescription opioid vs. heroin-using adolescents with opioid use disorder. *Drug Alcohol Depend.* 2009; 101:13–19. [PubMed: 19081205]
9. Torrington M, Domier CP, Hillhouse M, Ling W. Buprenorphine 101: Treating opioid dependence with buprenorphine in an office-based setting. *J Addict Dis.* 2007; 26:93–99. [PubMed: 18018812]

10. Brands B, Blake J, Sproule B, Gourlay D, Busto U. Prescription opioid abuse in patients presenting for methadone maintenance treatment. *Drug Alcohol Depend.* 2004; 73:199–207. [PubMed: 14725960]
11. Wu LT, Woody GE, Yang C, Blazer DG. How do prescription opioid users differ from users of heroin or other drugs in psychopathology: Results from the national epidemiologic survey on alcohol and related conditions. *J Addict Med.* 2011; 5:28–35. [PubMed: 21532972]
12. Dreifuss JA, Griffin ML, Frost K, Fitzmaurice GM, Potter JS, Fiellin DA, Weiss RD. Patient characteristics associated with buprenorphine/naloxone treatment outcome for prescription opioid dependence: results from a multisite study. *Drug Alcohol Depend.* 2013; 131:112–118. [PubMed: 23333292]
13. Sigmon SC, Dunn KE, Saulsgiver K, Patrick ME, Badger GJ, Heil SH, Higgins ST. A randomized, double-blind evaluation of buprenorphine taper for the treatment of prescription opioid dependence. *JAMA Psychiatry.* 2013; 70:1247–54.
14. McLellan AT, Luborsky L, Cacciola J, Griffith J, Evans F, Barr HL, O'Brien CP. New data from the Addiction Severity Index. Reliability and validity in three centers. *J Nerv Ment Dis.* 1985; 173:412–423. [PubMed: 4009158]
15. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: Psychometric properties. *J Consult Clin Psychol.* 1988; 56:893–897. [PubMed: 3204199]
16. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry.* 1961; 4:561–571. [PubMed: 13688369]
17. Derogatis, LR. Brief symptom inventory. National Computer Systems, Inc.; Minneapolis, MN: 1993.
18. Selzer ML. The Michigan Alcoholism Screening Test: The quest for a new diagnostic instrument. *Am J Psychiatry.* 1971; 127:1653–1658. [PubMed: 5565851]
19. Center for Substance Abuse Treatment. A guide to substance abuse services for primary care clinicians: Treatment improvement protocol (TIP) series. U.S. Government Printing Office; Washington, DC: 1997. number 24 (DHHS Pub. No. SMA 97-3139 ed.)

Highlights

- We examined intake characteristics in PO abusers with and without lifetime heroin use.
- H⁺ participants had more severe opioid use characteristics than H⁻ participants.
- H⁺ participants reported greater non-opioid drug use than H⁻ participants.
- H⁺ participants trended toward poorer treatment outcomes than H⁻ participants.
- PO abusers with a history of heroin use may possess unique treatment needs.

Figure 1.

Treatment response among 22 PO-dependent outpatients receiving buprenorphine stabilization, 4-week buprenorphine taper and subsequent naltrexone. Data are shown for H^+ (black bars) and H^- (grey bars) participants. The upper panel presents data on illicit opioid abstinence, defined as the percent of participants testing biochemically negative for all opioids at the end of treatment. The lower panel presents data on treatment retention, defined as the percent of participants still retained in treatment at the end of the 12-week study.

Table 1

Opioid use characteristics

	All Subjects (n = 89)	H ⁺ (n = 41)	H ⁻ (n = 48)	p-value
<u>Initiation of illicit opioid use</u>				
Age at first illicit opioid use	18.7 (5.6)	18.5 (6.5)	18.9 (4.8)	0.73
Primary route of first use of illicit opioid (%)				
Oral	33	37	29	0.46
Intranasal	63	56	69	0.22
Intravenous	4	7	2	0.24
Age at which regular ^a illicit opioid use began	21.4 (5.8)	21.5 (6.7)	21.2 (4.9)	0.84
Duration of regular illicit opioid use (years)	4.9 (3.9)	6.1 (4.1)	3.9 (3.5)	0.009
Primary route of regular illicit opioid use (%)				
Oral	8	5	11	0.32
Intranasal	76	71	81	0.27
Intravenous	15	24	6	0.02
<u>Lifetime illicit opioid use</u>				
Ever used heroin (%)	58	100	23	<0.001
Age of first heroin use	21.6 (5.4)	21.5 (5.9)	21.8 (3.5)	0.86
Duration of heroin use among those reporting any use (years)	1.3 (2.3)	1.6 (2.5)	0.01 (0.03)	0.05
Bags per day at peak use	10.2 (15.2)	11.9 (16.1)	1.4 (1.4)	0.07
Primary route of heroin administration (%)				
Oral	0	0	0	
Intranasal	54	46	82	0.04
Intravenous	46	54	18	0.04
Ever used an illicit opioid by IV route (%)	43	76	15	<0.001
Ever received treatment for opioids (%)	35	49	23	0.01
<u>Current illicit opioid use</u>				
Primary PO at study intake				
Oxycodone (%)	54	46	60	0.18
Dose, mg	108.1 (73.6)	148.4 (90.5)	81.7 (44.6)	0.006
Buprenorphine (%)	40	49	33	0.14
Dose, mg	8.9 (5.5)	9.1 (6.1)	8.7 (4.9)	0.83
Hydrocodone (%)	3	2	4	0.65
Dose, mg	55.8 (17.7)	40	63.8 (15.9)	0.44
Hydromorphone (%)	1	0	2	0.28
Dose, mg	4		4	
Morphine (%)	1	2	0	0.35
Dose, mg	200	200		
% reporting occasional heroin use at intake	4	10	0	0.03
Primary route of PO administration at study intake (%)				

	All Subjects (n = 89)	H ⁺ (n = 41)	H ⁻ (n = 48)	p-value
Oral	15	12	17	0.55
Intranasal	69	61	75	0.16
Intravenous	17	27	8	0.02

Note: Values represent mean (SD) unless otherwise indicated.

^a 3x per week