Primary Care Office-based Buprenorphine Treatment: Comparison of Heroin and Prescription Opioid Dependent Patients

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BACKGROUND: Prescription opioid dependence is increasing, but treatment outcomes with office-based buprenorphine/naloxone among these patients have not been described.

METHODS: We compared demographic, clinical characteristics and treatment outcomes among 200 patients evaluated for entry into a trial of primary care office-based buprenorphine/naloxone treatment stratifying on those who reported exclusive heroin use (n=124), heroin and prescription opioid use (n=47), or only prescription opioid use (n=29).

RESULTS: Compared to heroin-only patients, prescription-opioid-only patients were younger, had fewer years of opioid use, and less drug treatment history. They were also more likely to be white, earned more income, and were less likely to have Hepatitis C antibodies. Prescription-opioid-only patients were more likely to complete treatment (59% vs. 30%), remained in treatment longer (21.0 vs. 14.2 weeks), and had a higher percent of opioid-negative urine samples than heroin only patients (56.3% vs. 39.8%), all p values < .05. Patients who used both heroin and prescription opioids had outcomes that were intermediate between heroin-only and prescription-opioid-only patients.

CONCLUSIONS: Individuals dependent on prescription opioids have an improved treatment response to buprenorphine/naloxone maintenance in an office-based setting compared to those who exclusively or episodically use heroin.

KEY WORDS: buprenorphine/therapeutic use; primary health care; opioid-related disorders.
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INTRODUCTION

The abuse of prescription opioids has increased substantially in the past 15 years. Few studies have examined characteristics of prescription opioid users.[1–4] A recent study examining characteristics of heroin-only, oxycodone-only, and heroin-and-oxycodone users, found that oxycodone-only users were more likely to be younger, female, white, and have lower income than heroin-only users.[1] Although these findings suggest that prescription opioid users differ from heroin users, to our knowledge no study has compared their treatment response to primary care office-based treatment with buprenorphine. Buprenorphine, a partial mu opioid agonist, that is combined with the opioid antagonist naloxone, can be prescribed by office-based physicians who have undergone the necessary training and certification.[5–8] The purpose of this post hoc analysis was to compare demographic, psychosocial, and substance-use characteristics and treatment responses to buprenorphine/naloxone among prescription-opioid-only, heroin-only, and prescription-opioid and heroin users.

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METHODS

Participants

Two hundred adults (≥18 years) seeking primary-care-based buprenorphine treatment were referred from physicians, methadone treatment, and word of mouth. All participants met DSM-IV TR[9] criteria for opioid dependence. Patients were excluded if they were dependent on alcohol (n=4), cocaine (n=2), sedatives (n=0), or benzodiazepines (n=2), or had a medical or psychiatric disorder that precluded participation (n=19). Twenty-five eligible individuals did not complete the intake. Thirty-four did not complete the 2-week induction. One hundred and sixty-six participants were randomized in a clinical trial evaluating counseling intensity and medication dispensing frequency. This research was approved by Yale University; all patients provided informed consent.

Measures

Sociodemographic, medical, psychosocial, drug use, and treatment information was collected before treatment. Assessment instruments included the Center for Epidemiological Studies Depression Scale (CESD),[10] the Treatment Motivation Scale (TMS),[11] and the Addiction Severity Index (ASI).[12] The ASI was only collected for the 166 individuals who entered the trial.

To evaluate treatment outcomes, 2 measures of the percent of weekly opioid-negative (based on standard opiate tests) and cocaine-negative urine toxicologies were computed, with missing samples counted as positive, or evaluating only provided

Table 1. Baseline Sociodemographic, Medical, and Psychosocial Characteristics of Opioid Use Groups

Characteristic	Prescription-opioid-only users	Heroin-only users	Heroin-and-prescription opioid users	*P* value*
Sociodemographics				
Age ≤35 years, % (*n*)	69 (20)	40 (49)	45 (21)	.02†
Male, % (*n*)	83 (24)	71 (88)	87 (41)	.06
White, % (*n*)	97 (28)	68 (84)	87 (41)	.001†, ‡
Full-time employment, % (*n*)	39 (11)	37 (44)	35 (16)	.93
High School or greater, % (*n*)	86 (24)	75 (90)	87 (40)	.16
Monthly income, ≥ $1,000, % (*n*)	69 (20)	42 (39)	53 (24)	.04†
Never married, % (*n*)	48 (14)	56 (69)	63 (30)	.39
Medical characteristics				
ASI medical, % > 0 (*n*)	28 (8)	12 (11)	16 (7)	.13
HCV status, negative, % (*n*)	86 (24)	58 (66)	72 (33)	.01†
Pyschosocial characteristics				
ASI employment, mean (SD)	0.30 (.30)	0.41 (.30)	0.37 (.30)	.23
ASI legal, > 0, % (*n*)	34 (10)	33 (30)	27 (12)	.72
ASI family/social, mean (SD)	0.27 (.21)	0.26 (.19)	0.31 (.22)	.31
ASI psychiatric, > 0, % (*n*)	34 (10)	27 (25)	41 (18)	.26
CESD, mean (SD)	16.3 (12.1)	16.4 (12.1)	18.7 (11.6)	.54
Drug use and treatment history				
Years of opioid use, mean (SD)	4.0 (5.6)	9.4 (7.6)	7.9 (8.9)	.005†
Days of opioid use in prior 30, mean (SD)	28.4 (4.3)	28.4 (4.7)	28.0 (4.9)	.87
ASI Drug, 1> 0.30, % (*n*)	90 (26)	65 (60)	69 (31)	.04†
Treatment motivation scale, mean (SD)	4.8 (0.5)	4.9 (0.4)	5.1 (0.4)	.08
Drug treatment history, > 1 prior treatment, % (*n*)	28 (8)	65 (59)	69 (31)	.001†, §
Use of other drugs in prior 30 days, % (*n*)				
Alcohol	52 (15)	47 (43)	51 (23)	.84
Cocaine	28 (8)	38 (35)	40 (18)	.52
Marijuana	45 (13)	25 (23)	38 (17)	.08
Other	21 (6)	13 (12)	27 (12)	.14
ASI Alcohol, % > 0 (*n*)	52 (15)	47 (43)	51 (23)	.84

*Based on chi-square tests for categorical variables and one-way ANOVA for continuous measures
†Heroin-only users ≠ prescription opioid–only users.
‡Heroin-only users ≠ heroin-and-prescription-opioid users.
§Prescription-opioid-only users ≠ heroin-and-prescription-opioid users.

samples. The maximum consecutive weeks of abstinence from illicit opioids and cocaine were computed for each patient.

Treatment

We used the buprenorphine/naloxone sublingual tablet formulation provided at 16 mg daily after a 2-week induction. Two dose upgrades to 20 and 24 mg were possible. Medication was provided for daily self-administration.

Participants were randomized to 1 of 3 psychosocial treatments after the 2-week induction, Standard Medical Management (SMM) and medication pickup once weekly, SMM and medication pickup thrice weekly, or Enhanced Medical Management (EMM) and medication pick-up thrice weekly. SMM involved 20-minute manual-guided addiction counseling sessions provided weekly by a trained nurse: EMM sessions lasted 45 minutes. Study design and results have been published separately.[13]

Data Analysis

Univariate comparisons of prescription-opioid-only, heroin-only, and combined-use patients were conducted using chi-square tests and analyses of variance (ANOVAs). Variables with skewed distributions were dichotomized (see Table 1). Retention was examined using Kaplan–Meier survival analysis. When the overall test was significant, post hoc follow-up comparisons were conducted using Bonferroni adjustment. In the treatment outcome analyses treatment group assignment was statistically controlled.

We conducted multinomial logistic regression to examine group differences controlling for predictor variables.[14] We examined 2 variable domains: Sociodemographic, medical and psychosocial characteristics, and baseline substance-use variables, with variable entry based on univariate $p<.20$.[14] Likelihood ratio tests examined individual variables, with Bonferroni adjusted follow-ups. To examine differences in treatment response while controlling for baseline differences, we conducted analysis of covariance (ANCOVA) with each

outcome using significant individual variables from the multinomial regressions.

RESULTS

Categorization of Opioid Use Group

In the week before treatment, 29 patients reported prescription-opioid-only use, 124 reported heroin-use only, and 47 reported both heroin and prescription opioid use. Data regarding opioid used for the prior month was available for the subset of individuals who completed the 2-week induction (n=166). The concordance between categorizations based on past-week and past-month use was high, with 125 of 166 (75%) categorized the same on both, and only 3 of 29 (10%) classified as prescription-opioid-use only in the past week reporting heroin use in the preceding 30 days.

Among patients reporting only prescription opioid use, sustained release oxycodone (Oxycontin, 57%) was the most common prescription opioid reported, with oxycodone/acetaminophen (Percocet, 18%) and hydrocodone/acetaminophen (Vicodin, 8%) reported less frequently. Over the 4 years of the study the percent of prescription-opioid-only users increased from 6% to 29% (p=.02).

Univariate Analyses

Patients who used only prescription opioids were younger and had fewer years of opioid use and less drug treatment history, yet reported higher ASI drug severity than heroin-only patients (Table 1). They also earned more income, were more likely to be white, and were less likely to have Hepatitis C (HCV) antibodies. Additionally, combined users were more likely to be white than heroin-only patients. Prescription-opioid-only users also had less drug treatment history than combined users.

Multinomial Logistic Regression Analyses

For the multinomial logistic regression examining sociodemographic and clinical characteristics, the variable set of age, gender, race, income, HCV status, and ASI medical score significantly differentiated among the groups (N=166, p<.001). The set of ASI drug composite score, treatment motivation, drug treatment history, recent marijuana use, and recent other drug use significantly differentiated among groups (N=166, p<.001). Race, income, years of opioid use, and drug treatment history were the only significant individual variables (same direction as univariate results).

Treatment Outcomes

Prescription-opioid-only patients were significantly more likely to complete treatment than heroin-only patients (Table 2). In addition, both prescription-only and combined-use patients remained in treatment longer than heroin only patients. Twenty-four percent of heroin-only patients dropped out during induction compared to 2% of combined-use patients and none of the prescription-opioid-only patients (p<.001). Controlling for assigned treatment, prescription-opioid-only patients had a higher percentage of opioid-negative urines than heroin-only and combined-use patients, and achieved longer durations of continuous opioid abstinence than combined-use patients. In the third year of the trial, we began routinely testing all samples for oxycodone and methadone. The findings did not change if these results were included.

Based on multinomial regression, race, income, drug treatment history, and years of opioid use were included in ANCOVAs. Prescription-opioid-only patients still showed higher percent of opioid-negative urines (p=.03), higher percent of opioid negative urines of tests provided (p=.008), and more continuous weeks of opioid abstinence (p=.04) than heroin-only patients. Percent of cocaine-negative urine samples with missing counted as positive (p=.20), percent of cocaine-negative urines of tests provided (p=.22), and weeks of cocaine abstinence (p=.20) did not differ.

Table 2. Treatment Outcome of Opioid Use Groups

Characteristic	Prescription-opioid-only users	Heroin-only users	Heroin-and-prescription-opioid users	*P* value*
Treatment outcome				
Treatment completion, % (*n*)	59 (17)	30 (37)	38 (18)	.01†
Retention, mean no. of weeks (SD)	21.0 (6.7)	14.2 (9.5)	18.9 (6.7)	.002†, ‡
Percent opioid-negative urines with missing counted as positive, mean (SD)	56.3 (33.0)	39.8 (36.2)	35.3 (30.2)	.03†, §
Percent opioid-negative urines of samples collected, mean (SD)	75.3 (33.1)	52.9 (39.0)	48.8 (33.9)	.007†, §
Weeks of cont. opioid abstinence, mean (SD)	8.2 (6.2)	5.9 (6.6)	4.5 (4.8)	.04§
Percent cocaine-negative urines with missing counted as positive, mean (SD)	55.5 (32.5)	46.5 (36.8)	45.5 (31.2)	.42
Percent cocaine-negative urines of samples collected, mean (SD)	79.7 (32.4)	72.9 (33.6)	69.4 (31.7)	.43
Weeks of cont. cocaine abstinence, mean (SD)	7.4 (7.6)	8.7 (6.8)	6.8 (6.0)	.55

*Based on logistic regression for categorical variables and one-way ANCOVA for continuous measures controlling for assigned treatment group
†Heroin-only users ≠ prescription-opioid-only users.
‡Heroin-only users ≠ heroin-and-prescription-opioid users.
§Prescription-opioid-only users ≠ heroin-and-prescription-opioid users.

DISCUSSION

The findings from this study indicate that patients using only prescription opioids showed better treatment response than patients using heroin, even controlling for potential confounders. Fifty-four percent of urine samples of patients with only prescription opioid use were negative for opioids during the trial. Prescription-opioid-only patients were more likely to complete the 2-week induction, whereas nearly a quarter of heroin-only patients did not. The study results do not indicate, however, that heroin-dependent patients experience poor treatment outcomes with office-based buprenorphine/naloxone treatment as treatment outcomes were comparable to prior studies of heroin-dependent patients in agonist treatment.[5,6,15,16]

Compared to heroin-only users, prescription-opioid-only users were less likely to have HCV antibodies, had fewer years of opioid use, and were less likely to have a history of drug treatment, suggesting that patients using prescription opioids alone are seeking treatment earlier in their disorder. Office-based buprenorphine/naloxone treatment may be particularly attractive for these patients because it provides greater privacy, is similar to treatment for other medical problems, and reduces patients' time commitment compared to methadone maintenance. The study findings suggest that office-based treatment engages patients with prescription opioid dependence in treatment earlier, which is consistent with mainstreaming opiate agonist treatment[17] and with prior research.[18,19]

Limitations of our study should be noted. First, the randomized clinical trial was not designed to examine characteristics and treatment response differences between opioid users; therefore, our findings are exploratory. Second, opioid use categorization was based on only 1 week of self-reported use. This was intended to provide information on individual's opioid use before treatment rather than a comprehensive measure of lifetime use. Defining subtypes of opiate users may require several types of converging information and deserves further research. Third, the prescription-opioid-only group was relatively small (n=29), which limits power to detect group differences. The fact that differences were found suggests such effects are large and in some cases clinically significant. Fourth, the sample represents only treatment-seeking opioid-dependent individuals at 1 clinical site and may not generalize to other patients seeking treatment in primary care.

The current findings suggest that type of opioid use is an important factor in office-based buprenorphine/naloxone treatment. Research is needed to evaluate whether prescription-opioid-only users show better treatment response in settings such as methadone maintenance. Despite the improved outcome of prescription-opioid-only patients compared to combined and heroin-only patients, there is still room to optimize treatment response.

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Potencial Financial Conflict of Interest: *Dr. Pantalon reported being a consultant for Bristol-Myers Squibb, and Dr. Schottenfeld reported owning stock in astra Zeneca, GlaxoSmithKline, Pfizer, Sanofi-Synthelab, Wyeth, and Stryker Corporation. The other authors reported no conflicts of interest.*

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REFERENCES

1. Office of Applied Studies. Results from the 2003 National Survey on Drug Use and Health: National findings (DHHS Publication No. SMA 04-3964, NHSDA Series H-25). Rockville, MD: Substance Abuse and Mental Health Services Administration; 2004.
2. **Potter JS, Hennessy G, Borrow JA, Greenfield SF, Weiss RD.** Substance use histories in patients seeking treatment for controlled-release oxycodone dependence. Drug Alcohol Depend. 2004;76:213–15.
3. **Simoni-Wastila L, Strickler G.** Risk factors associated with problem use of prescription drugs. Am J Public Health. 2004;94:266–8.
4. **Simoni-Wastila L, Ritter G, Strickler G.** Gender and other factors associated with the nonmedical use of abusable prescription drugs. Subst Use Misuse. 2004;39:1–23.
5. **Fiellin DA, Pantalon MV, Pakes J, O'Connor PG, Chawarski M, Schottenfeld RS.** Treatment of heroin dependence with buprenorphine in primary care. Am J Drug Alcohol Abuse. 2002;28:231–41.
6. **Stein MD, Cioe P, Friedmann PD.** Buprenorphine retention in primary care. J Gen Intern Med. 2005;20:1038–41.
7. **Turner BJ, Laine C, Lin YT, Lynch K.** Barriers and facilitators to primary care or human immunodeficiency virus clinics providing methadone or buprenorphine for the management of opioid dependence. Arch Intern Med. 2005;165:1769–76.
8. **Krantz MJ, Mehler PS.** Treating opioid dependence. Growing implications for primary care. Arch Intern Med. 2004;164:277–88.
9. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994.
10. **Radloff LS.** The CES-D Scale: a self-report depression scale for research in the general population. Appl Psychol Meas. 1977;1:385–401.
11. **Knight K, Halcom M, Simpson DD.** TCU psychosocial functioning and motivation scales: Manual on psychometric properties. Institute for Behavioral Research: Texas Christian University; 1994.
12. **McLellan AT, Kushner H, Metzger D, et al.** The fifth edition of the Addiction Severity Index. J Subst Abuse Treat. 1992;9:199–213.
13. **Fiellin D, Pantalon MV, Chawarski M, et al.** Buprenorphine maintenance in primary care: a randomized controlled trial of counseling conditions and medication dispensing. N Engl J Med. 2006;355:365–74.
14. **Hosmer DW, Lemeshow S.** Applied Logistic Regression. New York: John Wiley & Sons; 2000.
15. **Fiellin DA, O'Connor PG, Chawarski M, Pantalon MV, Schottenfeld RS.** Office versus narcotic treatment program-based buprenorphine for opioid dependence. Drug Alcohol Depend. 2002;66:S55–6.
16. **Fudala PJ, Bridge TP, Herbert S, et al.** Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. N Engl J Med. 2003;349:949–58.
17. **Fiellin DA, O'Connor PG.** New Federal initiatives to enhance the medical treatment of opioid dependence. Ann Intern Med. 2002;137:688–92.
18. **Sullivan LE, Chawarski M, O'Conner PG, Schottenfeld RS, Fiellin DA.** The practice of office-based buprenorphine treatment of opioid dependence: is it associated with new patients entering treatment? Drug Alcohol Depend. 2005;79:113–6.
19. **McLeod CC, Kissin WB, Stanton A, Sonnefeld J.** 30-day outcomes for buprenorphine patients treated by a national sample of qualified physicians. College on Problems of Drug Dependence. Orlando, FL; 2005.