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Clinical Correlates of Smoking Status in Men and Women with Opioid Use Disorder

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Abstract

Background: Smoking is highly prevalent in people with opioid use disorder (OUD) and is a significant contributor to morbidity and mortality in this population. However, little is known about the differences between those with OUD who do and do not smoke cigarettes.

Objectives: Our aim was to investigate differences between treatment-seeking adults with OUD who did and did not smoke.

Methods: Participants (N=568; 30% female) completed a battery of self-report questionnaires including measures of current smoking status and number of cigarettes smoked per day as well as measures of clinical characteristics (e.g., craving, anxiety).

Results: Of the total sample, 77% were current smokers. Multivariable logistic regression identified heroin use (OR = 2.20, 95% CI = 1.38, 3.53) and younger age (OR = 0.97, 95% CI = 0.95, 0.997) as strong correlates of smoking status; other characteristics were not significant. Older age and opioid craving were associated with more cigarettes smoked per day. Notably, these patterns differed for males and females; opioid craving (B = 0.62, SE_B = 0.24) was associated with the number of cigarettes smoked among men, and anxiety (B = 0.39, SE_B = 0.19) was associated with the number of cigarettes smoked among women.

Conclusion: Adults with OUD who used heroin in the past month were more likely to be current smokers. No sex differences were observed in likelihood of smoking; however, the predictors of smoking status and severity differed between men and women.

Keywords

opioid use disorder; smoking; sex differences; anxiety

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Declaration of Interests

Dr. Weiss has been a consultant to Indivior, Alkermes, Braeburn Pharmaceuticals, GW Pharmaceuticals, US World Meds, Janssen Pharmaceuticals and Daiichi Sankyo. Drs. McHugh, Janes, Griffin, and Greenfield and Ms. Taghian report no potential conflicts of interest relevant to this manuscript.

Introduction

Opioid and nicotine use independently confer significant health risks and contribute to early mortality (Centers for Disease Control and Prevention, 2017). Moreover, opioids and nicotine are often used concurrently (John et al., 2018; Young-Wolff, Klebaner, Weisner, Von Korff, & Campbell, 2017; Zale et al., 2015), exposing people to the negative effects of both substances. Tobacco smoking among people with opioid use disorder (OUD) is 4–5 times more common than among the general population (Parker, Streck, & Sigmon, 2018) and among people in primary care settings (John et al., 2018). Furthermore, the severity of both nicotine dependence (Parker et al., 2018) and opioid use (Young-Wolff et al., 2017) is greater in those who misuse both substances and smoking cessation treatments are less effective among people with OUD, relative to those without (Miller & Sigmon, 2015).

Despite increasing evidence for heightened vulnerability to smoking among people with OUD, relatively little is known about differences between people with OUD who do and do not smoke. This may be attributable, at least in part, to the very high prevalence of smoking in people with OUD. Many studies of smoking in this population have focused on people receiving OUD treatment (predominantly opioid agonist therapy), and in these studies the rates of current smoking are typically in the range of 75%–95% (e.g., Chisolm et al., 2013; Patkar et al., 2002; Richter, Gibson, Ahluwalia, & Schmelzle, 2001). Of the studies that have compared people with respect to smoking status, findings generally suggest worse overall clinical severity in smokers, such as deficits in decision making (Rotheram-Fuller, Shoptaw, Berman, & London, 2004), worse health (Patkar et al., 2002), and more depressive symptoms (Meyer, Lin, & Brown, 2006). Improved understanding of the differences between smokers and non-smokers will help to identify vulnerability and resilience factors in this population and to understand the clinical needs of smokers with OUD. Critically, because of the lower cessation success in this population, understanding clinical correlates of smoking can provide insight into potential novel or adjunctive treatment targets to improve outcomes.

Additionally, there are a number of sex differences that have been observed related to both OUD (McHugh et al., 2013) and tobacco use (Benowitz & Hatsukami, 1998; Dumais et al., 2017). Notably, women with OUD are more likely to use opioids to cope with stress (McHugh et al., 2013) and anxiety is a predictor of the use of anxiolytic drugs in women, but not men (McHugh, Votaw, Bogunovic, et al., 2017), suggesting a key role of anxiety in OUD among women. However, little is known about sex differences in smoking in OUD. A large study of people receiving methadone maintenance therapy (N=550) found that women were more likely to smoke than men (84% vs. 75%), but there was no sex difference in the number of cigarettes smoked (Richter et al., 2001).

The purpose of this secondary analysis was to characterize differences between smoking and nonsmoking adults with OUD. The first aim was to characterize demographic and clinical differences between smokers and non-smokers. The second aim was to characterize correlates of smoking severity (measured as average number of cigarettes smoked per day) and to investigate whether these results differed between men and women. This was an exploratory (hypothesis-generating) analysis.

Methods

Participants

Adults aged 18 and older were recruited from an inpatient substance use disorder treatment unit at a psychiatric hospital for a one-time survey study. Participants in this study include the subset of the parent sample with a current diagnosis of OUD (N=568). Participants were excluded if they had a current medical or psychiatric condition that would interfere with the ability to provide informed consent or to complete a brief (approximately 30- minute) battery of questionnaires.

The sample consisted of 568 participants (30% female) with a mean age of 31.5 years (SD = 11.1). The sample predominantly self-reported race and ethnicity as White (91.4%) and non-Hispanic (93.8%), and approximately 41.8% of the sample was employed.

Procedures and Measures

Participants completed the survey on a tablet computer. All procedures were approved by the local institutional review board. Opioid use disorder diagnosis was based on clinical assessment at intake. Clinical diagnoses were extracted from the medical chart. Participants self-reported clinical and demographic information.

The Brief Addiction Monitor (Cacciola et al., 2013) was used to assess substance use in the past 30 days. Participants were asked to report days of substance use by substance type and this was used as our marker of opioid use frequency. Participants were asked separately about heroin use and opioid analgesic use. Participants also reported current smoking status and number of cigarettes smoked, on average, in the prior 30 days. Participants completed the Overall Anxiety Symptom and Impairment Scale (Norman, Cissell, Means-Christensen, & Stein, 2006), a 5-item measure of anxiety symptom severity; screening for the presence of chronic pain (defined as a minimum of 3 months of consecutive significant pain, not related to substance withdrawal); and the Opioid Craving Scale (Weiss et al., 2003), a 3-item validated measure of opioid craving.

Data Analysis

We first evaluated variables of interest for skewness and univariate outliers. We then compared smokers and non-smokers with respect to variables of interest using t-tests and χ^2 tests. In a multivariable analysis, we included all variables of interest in a logistic regression with smoking status as the dependent variable to determine the most robust correlates of smoking status. To minimize collinearity, only clinical variables significantly associated with smoking in bivariate analyses were included. A linear regression was used to examine correlates of number of cigarettes smoked per day. Finally, the regression models were repeated separately for men and women to determine whether these effects differed by sex. Covariates in regression models included age, marital status (binary: never married vs. other), anxiety symptom severity, opioid craving and presence of heroin use in the past 30 days. Although sex was not significantly associated with smoking status in bivariate models, this was retained as a covariate to investigate sex differences in adjusted models.

Results

Of the 568 participants included in our analyses, 76.8% identified as current smokers. Of those who smoked, the average number of cigarettes smoked per day in the previous month was 15.2 ($SD = 8.4$; range = 0 to 50). All participants were diagnosed with OUD; 70.1% reported use of heroin in the past 30 days and 62.7% reported use of opioid analgesics (43.8% of the sample reported use of both opioid types, 4.6% reported that they had not used an opioid in the past 30 days).

Table 1 presents the results of the bivariate analyses. Smokers were younger and less likely to be married. There was no significant sex difference in likelihood of smoking (81.2% of women and 74.9% of men were smokers). These analyses indicated that smokers reported significantly higher anxiety symptoms and higher opioid craving. There was no difference in the likelihood of current chronic pain. Smokers were significantly more likely to have used heroin in the past 30 days.

Multivariate analyses with smoking status as the dependent variable (Table 2) indicated that heroin use was a strong correlate of smoking status ($OR = 2.20$, 95% $CI = 1.38, 3.53$, $p < .01$). The only other significant correlate was age, with younger participants more likely to smoke ($OR = 0.97$ 95% $CI = 0.95, 0.997$, $p < .05$).

Among smokers, results of a linear regression with number of cigarettes smoked on average per day found that age ($B = 0.15$, $SE_B = 0.06$, $p < .01$), and greater opioid craving ($B = 0.58$, $SE_B = 0.20$, $p < .05$) were significantly associated with more cigarettes smoked per day. No other variables were significant.

To examine sex differences, regression models for smoking were examined in men and women, separately. The results of the logistic regression indicated that none of the predictors were significantly associated with smoking status among women, but that age ($OR = 0.97$, 95% $CI = 0.95, 0.996$, $p < .05$) and heroin use ($OR = 2.27$, 95% $CI = 1.33, 3.87$, $p < .01$) were associated with smoking among men. The linear regression models predicting average number of cigarettes smoked per day also indicated a sex difference. Specifically, greater anxiety severity ($B = 0.39$, $SE_B = 0.19$, $p = .05$) and heroin use ($B = 4.77$, $SE_B = 2.10$, $p < .05$) were associated with more cigarettes per day among women, whereas never being married ($B = 2.74$, $SE_B = 1.34$, $p < .05$) and greater opioid craving ($B = 0.62$, $SE_B = 0.24$, $p < .05$) were associated with more cigarettes per day among men. No other variables were significant in either linear model.

Discussion

The results of this secondary data analysis suggest that people with OUD who smoke have a worse overall clinical presentation, characterized by higher opioid craving, severity of anxiety symptoms, and presence of heroin use (compared to opioid analgesic use alone). In multivariable models, the use of heroin was strongly linked with smoking status beyond the contribution of sociodemographic and other clinical variables. Participants who had used heroin in the past 30 days had 2.2 times higher odds of being a current smoker. This is consistent with evidence that heroin use (relative to opioid analgesic use alone) is a poor

prognostic variable in people with OUD (Dreifuss et al., 2013). Although younger age was associated with a higher likelihood of smoking, older smokers smoked more cigarettes per day. Opioid craving was associated with the severity of smoking, as reflected by more cigarettes smoked on average per day.

Several sex differences also emerged in our analyses. Contrary to general population data, men were not more likely to be smokers (Jamal et al., 2018), and did not smoke more cigarettes per day relative to women. However, it is of note that although the prevalence of smoking was not significantly different between men and women, the magnitude of difference in prevalence was comparable to a prior study. In our study 81% of women and 75% of men were current smokers, similar to Richter and colleagues (2001), who found that 84% of women and 75% of men with OUD were current smokers. Furthermore, correlates of smoking status and severity differed between men and women. Younger age and past 30 day use of heroin were associated with greater likelihood of smoking in men, but not in women. Among women, more severe anxiety symptoms and heroin use were associated with more cigarettes smoked per day. In contrast, among men, never being married and more opioid craving were associated with more cigarettes smoked per day. This finding is consistent with prior studies suggesting that women are more likely to use opioids to cope with negative affect relative to men with OUD (McHugh et al., 2013) and nicotine dependence (Benowitz & Hatsukami, 1998). Although there were no sex differences in the likelihood of smoking between men and women, the current findings contribute to the literature demonstrating that motivating factors for smoking may differ based on sex.

These findings are consistent with several prior studies demonstrating the relationship between tobacco and opioid use. For instance, individuals may co-use nicotine and opioids as nicotine's stimulant properties appear to mitigate some perceived unwanted effects of opioids, such as difficulty concentrating or fatigue (Young-Wolff et al., 2017). Nicotine and opioids also have a shared influence on pain, as acute nicotine attenuates pain sensitivity (Perkins et al., 1994). However, chronic nicotine use appears to have the opposite effect with smokers showing greater pain intensity than non-smokers (Palmer, Syddall, Cooper, & Coggon, 2003), which may explain the higher doses of opioids used by smokers (Plesner, Jensen, & Hojsted, 2016). Such effects on pain appear to be sex-dependent as acute nicotine administration reduces pain sensitivity in male, but not female smokers (Jamner, Girdler, Shapiro, & Jarvik, 1998); this further supports the hypothesis that men and women differ on motivators for substance use.

Although this study was cross-sectional in nature, it raises potential clinical implications. First, smokers exhibited a worse overall clinical presentation than non-smokers, suggesting that this group may be particularly difficult to treat. Second, there may be sex-specific motivators for tobacco use, such as managing anxiety in women. In a prior analysis, we demonstrated that anxiety sensitivity was associated with more barriers to smoking cessation in people with OUD (McHugh, Votaw, Fulciniti, et al., 2017). This study further highlights the importance of addressing anxiety in smokers with OUD, particularly women.

This study has several limitations. First, we relied exclusively on self-report data for smoking status and severity. Second, this study was cross-sectional and thus the longitudinal

associations among these variables remain unknown. Our sample was predominantly white and non-Hispanic, and thus replication in more racially and ethnically diverse samples is needed. Finally, we did not collect data on history of smoking, and thus prior smoking status could not be considered in our analyses.

In summary, this study found that smoking is highly prevalent in treatment-seeking adults with OUD. Smoking was associated with a more severe clinical profile, most predominantly characterized by the use of heroin. Furthermore, some evidence suggested sex-specific risks for smoking severity, with anxiety associated with smoking more cigarettes per day for women and craving associated with more cigarettes per day for men. Future studies attempting to better understand this sex difference, and potential underlying mechanisms, will be an important next step.

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Table 1.

Sample Characteristics and Bivariate Analyses

Variable	Total Sample (N=568)	Smokers (N=436)	Non-Smokers (N=132)	t/ χ^2	p
age (mean, SD)	31.54 (11.14)	30.33 (10.23)	35.54 (12.98)	4.80	<.001
sex (% male)	67.40%	68.10%	75.60%	2.65	.10
marital status (% never married)	69.10%	72.70%	57.30%	11.32	<.01
employment (% employed)	41.80%	39.70%	48.80%	3.43	.06
chronic pain (%)	30.80%	31.30%	29.40%	0.16	.69
opioid craving (mean, SD)	5.49 (2.50)	5.70 (2.43)	4.83 (2.59)	-3.48	<.01
anxiety severity (mean, SD)	11.72 (4.69)	11.98 (4.67)	10.86 (5.00)	-2.37	.02
anxiety sensitivity (mean, SD)	24.97 (16.30)	25.33 (16.48)	23.80 (15.71)	-0.93	.35
heroin use past 30 days (%)	73.60%	78.90%	55.60%	26.57	<.001

Table 2.

Logistic Regression Predicting Smoking Status

Variable	<i>B</i>	<i>SE_B</i>	<i>p</i>	<i>OR</i> (95% CI)
Age	−0.03	0.01	0.02	0.97 (0.95, 0.997)
Sex (ref=female)	−0.18	0.27	0.50	0.83 (0.49, 1.41)
Marital status (ref=ever married)	0.20	0.27	0.46	1.22 (0.72, 2.06)
Anxiety severity	0.03	0.03	0.33	1.03 (0.98, 1.08)
Opioid craving	0.05	0.05	0.26	1.05 (0.96, 1.16)
Any heroin use (past 30 days)	0.79	0.24	<.01	2.20 (1.38, 3.53)