Published in final edited form as:

J Subst Abuse Treat. 2010 December ; 39(4): 378–383. doi:10.1016/j.jsat.2010.06.012.

Physician Introduction to Opioids for Pain Among Patients with Opioid Dependence and Depressive Symptoms

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Abstract

This study determined the frequency of reporting being introduced to opioids by a physician among opioid dependent patients. Cross-sectional analyses were performed using baseline data from a cohort of opioid addicts seeking treatment with buprenorphine. The primary outcome was response to the question: “Who introduced you to opiates?” Covariates included sociodemographics, depression, pain, current and prior substance use. Of 140 participants, 29% reported that they had been introduced to opioids by a physician. Of those who were introduced to opioids by a physician, all indicated that they had initially used opioids for pain, versus only 11% of those who did not report being introduced to opioids by a physician ($p<0.01$). There was no difference in current pain (78% vs. 85%, $p=0.29$), however participants who were introduced to opioids by a physician were more likely to have chronic pain (63% vs. 43%, $p=0.04$). A substantial proportion of individuals with opioid dependence seeking treatment may have been introduced to opioids by a physician.

Introduction

Based on 2008 national data, nearly 2 million individuals in the U.S. have opioid abuse or dependence, with the majority reporting abuse of prescription opioids (Substance Abuse and Mental Health Services Administration, 2009). Individuals may be introduced to opioids through a variety of non-medical and medical situations. Patients who are introduced to opioids through a physician may subsequently develop abuse or dependence either through continued use of prescription opioids or heroin. However, the majority of persons who have misused prescription opioids report receiving them from a friend or relative (Substance Abuse and Mental Health Services Administration, 2009) and others may purchase diverted opioids from other sources (Inciardi, Surratt, Cicero, & Beard, 2009). Therefore, prescription opioid abuse and dependence may develop without provision of script from a physician. At the same time, physician prescribing rates for opioids are increasing (Caudill-Slosberg, Schwartz, & Woloshin, 2004; Gilson, Ryan, Joranson, & Dahl, 2004; Olsen,

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Daumit, & Ford, 2006; Sullivan, et al., 2008), raising concern that the medical providers may share responsibility for the rise in opioid abuse and dependence.

The risk of developing opioid abuse or dependence after being prescribed opioids for acute or chronic pain by a physician is unknown. A meta-analysis of iatrogenic addiction (defined as an “addiction of a patient to a drug initially prescribed for a medical condition”) concluded that the literature could not establish whether the risk was high (>10%) or low (<0.1%) (Wasan, Correll, Kissin, O’Shea, & Jamison, 2006). However, the practice of prescribing opioids for pain is fairly common: studies suggest that the prevalence of prescribed opioid use in adults is approximately 20% (MMWR, 2010; Williams, Sampson, Kalilani, Wurzelmann, & Janning, 2008). Even if the true risk is low, the widespread practice of prescribing opioids could still result in a substantial absolute number of cases of opioid abuse and dependence, thereby contributing to the problem. Therefore, assessing the frequency of reporting a physician introduction to opioids in a population of opioid addicts entering treatment provides insight to the relative contribution that iatrogenic addiction makes to the epidemic of opioid abuse and dependence. Furthermore, it is important to examine the phenomenon of physician introduction to opioids among a population of prescription and non-prescription opioid users since: 1) patients who were initially introduced to opioids by a physician may have shifted their use to heroin and 2) prescription opioids can be procured without use of a physician script.

This study examined the prevalence of reporting being introduced to opioids by a physician among a cohort of patients with opioid dependence who were seeking addiction treatment with buprenorphine. In addition, we performed descriptive analyses to understand how participants who reported opioid introduction through a physician differed from those who did not. We hypothesized that opioid dependent participants who had been introduced by a physician would be more likely to use prescription opioids as opposed to heroin, and would be more likely to have pain since this would be an underlying reason for an initial introduction to opioids by a physician.

Methods

Study Sample and Design

This cross-sectional study used baseline data from participants in a randomized, controlled trial to determine whether treatment for depressive symptoms increases treatment retention among opioid dependent patients initiating buprenorphine (Stein MD, et al. in press). Participants were recruited through community advertising, physician referrals and word-of-mouth. Study inclusion criteria included: age 18–65, a DSM-IV diagnosis of opioid dependence, a score on the Modified Hamilton Depression Revised Scale (MHDRS) greater than 14 (Miller, Bishop, Norman & Maddover, 1985), the absence of significant suicidal ideation, willingness and ability to complete a 3-month treatment with buprenorphine, no history of severe mental illness (bipolar disorder, schizophrenia, schizo-affective, or paranoid disorder), no currently prescribed medications for depression (participants were not specifically excluded if they were taking a tricyclic anti-depressant only for pain), and the ability to complete the study assessment in English. The study was approved by the Rhode Island Hospital and Butler Hospital Institutional Review Boards.

Between November 2006 and May 2009, 932 individuals were screened by telephone, and of those, 394 callers appeared eligible for the study and were invited for an in-person screening visit. Of the 226 who attended this visit, 147 fully met criteria and agreed to enroll in the parent study. Seven participants (4.8%) were missing data on the question which asked whether a physician had introduced them to opiates and were excluded from the analyses leaving a final study cohort of 140.

Measures

The primary outcome examined was participants' responses to the question: "Who introduced you to opiates?" Possible responses included physician, sexual partner, friend, family member, stranger and no one. Covariates included the demographic variables age, sex, race (white v. non-white), current (past 30 day) employment and insurance status. Clinical variables included severe depression, current pain, chronic pain, self-report of starting opioids for pain, having a primary care provider, and regular use of alcohol, marijuana or cocaine prior to opioid use. Severe depression was defined as a score greater than 28 on the Beck Depression Inventory II (Beck, Steer, & Brown, 1996). Current pain was defined as having any pain in the past week; chronic pain was defined as pain that had been present for at least 6 months. Current pain was rated in severity by using the Visual Analog Scale (VAS) (Melzack, 1987). Chronic severe pain was defined as pain ≥ 6 months that: 1) caused at least moderate interference (defined by a single question from the Short Form-12 Questionnaire (Ware, Kosinski, & Keller, 1996)) or 2) was of at least moderate in intensity (defined as a score above the median VAS score for the group). This definition was adapted from a study of chronic severe pain in methadone maintenance patients by the Rosenblum et. al. (Rosenblum, et al., 2003) Initiation of opioids for pain was defined as positive response to the question: "Do you believe that you started using your primary opiate of addiction to relieve physical pain?" Information on current (last 30 days) and past use of prescription opioids and heroin (including route of administration) was obtained using the Addiction Severity Index (ASI) (McLellan, et al., 1992). Regular use of alcohol, marijuana and cocaine was determined by the question "Prior to starting opiates, did you ever have daily or regular use of (drug)?"

Statistical Analysis

All analyses were performed using baseline study data. The prevalence of physician introduction to opioids was determined by calculating the proportion with that report from the total sample. Descriptive analyses were performed comparing individuals who reported a physician introduction to opioids to those who did not report a physician introduction. We examined differences in demographic, clinical, and substance use-related variables between participants using Student t-tests and Pearson chi-square tests. All statistical analyses were conducted using Stata version 10.0 (College Station, TX, USA).

Results

Of the 140 opioid dependent participants seeking treatment in the sample, 40 (29%) reported that they had been introduced to opioids by a physician. The mean age in the sample was 38 years (± 10 SD), 24% were female, and the average duration of opioid use was 9 years. There were no significant differences in gender, age, race, marital status, employment, or insurance status among individuals who did and did not report being introduced to opioids by a physician (Table 1). Individuals who were introduced to opioids through a physician were less likely to have injected drugs. Regular use of alcohol prior to starting opioids was equally reported among those who were and were not introduced by a physician to opioids. However, individuals who were introduced by a physician were significantly less likely to report prior use of marijuana and cocaine.

All of the participants who reported being introduced to opioids by a physician indicated that they had started using opioids to treat pain compared to only 11% of those not introduced to opioids by a physician (Table 2). The prevalence of any current or chronic pain was high in the sample overall (83% and 49%, respectively). There were no significant differences in the proportions reporting current pain (any pain in the past week) between individuals who had and had not been initially introduced to opioids by a physician (Table

2). Among individuals who reported pain, the mean VAS score between the two groups did not significantly differ (57 (SD±4) for physician introduced v. 60 (±3) for not physician introduced; p -value=0.57). Individuals who had been introduced to opioids by a physician were more likely to have chronic pain and chronic severe pain. The percentage of individuals with severe depression did not differ between the two groups. Participants who were introduced to opioids by a physician were more likely to admit to using a physician to procure a prescription for opioids to get high with, and to seek out a physician who “gives opiate prescriptions without asking too many questions.”

Participants introduced to opioids by a physician were more likely to be currently using prescription opioids only (Figure 1) compared with participants who were not introduced by physician (Chi-square p -value<0.01). However, 32% of opioid dependent individuals who were physician introduced reported currently using heroin in combination with prescription opioids, and 10% were using heroin exclusively. Likewise, participants who were introduced to opioids by a physician were half as likely to currently inject drugs (28 v. 57%, p -value<0.01).

Discussion

Opioids are prescribed in medical settings for acute and chronic pain, and physicians may provide an introduction to opioids in individuals who subsequently develop opioid abuse and dependence. This study found that among a cohort of opioid dependent patients who were seeking addiction treatment with buprenorphine, 29% reported that they had been introduced to opioids through a physician treating their pain. To our knowledge, this is the first study to assess this question in a population of opioid dependent patients who were users of both prescription and non-prescription opioids. This study, while it does not define the risk of developing opioid abuse or dependence among patients who are prescribed opioids in a medical setting, provides insights on the fraction of patients whose opioid dependence can be linked to a medical introduction to opioids.

This study expands the current understanding of physicians' roles in the growing trend of opioid abuse and dependence. Prescription opioid misuse is reportedly increasing (Gilson, et al., 2004; Zacny, et al., 2003), as are overdose deaths related to prescription opioids (Hall, et al., 2008; Warner, Chen, & Makuc, 2009). Concurrently, physician prescribing rates for opioids are increasing (Caudill-Slosberg, et al., 2004; Gilson, et al., 2004; Olsen, et al., 2006; Sullivan, et al., 2008), raising concern that the medical providers may share responsibility for the current trend. Physicians are encouraged to screen for and treat pain, and opioids are effective in treating pain (Ballantyne & Mao, 2003) though the risk for subsequent addiction is not known (Wasan, et al., 2006). Even if the risk is low, the widespread practice of prescribing opioids among physicians could still result in a substantial absolute number of cases of opioid dependence, and thereby contribute to the problem of opioid dependence. This study suggests that physician introduction to opioids is a factor for a sizeable proportion of individuals who have opioid dependence requiring addiction treatment.

The finding that participants who reported being introduced to opioids through a physician were more likely to have chronic pain is consistent with prior research. Studies of opioid dependent patients on methadone maintenance show that more than a third report chronic pain (Rosenblum, et al., 2003; Rosenblum, et al., 2007). At least two prior studies have found a higher prevalence of chronic pain among opioid dependent patients who were primarily prescription drug users compared to non-prescription drug users (Brands, Blake, Sproule, Gourlay, & Busto, 2004; Rosenblum, et al., 2007). However, it is interesting to note that the proportion of individuals with current pain was similar among those who did

and did not report a physician introduction to opioids. It is possible that some participants who did not initiate opioids for pain may have developed pain for reasons related to their opioid use. Such causes for pain in this cohort might include injuries from trauma, depression (Bair, Robinson, Katon, & Kroenke, 2003), chronic medical conditions that are associated with pain such as hepatitis C virus (Barkhuizen, et al., 1999; Silberbogen, Janke, & Hebenstreit, 2007; Thompson & Barkhuizen, 2003), or opioid induced hyperalgesia (Chu, Angst, & Clark, 2008).

Our study cohort included both current users and non-users of prescription opioids, and results demonstrated that the majority of individuals who were introduced to opioids by a physician for pain continued to use prescription opioids over heroin. Still, 42% of participants who reported that a physician introduced them to opioids were currently using some heroin (either exclusively or in combination with prescription opioids) and over a quarter were injecting opioids, which confirms prior research that suggest shifting trajectories of opioid abuse among individuals who are initially prescribed opioids. A study of opioid dependent patients in a methadone treatment program in Canada found that 24% of participants reported using prescription opioids (medically or non-medically) initially and heroin later (Brands, et al., 2004), and a study of 72 methadone maintenance treatment programs in the U.S. found that 69% of primary heroin users had ever used prescription opioids (Rosenblum, et al., 2007). Our finding that opioid dependent individuals who are initially introduced to opioids for pain are more likely to admit to prescription drug aberrant behaviors (telling a doctor they had pain to obtain opioids so that they could get high, or seeking out a physician known to prescribe opioids “without asking too many questions”) suggests that the patients who display drug aberrant behaviors are more likely to have developed their opioid addiction in the context of pain management through a physician, as opposed to initiating use through illicit opioids. This may be relevant to dispelling the bias against use of effective pain medicines for injection drug users (Breitbart, et al., 1996).

There are several limitations to this study. The relatively small sample size limited power to detect statistically significant differences. The study questionnaire asked whether the participant was introduced to opioids by a physician, but did not obtain detailed information on the setting (e.g. office or emergency department), the respondent’s ongoing relationship with that prescribing physician, or the amount and duration of the initial opioid prescription. Furthermore, this question relied on patient recall which could be subject to bias in either direction, and patients’ conceptions of what constitutes an “introduction” to opiates may have differed. Second, our study was conducted among a sample of opioid dependent individuals with depressive symptoms who were seeking treatment with buprenorphine, which may limit generalizability. However, depression is common among opioid addicts: studies estimate that approximately a third to one half suffer from depression (Brienza, et al., 2000; Croughan, Miller, Wagelin, & Whitman, 1982; Khantzian & Treece, 1985; Rounsaville, Weissman, Crits-Christoph, Wilber, & Kleber, 1982). Furthermore, our sample appears to be similar to other populations of buprenorphine treated patients with regards to the proportion currently using heroin v. non-heroin opioids, supporting its overall general representativeness (Stanton, McLeod, Luckey, Kissin, & Sonnenfeld). Finally, by excluding individuals on antidepressants, which may include a small subset on tricyclic antidepressants for depression and pain, ours may be an underestimate of the true proportion of opioid dependent individuals who are introduced to opioids by a physician for pain.

In summary, this study found that 29% of patients who were presenting for treatment for opioid dependence reported that a physician had introduced them to opioids. This finding reinforces the need for physicians to carefully select patients before initiating an opioid therapeutic trial and, once prescribing, to monitor patients regularly for opioid misuse, abuse and dependence (Passik, 2009). More prospective research is needed to examine the

trajectories of opioid use that occur among individuals who introduced to opioids through a physician, and to develop strategies to prevent patients from developing addiction to opioids.

Acknowledgments

This study was funded by the National Institute on Drug Abuse (DA 022207), Clinical Trial # NCT 00475878. Dr. Stein is a recipient of a NIDA Mid-Career Award (DA 000512)

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Figure 1.
Patterns of Current Opioid Use Among Opioid Dependent Participants Who Were and Were Not Introduced to Opioids By a Physician

Table 1

Characteristics of Opioid Dependent Patients Who Do and Do Not Report a Physician Introducing Them to Opioids

	Physician Introduced (n=40) % or Mean ($\pm$ SD)	Physician Did Not Introduce (n=100) % or Mean ($\pm$ SD)	p-value
Age	38 ($\pm$ 9)	37 ($\pm$ 10)	0.87
Female	28	22	0.49
Non-white	15	22	0.35
Married	10	7	0.52
Employed	45	56	0.24
Has Health Insurance	44	33	0.24
Has a Primary Care Provider	38	37	0.96
Duration of Opioid Use	9 ($\pm$ 8)	9 ($\pm$ 7)	0.74
Prior Injection Drug Use	38	76	<0.01
Regular Use of Alcohol prior to Opioids	35	34	0.91
Regular Use of Marijuana prior to Opioids	53	72	0.03
Regular Use of Cocaine prior to Opioids	23	45	0.01

Table 2

Pain, Depression, and Drug Related Aberrant Behaviors Among Opioid Dependent Patients Who Do and Do Not Report a Physician Introducing Them to Opiates

	Physician Introduced (n=40) %	Physician Did Not Introduce (n=100) %	p-value
Introduced to Opioids for Pain	100	11	<0.01
Current (past week) Pain	78	85	0.29
Chronic (>6 mo.) Pain	63	43	0.04
Chronic Severe Pain	53	30	0.01
Severe Depression	38	48	0.26
Regular Opioid Use Was Prescribed by a physician	85	14	<0.01
Ever used a physician to procure a prescription for opioids to get high	50	32	0.05
Ever used a physician to procure a prescription for opioids to sell to others	10	4	0.17
Ever sought out a physician known to easily prescribe opioids	33	17	0.04