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Sublingual buprenorphine for chronic pain: A survey of clinician prescribing practices

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Abstract

Objectives—Sublingual buprenorphine, with and without naloxone, is indicated for the treatment of opioid use disorders. Although not approved for pain, some evidence suggests it may be a safe and effective alternative to conventional opioid analgesics, particularly for those with addiction problems. This study surveyed pain specialists to examine the extent to which sublingual buprenorphine was prescribed for chronic pain and explore associated clinician attitudes and characteristics.

Method—A 36-item survey examining clinician attitudes and characteristics related to sublingual buprenorphine and other opioids was distributed to 1,307 members of the American Pain Society, a multi-disciplinary professional group. Members were provided a paper copy of the survey and URL to an on-line version. A follow up letter was mailed after 2 weeks.

Results—Overall, 230 completed surveys were returned (18.5%). Of clinicians who prescribed opioids for chronic pain (92.5%), 19.7% reported prescribing sublingual buprenorphine for chronic pain at least once; of these prescribers, 39.6% did not have a DEA X-waiver to prescribe sublingual buprenorphine for opioid dependence. Prescribers were more likely than non-prescribers to find sublingual buprenorphine effective for chronic pain. Prescribers were also significantly more likely to view sublingual buprenorphine as safer than full agonists in terms of addiction, overdose, and drug interaction. No differences emerged between prescribers and non-prescribers regarding perceptions of potential for drug diversion or in terms of overall opioid prescribing behaviors.

Discussion—Results suggest that sublingual buprenorphine is indeed being used to treat chronic pain; however, the circumstances when this occurs are not entirely clear.

Keywords

chronic pain; sublingual buprenorphine; opioids; attitudes; practices

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Introduction

Sublingual buprenorphine, a partial μ -opioid agonist and κ -opioid antagonist, is approved in the United States for the treatment of opioid use disorders. Sublingual buprenorphine has two formulations: with and without naloxone. The addition of naloxone, an opioid antagonist, is intended to inhibit potential opioid effects [1] thereby minimizing abuse liability and discouraging diversion without reducing the clinical efficacy [2]. Buprenorphine's high affinity with the μ -opioid receptor allows for a slow dissociation, resulting in a long duration of action and mild withdrawal symptoms [3]. These properties have made the sublingual (i.e., under the tongue) formulation, either tablet or film, a highly effective treatment for DSM-IV-TR opioid dependence [4, 5, 6, 7].

Since 2000 [8], physicians completing basic training on its use may apply for a DEA X-waiver to prescribe sublingual buprenorphine for opioid dependence in outpatient settings. The rationale for the X-waiver mechanism was to increase access to a safe and effective treatment using an opioid replacement treatment. Previously, opioid replacement treatment was only available in highly regulated clinics, i.e., methadone. Providing treatment in the privacy of a physician's office as opposed to a maintenance program minimizes barriers to treatment and helps destigmatize treatment of opioid use disorders [9].

Research has indicated sublingual buprenorphine may be an effective treatment for reducing chronic pain symptoms [5]. Further, evidence suggests sublingual buprenorphine is currently being used by clinicians to treat chronic pain [4, 5, 10, 11]. However, while other formulations (e.g., transdermal) are approved for pain management, the sublingual formulation, tablet and film, does not carry a pain indication. Experts in addiction and pain may select buprenorphine over a full agonist (albeit in divided doses) to minimize risk of abuse and diversion in addicts [12].

Little information is available regarding the extent to which off-label use of sublingual buprenorphine is occurring and under what circumstances. The purpose of this study was to examine the extent to which sublingual buprenorphine is used by pain specialists to treat chronic pain, as well as explore clinician attitudes and characteristics associated with its use.

Materials and Methods

Study sample

Prospective respondents were the 2,539 members of American Pain Society (APS), a large, multidisciplinary professional pain society. Those identified as being a medical doctor (M.D. or D.O.), physician assistant (P.A.), or nurse with prescriptive authority in the United States (e.g., Nurse Practitioner, Clinical Nurse Specialist, Advanced Practice Nurse) were invited to participate. Members with addresses outside the United States of America and its territories were excluded. After identifying potentially eligible respondents, the survey was distributed to 1,307 members between April and May, 2010. Respondents were not compensated for their participation. Sixty-one surveys were returned either as undeliverable or the potential respondent was no longer eligible (e.g., no longer practicing).

Materials

The 36-item survey was developed by the authors based on a review of literature on clinicians' prescribing practices. The survey used a combination of multiple choice, fill in the blank, ranked items, and items scored on a 5 point Likert-type scale. Some items included were derived from existing surveys including questions on attitudes [13], patient and clinician characteristics [14], and demographics [15, 16]. The survey focused on practice characteristics and prescribing behaviors related to sublingual buprenorphine and

other opioids, and was organized into the following four sections (in order of presentation): (a) clinician characteristics, including professional title, size of community, medical specialty, board certification, and years in practice, (b) patient characteristics, including number of patients, percentage of patients with chronic pain, and proportion of patients maintained on opioids, (c) sublingual buprenorphine-prescribing behaviors, including prescribing practices, formulations used, dosing, reasons for using, and concerns about safety and effectiveness, and (d) opioid-related attitudes and behaviors, including opioid prescribing concerns and likelihood to prescribe opioids to patients with various substance use histories. A pilot version of the survey was reviewed by experts in the areas of pain and addiction, including anesthesiologists, psychologists, and addiction psychiatrists, and feedback was incorporated into the final version.

Procedure

Because email addresses were not provided, eligible respondents received a paper copy of the survey by mail, as well as a prepaid business reply envelope and a cover letter explaining the study and requesting participation. The cover letter included the URL to an on-line version of the survey. Respondents were instructed to complete and return the survey anonymously. Two weeks following the initial mailing, all potential respondents received a follow-up letter reminding them about the survey. A study flow diagram is provided in Figure 1 describing the number of respondents in the final analytic data set.

Data Analysis

Data was analyzed using SPSS version 19. Descriptive statistics for survey respondents were calculated. Chi Square tests were performed to compare characteristics of sublingual buprenorphine prescribers to those of non-prescribers. T-tests examined group characteristics and differences between buprenorphine prescribers and non-prescribers' attitudes regarding buprenorphine and opioids overall. An alpha level of .05 was used for all tests.

Results

Physician characteristics

Overall, 230 completed surveys were returned (18.5%). Except where noted, this is the sample about which results are presented. Because surveys were completed anonymously, we were unable to compare responders with non-responders. To understand the characteristics of responders to the extent possible, we compared responders with current APS membership characteristics. A review of society membership statistics [17] indicated that respondents represented the range of clinical specialties with the society membership. Table 1 describes clinician characteristics. Respondents were distributed throughout the United States. The majority of respondents were from larger communities (52.4%), board-certified physicians with 10–19 years in practice (31.1%). Most had completed a fellowship (66.5%) and held an academic appointment (50.9%). Primary clinical settings were most often group practices (38.5%), academic/Veteran's Health Care (36.7%), and community hospitals (21.7%). Among respondents, 18.6% were certified by American Society of Addiction Medicine (ASAM) or American Board of Addiction Medicine (ABAM).

Practice Characteristics and Setting

Number of patients varied greatly among clinicians ($M=1035.3$, $SD=1315.2$, $Median=500.0$). Not surprisingly, chronic pain was a common patient complaint (79.2%); for 71.7% it was the chief complaint. Overall, 92.5% of clinicians reported prescribing

opioids for the treatment of chronic pain with 53.4% of their patients maintained on opioid therapy (table 1).

Buprenorphine prescribers

Overall, 45 respondents (19.7%) reported some experience using sublingual buprenorphine (with and without naloxone) to treat chronic pain. Hereafter, the term sublingual buprenorphine is used to describe both sublingual formulations, i.e., with and without naloxone, except where noted. Compared to prescribers, non-prescribers were less likely to work in academic medical centers (Table 1). When asked to compare themselves to colleagues in their specialty, non-prescribers viewed their use of opioid analgesics for chronic pain as less frequent relative to other prescribers.

Among sublingual buprenorphine prescribers, 52.3% used the buprenorphine/naloxone formulation, although 43.2% of prescribers used both formulations. Physicians reported that, during the preceding 6 months, prescriptions for sublingual buprenorphine/naloxone ($M=51.9$, $SD=125.5$) were greater than prescriptions for sublingual buprenorphine without naloxone ($M=8.8$, $SD=21.3$). A majority of sublingual buprenorphine prescribers (61.4%) had DEA X-waivers authorizing use of buprenorphine for an opioid use disorder. As shown in Table 2, the extent of sublingual use and dosing practices was quite variable. Among prescribers, 65.0% reported that switching to buprenorphine from another opioid was their greatest challenge.

Opioid related practice behaviors and attitudes

As shown in Table 3, no significant differences were observed between non-prescribers and prescribers of sublingual buprenorphine in terms of opioid prescribing behaviors, although three concerns did trend toward significance, including concerns with side effects, tolerance, and diversion.

With regards to likelihood to prescribe to patients with a history of various substance use disorders, non-prescribers reported a lower likelihood of prescribing opioids to patients with prior opioid and alcohol problems. No differences were observed between non-prescribers and prescribers with regards to prescribing opioids for a patient with prior non-opioid substance use problems. Non-prescribers were also slightly less likely to prescribe any opioid to patients with current alcohol or non-opioid substance use problems than were sublingual buprenorphine prescribers.

Discussion

The purpose of this study was to examine the extent to which pain specialists prescribed sublingual buprenorphine for chronic pain and to describe clinician attitudes and behaviors associated with prescribing. Among clinicians prescribing opioids, 19.7% prescribed sublingual buprenorphine, most often with naloxone. However, there was considerable variation in frequency of use. This is consistent with reports suggesting this buprenorphine formulation is thought to be a viable pain management option [4, 5, 10, 11]. While this may not be surprising given buprenorphine's known analgesic properties, the extent of use have not been previously documented to our knowledge.

This raises the issue of why some clinicians prescribe sublingual buprenorphine for chronic pain as opposed to conventional opioid analgesics, and under what circumstances. Not surprisingly, sublingual buprenorphine prescribers viewed its use for pain more positively with respect to safety and effectiveness than non-prescribers. However, overall attitudes and behaviors towards opioid analgesics did not differentiate prescribers from non-prescribers. Both prescribers and non-prescribers of sublingual buprenorphine held similar concerns

regarding prescribing opioids for chronic pain in terms of safety. This is consistent with prior reports of clinician attitudes and behaviors about opioid analgesics [13, 14, 18]. Nor were there differences with regards to willingness to prescribe opioid analgesics to a patient with a prior non-opioid substance use problem. These similarities indicate that clinician and the clinical environment and commonly investigated opioid analgesic-related attitudes and behaviors did not predict whether a clinician may be more likely to prescribe sublingual buprenorphine for chronic pain. It is possible that other factors, including patient characteristics beyond substance abuse, are associated with likelihood to prescribe sublingual buprenorphine. For example, it may be important to examine what role, if any, gender and other sociodemographic characteristics as well as other comorbidities, including psychiatric disorders, play in opioid prescribing.

This study is not without its limitations. The small sample size and low response rate limit the generalizability of the findings reported. The actual prevalence of sublingual buprenorphine prescribing may be different. Indeed, it is reasonable to expect that prescribing has increased since the time of this survey. Among the surveys received, there were incomplete surveys that were unusable in the data set due to a significant amount of missing information. Additionally, the sample was drawn from a professional society for pain specialists. The findings might be different were the sample drawn from members of other pain societies with different perspectives on opioid therapy or from a more general set of clinicians who prescribe opioids, for example primary care clinicians. Finally, the data was collected prior to the availability of transdermal buprenorphine patches and sublingual buprenorphine/naloxone formulation as a soluble film [19, 20]. It is unknown how the availability of a transdermal formulation with a chronic pain indication may impact use of the sublingual formulations.

In spite of the above, this report demonstrates that sublingual buprenorphine is being prescribed off-label by pain clinicians, many of whom may not have DEA X-waivers, to treat pain in chronic pain patients. It seems unlikely that this prescribing results from efforts to circumvent the DEA X-waiver as this was a sample of pain specialists. It seems more likely that sublingual buprenorphine is being prescribed specifically for pain rather than for co-occurring chronic pain and opioid dependence. This is supported by the finding that prescribers reported no difference in their willingness to prescribe opioids for an individual with a substance use history. While this suggests a perceived benefit, efficacy and safety of this formulation for chronic pain is uncertain.

As noted above, it is unclear why and under what circumstances clinicians elect to prescribe sublingual buprenorphine for pain. Understanding why some clinicians are more likely to prescribe buprenorphine to treat pain may identify conditions in which it may be most suitable for treating chronic pain. Such practice-based information may inform future clinical research on buprenorphine to subsequently inform clinical practice. As findings from this study did not clarify a clear rationale for its use and given the prevalence of off-label use, additional research examining its safety and effectiveness for chronic pain is warranted to assist clinicians in determining whether sublingual buprenorphine is an appropriate treatment for chronic pain.

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Figure 1.
Study flow diagram of the number of respondents included in the final analytic data set.

Table 1
Physician and Practice Characteristics by Sublingual Buprenorphine Prescriber Status*

Demographics	Prescriber No. (%) / M (SD)	Non-Prescriber No. (%) / M (SD)	χ^2/t	df	P value
State or territory of practice	(n=45)	(n=180)	5.56	4	0.24
South	16(35.6%)	54(30.0%)			
West	17(37.8%)	45(25.0%)			
Midwest	7(15.6%)	44(24.4%)			
Northeast	5(11.1%)	36(20.0%)			
Puerto Rico	0	1(.60%)			
Community size	(n=45)	(n=183)	4.72	2	0.10
< 100,000	6(13.3%)	39(21.3%)			
100,000 to 500,000	9(20.0%)	55(30.1%)			
> 500,000	30(66.7%)	89(48.6%)			
Professional degree	(n=44)	(n=184)	0.67	1	0.41
Physician	39(88.6%)	154(83.7%)			
Prescribing nurse	5(11.4%)	30(16.3%)			
Board certified	(n=43)	(n=177)	1.28	1	0.26
Years in practice	41(95.3%)	159(89.8%)			
< 10 years	(n=44)	(n=183)	3.43	3	0.33
10 to 19 years	6(13.6%)	48(26.2%)			
20 to 29 years	16(36.4%)	54(29.5%)			
> 30 years	13(29.5%)	43(23.5%)			
Fellowship in specialty	9(20.5%)	38(20.8%)			
Hold academic appointment	(n=39)	(n=160)	0.65	1	0.42
Primary clinical setting	28(71.8%)	104(65.0%)			
Academic/VA medical center	(n=44)	(n=183)	0.70	1	0.40
Community hospital/clinic/group practice/other	20(45.5%)	96(52.5%)			
Primary clinical setting	(n=44)	(n=182)	9.97	3	0.02
Academic/VA medical center	10(22.7%)	73(40.1%)			
Community hospital/clinic/group practice/other	10(22.7%)	39(21.4%)			

	Prescriber No. (%) / M (SD)	Non-Prescriber No. (%) / M (SD)	χ^2/t	df	P value
Group practice	20(45.5%)	67(36.8%)			
Other	4(9.1%)	3(1.6%)			
ASAM/ABAM certification	(n=38)	(n=172)	0.19	1	0.66
Primary medical specialty	8(21.1%)	31(18.0%)			
Anesthesiology	(n=45)	(n=181)	4.09	6	0.66
Physical medicine and rehabilitation	21(46.7%)	72(39.8%)			
Neurology	4(8.9%)	21(11.6%)			
Family practice/Internal medicine	2(4.4%)	16(8.8%)			
Psychiatry	11(24.4%)	32(17.7%)			
Surgery	2(4.4%)	6(3.3%)			
Other	0	3(1.7%)			
	5(11.1%)	31(17.1%)			
Practice Setting (by clinician)					
Current number of patients by clinician	(n=38)	(n=156)	0.44	192	0.66
% patients with Chronic Pain (CP)	951.6 (1199.3)	1055.7 (1344.7)			
	(n=45)	(n=183)	-1.11	226	0.27
% patients with CP as primary problem	83.5(27.0)	78.1(29.8)			
	(n=44)	(n=181)	-1.83	223	0.07
Prescribe opioids for CP	79.7(28.5)	69.7(33.5)			
	(n=44)	(n=183)	2.14	1	0.14
% patients maintained on opioids for CP	43(97.7%)	167(91.3%)			
	(n=43)	(n=182)	-1.41	223	0.16
Prescribe chronic opioid therapy, compared to others in specialty	59.7(29.0)	51.9(33.6)			
Less often	(n=37)	(n=179)	7.30	2	0.03
About the same	4(10.8%)	43(24.0%)			
More often	14(37.8%)	83(46.4%)			
	19(51.4%)	53(29.6%)			

* Sample size noted for individual variables.

Table 2

Prescribers of Sublingual Buprenorphine for Chronic Pain*

	No.(%)/M (SD)
Buprenorphine Prescriber Characteristics	
Possess DEA X-waiver (n=44)	27(61.4%)
Buprenorphine prescribers by formulation (n=44)	
Buprenorphine/naloxone	23(52.3%)
Buprenorphine without naloxone	2(4.5%)
Both	19(43.2%)
Number prescriptions past 6 months	
Buprenorphine/naloxone (n=44)	51.9(125.5)
Buprenorphine without naloxone (n=30)	8.8(21.3)
Buprenorphine doseage	
Typical starting dose (n=44)	
4 mg	24(54.5%)
8 mg	12(27.3%)
12 mg	1(2.3%)
16 mg	6(13.6%)
24 mg	1(2.3%)
Maximum dose (n=44)	
8 mg	3(6.8%)
12 mg	6(13.6%)
16 mg	6(13.6%)
24 mg	10(22.7%)
32 mg	17(38.6%)
32 mg	2(4.5%)
Average dose (n=43)	
4 mg	1(2.3%)
8 mg	13(30.2%)
12 mg	8(18.6%)
16 mg	15(34.9%)
24 mg	5(11.6%)
32 mg	1(2.3%)
Buprenorphine management challenges (n=40)	
Switching to	26(65%)
Switching from	9(22.5%)
Titrating	5(12.5%)

* Sample size noted for individual variables.

Table 3
Comparing Sublingual Buprenorphine Prescriber & Non-Prescriber Opioid Related Practice Behaviors and Attitudes

	Prescriber		Non-Prescriber		t	df	p value
Concerns about prescribing opioids for chronic pain (0=Not at all concerning, 4=Extremely concerning)	M (SD)		M (SD)				
Efficacy	2.5(1.3)		2.1(1.2)		-1.49	212	0.14
Side effects	2.6(1.0)		2.3(1.0)		-1.78	213	0.08
Tolerance	2.3(1.1)		2.0(1.1)		-1.70	214	0.09
Interaction with other medication	2.1(0.7)		2.1(1.0)		-0.44	213	0.66
Opioid misuse	2.9(0.9)		2.7(1.0)		-1.15	215	0.25
Addiction	2.1(1.1)		2.2(1.2)		0.52	216	0.60
Dose escalation	2.4(1.1)		2.3(1.1)		-0.54	214	0.59
Attitudes of other doctors/colleagues	1.3(1.2)		1.3(1.3)		0.02	215	0.98
Diversification	2.8(1.1)		2.5(1.1)		-1.92	215	0.06
No exit strategy	1.6(1.2)		1.7(1.2)		0.32	213	0.75
Regulatory burden/DEA	1.6(1.3)		1.8(1.2)		0.91	214	0.36
Medical liability	1.8(1.3)		1.9(1.1)		0.50	213	0.62
Long-term safety	2.2(1.3)		2.1(1.1)		-0.62	215	0.54
Likelihood to prescribe by substance use problem (0=Not at all, 4=Extremely)							
Prior opioid problem	1.2(1.0)		1.0(0.9)		-1.35	213	0.18
Prior alcohol problem	1.6(0.9)		1.4(0.8)		-0.78	215	0.44
Prior non-opioid problem	1.5(1.0)		1.5(0.8)		0.10	212	0.92
Current alcohol problem	0.7(1.0)		0.5(0.8)		-1.02	216	0.31
Current non-opioid problem	0.8(1.1)		0.7(0.8)		-0.45	214	0.65

Note: $p < 0.05$ (two-tailed tests)