

Abuse of Buprenorphine in the United States: 2003-2005

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ABSTRACT. This study examines trends in the reported abuse of two sublingual buprenorphine products, Subutex[®] and Suboxone[®], in the United States. Quarterly counts of abuse cases were obtained from 18 regional poison control centers (PCCS) for 2003-2005. Seventy-seven abuse cases were reported, of which 7.8 percent involved Subutex[®] and 92.2 percent involved Suboxone[®]. The average quarterly ratio of abuse cases per 1,000 prescriptions dispensed was 0.08 (SD \pm 0.09) for Subutex[®], and 0.16 (SD \pm 0.08) for Suboxone[®]. Findings suggest that these sublingual buprenorphine formulations have a low rate of abuse based on toxico-surveillance data. doi:10.1300/J069v26n03_12 [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <http://www.HaworthPress.com> © 2007 by The Haworth Press, Inc. All rights reserved.]

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INTRODUCTION

Buprenorphine, a partial μ opioid agonist, has been used as a pain medication for several

decades in the United States (U.S.).¹ In October 2002, two new sublingual buprenorphine formulations, Subutex[®] and Suboxone[®] (Reckitt Benckiser), were approved for the office-based

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treatment of opioid dependence consistent with the Drug Addiction Treatment Act of 2000.² Subutex[®], a single entity buprenorphine hydrochloride product, was intended for use during the initiation phase of substitution therapy while Suboxone[®], a buprenorphine-naloxone combination drug, was intended for the maintenance phase.³

Buprenorphine's partial agonist properties, coupled with its slow rate of dissociation from the μ receptor after binding and ceiling effect at higher doses, contributed to its classification as a Schedule III drug with lower abuse potential than full μ opioid agonists.⁴ With the increased medical availability of buprenorphine, however, concerns have mounted regarding its abuse potential.¹ Internationally, cases of buprenorphine misuse and abuse-related morbidity and mortality have been documented in numerous countries where the drug has been approved for use in opioid dependence treatment.⁵⁻¹⁰ In Finland, where both single entity buprenorphine and buprenorphine-naloxone combination products are available for clinical use, intravenous abuse of these drugs has been reported among untreated intravenous users (IVs).¹¹

To date, however, little is known concerning the abuse of these sublingual buprenorphine products in the U.S. To address this issue, we assessed trends in the reported abuse of buprenorphine and buprenorphine-naloxone combination using data from regional toxic-surveillance systems.

METHODS

Study data consisted of calls received between 4th quarter, 2003 through 4th quarter, 2005 by 18 regional poison control centers (PCCs) covering a total of 103.1 million individuals in 20 different states. Call inclusion criteria specified that (a) the exposure resulted from an intentional improper or incorrect use of a substance with an attempt to get "high," produce euphoria, or other psychotropic effect (defined as "Abuse" per PCC rating criteria); and (b) the substance involved was Subutex[®] or Suboxone[®]. Each call was reviewed and classified by a Specialist in Poison Information (SPI), a professional trained in nursing and/or

pharmacology. Clinician review has shown good correspondence between PCC opioid analgesic cases categorized as "abuse" and standard nosological classifications of opioid abuse and dependence.¹² As a proxy for legitimate use, data were obtained on the estimated number of prescriptions dispensed for Subutex[®] and Suboxone[®] by retail pharmacies from IMS Health, Inc., a commercial vendor of healthcare data.¹³

Statistical Analysis

We tabulated the number of abuse cases and prescriptions dispensed for each drug by quarter for the nine quarter study period. We also calculated the mean number and standard deviation of abuse cases and the ratio of abuse cases to 1,000 prescriptions dispensed.

RESULTS

Table 1 presents the number of abuse cases and prescriptions dispensed for each drug by calendar quarter. Seventy-seven PCC abuse cases were reported for the two drugs combined. Of these, 7.8 percent involved Subutex[®]; and 92.2 percent involved Suboxone[®]. The mean number of abuse cases per quarter was 0.66 (standard deviation ± 0.71) for Subutex[®],

TABLE 1. Number of abuse cases and estimated number of prescriptions dispensed on an outpatient basis for Suboxone[®] and Subutex[®] by quarter in the United States (US), 4th quarter 2003-4th quarter 2005.

	# Abuse Cases Subutex [®]	# Prescriptions Subutex [®]	# Abuse Cases Suboxone [®]	# Prescriptions Suboxone [®]
4Q03	0	3,239	1	14,568
1Q04	1	4,611	4	19,924
2Q04	0	6,259	1	27,946
3Q04	1	7,726	9	35,049
4Q04	1	8,722	6	43,313
1Q05	1	10,445	9	54,253
2Q05	0	11,239	19	66,655
3Q05	0	10,749	11	65,360
4Q05	2	11,696	11	73,106
Total	6	74,686	71	400,174

and 7.88 (standard deviation \pm 5.68) for Suboxone[®].

Of the estimated 474,860 prescriptions dispensed for the 2 drugs, 15.7 percent were for Subutex[®]; and 84.3 percent were for Suboxone[®]. The number of prescriptions dispensed for each product rose during the study period. The change was most pronounced for Suboxone[®], which showed a 402 percent increase in the volume of prescriptions dispensed during the nine quarter period compared to a 261 percent increase for Subutex[®].

Figure 1 presents the ratio of abuse cases to 1,000 prescriptions dispensed per quarter by drug. For Subutex[®], the average quarterly ratio of abuse cases per 1,000 prescriptions dispensed was 0.08 (SD \pm 0.090), while for Suboxone[®] the average quarterly ratio of abuse cases per 1,000 cases dispensed was 0.16 (SD \pm 0.080).

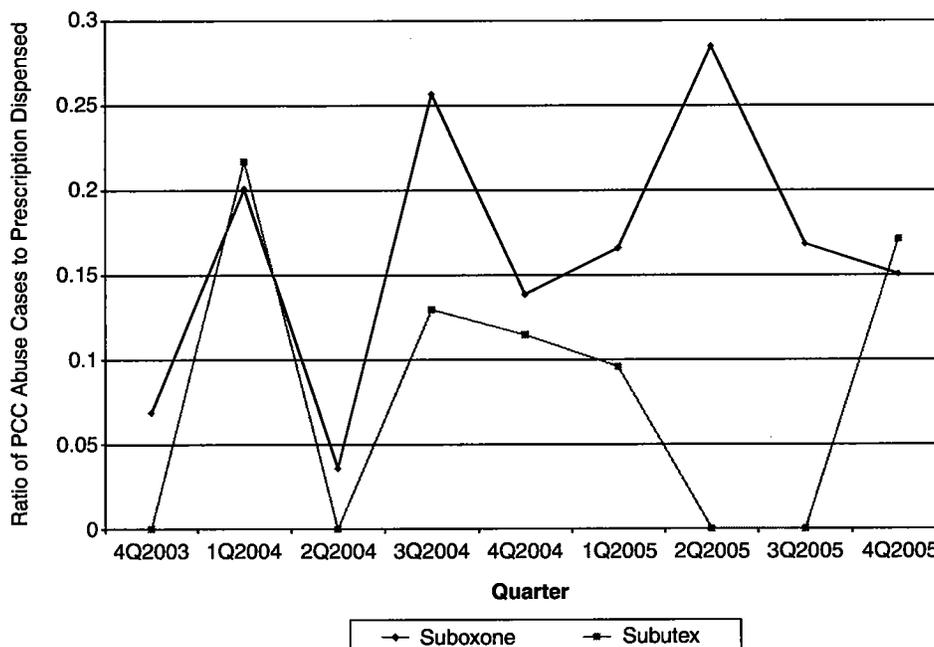
DISCUSSION

Our data indicate that the medical availability of both Suboxone[®] and Subutex[®] increased

steadily in the U.S. between 4th quarter, 2003 and 4th quarter, 2005. The rise was particularly marked for Suboxone[®] which accounted for approximately 84 percent of the total number of prescriptions dispensed for both drugs during this time period. Suboxone[®] also accounted for the majority (92 percent) of the 77 abuse cases reported in total for the two products combined.

After adjusting for differences in the degree of dispensing of these two drugs, the ratio of abuse cases was slightly higher on average for Suboxone[®] than for Subutex[®] (0.16 versus 0.08 abuse cases per 1,000 prescriptions dispensed, respectively). These ratios are low in comparison to similar data on opioid analgesic abuse. Zacny and colleagues calculated the ratio of drug-abuse related emergency department (ED) mentions per 1,000 prescriptions dispensed for five opioids for the period 1994-2001.¹⁴ Hydromorphone had the highest average ratio (1.80 ED mentions per 1,000 prescriptions dispensed), while fentanyl had the lowest (0.013 ED mentions per 1,000 prescriptions dispensed).

FIGURE 1. The ratio of Suboxone[®] and Subutex[®] abuse cases to 1,000 prescriptions dispensed as reported to participating poison control centers by quarter, 4th quarter, 2003-4th quarter 2005.



Our finding that Suboxone® had a higher abuse ratio than Subutex® is intriguing. One possible explanation is that the degree of patient exposure to Subutex is likely much lower than that for Suboxone. According to the product package insert, Subutex is preferred for use during induction, and the use of Subutex for unsupervised administration should be limited to those patients who cannot tolerate Suboxone.¹⁷ Suboxone®, in contrast, is recommended for use in all 3 phases of treatment, including long-term maintenance, and in a much broader array of patients.¹⁵

Information concerning the route of buprenorphine administration used by abusers would have aided us in interpreting our study results. Data show that, in non-dependent opioid abusers, the opioid agonist effects of sublingually administered Suboxone® closely resemble those seen for Subutex®.¹⁶ Similarly, it has been demonstrated that, when administered parenterally, naloxone's functional blockade of buprenorphine's action is only partial and short-lived in nature.¹⁷ A recent study of untreated intravenous abusers in Finland revealed that 68 percent reported abusing Suboxone intravenously.¹¹ Moreover, 66 percent of those who had abused the drug once admitted that they had abused it at least once subsequently, or even regularly thereafter, despite describing the effect as a "bad experience." Future research is needed to examine the characteristics of buprenorphine abusers in more detail and explore whether and to what extent route of administration varies by type of abuser.

In addition to lacking data on route of administration, our study was limited by the fact that the geographical coverage of participating PCCs was not nationally representative. It is important to note, however, that all major regions of the U.S. were included.

Our results suggest that while both Subutex® and Suboxone® are being abused in the post-marketing context, the level of such abuse is low relative to the number of prescriptions dispensed. These findings are especially noteworthy in light of the fact that both these products are prescribed for use in a population at high risk for drug abuse. Ongoing monitoring of these new products is vital in order to determine whether these trends will continue.

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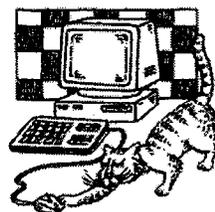
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