DECREASED OPIOID PRESCRIBING IN A PEDIATRIC EMERGENCY DEPARTMENT AFTER THE RESCHEDULING OF HYDROCODONE

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Abstract—Background: The Drug Enforcement Administration (DEA) changed hydrocodone-containing products (HCPs) from Schedule III to II status on October 6, 2014, making codeine-containing products (CCPs) the only non-Schedule II oral opioid agents. Objectives: We sought to describe prescribing patterns of oral opioid agents in the pediatric emergency department before and after the 2014 DEA rescheduling of HCPs. Methods: We performed a cross-sectional study evaluating prescribing patterns in the pediatric emergency department at an urban, academic, quaternary care children’s hospital system for 6 months before and 6 months after the DEA rescheduling of HCPs. Differences in patient demographics, provider type, and diagnoses were assessed during the two time periods using Pearson’s chi-squared test. The Breslow–Day statistic was used to assess differences in prescribing patterns by provider type. Results: There were 1256 prescriptions for HCPs and CCPs in our pediatric emergency department during the study period, and only 36 prescriptions for alternate oral opioid medications. Prescriptions of all opioid pain medications decreased by 55% after rescheduling. The odds of prescribing HCPs were reduced by 60% after the DEA rescheduling (odds ratio 0.40 [95% confidence interval {CI} 0.30–0.54]; p < 0.001). There was no difference between monthly ordering frequencies for CCPs before or after the DEA rescheduling (p = 0.75). Conclusions: The period after rescheduling of HCPs was associated with a lower odds of HCP prescriptions in our emergency department without an increase in the prescription of CCPs. © 2016 Elsevier Inc. All rights reserved.

Keywords—codeine; DEA rescheduling; emergency department; hydrocodone; pediatric

INTRODUCTION

There are nearly 25 million pediatric emergency department (ED) visits each year, and 75% of these visits involve a medication being administered or prescribed (1,2). Hydrocodone and hydrocodone-containing products (HCPs) are among the most prescribed oral opioid medications in the United States (US) and have a good safety profile in children (3,4). Codeine and codeine-containing products (CCPs) are also widely available, but safety concerns have been raised about use in children because of genetic variability in metabolism (5). The enzyme cytochrome 2D6 catalyzes the conversion of codeine to morphine, and its variable activity can lead to both therapeutic failure and toxicity (6–8).

Between 2001 and 2010, the percentage of ED visits in which an opioid analgesic was prescribed in adult EDs rose from 20.8% to 31.0%, while codeine use declined, but opioid prescriptions for children have remained stable.
over the same period (9,10). In addition, codeine use in pediatric EDs accounted for nearly one-third of the overall codeine prescriptions (11). Extrapolating from these numbers suggests that up to 57,000 children with the ultrarapid metabolizing phenotype of cytochrome 2D6 were at risk of developing toxic levels of morphine and 250,000 children with the poor metabolizing phenotype were at risk of inadequate analgesia from CCPs (11).

Multiple warnings have been issued regarding the dangers of CCP use in children. The American Academy of Pediatrics issued guidelines about the potential danger and lack of documented efficacy of CCPs for children with cough or upper respiratory infections in 2006 (12,13). The US Food and Drug Administration (FDA) issued a statement of concern regarding the risk of serious or fatal respiratory depression in nursing infants (14). In 2012, the World Health Organization removed CCPs from its analgesic ladder (15). Despite such warnings, the use of CCPs is still a point of much debate (16).

Recent changes to the US Drug Enforcement Administration (DEA) narcotic classification of HCPs have resulted in a new focus on hydrocodone and codeine. Effective October 6, 2014, HCPs were changed from Schedule III to Schedule II status in the Controlled Substance Act, which is a more stringent classification requiring a triplicate prescription for outpatient use in many states (17,18). The purpose of this rescheduling was to make access to these commonly abused agents more difficult (19). At this time, the only non–Schedule II narcotic available in the United States is codeine and related CCPs. The objective of this study is to describe prescription patterns of HCPs and CCPs in the pediatric ED before and after the 2014 DEA rescheduling of HCPs. We hypothesized a decline in HCP prescriptions and an increase in CCP prescriptions after the DEA scheduling change.

MATERIALS AND METHODS

Study Design and Population

This was a cross-sectional study in patients who presented to the EDs of two urban, academic, free-standing children’s hospitals in our hospital system. Data were divided into two groups: prescriptions ordered from April 6, 2014 to October 5, 2014 and prescriptions ordered from October 6, 2014 to April 6, 2015, representing 6 months before and 6 months after the DEA rescheduling of HCPs. During that period, there were 117,955 patient encounters in the two EDs.

All patients that presented to the ED and received a prescription for an oral opioid medication were included. CCPs consisted of acetaminophen-codeine oral elixir 24–2.4 mg/mL, and codeine sulfate 30 mg oral tablets. HCPs were hydrocodone-acetaminophen oral solution 2.5–108.3 mg/5 mL and 3.75–162.5 mg/7.5 mL. Patients who were prescribed hydromorphone 2 mg oral tablets, morphine sulfate 10 mg/5 mL oral solution, morphine sulfate 15 mg oral tablets, morphine sulfate extended release tablets, oxycodone-acetaminophen oral tablets, and tramadol 50 mg oral tablets were also evaluated but were excluded from detailed analysis because of the small sample size (n = 36). This study was approved by our local institutional review board.

RESULTS

During the study period, 1044 prescriptions were written for oral HCPs, 212 prescriptions for CCPs, and 36 prescriptions for other opioid medications. Of the 1256 HCPs and CCPs, all were combined with acetaminophen except three codeine tablet prescriptions. There was no significant difference in patient sex, ethnicity, and race between the rescheduling periods (Table 1). The unadjusted OR of oral opioid prescription was 0.40 when comparing prescriptions before and after the DEA rescheduling (Table 2). After adjusting for race, provider type, and diagnosis, the odds of ordering HCPs were reduced by 54% after DEA rescheduling compared to...
the study period before the FDA rescheduling of HCPs (OR 0.46 [95% CI 0.33–0.64]; p < 0.001).

Using the independent t-test, there were no significant differences between monthly ordering frequencies before or after DEA rescheduling for CCPs (p = 0.75), but there was a difference in the frequency of HCP prescriptions (p < 0.001; Table 3). In addition, there were significant differences before and after the DEA rescheduling between CCPs and HCPs, with a mean reduction in HCPs after rescheduling (p < 0.001 and p = 0.001, respectively; Table 3; Figure 1). Less than 5% of the included patients had an active prescription for an opioid medication recorded in the electronic medical record at the time of the ED visit.

Residents and some fellows do not have DEA numbers and, consequently, are unable to write triplicate prescriptions for outpatient Schedule II opioid medications at our institution, and therefore we assessed differences in provider prescribing patterns based on provider type. For all provider subgroups, the odds of prescribing HCPs were significantly reduced after DEA rescheduling (Table 4). There were prescribing differences between pediatric emergency medicine board eligible/certified attendings, general pediatricians working in the ED, and advanced practice providers (Breslow–Day p = 0.001). Pediatric emergency medicine providers, fellows, and residents collectively prescribed fewer HCPs after the DEA rescheduling of HCPs, but this reduction in prescriptions was less pronounced than that observed among general pediatricians (Breslow–Day p < 0.001).

**DISCUSSION**

To our knowledge, this is the first study assessing the effect of the DEA rescheduling of HCPs on prescribing patterns in the pediatric ED. While this policy change was intended to make HCPs less available given their potential for abuse, these results suggest an overall decrease

| Table 1. Demographic Comparisons of Patients Who Received an Outpatient Prescription for an Oral Opioid Medication Before and After the Rescheduling of Hydrocodone-Containing Products (N = 1256) |
|---|---|---|---|
| Before DEA Rescheduling, N = 881 (70.1%) | After DEA Rescheduling, N = 375 (29.9%) | p Value |
| Female sex, n (%) | 429 (48.7) | 172 (45.9) | 0.36 |
| Hispanic, n (%) | 382 (43.8) | 174 (46.6) | 0.35 |
| Race, n (%) |  |  | 0.08 |
| White | 632 (72.6) | 267 (72.2) |  |
| African American | 204 (23.4) | 97 (26.2) |  |
| Other* | 34 (4.0) | 6 (1.6) | 0.002 |
| Diagnosis, n (%) |  |  |  |
| Musculoskeletal | 433 (49.1) | 213 (56.8) |  |
| Fracture | 230 (53.1) | 105 (49.2) |  |
| Sickle cell disease | 30 (6.9) | 27 (12.7) |  |
| Chest pain | 11 (2.5) | 8 (3.8) |  |
| Abdominal pain | 136 (15.4) | 48 (12.8) |  |
| Tooth/mouth/ear/eye | 145 (16.5) | 35 (9.3) |  |
| Herpangina/pharyngitis | 69 (47.6) | 16 (45.7) |  |
| Peritonsillar abscess | 12 (8.3) | 1 (2.9) |  |
| Skin problems | 109 (12.4) | 55 (14.7) |  |
| Abscess | 50 (45.9) | 21 (38.1) |  |
| Genitourinary pain | 26 (3.0) | 17 (4.5) |  |
| Headache | 32 (3.6) | 7 (1.9) |  |

DEA = U.S. Drug Enforcement Administration.
* Includes Asian, American Indian/Alaskan Native, and Native Hawaiian/other Pacific Islander.

| Table 2. Unadjusted Odds for Prescriptions for Codeine-Containing Products and Hydrocodone-Containing Products Before and After the Rescheduling of Hydrocodone-Containing Products for Schedule III to II (N = 1256) |
|---|---|---|---|
| Codeine-Containing Products, n (%) | Hydrocodone-Containing Products, n (%) | Odds Ratio | 95% CI | p Value |
| Before DEA rescheduling | 112 (52.8) | 769 (73.7) | 0.40 | 0.30–0.54 | <0.001 |
| After DEA rescheduling | 100 (47.2) | 275 (26.3) |  |

CI = confidence interval; DEA = U.S. Drug Enforcement Administration.
* Acetaminophen-codeine no. 3 300-30 mg oral tablets, acetaminophen-codeine 120-12 mg/5 mL oral elixir, acetaminophen-codeine oral elixir 24 mg-2.4 mg/mL, and codeine sulfate 30 mg oral tablets.
† Hydrocodone-acetaminophen 5-325 mg, 75-325 mg, 10-325 mg oral tablets and hydrocodone/acetaminophen PO solution 2.5 mg-108.3 mg/5 mL or 3.75 mg-162.5 mg/7.5 mL.
in the frequency of oral opioid-containing analgesics in the pediatric ED at our institution (17,18). Contrary to our hypothesis, the rescheduling of HCPs did not result in an increase in the prescription of CCPs. However, this rescheduling did not appear to equally affect prescribing habits among all levels of providers, because attending physicians had a less dramatic decrease in HCP prescribing over the study period when compared to nurse practitioners and physician’s assistants.

While others have reported that health advisories have not led to decreased prescriptions of other opioid-containing medications, such as CCPs, our findings suggest that the DEA rescheduling of HCPs led to a significant decrease in the prescription of HCPs in our pediatric ED (20). The overall decreased frequency of oral opioid analgesic prescription among children may be an unintended consequence of the DEA rescheduling of HCPs. A recent study using data from the National Prescription Audit noted a 22% decline in HCPs after rescheduling, although 73.7% of this decline was related to refill prescriptions (21). Refill prescriptions for analgesics are not a common occurrence in our ED, making the observed 60% decline in HCP prescriptions after rescheduling even more clinically relevant.

Our study suggests that codeine was not prescribed more frequently in the ED after the DEA rescheduling. This finding is reassuring in light of myriad warnings against the prescription of codeine in children (12–14,22,23). Moreover, studies have shown that HCPs have gained popularity over CCPs in recent years, given the understanding of pharmacogenomics and the potential for undertreatment or fatal toxicities from CCPs (24). Provider understanding of such genetic variation may have contributed to the constant rate of CCP prescription in our pediatric ED. In addition, several studies have shown ibuprofen to have equal to superior efficacy compared with codeine products in treatment of pain caused by injuries, which may have also contributed to the consistently low prescription frequency of CCPs seen in this study (25–27).

While all providers prescribed fewer HCPs after the DEA rescheduling, the difference was less pronounced among attending physicians. This is perhaps because some residents, fellows, nurse practitioners and physician’s assistants do not have DEA numbers and therefore cannot write paper prescriptions for outpatient Schedule II medications, but other studies have shown that trainees are less likely to prescribe CCPs than attending physicians (11). Moreover, other studies have shown that simple interventions including pocket-sized reference cards distributed to residents at a children’s hospital have led to decreased prescribing of HCPs and CCPs (28).

**Limitations**

This cross-sectional study is subject to limitations. First, our study was conducted in the pediatric ED from a single system with two children’s hospitals and may not represent changes in oral opioid prescribing patterns across
the United States. Second, this study was conducted within an academic training facility where residents and fellows may not all have their own DEA numbers. This limitation should be noted, because the decline in HCP prescriptions may not have been as pronounced in nonacademic institutions. Third, we did not assess increased adverse consequences, such as return visits or missed school or work days as a result of the FDA change. Fourth, the measured outcome for HCP prescriptions was abstracted from the electronic medical record and may be an underrepresentation of HCP prescriptions, because all Schedule II medications should have both a paper prescription. Finally, we did not include nonopioid oral analgesics in our analysis, which may have been prescribed more frequently in the pediatric ED in light of the DEA rescheduling of HCPs. This is because prescriptions are often not written for these over the counter medications, and a precise method to capture these data was not available at the time.

CONCLUSION

The DEA rescheduling of HCPs led to an overall decrease in the frequency of HCP prescriptions in the pediatric ED without an accompanying increase in the prescription of CCPs.

REFERENCES


ARTICLE SUMMARY

1. Why is this topic important?
   Hydrocodone and hydrocodone-containing products (HCPs) are among the most prescribed oral opioid medications in the United States and have demonstrated a good safety profile in children. The Drug Enforcement Administration changed hydrocodone-containing products from Schedule-III to II status on October 6, 2014, making codeine-containing products (CCPs) the only non-Schedule II oral opioid agents.

2. What does this study attempt to show?
   We aimed to describe the impact of the 2014 DEA rescheduling of HCPs on the prescribing patterns of oral opioid agents in the pediatric emergency department. We hypothesized a decline in HCP prescriptions and an increase in CCP prescriptions after the DEA scheduling change.

3. What are the key findings?
   Prescriptions of all opioid pain medications decreased by 55% after the DEA rescheduling of HCPs. There was no difference between monthly ordering frequencies for CCPs before or after the DEA rescheduling at our institution. Attending physicians demonstrated a less dramatic decrease in HCP prescribing over the study period when compared to nurse practitioners and physician’s assistants.

4. How is patient care impacted?
   The prescribing of HCPs is now more difficult than prescribing CCPs, which are a potentially dangerous medication in children. Our data suggest that the DEA rescheduling of HCPs was associated with a significant decline in the prescribing of all oral opioid agents during the study period.