The Journal of Emergency Medicine, Vol. 52, No. 4, pp. 547–553, 2017

0736-4679/$ - see front matter

http://dx.doi.org/10.1016/j.jemermed.2016.08.026

Pharmacology in Emergency Medicine

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**

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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

Received: 20 June 2016; Final submission received: 14 August 2016;
Accepted: 22 August 2016

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 no. 3 300 mg/30 mg oral tablets, acetaminophen-codeine 120-12 mg/5 mL oral elixir, acetaminophen-codeine oral elixir 24–2.4 mg/mL, and codeine sulfate 30 mg oral tablets. HCPs were hydrocodone-acetaminophen 5-325 mg, 75-325 mg, 10-325 mg oral tablets and 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 15 mg oral controlled release tablets, oxycodone-acetaminophen 5-325 mg 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.

Study Protocol

Data extracted from the electronic medical record included patient demographics (e.g., age, sex, height, and weight), medication administration information (e.g., date, route, dose, and frequency of any oral opioid analgesic), medication prescriber type, and diagnosis.

Analysis

Demographic differences were assessed during the two time periods using Pearson's chi-squared or Fisher's exact tests for categorical variables. The Breslow–Day statistic was used to assess differences in prescribing of CCPs and HCPs among provider level of training. Two-tailed Student's *t*-tests assessed any differences between the monthly frequencies during the two time periods. Unadjusted odds ratios (ORs) were calculated to estimate the odds of prescribing HCPs after the DEA rescheduling. Statistical significance was defined as $p < 0.05$. All statistics were computed using the Statistical Package for the Social Sciences software (version 23; IBM Corp., Armonk, NY).

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