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#### **Original Contribution**

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Maryann Mazer-Amirshahi, PharmD, MD, MPH <sup>a,b,\*</sup>, Kayla Dewey, MD <sup>a</sup>, Peter M. Mullins, MA <sup>c</sup>, John van den Anker, MD, PhD <sup>b,d,e,f</sup>, Jesse M. Pines, MD, MBA, MSCE <sup>c,g</sup>, Jeanmarie Perrone, MD <sup>h</sup>, Lewis Nelson, MD <sup>i</sup>

- <sup>a</sup> Department of Emergency Medicine, MedStar Washington Hospital Center, Washington, DC
- <sup>b</sup> Department of Clinical Pharmacology, Children's National Medical Center, Washington, DC
- <sup>c</sup> The George Washington University, School of Medicine and Health Sciences, Washington, DC
- <sup>d</sup> Department of Pediatrics, The George Washington University, Washington, DC
- <sup>e</sup> Intensive Care, Erasmus Medical Center-Sophia Children's Hospital, Rotterdam, the Netherlands
- <sup>f</sup> Department of Pediatric Pharmacology, University Children's Hospital Basel, Switzerland
- <sup>g</sup> Department of Emergency Medicine, the George Washington University, Washington, DC
- <sup>h</sup> Department of Emergency Medicine, University of Pennsylvania, Philadelphia, PA
- <sup>i</sup> Department of Emergency Medicine, New York University, New York, NY

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#### ABSTRACT

*Objective:* Although not recommended as first line therapy by consensus guidelines, opioid analgesics are commonly used to treat headaches. This study evaluates trends in opioid use for headaches in US emergency departments (EDs).

Methods: We performed a retrospective review of the National Hospital Ambulatory Medical Care Survey, 2001 through 2010. Adult headache-related visits were identified. Medications (opioid and nonopioid) used for the treatment of headache were categorized based on medication class. Trends in ED use of the most common opioids (codeine, hydrocodone, hydromorphone, morphine, and oxycodone) were explored. The proportion of visits for which each medication was used was tabulated, and trends were analyzed using survey-weighted logistic regression.

Results: Headache visits during which any opioid was used increased between 2001 (20.6%; 95% confidence interval [CI], 18.1-23.4) and 2010 (35.0%; 95% CI, 31.8-38.4; P < .001). Prescribing of hydromorphone, morphine, and oxycodone increased, with the largest relative increase (461.1%) in hydromorphone (2001, 1.8% [95% CI, 1.2-2.6]; 2010, 10.1% [95% CI, 8.2-12.4]). Codeine use declined, and hydrocodone use remained stable. Use of opioid alternatives, including acetaminophen, butalbital, and triptans did not change over the study period, whereas use of nonsteroidal anti-inflammatory drugs increased from 26.2% (95% CI, 23.0-29.7) to 31.4% (95% CI, 28.6-34.3). Prescribing of antiemetic agents decreased from 24.1% (95% CI, 19.6-29.2) to 23.5% (95% CI, 21.1-26.0). Intravenous fluid use increased from 20.0% (95% CI, 17.0-23.4) to 34.5% (95% CI, 31.0-38.2) of visits.

*Conclusions:* Despite limited endorsement by consensus guidelines, there was increased use of opioid analgesics to treat headaches in US EDs over the past decade.

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#### 1. Introduction

Headache is a common presenting complaint in US emergency departments (ED). In 2008, there were more than  $5.5\,$  million

E-mail address: maryannmazer@gmail.com (M. Mazer-Amirshahi).

headache-related ED visits. Care for headache in the ED is aimed at ruling out serious causes, such as meningitis and intracranial hemorrhage, and at symptomatic relief. Migraines are the most common type of headache encountered in the ED, comprising approximately 34.6% of primary headache-related visits. In addition, migraines accounted for 63.1% of headache complaints that resulted in hospital admission [1,2].

The medical treatment to alleviate headache symptoms in the ED varies depending upon the etiology. Consensus guidelines regarding the management of headache in the acute setting recommend against the use of opioid analgesics as first-line therapy for most types of headache. The American College of Emergency Physicians clinical policy recommends use of agents with serotonergic receptor activity,

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<sup>\*</sup> Corresponding author at: 110 Michigan Avenue NW, Washington, DC 20010. Tel.: +12152190242.

such as prochlorperazine, metoclopramide, or triptans in acute headache [3]. The American Academy of Neurology also recommends serotonergic agents for the treatment of acute migraine. The American Academy of Neurology recommends opioid analgesics be used only on a limited basis for rescue therapy in the setting of moderate to severe migraine [4].

In recent years, there has been a broad increase in the use of opioid analgesics in ED patients [5]. In a study examining trends in opioid use in US EDs, headache was one of the major reasons for visit associated with this large rise in opioid use [5]. Higher opioid use in EDs is concerning given rising rates of prescription opioid abuse, overdose, and related fatalities [6-9]. In this study, we characterize trends in opioid analgesic use in US EDs for headache-related visits, extend previous work by describing specific medications that may be responsible for the rise in opioid use in headache, and explore concurrent trends in alternative, nonopioid headache treatments.

#### 2. Methods

#### 2.1. Study design

We performed a retrospective review of data from the National Hospital Ambulatory Care Survey (NHAMCS) from 2001 to 2010. National Hospital Ambulatory Care Survey is an annual multistage probabilistic sample of visits made to US EDs conducted by the Centers for Disease Control and Prevention, National Center for Health Statistics. The survey is designed to make national-level estimates about the use and provision of services in hospital-based EDs. The NHAMCS survey instrument is a patient record form, which is completed by trained staff for a random sample of visits during randomly assigned reporting periods. Specific data included are patient demographics, payment source, reason for visit, recent admissions or ED visits, diagnosis, services provided, type of provider seen, cause of injury, medications prescribed, procedures performed, and patient disposition. Data on facility characteristics are also included, such as geographic region, metropolitan status, and funding source. Data are deidentified and publically available, and as such, this study was exempt from institutional board review [10].

#### 2.2. Methods and measurements

In NHAMCS, there are up to 3 reasons for visits listed. All ED visits during the study years where there was any reason for visit that was headache-related (such as headache, head pain, migraine) were included in the analysis. Although up to 8 medications administered in the ED and prescribed at discharge are included in NHAMCS in recent years; this number increased from 6 medications in 2004. To ensure consistent results, analysis was therefore restricted to the first 6 medications listed in each visit. Opioid analgesics in the database were identified, and analysis was focused on the 5 opioid analgesics most commonly prescribed in the ED: codeine, hydrocodone, hydromorphone, morphine, and oxycodone [5]. All single-agent and combination opioid preparations (eg, oxycodone/acetaminophen) were included. For some portions of the analysis, these opioids were grouped together, whereas for others, trends in specific agents were individually explored. Common nonopioid therapies that are used to treat headaches were also identified and categorized based on the mechanism of action. Nonopioid alternative therapies included acetaminophen alone, antiemetic agents, butalbital preparations, intravenous (IV) fluids, nonsteroidal anti-inflammatory drugs (NSAIDs), and triptans. A single author (M.M.A.) who is board certified in emergency medicine and medical toxicology and is also a registered pharmacist performed all medication coding. A list of included medications is provided in a Supplemental Appendix.

The sample was restricted to visits involving patients 18 years of age or older. Additional patient demographic data analyzed included

65 years of age or older, sex, race, and source of payment (Medicare, Medicaid, self-pay, private, other). Hospital characteristics such as geographic region, location, and hospital type were also explored.

We tabulated the proportion of visits during which each of the drug classes and each of the 5 specific opioids was used (administered in the ED or prescribed at discharge). For the years 2005 through 2010, NHAMCS differentiated whether a particular medication was administered in the ED or prescribed at discharge. For this period, we performed a separate analysis to distinguish between medications given in the ED vs at discharge. In addition, we investigated the proportion of visits in which opioids were used in conjunction with another class of drug. Because of insufficient sample size in individual years, these analyses were conducted over the study period as a whole. To assess for trends over the study period, we conducted survey-weighted logistic regression analyses, including all years in the study period, with year as the independent variable. To assess the magnitude of absolute difference between 2001 and 2010, we calculated survey-weighted linear combinations of estimators. Both the absolute difference and relative percentage changes in prescribing between 2001 and 2010 for each subcategory were calculated using the tabulated proportions. A P < .05 was considered significant for assessing whether trends were significant in all analyses. The National Center for Health Statistics guidelines for analysis of these databases were adhered to, and only variables with 30 or more cases were included in analysis. All analyses were performed using Stata, version 12 (Stata Corp LP, College Station, TX).

#### 3. Results

#### 3.1. Trends in opioid vs nonopioid use

The estimated number of visits for acute headache increased from 5.5 million in 2001 to 7.7 million in 2010. The overall use of opioid analgesics increased from 20.6% (95% confidence interval [CI], 18.1-23.4) to 35.0% (95% CI, 31.8-38.4) (69.9%, P=.001) during the study period (Figure). There were no significant changes in the use of acetaminophen, butalbital products, or triptans. There was a modest increase in NSAID use from 26.2% (95% CI, 23.0-29.7) to 31.4% (95% CI, 28.6-34.3) (P=.019). There was a decrease in the use of antiemetic agents from 24.1% (95% CI, 19.6-29.2) to 23.5% (95% CI, 21.1-26.0) (P=.08). Administration of IV fluids increased significantly (Table 1).

#### 3.2. Demographics of opioid use

There were variable increases in opioid use across demographic groups. Opioid analgesic use increased in both men and women and across different racial groups. There was a larger relative increase in opioid use in visits involving black patients over the study period. Use rates for this population were lower at the beginning of the study period (16.7% for blacks in 2001 compared with 21.9% for nonblacks), but this was not significant (P = .06). Opioid use was most common in visits where patients had Medicaid insurance, but the largest relative increase was found in visits where Medicare was the primary insurance (Table 2).

#### 3.3. Provider and hospital-level factors

Opioid use increased among visits evaluated by attending physicians only as well as those involving residents. The percentage increase in opioid use by midlevel providers was smaller and did not reach statistical significance. There was an increase in use noted in both teaching and nonteaching hospitals, but there was a greater relative increase in teaching institutions. There were significant increases in opioid use in all geographic areas except the northeast region. Prescribing rates were overall highest in the west, and that region also experienced the largest proportional increase. Increased

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