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Researched Abuse, Diversion and Addiction-Related Surveillance System



First Quarter 2015 Technical Report

Comparative Rates of Mortality and Severe Medical Effect Among Commonly Prescribed Opioid Analgesics: Calls to US Poison Centers Reporting Opioid Overdose Due to Intentional Abuse and Misuse Exposures

Key Points:

1. The rising epidemic of prescription opioid overdose and mortality parallels the dispensing rates of prescription opioids, and the availability of increasingly potent opioid analgesics.
2. This report uses data from the RADARS[®] System Poison Center Program to compare the rate of Death or Major Medical Effect for commonly prescribed opioid analgesics due to abuse and misuse.
3. The rate of Death or Major Medical Effect varied substantially among opioid analgesics. A 28-fold difference was observed when comparing the analgesics with the highest and lowest rates.
4. After correcting for potency, a highly linear correlation was observed when comparing rates of outcome. Eighty-nine percent of the variation observed was due to morphine milligram equivalents (i.e. potency) alone.

Background

Misuse and abuse of prescription opioids in the U.S. has reached epidemic proportions. While prescription opioids are effective for pain management, several significant adverse associations exist including abuse, dependence, addiction, healthcare costs, overdose and death. In 2010, two million Americans used prescription analgesics for non-medical purposes for the first time (1). In 2011, there were 238 million prescriptions for opioid analgesics (2), of which hydrocodone- and oxycodone-containing products accounted for approximately 85% of opioid prescriptions dispensed in the U.S. (3). Increasing supply and consumption of opioid analgesics trends with a rise in mortality from prescription opioid overdose, which is now the leading cause of accidental death in most U.S. states (4). In addition to the increasing number of opioid analgesics prescribed, a 2015 NCHS Data Brief identified that the percentage of opioid analgesics stronger than morphine dispensed have doubled over the last decade (5).

Previous investigations have identified specific opioid analgesics known to cause substantial burden of death. These analgesics have been identified by their contribution to gross number of deaths (6) and population mortality rates (7). Existent epidemiologic data have shown a positive relationship with prescription opioid sales and opioid morbidity and mortality (8). While it is commonly presumed that increasing potency among opioid analgesics is linked to higher rates of adverse outcomes, this claim has not been substantiated in the literature.

Methods

Program & Statistical Analysis

Intentional abuse and misuse exposures were collected by the RADARS[®] System Poison Center Program from January 2010 through June 2014. Death and Major Medical Effect, classified according to AAPCC guidelines, were recorded for tablets containing six commonly prescribed opioid analgesics: oxycodone, hydrocodone, morphine, hydromorphone,

oxymorphone, and tramadol. Amount of drug dispensed nationally was obtained from IMS Health. **Inclusion criteria:** All cases regarding opioid prescription medication exposures resulting in Death and Major Medical Effect were included for analysis. Schedule II controlled substances were included for analysis given their high abuse potential and risk of severe psychological or physical dependence. Tramadol (schedule IV) was included to compare the less potent opioids with more potent opioids. **Exclusion criteria:** Moderate Medical Effect and less serious exposures were excluded from review. Fentanyl was excluded due to its primary parenteral route of administration. We restricted analysis to opioid exposure in single product exposure cases.

Primary outcome was defined as the rate of Death or Major Medical Effect. Outcome rate per 100,000 grams dispensed was regressed on morphine milligram equivalents (MME).

Results

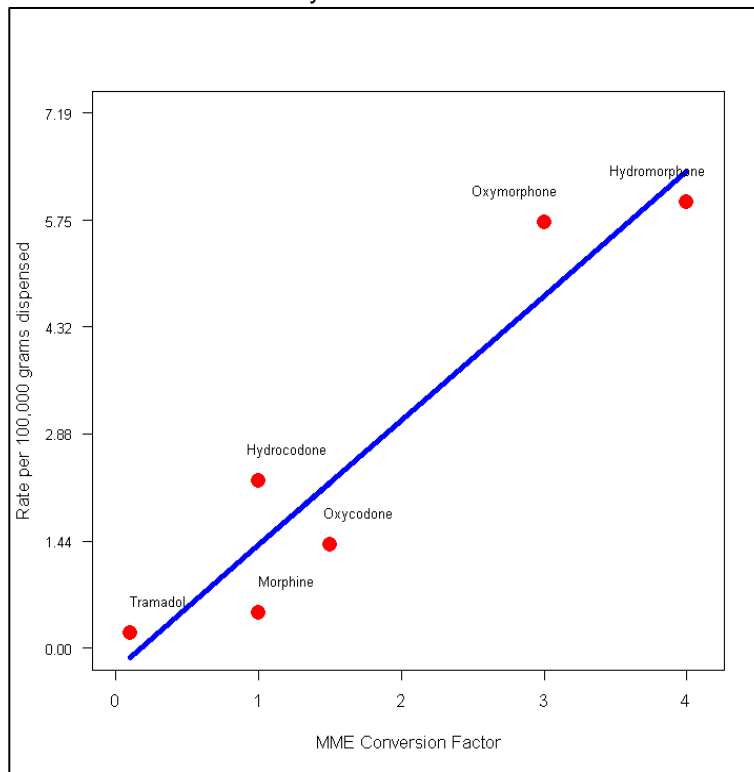
- We identified 11,380 cases; 95% of cases had a known medical outcome
- Among commonly prescribed opioid analgesics, the rate of Death or Major Medical Effect varied substantially. The top four offenders were hydromorphone, oxymorphone, hydrocodone, and oxycodone.
- A 28-fold difference was observed when comparing the analgesics with the highest rate of Death or Major Medical Effect (hydromorphone, 5.99/100kg dispensed) with the lowest (tramadol, 0.21/100kg dispensed).
- After correcting for potency, a highly linear correlation was observed when comparing rates of outcome, and 89% of the variation observed was due to MME alone. This observation was supported by additional sensitivity analyses.
- For each 1 unit change in MME, an increase of 1.7 cases of Death or Major Medical Effect are reported to Poison Centers per 100 kilograms drug dispensed ($p=0.004$).
- We evaluated the rate of outcome utilizing several denominators including number of prescriptions written, number of pills dispensed, number of milligrams of drug dispensed, and number of individuals filling prescriptions. Interestingly, the observed positively linear relationship for increasing potency and rate of outcome was found only for the total amount of drug dispensed.

Table

Rate of Death or Major Medical Effect Associated with Commonly Prescribed Opioid Analgesics
January 2010 to June 2014

Opioid Drug	Rate of Death or Major Medical Effect per 100,000 Grams	Rank Order	Number of Grams Dispensed to Cause one Death or Major Medical Effect (NNH)	Morphine Milligram Equivalents (MME)
Hydromorphone	5.99	1	16,686	4
Oxymorphone	5.73	2	17,450	3
Hydrocodone	2.25	3	44,506	1
Oxycodone	1.39	4	71,719	1.5
Morphine	0.48	5	208,398	1
Tramadol	0.21	6	486,700	0.1

Figure
Rate of Death or Major Medical Effect versus Opioid Potency
January 2010 to June 2014



Conclusions

Potency of prescription opioid analgesics demonstrates a significant, highly positive linear relationship with Death or Major Medical Effect of reported opioid exposures to U.S. Poison Centers. It is unknown whether the drug or the associated abuse behaviors ultimately cause death, but prescribers can select opioids with lower rates of associated major health outcomes. Such mindfulness when selecting opioid analgesics may contribute to decreasing severe adverse effects and mortality due to opioid overdose.

Suggested Citation

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References

1. Substance Abuse and Mental Health Services Administration, Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-41, HHS Publication No. (SMA) 11-4658. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2011.
2. Manchikanti L, Helm S, Fellows B, et al. Opioid epidemic in the United States. *Pain Physician*. 2012;15(3 Suppl):ES9-38.
3. Volkow ND, McLellan TA, Cotto JH, Karithanom M, Weiss SR. Characteristics of opioid prescriptions in 2009. *JAMA*. 2011;305(13):1299-301.
4. Holman JE, Stoddard GJ, Higgins TF. Rates of prescription opiate use before and after injury in patients with orthopaedic trauma and the risk factors for prolonged opiate use. *J Bone Joint Surg Am*. 2013;95(12):1075-80.
5. Frenk SM, Porter KS, Paulozzi LJ. Prescription opioid analgesic use among adults: United States, 1999-2012. *NCHS Data Brief*. 2015;(189):1-8.

6. Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. JAMA. 2008;300(22):2613-20.
7. Paulozzi LJ, Ryan GW. Opioid analgesics and rates of fatal drug poisoning in the United States. Am J Prev Med. 2006;31(6):506-11.
8. Fischer B, Jones W, Urbanoski K, Skinner R, Rehm J. Correlations between prescription opioid analgesic dispensing levels and related mortality and morbidity in Ontario, Canada, 2005-2011. Drug Alcohol Rev. 2014;33(1):19-26.

