



Clinical Potpourri

Opioid overdose leading to intensive care unit admission: Epidemiology and outcomes☆☆☆



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ABSTRACT

Purpose: There is a scarcity of studies assessing the patient population admitted to the intensive care unit (ICU) with opioid overdose. We sought to characterize the epidemiologic features and outcomes of this patient population.

Materials and methods: This is a retrospective cohort study of adult patients admitted to the ICU at University of Louisville Hospital for opioid overdose. We reviewed each patient's hospital record for demographic data, comorbidities, opioid used, coingestions, and outcomes.

Results: We included 178 adult patients, of which 107 (60%) were females. The median age was 41 years (interquartile range [IQR], 23). Oxycodone and hydrocodone were the 2 most commonly abused opioids. Benzodiazepines were the most common drug coingested, followed by amphetamines. Tobacco smoking, chronic pain, and alcoholism were the most frequent comorbidities identified. Mental disorders were also common. Most patients required invasive mechanical ventilation (84.8%). Median ICU length of stay was 3 days. Eighteen patients (10.1%) died in the hospital, whereas 6 patients (3.4%) were discharged to a nursing home. Patients who had any coingestion were significantly more likely to undergo invasive mechanical ventilation (91% vs 77%; $P = .014$) and had longer ICU length of stay (3 [IQR, 2] vs 2 [IQR, 1.8] days; $P = .024$).

Conclusion: Opioid overdose is a common cause of ICU admission and affects a relatively young population. Most have respiratory failure requiring mechanical ventilation. It is associated with a relatively high inhospital mortality. Coingestions appear to have an impact on outcomes.

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1. Introduction

Misuse of prescription and nonprescription opioids has been increasing since 2003. The increase in abuse of opioids runs parallel to prescribing practices that saw a marked increase in prescription opioids dispensed from 2002 to 2012. Over this same time frame, the rate of death from opioid analgesic and heroin poisonings has quadrupled. This epidemic cost the US health care system an estimated 9.6 billion dollars in 2005 [1–3]. Although legislative efforts have met with some initial success, the use of heroin has steadily increased since 2010, with the southwestern United States and Appalachia seeing the largest per capita increase in death rate from both prescription and illicit drug overdose [3–5].

Some European retrospective studies have attempted to determine prognostic factors in patients requiring stay in a medical intensive care unit (ICU) after opioid overdose. Median stays in the ICU ranged from 2 to 3.2 days, with 71% to 88% of patients requiring mechanical

ventilation. Mortality ranged from 2% to 14%, with variable causes including hypoxic brain injury, sepsis, and acute lung injury [6–8]. However, there is a scarcity of epidemiologic studies assessing this patient population in the United States. With this study, we sought to characterize the epidemiologic features and outcomes of patients with opioid overdose who are admitted to the ICU.

2. Materials and methods

2.1. Study design

We performed a retrospective cohort study that included patients from medical ICU at University of Louisville Hospital, an academic tertiary care center. Our protocol was reviewed and approved by our institutional review board, and informed consent was waived (IRB no. 14.0798).

2.2. Patients

We reviewed charts of patients admitted between 2011 and 2014. Patients were identified as candidates if opioid overdose was listed as

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a final diagnosis via the International Classification of Diseases codes at hospital discharge. This generated a cohort of 198 potential patients, the charts of whom were reviewed. Patients were included in the study if they had a positive test for opioid use by toxicology screening and/or a self-reported history of opioid misuse. We excluded patients if the opioid drug screen was negative. These criteria resulted in a final population of 178 patients.

2.3. Measurements

We reviewed each patient's hospital record for demographic data (age, race, sex, and medical history), laboratory results on admission, and the type of opioid used. Further analysis of our data included an evaluation of coingestion. *Coingestion* was defined as a study subject with a urine drug screen positive for opioids as well as one or more of the following: tricyclic antidepressants, benzodiazepines, amphetamines, acetone, methanol, or cocaine.

Outcome variables included need for mechanical ventilation, ICU and hospital length of stay, disposition at time of hospital discharge, re-admission within 30 days, and in-hospital mortality.

2.4. Statistical analysis

Continuous variables are reported as median and interquartile range (IQR). Categorical variables are reported as percentages. Statistical inference was conducted by 2 primary methods. Evaluation of associations between categorical data was performed using Pearson χ^2 test. When appropriate, Fisher exact test was used. To evaluate differences between 2 continuous variables, the Mann-Whitney *U* test was performed. All data were analyzed in R version 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria) [9]. For the purposes of our research, $P \leq .05$ was considered statistically significant.

3. Results

Our sample population consisted of 178 adult subjects, of which 107 (60%) were females. The median age was 41 years (IQR, 23). Tobacco smoking, chronic pain, and alcoholism were the most frequent comorbidities identified in the study population (48.2%, 44.6%, and 39.3%, respectively). Mental health comorbidities were also identified including depression, anxiety disorder, and bipolar disorder (28.9%, 14.8%, and 10.2%, respectively). For details of baseline characteristics, see Table 1. Table 2 shows the frequency with which specific opioids were abused, with oxycodone and hydrocodone being the 2 most common (31.4% and 27.5%, respectively).

Table 1
Baseline characteristics of the patients

Patient demographics	
Age, mean (\pm SD)	40 (14)
Female, n (%)	107 (60)
Ethnicity, n (%)	
White, n (%)	157 (88.2)
African American, n (%)	18 (10.1)
Hispanic, n (%)	1 (0.5)
Native American, n (%)	2 (1.12)
Comorbidities	
Smoking, n (%)	84 (48.27)
Chronic pain, n (%)	79 (44.63)
Alcoholism, n (%)	68 (39.3)
Depression, n (%)	51 (28.97)
Anxiety disorder, n (%)	26 (14.85)
Bipolar disorder, n (%)	18 (10.22)
PTSD, n (%)	6 (3.4)
HIV infection, n (%)	3 (1.74)
Schizophrenia, n (%)	3 (1.7)

PTSD indicates posttraumatic stress disorder.

Table 2
Most common opioids used per report

Opioid	n (%)
Oxycodone	60 (31.41)
Hydrocodone	52 (27.51)
Heroin	31 (16.23)
Methadone	31 (16.14)
Morphine	13 (6.91)
Fentanyl	9 (4.78)
Hydromorphone	3 (1.50)
Codeine	1 (0.52)

3.1. Coingestions

Coingestion occurred in 112 patients (62.9%). Benzodiazepines were the most common drug coingested followed by amphetamines. Table 3 gives details of coingestions detected on drug screen testing.

3.2. Outcomes

Most of our study population required invasive mechanical ventilation (84.8%). Median ICU length of stay was 3 days. Eighteen patients (10.1%) died in the hospital, whereas 6 patients (3.4%) were discharged to a nursing home. Of the 18 patients who died, 9 had a coingestion. Of those who died, 8 (44.4%) had acute respiratory distress per the Berlin definition [10], 15 (83.3%) had pneumonia or pneumonitis (defined as new lung infiltrates with hypoxia, fever, or purulent sputum), 9 (50%) had acute kidney failure by RIFLE criteria [11], 17 (94.4%) had multiple-organ dysfunction syndrome, and 9 (50%) had hypoxic brain injury.

Causes of death included hypoxic brain injury in 9 (50%), acute respiratory failure in 5 (27.7%), bowel infarction in 1 (5.6%), myocardial infarction in 1 (5.6%), circulatory shock in 1 (5.6%), and sepsis in 1 (5.6%).

Patients who had any coingestion were significantly more likely to undergo invasive mechanical ventilation (91% vs 77%; $P = .014$) and had longer ICU length of stay (3 [IQR, 2] vs 2 [IQR, 1.8] days; $P = .024$).

4. Discussion

Our study showed that invasive mechanical ventilation is required in a high proportion of patients with opioid overdose admitted to the ICU. Coingestion is frequent and appears to impact the outcomes. The overall mortality of 10% is substantial, especially considering the relatively young age of our study population.

The high prevalence of benzodiazepine use in self-poisoning has been reflected in similar studies [4,6,12]. A Centers for Disease Control and Prevention report shows a rise in the number of overdose deaths involving benzodiazepine consumption since 1999 [4]. Benzodiazepines were coingested in 27.5% of deaths in a study of opioid overdose deaths in San Francisco, California, between 2010 and 2012 [12].

The most common opioids reported in our patient population included oxycodone, hydrocodone, and heroin (31.14%, 27.51%, and 16.23%, respectively). Other opioids found less commonly in our study included morphine sulfate, fentanyl, hydromorphone, and codeine. These findings coincide with oxycodone and hydrocodone being prescribed at a higher rate than other opioids [13]. It is not surprising that the most commonly prescribed and, therefore, most available opioids are most frequently linked with abuse.

Our data are limited by our inability to determine whether most patients overdosed on prescribed or illicitly obtained medications. However, it has been previously published that natural and semisynthetic opioids (oxycodone, hydrocodone, and morphine) are more commonly abused than synthetic opioids (methadone and fentanyl) by both prescription and nonprescription users [4,14,15].

In our study, white females in their fifth decade were the most common patients to require ICU stays. This was unexpected as data show that men are more likely to visit emergency departments for opioid

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