Retrospective case series analysis of characteristics and trends in unintentional pharmaceutical drug poisoning by methadone, opioid analgesics, antidepressants and benzodiazepines in Clark County, NV 2009–13

Tamara Bruno, Jennifer R. Pharr

Department of Global and Environmental Health, School of Community Health Sciences, University of Nevada, Las Vegas, NV 89154, USA

Address correspondence to Jennifer R. Pharr, E-mail: jennifer.pharr@unlv.edu

ABSTRACT

Background  Poisoning has become the leading cause of injury death in the USA—with opioid analgesics involved in more fatal poisonings than any other drug, including cocaine and heroin. The epidemic of prescription drug poisonings is a public health concern. This study aimed to define potential high-risk groups for unintentional prescription drug poisoning by methadone, opioid analgesics, antidepressants or benzodiazepines.

Methods  A hospital-based retrospective case series analysis of admissions related to prescription drug poisonings associated with methadone, opioid analgesics, antidepressants or benzodiazepines for hospitals in Clark County, Nevada between 2009 and 2013 was employed.

Results  There were 7414 admissions with a primary diagnosis of an unintentional poisoning due to methadone, opioid analgesics, antidepressants or benzodiazepines. Women had the highest rate of admissions particularly in the 45–54 age group. Higher rates of admissions were also found among non-Hispanic whites, single and uninsured populations. There were concerning increases in admissions among 65+ and Native American/Alaskan Native subgroups in 2013. Benzodiazepines and opioid analgesics were the most prevalent drug categories for prescription drug poisoning admissions.

Conclusion  Public health professionals can utilize hospital data to identify populations at risk and in need of targeted interventions.

Keywords  emergency care, morbidity and mortality, public health

Introduction

Drug overdose has become the leading cause of injury death in the USA. In 2007, the US witnessed approximately 27 000 unintentional drug overdose deaths, equating to 1 every 19 min. In 2012, approximately 9 of every 10 poisonings were caused by drugs, and of those, opioid analgesics were involved in more fatal poisonings than any other drug, including cocaine and heroin. According to the Centers for Disease Control and Prevention (CDC), 46 people die every day from prescription painkillers.

In addition to an increase in prescription drug poisoning mortality, this epidemic is also associated with increased morbidity. A review of drug-related hospital emergency department (ED) data from 2004 to 2008, showed an estimated 111% increase in ED visits for nonmedical use of opioid analgesics during the study period and an 89% increase in visits associated

with nonmedical use of benzodiazepines. According to the CDC, for every unintentional opioid analgesic related overdose death, 9 persons are admitted for substance abuse treatment, 35 visit the ED, 161 report drug abuse or dependence and 461 report nonmedical uses of opioid analgesics. Beyond admissions to the ED or treatment facilities, prescription drug abuse and/or misuse is associated with an increased risk of HIV or Hepatitis B infection resulting from the transition from prescription to injection drugs. Increased falls and fractures are associated with prescription drug abuse and/or misuse in the elderly, and neonatal opioid withdraw syndrome is related to opioid use during pregnancy.
The trends in mortality and morbidity are highly correlated with both the increase in the medical use of pain analgesics and the trend in substance use and abuse among North-Americans. Prescription drug abuse has been the fastest growing drug problem in the USA in recent years, and is the second most commonly abused category of drugs, after marijuana. Between 1992 and 2003, a period that witnessed a 14% population increase, the number of people abusing controlled prescription drugs rose 81%, significantly more than the increase in the number of people abusing marijuana (2 times more), cocaine (5 times more) and heroin (60 times more). Although North-Americans only comprised 4.6% of the world population in 2008, the nation was consuming 80% of the global opioid supply, 99% of the world’s hydrocodone and two-thirds of illegal drugs globally. Hydrocodone became the most frequently prescribed drug in the USA and 120 million prescriptions for it were issued from 2005 to 2006. Eighty percent of North-Americans between the ages of 12 and 20 reported having used a controlled substance not prescribed to them, and every year since 2002, 2.5–2.8 million North-Americans abuse prescription drugs for the first time, outpacing all drugs except marijuana.

The epidemic of prescription drug abuse has great health, social and economic costs. Reducing the morbidity and mortality associated with prescription drug abuse is challenging because multiple factors contribute to the problem. Prescribing behaviors and the lack of education among providers and pharmacists along with inadequate counseling and monitoring of patients prescribed pain medication are important factors. Patients’ misuse or abuse, diversion and doctor shopping also contribute to the problem. Where they exist, prescription drug monitoring programs are underfunded and ineffective. Gilson and Kreis suggest that a better, more accurate understanding of prescription drug abuse/misuse is needed. Implementing strategies that target populations at greatest risk requires collaboration among local, state, federal and tribal health entities along with community partners. For development and implementation of effective interventions, further defining of populations at greatest risk is critical. This study aimed to contribute to the understanding of the problem by defining potential high-risk groups and identifying patterns of common drug use among unintentional drug overdose admissions for prescription drugs.

Methods

Study design

This study is a hospital-based retrospective case series analysis of hospital admissions related to prescription drug poisonings associated with methadone, opioid analgesics, antidepressants or benzodiazepines for hospitals in Clark County, Nevada between 2009 and 2013. Admissions were identified by analyzing discharge data obtained from the Center for Health Information Analysis (CHIA). CHIA receives data from hospital inpatient and outpatient (emergency) departments. CHIA data are compliant with the Health Insurance Portability and Accountability Act (HIPAA). Hospitals that provided data included 10 for-profit, 1 county and 4 non-profit hospitals. They cover the population within Clark County and are considered to be urban hospitals.

Research questions

This study attempted to answer three questions: (i) What were the trends in unintentional prescription drug poisoning by methadone, opioid analgesics, antidepressants and benzodiazepines admissions in Clark County, Nevada between 2009 and 2013? (ii) What were the demographic distributions of unintentional prescription drug poisoning by methadone, opioid analgesics, antidepressants and benzodiazepines? and (iii) What were the most common drugs, among the selected drug classes (methadone, opioid analgesics, antidepressants and benzodiazepines) related to unintentional prescription drug poisoning admissions?

Case selection—unintentional prescription drug poisoning case

All hospital admissions (inpatient and ED) related to unintentional prescription drug poisonings in Clark County, Nevada between 2009 and 2013 for methadone, opioid analgesics, antidepressants or benzodiazepines were identified. Cases were found by querying hospital discharge data for the appropriate International Classification of Diseases, Ninth Revision (ICD-9) diagnosis codes. Cases were included if the admission listed a primary diagnosis of drug poisoning by one of the four major drug categories of interest (methadone; opioid analgesics and related narcotics; antidepressants, sedative-hypnotics, tranquilizers; or benzodiazepine-based tranquilizers) and a Supplementary Classification of External Causes of Injury and Poisoning external cause of injury code (E-code) suggesting the poisoning was accidental. ICD-9 and E-codes used included:

<table>
<thead>
<tr>
<th>Drug category</th>
<th>ICD-9</th>
<th>E-code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid analgesics and related narcotics</td>
<td>965.03–09</td>
<td>E850 (0.1–0.2)</td>
</tr>
<tr>
<td>Methadone</td>
<td>965.02</td>
<td>E850.1</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>969.4</td>
<td>E853.2</td>
</tr>
<tr>
<td>Antidepressants, barbiturates, tranquilizers, other psychotropic agents</td>
<td>966, 967, 969, 970, 854 (0.0–0.2, 0.8), 855.0</td>
<td>(E851–E853)</td>
</tr>
</tbody>
</table>
Codes for opium (965.00) and heroin (965.01) were excluded from this analysis. Drug poisonings involving illicit drugs, non-opioid painkillers, and certain stimulants were not included. Also excluded were poisonings that listed excessive alcohol consumption as primary cause of injury even where E-codes indicating unintentional drug poisoning was present. The case selection methodology closely follows the recommendations suggested by the Safe States Injury Surveillance Workgroup’s Consensus Recommendations for National and State Poisoning Surveillance.23

Statistical analysis
Statistical methods were primarily descriptive. Demographic characteristics of age, gender, race/ethnicity, marital status and insurance type were analyzed. Age and gender-specific rates were calculated using county-level population estimates from the American Community Survey (ACS) for the corresponding study year. The overall and gender-specific rates were calculated as a weighted number of discharges per 100,000 population in each age grouping. Ages were grouped as follows: 18–24, 25–34, 35–44, 45–54, 55–64 and 65 and older. Additionally, race/ethnic group, marital status and insurance type (insured and uninsured) specific rates were calculated per 100,000 population. ACS only began providing county level data by insurance type (e.g. private, Medicaid, Medicare, VA) in 2013. We did have ACS data for the Clark County population with and without health insurance, so we compared insured versus uninsured admission rates per 100,000. Hospital admission rates for unintentional prescription drug poisonings were calculated for ED and inpatient admissions per 100,000 hospital admissions. Counts and percentages were tabulated to determine significant differences in these rates. Counts and percentages were tabulated to determine significant differences in these rates. Counts and percentages were tabulated to determine significant differences in these rates.

Characteristics of the sample
Characteristics of persons admitted for an unintentional prescription drug poisoning by methadone, opioid analgesics, antidepressants and benzodiazepines are described in Table 1.

Gender
During the study period, significantly more women were admitted than men (P < 0.01). In each year of the study women represented over half of all admissions (Table 1). The average overall admissions rate for the 5-year study period among females was 85.23 per 100,000 compared with 65.37 per 100,000 males with women having higher rates for each age group except 18–24 (Fig. 2A and B).

Race
The highest rate of admissions occurred among persons 45–54 years old, particularly among women (Fig. 2A and B). Women age 55–64 also showed an upward trend during the study period. Rates among the youngest age group (18–24) were highest in 2009 with a decrease in 2012 and 2013. Admission rates increased among persons aged 65 and older. The difference in admissions between men and women was most substantial in the 45- to 54-year old age group.

Marital status
A significant difference was found in the marital status of those admitted during the time period (P < 0.01). Non-Hispanic whites accounted for the largest percentage (5 years average >75.1%; range 71.1–77.7%) and highest rates of drug-poisoning admissions (Table 1, Fig. 2C). A significant rate increase was observed among Native American/Alaskan Native subgroup where rates increased sharply between 2012 and 2013 from 13 to 120 per 100,000 population (Fig. 2C).

Insurance type
There was a significant difference in the insurance type of those admitted (P < 0.01). Uninsured was the most frequent...
payer type associated with drug poisoning admissions. Medicare and Medicaid were also common and combined these public payer types comprised 35.4% (2579 admissions) of all admissions. Private insurance payers accounted for 23.7% (1728 admissions) of admissions (Table 1). Rates of admissions were higher for the uninsured versus the insured (Fig. 1B).

**Types and common drugs associated with prescription drug poisonings**

Benzodiazepines and opioids were the most prevalent drug categories listed during the study period (Fig. 3C). Benzodiazepines were involved in 49% of all admissions and listed as the primary diagnosis category in 45% of admissions. Opioids and other related narcotics were the second most common drug type, listed as a primary diagnosis in 29% of all admissions. Women had higher rates of poisonings associated with benzodiazepines, antidepressants and opioids admissions (Fig. 3A and B). Drug poisoning rates by methadone were very low among both genders and all age groups, particularly the 65 and older group. Benzodiazepines poisonings were high among women aged 35–44 and 45–54 years.

Multiple drugs were listed in 25% of all inpatient admissions versus 20% of ED admissions and in 22% of all admissions. The most common drug combination found was an antidepressant and a benzodiazepine.
Main finding of this study
Women had a higher representation in the drug poisoning counts, percentages and rates in every year of this analysis. Additionally, women had higher rates of drug poisoning attributed to a benzodiazepine. Persons aged 45–54 years had higher rates of drug poisoning with an increase in admissions among people 65 and older during the study period. The non-Hispanic white and black populations, single people and the uninsured also had the high rates of hospital admissions for unintentional prescription drug poisoning. Benzodiazepines were the drugs most often involved.

What is already known on this topic
Other studies have demonstrated a differential risk for women. Coben et al. found that in comparison to patients hospitalized for poisoning from other substances, those hospitalized for prescription opioids, sedatives and tranquilizers were more likely to be women, aged >34 years.24 The prominent involvement of benzodiazepines in drug poisonings may contribute to the differential risk for women. These differences may be due to prescribing practices among providers, higher rates of chronic pain among women (e.g. fibromyalgia) or more anxiety or insomnia among women.25–29

Results of this study are consistent with the national pattern of drug poisoning among different age groups, particularly older adults.30 This may be related to the prevalence of chronic long-term opioid use.31 Currently, more than 3% of the US adults receive long-term opioid therapy for chronic non-cancer pain and patients that are on long-term regimens tend to take higher doses which puts them at greater risk.21 This may also contribute to the increasing incidence among people in the age of 65 and older, a group with more complex medical conditions that are often treated with narcotic pain medication.

What this study adds
The majority of unintentional prescription drug poisoning studies examine overdose death rather than hospital admissions. This study helps to answer the important question about ‘who’ is being treated for unintentional prescription drug overdose.

When examining the increased incidence in unintentional prescription drug poisoning among the 65+ age group, it is important to note that persons in this age group were more frequently admitted to the hospital, whereas the other age groups are more frequently seen in the ED only. This may be because older populations have more complex underlying medical conditions which may complicate the clinical course of a drug-poisoning event.

With regard to race, Native Americans exhibited the most dramatic increase in drug poisoning rates. The CDC also reported that age-adjusted death rates in 2010 were highest among this group.4 Although numbers of drug poisoning admissions are relatively low among Native Americans, these findings suggest a potentially emerging problem in this population that warrants further study.

Some studies have suggested an emerging problem of drug poisonings associated with methadone, an opioid traditionally used in the treatment of heroin abuse. A study conducted by the CDC of prescription overdose deaths in Washington from 2004 to 2007 demonstrated increased risk of overdose from methadone within the Medicaid population.32 The findings of this study did not support this. Methadone poisonings represented only 3.4% of drug poisoning in the Medicaid population and 3–4% of the overall admissions each year. However, since the national data suggest that methadone is being increasingly used in the treatment of chronic pain because it is relatively cheap, it has been observed to play a prominent role in overdose mortality. Further observation of the trend is recommended.

Our study showed higher rates of drug poisonings among uninsured persons. This may indicate that this population is acquiring prescription drugs through nonmedical distribution channels or diversion. Studies have shown that most (60%) people who use prescription drugs non-medically obtain them from a friend or family member to whom they were prescribed.33 A prescription pain medication is prescribed to one in every five North-Americans each day—enough medication to dose every adult American for one month.19 The increase in prescriptions and sales has led to an increase in accessibility and possible diversion. A study by Hall and colleagues found that 63% of prescription drug overdose was associated with
drug diversion. Our study suggests diversion may be a possible factor in the drug poisoning epidemic in Clark County, which warrants further investigation.

Limitations
It is possible that some of our findings were an artifact of a small sample size. For example, the rate increase observed among Native Americans may be due to the relatively small population size. The case selection method was dependent on the accurate coding by medical personnel at the reporting hospitals. It is possible that cases were missed due to provider bias in diagnosing and/or coding errors. There were 169 ICD-9 Codes which indicated drug poisoning which were missing E-codes and as such were excluded from our analysis.

Another limitation associated with coding of drug poisonings is that the codes are not specific enough to determine which drug was contributory in each category. Future studies should examine the possibilities of selecting for codes that indicate the specific drug type involved in the poisoning. We do not have data about the number of people living in Clark County who are using prescription drugs in general or about
the increase in prescription drug use in Clark County over the study period to control for cohort effects in this study. We used American Community Survey data to calculate rates for each year which are less precise that census data and have their own inherent limitations.35

**Conclusion**

The findings of this study provide information to suggest that interventions should be targeted at several demographic groups. Non-Hispanic whites and blacks, women age 45–54 and 55–64, single and uninsured groups prescribed benzodiazepines, antidepressants and opioid analgesics could benefit from risk reduction programs including education, substance abuse treatment and monitoring. Education about the risk associated with benzodiazepines for patients and health professional as well as monitoring programs are recommended as this category was associated with the most admission, particularly among women.

Studies like this should be replicated to further define the population at risk in order to develop strategies to reduce the associated morbidity and mortality burden of unintentional prescription drug poisoning. Public health professionals can utilize hospital data to identify populations at risk and in need of targeted interventions.

**Funding**

The project described was supported by a grant from the National Institute of General Medical Sciences (5 U54 GM104944).

**Conflict of interest**

None declared.
References


