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Clinical paper

Regional incidence and outcome of out-of-hospital cardiac arrest associated with overdose☆

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ABSTRACT

Background: The frequency of lethal overdose due to prescription and non-prescription drugs is increasing in North America. The aim of this study was to estimate overall and regional variation in incidence and outcomes of out-of-hospital cardiac arrest due to overdose across North America.
Methods: We conducted a retrospective cohort study using case data for the period 2006–2010 from the Resuscitation Outcomes Consortium, a clinical research network with 10 regional clinical centers in United States and Canada. Cases of out-of-hospital cardiac arrest due to drug overdose were identified through review of data derived from prehospital clinical records. We calculated incidence of out-of-hospital cardiac arrest due to overdose per 100,000 person-years and proportion of the same among all out-of-hospital cardiac arrests. We analyzed the association between overdose cardiac arrest etiology and resuscitation outcomes.
Results: Included were 56,272 cases, of which 1351 were due to overdose. Regional incidence of out-of-hospital cardiac arrest due to overdose varied between 0.5 and 2.7 per 100,000 person years ($p < 0.001$), and proportion of the same among all treated out-of-hospital cardiac arrests ranged from 0.8% to 4.0%. Overdose cases were younger, less likely to be witnessed, and less likely to present with a shockable rhythm. Compared to non-overdose, overdose was directly associated with return of spontaneous circulation (OR: 1.55; 95% CI: 1.35–1.78) and survival (OR: 2.14; 95% CI: 1.72–2.65).
Conclusions: Overdose made up 2.4% of all out-of-hospital cardiac arrest, although incidence varied up to 5-fold across regions. Overdose cases were more likely to survive than non-overdose cases.

Introduction

Out-of-hospital cardiac arrest (OHCA) is the common endpoint of many pathological processes. In the resuscitation literature, the etiology of OHCA is often dichotomized into OHCA of presumed cardiac origin and those of non-cardiac origin. This dichotomy largely corresponds to major differences in treatment strategies, with many focusing on the reversal of conditions that prevent an otherwise sound heart from functioning. One such condition is OHCA resulting from drug overdose (OD-OHCA).

Drug overdose is currently a major public health problem in the United States and Canada. According to the most recent statistics, in the United States the cause specific mortality rate for drug overdose in 2013 was approximately 9.5 per 100,000.[1] This estimate accounts for intentional and unintentional events, as well as legal and illegally obtained drugs. OD in the prehospital environment may frequently present to EMS as OD-OHCA, although the epidemiology of OD-OHCA – as opposed to drug-related mortality – is limited. Previous studies have described incidence and characteristics of OD-OHCA and its subsequent resuscitation.[2–7] A broad geographic analysis of OD-OHCA has not been conducted. Additionally, as OD continues to grow as a public health problem, the treatment of OD-OHCA may become more frequent and

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evidence-based treatment guidelines will be essential. Current advanced cardiac life support (ACLS) guidelines from the American Heart Association do not differ appreciably between the resuscitation of OD-OHCA and non-OD-OHCA.[8] However, previous studies suggest that real world ACLS care is different for OD-OHCA.[7,9]

We investigated regional variation in incidence, outcomes and characteristics of OD-OHCA in a large population-based cohort of OHCA across North America representing a population of 19.5 million. We further sought to determine whether previous observed differences in treatment of OD-OHCA reflect general phenomena throughout the US and Canada.

Methods

This study was conducted with de-identified data obtained from the Resuscitation Outcomes Consortium (ROC) through the cooperation of the University of Washington Clinical Trials Center (ROC Data Coordinating Center (DCC)). The structure, surveillance methodology, and participants of the ROC have been reported elsewhere.[10] In brief, the ROC is a clinical research consortium with 10 sites in the United States and Canada. The ROC conducts population-level regional OHCA surveillance, as well as clinical trials for the prehospital treatment of OHCA and major trauma. All non-traumatic cases of OHCA treated by emergency medical services (EMS) in 10 sites of the ROC in the time period spanning 2006–2010 were included in this analysis. Sites included Birmingham, Alabama; Dallas, Texas; Milwaukee, Wisconsin; Ottawa, Ontario; Pittsburgh, Pennsylvania; Portland, Oregon; San Diego, California; Seattle (King County), Washington; Toronto, Ontario; and Vancouver, British Columbia. Data from later than 2010 were not available due to clinical trial-related data availability limitations. For perspective, while this capture period includes the ROC-PRIMED clinical trial,[11] it excludes the currently on-going CCC and ALPS studies whose methodology have been published.[12–13]

Cases of OD-OHCA were identified through case record review by local data abstractors. These individuals had access to electronic and written prehospital patient care reports produced by emergency medical technicians and paramedics, digital defibrillator download files, and limited in-hospital records. Sufficient evidence of OD-OHCA necessitated explicit indication of the acute use of drugs at the time of the OHCA; case definition rules for OD required near certainty of case status. Examples of positively identifying circumstances included: in-hospital clinical notes indicating a positive toxicological screen, prehospital administration of naloxone (an opioid reversal agent), and paramedic notes explicitly stating that the patient had overdosed. Not all of these conditions were ascertainable for all cases due to differential case data availability throughout the study period. For example, prehospital naloxone administration was only collected globally throughout the ROC until 2009. Examples of insufficient identifying circumstances for OD-OHCA included: presence of drug paraphernalia at the scene of the OHCA, prior history of drug use, and patient characteristics suggesting drug overdose (e.g. young, asystolic patient).

The structure of the ROC necessitated a specialized incidence calculation methodology. Incidence of OD-OHCA was calculated by accounting for individual EMS agencies' participation in the ROC, ROC PRIMED trial, and associated surveillance activities. The service area of each EMS agency was used to approximate a service population from census data. For US agencies, 2000 US Census data was used, while Statistics Canada 2006 was used for Canadian agencies. Total person-years for each agency's service area were calculated by multiplying its participation period by its approximate service population. Incidence of OHCA and OD-OHCA were then calculated at the site level by dividing the number of events in each site by the accumulated person time of all of its participating agencies between 2006 and 2010. Incidence was reported per 100,000 person-years for ROC overall and by anonymized site ID.

The total catchment area of the participating ROC sites encompassed 35,331 square miles with an estimated combined population of 19.5 million. Underlying rates, outcomes and characteristics of all-cause OHCA throughout the participating areas have been described previously.[14] Environments include a mix of urban, suburban and rural settings, and EMS agencies included both basic and advanced life support capabilities.

Key covariates

The ability to assess individual patient characteristics was limited by the design of the underlying (or parent) OHCA surveillance system. Patient age, sex and presenting electrocardiogram (ECG) rhythm were the only universally available patient specific characteristics. Other factors of interest such as race, body-mass index, current medications and medical history were often not available. Presenting ECG rhythm was categorized as ventricular fibrillation/ventricular tachycardia (VF/VT), shockable by automated external defibrillator (AED), pulseless electrical activity (PEA), asystole, and no shock advised by an AED. However, numerous resuscitation characteristics were available, including event timing, witness status, cardiopulmonary resuscitation (CPR) quality characteristics, advanced airway placement, defibrillation, and administration of drugs. Available resuscitation drug variables included epinephrine, sodium bicarbonate, and atropine. Total medication dosage was available for epinephrine was reported in milligrams.

The earliest available CPR quality parameters for up to 20 min of CPR were compared between patients with and without OD-OHCA. The ROC captures chest compression rate (CCR), chest compression fraction (CCF), and depth when sufficient data streams are available in digital defibrillator files. Unfortunately, chest compression depth requires specialized hardware, which not all EMS agencies currently deploy. Therefore, we were only able to compare cases on the basis of CCR and CCF, which are nearly universally calculable with standard prehospital equipment.

Outcome measures

Three primary outcomes were ascertained in order to understand the effect of OD-OHCA case status on patient prognosis: return of spontaneous circulation (ROSC), survival to emergency department (ED), and survival to hospital discharge. ROSC was defined as the return of pulses at any time during the course of prehospital treatment, as indicated by prehospital patient care reports or digital defibrillator data. Survival to ED was defined as the patient attaining ROSC and maintaining ROSC for any duration until arrival at the ED. Survival to hospital discharge was defined as post-resuscitation discharge or transfer from the receiving hospital alive regardless of neurologic status.

Data management and quality assurance

Basic data quality was supported by ROC site-level and central quality assurance measures. Each ROC site conforms to uniform ROC data collection forms and procedures, but implements its own quality assurance procedures. These may, for instance, include re-review of randomly selected cases or prescreening of abstracted data for erroneous outlying values. The ROC DCC conducts internal quality control through self-checking electronic data entry forms, as well as through periodic random review of case data from regional sites.