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Clinical Paper

Recreational drug overdose-related cardiac arrests: Break on through to the other side☆

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ABSTRACT

Introduction: The annual rate of recreational overdose (OD)-related death is increasing exponentially, making unintentional overdose the leading cause of injury-related death in America. Unfortunately, little attention in the resuscitation community has focused on the post-arrest care of this rapidly growing population.

Methods: We included patients presenting between January 2009 and February 2014 after out-of-hospital cardiac arrest (OHCA) and abstracted baseline clinical characteristics and neurological outcomes. We considered an arrest to be an OD OHCA if toxicology screens were positive and not explained by therapeutic medication administration or home medications; or if there was a history strongly suggestive of OD. We compared the baseline clinical characteristics and outcomes between the OD and non-OD cohorts.

Results: In total, 591 OHCA patients were admitted, of which 85 (14%) arrests were OD-related. OD OHCA patients were significantly younger, had fewer medical comorbidities, were more likely to present with non-shockable rhythms and had worse baseline neurological function. However, overall survival, neurological outcomes and length of stay did not vary between groups. OD OHCA patients who survived to discharge had a significantly higher rate of favorable discharge dispositions (83% of OD OHCA survivors discharged to home or acute rehabilitation vs 62% of non-OD OHCA ($P = 0.03$)).

Conclusion: Patients who have suffered an OD OHCA make up a significant proportion of the overall OHCA population. Despite poor baseline prognostic factors, survival after OD OHCA was no worse than after non-OD OHCA, and among survivors a majority had a good neurological outcome.

1. Introduction

Recently, considerable media and public health attention has focused on what has been termed an "epidemic" of unintentional recreational drug overdose-related deaths in the United States.[1–3] The annualized rate of overdose-related death is increasing exponentially, making unintentional overdose the leading cause of injury-related death in America.[3] Respiratory depression leading to asphyxial cardiac arrest is the final common pathway of a majority of these deaths, especially after overdoses of opioids and/or sedative-hypnotic agents such as benzodiazepines. Indeed, drug overdoses make up between 2 and 29.4% of out-of-hospital cardiac arrests (OHCA), and are particularly common in young adults.[4–7]

Despite its public health significance, little attention in the resuscitation community has focused on the post-arrest management of this rapidly growing population. In the pre-hospital setting, physicians and emergency medical service (EMS) providers perceive and manage overdose-related OHCA due to common drugs of abuse (OD OHCA) differently than other arrest etiologies, despite the absence of evidence or consensus recommendations.[5,8] However, to our knowledge, no studies have specifically examined the cohort of OD OHCA patients that are resuscitated and survive to hospital admission.

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We describe the clinical characteristics and outcomes of patients successfully resuscitated from OD OHCA who survived to hospital admission. We hypothesized that this population would be demographically distinct from patients admitted after non-OD OHCA, and that patient outcomes would differ between these groups.

2. Methods

UPMC Presbyterian Hospital is a 795-bed tertiary care referral center. Since 2007, a unique Post-Cardiac Arrest Service (PCAS) has standardized care for the more than 200 patients annually who are successfully resuscitated and admitted after cardiac arrest, and maintains a prospective database including all patients.[9] The present study is a retrospective, observational cohort study including patients who presented between January 1, 2009 and February 12, 2014 after OHCA. We excluded patients for age under 18 years, in-hospital cardiac arrest, or uncertain location of arrest. We further excluded patients OHCA secondary to blunt or penetrating trauma, stroke or subarachnoid hemorrhage. The University of Pittsburgh Institutional Review Board deemed review of the database to be exempt from need for informed consent.

Our primary exposure of interest was OD OHCA in which the overdose was related to commonly abused drugs. We performed a structured chart review of all emergency department (ED) and inpatient admission notes, electronic medication administration record, and EMS trip sheets. We recorded the results of all serum and urine toxicology screens, ED or EMS administration of opiates and benzodiazepines, and historical details indicative of OD OHCA (i.e. found with drug paraphernalia or witnessed overdose). We considered an arrest to be overdose-related if toxicology screens were positive and not explained by therapeutic medication administration prior to sampling or home medication history; or if there was a documented history strongly suggestive of overdose. We did not consider arrests to be overdose-related when the only positive toxicology results were cannabis and/or ethanol, or if there was a clearly defined alternative etiology (e.g. strangulation or witnessed arrest during outpatient hemodialysis).

We abstracted baseline clinical characteristics from our registry, including age, sex, initial arrest rhythm (ventricular tachycardia/fibrillation (VT/VF), pulseless electrical activity (PEA), asystole, or unknown), bystander-administered cardiopulmonary resuscitation (CPR), Charlson Comorbidity Index, initial Glasgow Coma Scale score (GCS), use of mild therapeutic hypothermia, cardiac catheterization, and Pittsburgh Cardiac Arrest Category (PCAC). The PCAC is a validated clinical prediction tool that stratifies CA survivors by their risk of subsequent death or neurological deterioration based on clinical characteristics during the first 6 h after ROSC.[10] The tool stratifies survivors of CA into four categories that are strongly predictive of survival and functional outcome. In the subgroup of patients for whom the results of continuous electroencephalography (EEG) monitoring were available from previous work, we abstracted the presence (yes/no) of a suppression-burst pattern, generalized periodic epileptiform discharges, myoclonic status epilepticus, nonconvulsive status epilepticus, and reactivity in the first 72 h of monitoring.[11]

We also abstracted patient outcomes from our registry, including survival to hospital discharge, hospital length of stay, Cerebral Performance Category at hospital discharge, favorable discharge disposition (home or acute rehabilitation), and mode of death (brain death; withdrawal for poor anticipated neurological prognosis; re-arrest or refractory hemodynamic instability; or withdrawal based on surrogate representation of the patient's goals of care). We included multiple measures of outcome as they measure different components of recovery.[12]

We used descriptive statistics to summarize baseline characteristics and outcomes, and report means with standard deviations for continuous variables and numbers with corresponding percentages for categorical variables. We used *t*-tests or Chi-Square tests as appropriate to compare the cohort of OD OHCA patients to the cohort of non-OD OHCA. Finally, we constructed an adjusted logistic regression model to test for an independent association of OD OHCA with survival after controlling for potential confounders. We forced OD OHCA into the model, and included other predictors with an unadjusted association with overdose status. We excluded GCS from this model because it is collinear with PCAC. We used Stata Version 13.1 (StataCorp, College Station, TX) for all analyses.

3. Results

A total of 591 OHCA patients were admitted during the study period. There were 183 subjects with positive toxicology screens. Of these, 50 had received opioids or benzodiazepines by emergency providers prior to the toxicology screen, 15 had insufficient prehospital documentation to determine if opioids or benzodiazepines had been administered, 17 toxicology screens were positive only for ethanol or cannabis, and 16 had a clearly defined non-toxicologic etiology of arrest. Thus, 85 (14%) arrests were deemed to be recreational drug overdose-related. OD OHCA patients were significantly younger, had fewer medical comorbidities, were more likely to present with non-shockable rhythms, had worse baseline GCS and PCAC scores, and were less likely to undergo cardiac catheterization (Table 1). The most common agents identified on toxicology screens were opiates and benzodiazepines (Table 2), and the median number of positive results in the OD OHCA subgroup was 2 (interquartile range 1–3). Coingestion of opiates and benzodiazepines was common (35 patients (41%) of all overdoses). Only two patients (2%) in the OD OHCA cohort had isolated stimulant (cocaine and/or amphetamine) intoxication, while the remainder had toxicology screens that were also positive for benzodiazepines and/or opioids. Among OD OHCA patients, 40 (47%) received naloxone and naloxone use was not associated with survival ($P = 0.54$).

Continuous electroencephalographic data were available for 241 patients (33 overdose-related (39%) and 208 non-overdose (41%)). There was no difference in the incidence of various patterns between groups (Table 3). Overall survival, neurological outcome and length of stay did not vary between groups (Table 4), and OD OHCA was not independently associated with mortality in adjusted analysis (Table 5). However, OD OHCA patients who survived to discharge had a significantly higher rate of favorable discharge dispositions (83% of OD OHCA survivors discharged to home or acute rehabilitation vs 62% of non-OD OHCA ($P = 0.03$). Among those who did not survive to discharge, brain death accounted for 34% of deaths in the OD OHCA cohort compared to 12% in the non-OD OHCA cohort ($P = 0.002$).

4. Discussion

We report the demographics and outcomes of patients admitted after OD OHCA. Consistent with previous reports, OD OHCA was common, comprising 14% of our total OHCA population.[4–7] Importantly, despite a higher incidence of non-shockable arrest rhythm and deeper coma on presentation, survival after OD OHCA was no worse than after non-OD OHCA. Moreover, among survivors, 83% were discharged to home or acute rehabilitation. This suggests that despite the high incidence of poor baseline prognostic features after return of spontaneous circulation (ROSC), OD OHCA patients may have excellent neurological recoveries and warrant aggressive neurocritical care. Some patients required initial specialized toxicologic interventions such as antidotal therapy, treatment of sodium channel blockade and recurrent ventricular dysrhythmia, or seizures/agitation. However, the mainstay of