

RESEARCH ARTICLE



## Clinical and epidemiological characteristics of patients with acute drug intoxication admitted to ICU

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### ABSTRACT

**Background:** Drug overdose continues to be the most common cause of acute poisoning worldwide. There has been a substantial increase in drug overdose incidence and prevalence over the past decade, probably as a result of the emergence of new synthetic designer drugs. The purpose of this study is to describe the clinical and epidemiological characteristics of patients with acute drug intoxication admitted to the Intensive Care Unit (ICU).

**Methods:** A single center, prospective, observational study was conducted among all adult patients with clinical signs suggestive of acute drug intoxication admitted from the Emergency Department (ED) to ICU during a 6-month period (September to March).

**Results:** Sixty-five patients were admitted. Their median age was 49 years (mean 48.2, range 20–72), and the majority were male (48, 74%). Median Sequential Organ Failure Assessment (SOFA) score on admission to ICU was 6 (mean 6, range 0–13). Fifty-five patients (85%) had a positive urine and/or serum toxicology screen. Most commonly detected substances were: opiates (18, 33%), cocaine (13, 24%), methadone (12, 22%), benzodiazepines (10, 18%), and marijuana (9, 16%). In 16 patients (29%), >1 substance was isolated. Twenty-three patients (35%) had negative urine toxicology screen. Ethyl alcohol was detected in the serum of 23 patients (35%). Five patients (8%) expired in ICU.

**Conclusion:** Classic recreational drugs remain the most common substances involved in acute drug poisoning. More sensitive detection methods are warranted to identify new designer drugs of abuse such as synthetic cannabinoids.

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## 1. Introduction

Drug use and abuse continue to be a large public health concern worldwide. Over the past decade, novel or atypical psychoactive substances have emerged and become increasingly popular with a concomitant increment in reports to poison control centers and ED visits. Until recently, drug overdose was seen as a substance abuse or law enforcement problem and not as a public health issue. Although drug overdose-related deaths attract much public attention, there are substantial consequences of non-fatal overdoses including cardiac and musculoskeletal problems, aspiration pneumonia, cognitive impairment and hypoxic brain injury, renal dysfunction, and physical injuries sustained during the intoxication event. Unintentional overdose deaths are rarely instantaneous and drug users rarely overdose alone. As such, for the most part, overdose-related deaths are potentially avoidable [1]. Nevertheless, the annualized rate of drug overdose-associated deaths is increasing exponentially, making unintentional overdose the leading cause of injury-related death in USA [2]. Critical Care and Emergency Medicine

physicians are confronted with intoxicated patients on a routine basis, with clinical scenarios including known drug overdose, unknown illicit drug intoxication, suicidal attempts, and accidental exposures. Since the protean manifestations of acute drug poisoning are challenging, a high index of suspicion for intoxication is warranted in the practice of critical care medicine. In New York City (NYC), unintentional drug poisoning is the third leading cause of premature death, with opioids being the most commonly associated class of drugs [3]. Polysubstance intoxication is associated with a higher risk of death from overdose. According to the NYC Department of Health and Mental Hygiene (NYCDOHMH), about 98% of overdose-related deaths that occur in the city involve >1 substance [4]. In April 2015, the NYCDOHMH issued an alert about the increase in synthetic cannabinoids-related adverse events and ED visits. Precise assessment of their incidence is difficult to calculate due to the lack of widely available and rapid laboratory confirmation, the large variety of synthetic cannabinoids compounds, and the unknown number of exposed individuals.

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Nevertheless, classical recreational drugs such as heroin, cocaine, cannabis, ethyl alcohol, and benzodiazepines remain the most common substances associated with acute drug intoxication requiring emergency medical attention [5–9].

Health care costs resulting from overdose treatment are also increasing substantially. From 1999 to 2008, hospitalization rates for overdose in USA increased by 55%, costing about US\$737 million in 2008 [10]. Patients with acute drug intoxication represent 0.6–2.1% of all ED visits [11,12], and account for 3–14% of total Intensive Care Unit (ICU) admissions [13–16]. In the Western hemisphere, both ICU and in-hospital mortality of patients with acute drug intoxication are significantly lower than that of the general ICU population, at 0.2–4% [16,17]. The treatment and complications of patients with acute drug intoxication in ICU vary according to the nature of the substance ingested, individual amount of drug, and the concomitant use of other substances. The interventions requiring critical care in acute drug-poisoned patients include the need for airways protection and mechanical ventilation, hemodynamic stabilization and needs for vasopressors, and specific procedures that would enhance the clearance of the toxins involved. The clinical challenge is to safely treat patients who have ingested unknown substances, which should be achieved by identifying the toxidrome on presentation to ED. The paucity of analytical confirmation of hazardous substances may prevent clinicians from effectively managing these patients. The main objective of this study is to describe the clinical and epidemiological characteristics of patients with acute drug intoxication admitted to ICU.

## 2. Materials and methods

### 2.1. Study design and patient population

This study has a prospective, observational design. It was conducted in a general, community inner-city hospital located in Northern Brooklyn, New York, which provides health care to a population mainly composed of immigrant, low-income, and homeless individuals. The ICU works under a closed system, with the supervision of five board-certified intensivists who deliver 16 hours per day in-house coverage that includes weekends and holidays (8am–12am). It is composed of 12 beds, with an annual admission average of 600 patients. In addition, the hospital has a 12-bed Step-Down Unit (SDU) which is also supervised by the critical care medicine (CCM) service. The ED at our institution ranks among the busiest in NYC, with more than 120,000 visits per year.

All consecutive patients, 18 years or older, admitted to ICU with the possible diagnosis of

acute drug intoxication were enrolled in the study. The study period comprised the months between September 2015 and February 2016. Variables such as age, gender, reason for intoxication (recreational, suicidal, accidental), previous history of psychiatric disorder or substance abuse, Sequential Organ Failure Assessment (SOFA) score on admission to ICU, needs for mechanical ventilation and/or vasopressors therapy, urine and serum toxicology screen results, remarkable laboratory and clinical findings on arrival to ED, day of the week of admission to ICU, ICU length-of-stay (LOS), and outcome at ICU discharge were monitored. Clinical presentations resulting from the suspected use of classical recreational drugs (including ethyl alcohol), novel psychoactive substances such as synthetic cannabinoids, and/or other substances including prescribed medications were identified in ED. Patients were enrolled in the study if the admitting diagnosis was a confirmed acute drug intoxication within 12 hours prior to admission, and/or if blood and/or urine toxicology screens demonstrated the presence of non-prescribed, illicit drugs or inappropriately elevated levels of prescribed or over-the-counter medications. Patients with clinical signs and symptoms of acute drug poisoning on arrival to ED, in whom toxicology screens were not available at the time of admission to ICU, were also included in the study. Overdose and intoxication were defined as states of major disturbance of consciousness level, vital functions, and behavior following the consumption of psychoactive substances. In patients with suspicion of synthetic cannabinoids intoxication, a urine toxicology screen using liquid chromatography-tandem mass spectrometry was obtained. In patients readmitted to ICU during the study period, only data from the first admission was analyzed. To avoid selection bias, patients with history of recreational substance abuse and/or positive urine toxicology screen admitted to ICU for reasons other than acute drug intoxication were excluded from the study. Patients admitted to SDU with the diagnosis of acute drug intoxication were also excluded, since this treatment area could not be considered as a standard ICU given the staffing differences which included nurse:patient ratio. Also excluded were patients admitted to Medicine wards who later required to be transfer to ICU. The primary endpoint of this study was ICU mortality. Computerized electronic medical records were reviewed and clinical information was abstracted for each patient. After waiving the needs for informed consent, the Institutional Review Board approved the study.

### 2.2. Results

Sixty-five patients were admitted during the study period, representing 19% of total ICU admissions

**Table 1.** Profile of patients with elevated SOFA score (>4)

- Mostly male (38, 75%)
- Median age of 52 years (mean 49.1, range 20–72)
- Most common toxicological findings: ethyl alcohol (20, 39%), opiates (19, 37%), cocaine (10, 19%); 16 patients (31%) with polysubstance intoxication

(65/344). Only two patients (3%) were readmitted to ICU. Their median age was 49 years (mean 48.2, range 20–72) and the majority were male (48, 74%). Median SOFA score was 6 (mean 6, range 0–13) and 51 patients (78%) had SOFA score >4. Table 1 shows characteristics of patients with elevated SOFA scores. Overall, recreational drug overdose was the most common etiology of acute drug intoxication (55, 85%), while suicidal attempt was the reason for admission in eight patients (12%). Accidental poisoning was sought in two patients (3%). Mechanical ventilatory support was required in 50 patients (77%), which accounted for a total of 222 mechanical ventilation days. Median duration of mechanical ventilation was 3 days (mean 3.4, range 1–22), and three patients (6%) underwent tracheostomy procedure because of prolonged mechanical ventilation and inability to be weaned off from the ventilator. Mechanical ventilation was more commonly required among patients with polysubstance intoxication (17, 34%; RR = 0.9806, 95% CI = 0.7438–1.2929,  $p = .8898$ ), and in those abusing opiates (including methadone; 21, 42%; RR = 1.4241, 95% CI = 1.0753–1.8861,  $p = .0137$ ) and ethyl alcohol (17, 34%; RR = 0.9407, 95% CI = 0.7041–1.2567,  $p = .6792$ ). A total of eight patients (12%) received at least one vasoactive drug, and those intoxicated with opiates (including methadone; 4, 50%) more frequently developed hemodynamic instability.

Most common days of admission were: Saturdays (13, 20%), Sundays (11, 17%), Mondays (10, 15%), Tuesdays (10, 15%), Wednesdays (9, 14%), Thursdays (8, 12%), and Fridays (4, 6%). A total of 268 ICU days were utilized to treat these patients, with a median ICU LOS of 2 days (mean 4.1, range 1–21). Twenty-seven patients (42%) had ICU LOS of >2 days, and

they were usually intoxicated with ethyl alcohol (11, 41%) or opiates (including methadone; 9, 33%).

Most common clinical presentations on arrival to ED were: altered level of consciousness (including agitation, irrational behavior, stupor, coma; 33, 51%), seizures (13, 20%), tachypnea (13, 20%), and cardiac arrest (4, 6%). Most frequent laboratory abnormalities included: hypoxemia (39, 60%), acute kidney injury and electrolyte imbalance (27, 42%), hypercapnea (25, 39%), and elevated creatine kinase levels (16, 25%). Twenty-four patients (37%) had a history of psychiatric disorders, while 51 (79%) were previously admitted for acute drug intoxication.

Fifty-five patients (85%) had at least one substance detected in their urine and/or serum toxicology screen. Most commonly identified substances were: opioids (18, 33%), cocaine (13, 24%), methadone (12, 22%), benzodiazepines (10, 18%), and marijuana (9, 16%). In 16 patients (29%), >1 substance was identified. Twenty-three patients (35%) had negative urine toxicology screen. From those: two patients had acetaminophen intoxication, one patient ingested ethylene glycol, one patient ingested bleach, one patient consumed isopropyl alcohol, one patient overdosed with non-steroidal anti-inflammatory drugs plus dextylamine and diphenhydramine, and one patient abused antidepressants. Twenty-three patients (35%) had positive serum ethyl alcohol levels. Median serum ethyl alcohol level was 274 (mean 250, range 44–531). Ethyl alcohol was the only substance isolated in 11 of those patients (48%). From the group of patients with positive serum ethyl alcohol levels, 12 (52%) co-ingested other substances, most commonly opiates (including methadone; 7, 30%) and benzodiazepines (4, 17%).

Overall, twenty-one patients (32%) were additionally screened for synthetic cannabinoids, but none was positive. Table 2 shows characteristics of patients with suspicion for synthetic cannabinoids intoxication. Eight patients (12%) signed against medical advice while receiving treatment in ICU. Clinical features of these patients are highlighted in Table 3.

The approximate cost of ICU care for these patients was US\$1,045,200 (mean of US\$16,080 per

**Table 2.** Clinical profile of patients with suspicion for synthetic cannabinoids intoxication

- Mostly male (20, 95%)
- Median age of 47 years (mean 45.2, range 20–68)
- Median SOFA score of 6 (mean 5.9, range 1–13)
- Most common clinical presentation: altered mental status (14, 67%), seizures (4, 19%)
- Most frequent toxicological findings: opiates (11, 52%), marijuana (7, 33%), ethyl alcohol (5, 24%), benzodiazepines (4, 19%)
- Elevated creatine kinase levels (7, 33%)
- Negative serum and urine toxicology screen (5, 24%)

**Table 3.** Characteristics of patients who signed against medical advice

- Exclusively male
- Median age of 49 years (mean 44.8, range 23–55)
- Median SOFA score of 5 (mean 5.9, range 4–8)
- Most commonly presented with altered level of consciousness (5, 63%)
- Most frequently detected substances were benzodiazepines (3, 38%), ethyl alcohol (3, 38%) and marijuana (2, 25%)

patient), based on the daily cost of an ICU bed of US \$3,900 at our institution.

Five patients (8%) expired while receiving treatment in ICU. All of them were male, with a median age of 54 years (mean 52.2, range 37–72) and a median SOFA score on admission of 11 (mean 10.8, range 7–13). Their median ICU LOS was 7 days (mean 6.4, range 1–14), and median duration of mechanical ventilation was 7 days (mean 6.4, range 1–14). In three patients (60%), opiates (including methadone) were found in their urine toxicology screen. In two patients (40%), ethyl alcohol levels were positive in serum. One patient overdosed with cocaine. The other patient had negative urine and serum toxicology screens but was found to have oxalate crystals in the urine after the ingestion of ethylene glycol. Patients with acute opioids intoxication had increased mortality when compared to patients intoxicated with other substances (RR = 3.75 vs RR = 0.27).

### 3. Discussion

This study examined the clinical and epidemiological characteristics of patients with acute drug intoxication admitted to ICU. To our knowledge, this is the first study conducted in NYC addressing the utilization of ICU resources among patients with acute drug poisoning admitted to critical care units. The proportion of patients admitted to ICU in our study was substantially higher than previously reported in the literature [5,6,13–16,18–21], probably as a result of the hospital geographic location and our patients' socio-demographic characteristics. Despite the fact that our data is exclusively limited to results obtained from admissions during the autumn and winter, other related publications also showed a peak of ICU admissions during these seasons [21–23]. Although the majority of patients in this cohort were male, similarly to other related studies [5,6,24], our subjects were older when compared with other groups [5,6,16,18,19].

Organ dysfunctions and failures after drug overdose events are common, mostly transient, phenomena. Therefore, the criteria for multiorgan dysfunction among drug-intoxicated patients should be carefully and critically appraised. After extensive

review of published literature, we found only one study in which SOFA score was used as a tool to stratify the severity of illness among acutely intoxicated patients admitted to ICU. SOFA scores in our cohort were higher when compared to that publication [18]. Our results showed a linear relationship between increased SOFA score with advanced age, male gender, consumption of ethyl alcohol and opiates, and adverse outcome.

The majority of patients included in this cohort underwent mechanical ventilation, either from acute hypoxemic and/or hypercapnic respiratory failure, decreased level of consciousness with inability to safely protect airways, or cardiac arrest on arrival to ED. Even though the rate of mechanical ventilation reported in our study is significantly higher than in other similar publications [5,13,20,21,24–26], our ICU LOS is comparable to other related series [13,16,26]. As previously outlined in other reports, mechanical ventilation was most frequently required in patients with opiates intoxication [27,28].

As described in other large related cohorts [5,6,19,24], more than half of the admissions occurred during weekends, and clinical presentations as well as laboratory abnormalities were also equivalent to those previously outlined in other reports [5,6,16,18]. Our toxicology results are proportionate to formerly published data [5,6,13]. Including methadone, opiates was the most common substance detected in the urine toxicology screen of our subjects (30, 55%). More than one substance was identified in 16 patients (29%), and 23 patients (35%) had positive ethyl alcohol levels in serum.

Overall, acute drug intoxication accounted for 268 ICU bed days during the 6-month study period. Costing methodology calculated the median daily cost of an ICU bed at our institution to be US \$3,900. Based on this, the total cost of ICU care for these patients is estimated to be US\$1,045,200. It is worth noting that patients who would require additional invasive interventions such as hemodialysis, transfusion of blood and blood-related products, or surgical procedures would have higher daily cost of ICU care. Given the facts that our ICU LOS was relatively short, the proportionally high number of patients who signed against medical advice, and the number of patients who may have been admitted to



ICU for ‘observation’, we hypothesized that some of these intoxicated patients could have been possibly admitted to a less expensive level of care area such as SDU and telemetry units in which care for these patients could be delivered.

The unadjusted ICU mortality in our cohort was significantly higher than previously reported in other similar studies [5,6,13,16,18,20,24,26]. These patients were older, had higher SOFA scores on admission, and opiates were the most commonly detected substance in their toxicology screen. ICU mortality in patients with opioids overdose range is 2–14% [16,28,29]. In NYC, Siegler et al. reported that increased level of poverty, male gender, living in Brooklyn, age above 45 years, and white race were independent risk factors for fatal opioids overdose [30].

Our results suggest an interesting trend related to the increased reported use of novel psychoactive substances. Since January 2015, the NYCDOHMH surveillance has detected more than 8000 synthetic cannabinoids-related ED visits in NYC. The majority of these patients were male (90%), and their median age was 37 years. A notable geographic clustering of these ED visits was identified, with nearly half of those patients (46%) being residents near where our hospital is located. There were 10 fatalities related to the use of synthetic cannabinoids in 2015, with nine of these deaths involving multiple substances such as cocaine, benzodiazepines, heroin, and alcohol [31]. In 2015, there were 886 confirmed deaths in NYC as a result of unintentional drug poisoning [32]. The data associated with the consumption of synthetic cannabinoids in our cohort is based on patient’s self-reported use and/or reports from the Emergency Medical Service (EMS). Methods to detect, identify, and confirm synthetic cannabinoids lag behind the clinical spectrum of these drugs. Many of the cases depend upon self-report of the patients, whose information may be unreliable or inaccurate. In our cohort, 21 patients (32%) were screened for synthetic cannabinoids in the urine, using liquid chromatography-tandem mass spectrometry assay. Liquid chromatography-tandem mass spectrometry presents sufficient sensitivity to quantify synthetic cannabinoids in biological fluids such as urine [33,34].

This study has a few notable limitations. First, it was conducted in a single institution and, therefore, our results may not be applicable to other ICUs with different patients’ socio-economic and cultural demographics. Second, despite the large number of consecutive patients recruited, the study may have been underpowered and a larger sample size obtained by extending the study period would perhaps have revealed additional significant findings. Third, there were no data collected on long-term outcome of these patients after their

ICU and hospital discharge. Fourth, there was a lack of biological testing of blood specimens in patients with suspicion for synthetic cannabinoids intoxication. The main strength of this manuscript is its prospective design, with evaluation of all consecutive patients with acute drug intoxication admitted to ICU. Our data provides an interesting insight into the substances associated with acute drug toxicity presentations in patients admitted to ICU.

#### 4. Conclusion

Surveillance of drug abuse patterns is crucial to developing strategies to direct both clinical-based and community-based interventions. Creating a detailed understanding of current trends is challenging in the face of constantly evolving habits. Designer drugs intoxication should be considered in patients who present to ED with mental status changes and negative toxicology screens. More research is needed to determine how a multidisciplinary ICU team can best engage and support patients who survive an ICU admission after an acute drug intoxication event.

#### Disclosure statement

No potential conflict of interest was reported by the authors.

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