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Epidemiology and Treatment of Severe Poisoning in the Intensive Care Unit: Lessons from a One-Year Prospective Observational Study

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Abstract

Background: Acute poisoning is a frequent cause of admission to emergency departments (ED) and often requires treatment in the intensive care unit (ICU). The objective of this study is to characterize the patients admitted to an ICU in a toxicology referral center in Iran.

Methods: Prospective, observational study carried out from 1 January to 31 December 2008 at a 10-bed toxicology ICU in a referral hospital for poisoned patients in Tehran, Iran. All patients above 12 years of age with severe poisoning treated in the ICU were included.

Results: 175 out of 2187 patients admitted to the emergency department due to poisoning were admitted to the ICU. The intent was unintentional in 47 cases (27%) and suicidal in 128 Cases (73%). There were 99 males (57%) and 76 females (43%). The age of the patients ranged from 16 to 65 years, with a peak in the third decade of life. Benzodiazepines, cyclic antidepressants, pesticides and opiates were the most frequently used agents. The overall mortality rate in the ICU was 17.7%. Pesticides carried the highest mortality risk (41%). Coma, rhabdomyolysis and aspiration pneumonia were the most common complications.

Conclusion: Patients admitted to our ICU had a high mortality. This is likely related to the large number of highly toxic exposures but may also be related to sub-optimal treatment and facilities. We plan to implement standard diagnostic and therapeutic pathways in our ED and ICU to attempt to improve these outcomes.

Keywords: Poisoning; Intensive care unit; Complications; Epidemiology; Outcome

Introduction

Acute poisoning is a frequent cause of admission to emergency departments (ED) and often requires treatment in the intensive care unit (ICU). One to five percent of public hospital admissions worldwide are caused by unintentional or deliberate poisoning [1-5]. Early diagnosis and rapid initiation of appropriate therapy in ED and ICU are critical for lowering hospital morbidity and mortality in poisoned patients.

The clinical patterns of patients with severe poisoning vary markedly between different study centers [6-15]. In developed countries, the availability of prescription and non-prescription drugs has been associated with a significant increase in patients requiring hospital admission for medical drug overdose [16, 17]. In developing countries, the incidence of pesticide poisoning has doubled during the past decades and accounts for a large number of fatal outcomes despite increased availability of ICU facilities [18-20]. Recently published data from Iran have shown an important increase in aluminum phosphate poisoning while tramadol and opioid poisoning still constitutes a major challenge for hospitals and poisoning centers [20-28]. Since Baharloo hospital is one of the main referral hospitals for poisoned patients in Tehran, Iran, [29] we conducted a prospective observational study including all patients with severe poisoning admitted to the toxicology ICU. The objective of our study was identifying typical clinical and epidemiological patterns of severe poisoning requiring ICU treatment.

Methods

Design and setting

This was a prospective observational study designed to describe the clinical and epidemiological patterns of severe poisoning requiring ICU treatment .The study site was Baharloo Hospital, Tehran, Iran. The study started 1 January to and ended 31 December 2008 and was approved by our local institutional review board.

Baharloo Hospital serves as one of two main clinical toxicology centers for the Tehran region with an estimated population of over 8.5 million people. Baharloo Hospital is a teaching hospital of Tehran University of Medical Sciences [29]. It consists of 330 beds and 8 departments including pediatrics, gynecology, cardiology, general surgery, orthopedics, oto-rhino-laryngology, neurology, and critical

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care medicine. A separate 10-bed toxicology ICU provides highly-specialized care for patients with severe intoxications. This unit is equipped with 10 respirators and 6 dialysis machines, and staffed by intensivists, specialists in emergency medicine, clinical toxicologists and critical care nurses.

Patient management

Initial assessment and treatment of poisoned patients in the ED was performed by the physicians in charge (consultants, residents, interns). Depending on the severity of symptoms patients were either discharged home after at least 6 hours of observation in the ED, transferred to a specialized poisoning ward (25 beds) or - in case of life-threatening signs and symptoms - referred to the ICU. Admission decision was made by the physician in charge of the ICU. Criteria for ICU admission were as follows: deep unconsciousness (Reed coma grade II-IV),[3] respiratory distress (RR>35 breaths/minute), hemodynamic instability (Systolic arterial pressure < 80 mm Hg or 20 mm Hg below the patient's usual pressure), potentially lethal exposures (e.g. aluminum phosphide, strychnine, arsenic, cyanide), and seizure [30].

ICU treatment

Critically ill patients in the ICU were continuously monitored and received basic and advanced supportive care as appropriate. Indications for endotracheal intubation and mechanical ventilation in the ICU were: global respiratory insufficiency due to excessive airway mucus secretions, impaired consciousness with loss of airway protective reflexes, cardiac arrest, and severe metabolic acidosis (pH < 7.2) with hemodynamic instability (systolic blood pressure < 80 mm Hg). When indicated, gastric lavage followed by administration of activated charcoal via gastric tube, and cleansing of the patient's body with soap and water, was carried out. Forced diuresis and urinary pH manipulation were used to increase renal elimination of specific toxicants. Patients with impaired consciousness of unknown etiology received an intravenous injection of 100 mg thiamine, 50 ml of dextrose 50% and naloxone 0.4 to 2 mg up to a maximum 10 mg. Flumazenil was used as diagnostic and therapeutic agent in case of suspected benzodiazepine overdosage (0.01 mg flumazenil per kg body weight). Other specific antidotes were used when indicated. Plasma cholinesterase levels, ethanol serum levels and carboxyhemoglobin concentrations were determined in selected patients. Discharge from the ICU was based on the history of the ingestion, the status of the patient and the expected clinical course.

Coma grading

Level of coma was assessed according to the REED coma scale as described by others: [3] Grade I coma was defined as decreased consciousness with normal reflexes, respiration and circulation. Grade II coma was defined as decreased consciousness with no response to painful stimuli but intact deep tendon reflexes and vital signs. Grade III was defined as coma with no response to painful stimuli, absence of deep tendon reflexes but intact respiration and circulation. Grade IV coma was defined by respiration and circulation collapsed [3].

Data collection and statistics

All patients aged 12 and above and newly admitted to the medical ICU of Baharloo Hospital between 1 January 2008 and 31 December 2008 for treatment of poisoning was included. Pediatric patients below the age of 12 years were treated in a separate pediatric department and therefore excluded from the present analysis. Patients with adverse drug reactions as defined by World Health Organization and food poisoning were excluded from our analysis [31].

Patient data were systematically recorded by one investigator (AY) and entered on a spreadsheet. Charts abstracted by a second individual, who was blinded to the purpose of the study, with an inter-rater reliability assessment of the abstraction procedure. Standard data collection included the drugs and poisons involved in the exposure, demographics, clinical signs and symptoms, clinical course, treatment and outcome. The intent of poisoning was categorized as either suicidal or unintentional. The patient and family were interviewed to determine the intent and circumstances of the poisoning. Other information (such as remaining drug samples, poison debris, and the analysis of blood and urine samples) was also considered when available. We used WinStat for Excel (R. Fitch Software, Staufen, Germany) and Statistical Product and Service Solutions (SPSS) 12.0 (SPSS Inc., Chicago, IL, USA) software for data analysis. Categorical data are presented as absolute numbers with associated percentages.

Results

During the one year study period, 2187 patients were admitted to Baharloo Hospital for treatment of poisoning. Of these patients, 175 (8%) were referred to the ICU for the treatment of life-threatening poisoning. The intent was unintentional in 47 cases (27%) and suicidal in 128 (73%). There were 99 males (57%) and 76 females (43%). The age of the patients ranged from 16 to 65 years, with a peak in the third decade of life (Figure 1). Demographic and clinical characteristic are shown in Table 1. The mortality rate in the ICU was 17.7% (31/175). Pesticides carried the highest mortality risk (41%).

Only two out of 31 fatal cases were due to unintentional poisoning.

Table 2 displays the distribution of patients according to their occupation. No significant differences were found between survivors and non-survivors. Pharmaceuticals, in particular benzodiazepines and cyclic antidepressants, accounted for two thirds of cases (Table 3). In 72% of these cases, only one agent was used while two or more pharmaceutical agents were noted in 28% of patients. Survival was higher in poisoning with pharmaceuticals than in those caused by pesticides.

Monitoring and treatment procedures are shown in Table 4. Invasive ventilation and gastric decontamination were by far the most frequently performed procedures in the ICU. In addition, 28 patients (16%) received specific antidote treatment (e.g. flumazenil, naloxone, atropine, ethanol, N-acetylcysteine).

Coma was the most common clinical feature and all patients had at

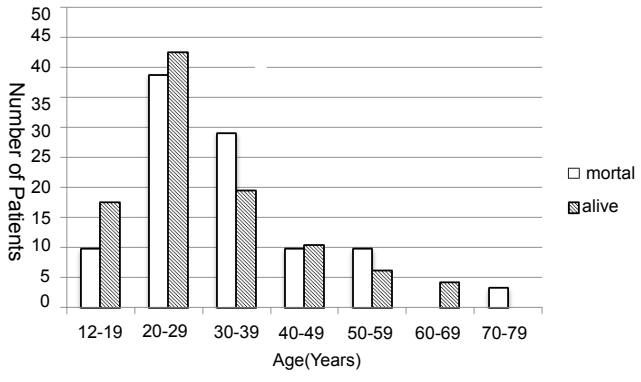

Figure 1: Age (in years) for patients with lethal and non-leathal poisnoing admitted to our ICU.

Patients	All study patients	Survivors	Non-survivors	p-value
	n=175 (100%)	n = 144 (100%)	n = 31 (100%)	
Age, years, median (IQR)	27 (22-36)	27 (22-37)	27 (23-36)	0.98
Male sex, n (%)	99 (57)	82 (57)	17 (55)	0.83
Accidental, *n* (%)	47 (27)	43 (30)	4 (13)	0.07
Suicidal, *n* (%)	128 (73)	101 (70)	27 (87)	0.07
Previous suicide attempts, *n* (%)	21 (12)	18 (13)	3 (10)	1.00
Drug addicts, *n* (%)	15 (9)	11 (8)	4 (13)	0.31
Psychiatric disease, *n* (%)	25 (14)	24 (17)	1 (3)	0.08
Latency period (ingestion-admission), hours, median (IQR)	5 (3-7)	5 (3-7)	6 (4-12)	0.05
ICU length of stay, days, median (IQR)	6 (4-9)	7 (4-10)	4 (2-6)	0.01

Table 1: Demographics and clinical information for or survivors and non-survivors admitted to our ICU for poisoning.

Patients	All study patients	Survivors	Non-survivors	p-value
	n=175 (100)	n = 144 (100)	n = 31 (100)	
Housewife, n (%)	50 (28.6)	39 (27)	11 (35)	0.35
Self- employee, *n* (%)	35 (20.0)	27 (19)	8 (26)	0.37
High-school student, n (%)	36 (20.6)	33 (23)	3 (10)	0.10
University student, n (%)	17 (9.7)	15 (10)	2 (6)	0.74
Driver, *n* (%)	14 (8)	9 (6)	5 (16)	0.08
Unemployed, *n* (%)	10 (5.7)	8 (6)	2 (6)	0.69
Worker, *n* (%)	9 (5.1)	8 (6)	1 (3)	1.00
Others (Soldier, Retired, Clerk), *n* (%)	5 (2.9)	5 (3)	0 (0)	0.59

Table 2: Occupation of or survivors and non-survivors admitted to our ICU for poisoning.

Patients/Drugs	All study patients	Survivors	Non-survivors	*p* Value
	n=175 (100)	n = 144 (100)	n = 31 (100)	
Pharmaceutical drugs	118 (67.4)	102 (71)	16 (52)	0.038*
Benzodiazepines	71 (40.5)	63 (44)	8 (26)	0.065
Cyclic antidepressants	63 (36)	54 (38)	9 (29)	0.373
Antipsychotics	17 (9.7)	15 (10)	2 (6)	0.499
Anti-convulsions	15 (8.6)	15 (10)	0 (0)	0.047*
Barbiturate	15 (8.6)	15 (10)	0 (0)	0.047*
Acetaminophen	13 (7.4)	10 (7)	3 (10)	0.821
Tramadol	12 (6.9)	11 (8)	1 (3)	0.336
Beta-blockers	6 (3.4)	6 (4)	0 (0)	0.305
Anti-histamines	4 (2.3)	4 (3)	0 (0)	0.455
Anti-cholinergic	4 (2.3)	1 (3)	3 (2)	0.855
Baclofen	4 (2.3)	4 (3)	0 (0)	0.455
Anti-depressive SSR	3 (1.7)	2 (1)	1 (3)	0.919
Analgesics	2 (1.3)	1 (1)	1 (3)	0.959
Anti-hyperglycemic	1 (0.6)	1 (1)	0 (0)	0.823
Anti-coagulants	1 (0.6)	1 (1)	0 (0)	0.823
Clonidine	1 (0.6)	1 (1)	0 (0)	0.823
Lithium	1 (0.6)	1 (1)	0 (0)	0.823
Antibiotics	1 (0.6)	1 (1)	0 (0)	0.823
Pesticides	27 (15,4)	16 (11)	11 (35)	0.002*
Organophosphate	12 (8)	7 (5)	5 (16)	0.040*
Aluminums phosphide	15 (8.6)	9 (6)	6 (19)	0.030*
Opioids	20 (11.4)	16 (11)	4 (13)	0.759
Others	16 (9)	11 (8)	5 (16)	0.969
Methanol	7 (4)	4 (3)	3 (10)	0.981
Carbon monoxide	6 (3.4)	6 (4)	0 (0)	0.305
Strychnine	1 (0.6)	0 (0)	1 (3)	0.177
Cyanide	1 (0.6)	0 (0)	1 (3)	0.177
Amphetamine	1 (0.6)	1 (1)	0 (0)	0.823

*Statistically significant

Table 3: Poison exposure for survivors and non-survivors of poisoning admitted to our Intensive Care Unit (ICU).

least some alteration in consciousness. Half of patients had grade II of coma (N=87, 49.7%), followed by grade III and grade IV in 41.7% and 8.6% of cases respectively. In almost half of the patients (46%) coma was longer than 48 hours. The duration of coma was 12 - 24 hours in 33 patients (18.9%), 24-48 hours in 32 patients (18.3%) and <12 hours in 29 patients (16.6%). Coma, rhabdomyolysis and aspiration pneumonia were the most common complications.Other clinical complications occurred less frequently (Table 5).

Discussion

Poisoning with pharmaceuticals, alcohol, illegal drugs, chemicals and other substances (e.g. plants, household products) have a significant impact on critical care resources worldwide [6-17], but the patterns of acute poisoning vary with place and time [16-17]. Previous studies from Iran on severe poisoning requiring ICU treatments have been retrospective and of limited statistical quality [1,32,33]. Hence, we used a prospective approach to identify typical clinical and epidemiological patterns of severe poisoning requiring ICU treatment in the large urban setting of Tehran, a metropolis with approximately 12 million inhabitants.

Our patients were mostly young (below 30 years); either employed, students or housewives, and had suicidal intentions. These findings are consistent with other study centers from developing countries including Iran [1,6, 12,16,17,20,34]. The number of patients with previous suicide attempts or preexisting psychiatric diseases, however, was lower than in two recently published analyses from Spain and Hong Kong [16,17]. Although Paracetamol poisoning is a major concern in the western countries, [35,36] benzodiazepines and tricyclic antidepressants were by far the most common agents of poisoning in our analysis. This finding is not suppressing and reflects a trend which is typical for many developed and a growing number of developing countries include Iran [1,11,17,20,32,33,37-40]. The considerably high number of patients with opioid poisoning in our analysis is in agreement with previous observations from Tehran [41].

In our study population, 17.7% of patients died during treatment in the ICU. This mortality rate is quite high and thus demands critical analysis. In previous studies from Iran, ICU mortality in poisoned patients was in the same range (11.6 to 18.6 %) [31, 33]. Similar mortality rates were found in other developing countries.42, 43 By contrast, two recent studies from Germany and Hong Kong reported ICU mortality in poisoning of 0.7 and 3%, respectively [12,17]. There are several reasons that might account for the extreme variation in mortality reported in different countries. One possibility is that our status as a referral center for poisoning may increase the incidence of severe cases. Another possibility is that criteria for ICU admission of patients vary widely across hospitals and countries [17]. In our setting, ICU admission was strictly limited to obviously severe and life-threatening poisoning, while other institutions routinely admit all poisoned patients to the ICU, regardless of the severity of symptoms at the time of entry [12]. ICU admission decisions are influenced by a number of different factors, including resource availability and physician prognostication [44] Standardized diagnostic pathways may be helpful in reducing the risk of false or delayed admissions to the ICU [30] Recently, criteria for ICU admission in poisoned patients presenting to the ER have been described in a clear and concise manner [45] We are implementing these criteria in our hospital and hope this process may improve our outcomes.

Another option for hospitals in emerging and developing countries to improve treatment outcome in poisoned patients is to improve monitoring and surveillance in a lower intensity setting. These `intermediate care´ areas may further unburden doctors in the ER, particularly in cases where the poison or expected course is unclear.

We were surprised to find that gastric lavage was administered to the large majority (88%) of patients admitted to our ICU. This finding was even more striking because the median time between ingestion and hospital admission was 5 to 6 hours. Lavage has serious risks include hypoxia, dysrhythmias, laryngospasm, perforation of the GI tract or pharynx, fluid and electrolyte abnormalities, and aspiration pneumonitis [46]. We believe the high rate of lavage observed in our study suggests over-use and that we need to educate our emergency department physicians to reserve lavage for early presenting patients with life-threatening exposures.

Our study has several limitations. First, we did not calculate mortality and outcome in poisoned patients presenting to the ER but not referred to the ICU. Hence, we could not determine the overall in-hospital mortality rate in all poisoned patients. The external validity of our study is limited the use of a single center. Although our center is one of the two main referral hospital for poisoned patients and covers a population over than 8.5 million of Tehran.

In summary, this is the first Iranian prospective observational study of poisoned patients admitted to the ICU. Our study shows two trends in severe poisoning: a high number of poisonings caused by psychotropic drugs with moderate mortality and a significant number of deaths due to pesticide poisoning. Our findings suggest several opportunities to improve treatment by standardizing the evaluation

Patients	Number of patients (%)
Monitoring and basic supportive care	**175 (100)**
continuous monitoring (ECG, oxygen status, blood pressure)	175 (100)
intravenous fluid and electrolyte replacement	166 (95)
oxygen supply	158 (90)
central venous catheterization	16 (9)
Advanced supportive care	**167 (95)**
invasive ventilation	166 (95)
gastric lavage	154 (88)
inotropic drug therapy	53 (30)
renal replacement therapy	19 (11)

Table 4: Monitoring and supportive care procedures for survivors and non-survivors admitted to our ICU for poisoning.

Complications	Number of patients (%)	THE MOST FREQUENT AGENT INVOLVED
Deep coma (grade 3 or 4)	88 (50)	Benzodiazepin(n=46)
Respiratory failure (bradypnea)	96 (55)	Benzodiazepin(n=42)
Aspiration pneumonia	14 (8)	Benzodiazepin(n=7)
Rhabdomyolysis	11 (6)	Tricyclic anti depressant(TCA) (n=8)
Seizure	4 (2)	Tramadol(n=2)
Nosocomial infection	2 (1)	phenobarbital
Subarachnoid hemorrhage	2 (1)	Tricyclic anti depressant(Tca)
Permanent blindness	2 (1)	Methanol(n=2)
Hemoptysis	1 (0.6)	orgnophospht(n=1)
Gastrointestinal bleeding	1 (0.6)	Acetamionophen(n=1)
Persistent vegetative state	1 (0.6)	Tricyclic anti depressant(Tca) (n=1)
Acute respiratory distress syndrome (ARDS)	1 (0.6)	opium(n=1)

Table 5: Complications for patients admitted to our Intensive Care Unit (ICU) for poisoning.

and treatment and by the use of evidence based therapies to treat poisoned patients in our hospital.

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Declaration of interest

The authors report no conflict of interest. The Authors alone are responsible for the content and writing of this paper.

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