Retrospective Evaluation of Intoxication Cases Followed in Pediatric Intensive Care: A 5-Year Experience

Muhterem Duyu1, Şeyma Köksal Atış2

1Department of Pediatrics, Pediatric Intensive Care Unit, Istanbul Medeniyet University, Goztepe Training and Research Hospital, Istanbul, Turkey
2Department of Pediatrics, Istanbul Medeniyet University, Goztepe Training and Research Hospital, Istanbul, Turkey

Abstract

Introduction: This study was designed to investigate the demographic, epidemiologic and clinical characteristics of cases admitted to the pediatric intensive care unit (PICU) with a diagnosis of intoxication.

Methods: Inpatient intoxication cases who were treated in the PICU between May 2015 and May 2020 were analyzed retrospectively.

Results: A total of 86 patients were included in the study. The average age was 10.8 ± 6.4 years and 53.5% of the cases were aged between 13-18 years. In terms of gender, 48.8% of the cases were male. Almost half of the (53.5%) intoxications occurred due to attempted suicide, 39.6% were accidental, 4.6% were due to substance abuse and 2.3% were due to incorrect drug dosage. Pharmaceutical agents were responsible for intoxication in the majority (79.1%) of patients, and among these, central nervous system (CNS) drugs were the most common (41.8%). Carbon monoxide poisoning was the most common nonpharmaceutical agent cause (8.1%). The agents that caused the intoxication were taken orally in 91.8% of cases. The average time from consumption to admission was 239±423.9 minutes. Gastric lavage was applied to 41.9% of the cases and activated charcoal was applied to 44.1%. Mechanical ventilation support was given to 32.6% of the patients. The most common findings were CNS symptoms (in 54.6% of patients). The mean length of stay (LOS) in PICU was 4.3±6.7 days and LOS in the hospital was 5.8±7.1 days. Mortality rate was 1.2%.

Discussion and Conclusion: Knowing the epidemiology of intoxication is of great importance for rapid and correct treatment. Multicenter comprehensive studies are needed to reveal risk factors related to mortality.

Keywords: Drug; intoxication; pediatric intensive care; suicide.

Intoxication is common in the childhood and represents one of the preventable causes of mortality and morbidity. It remains among the leading causes of hospitalization throughout the world[1,2]. Although progress has been made in the prevention of accidental intoxications, the utilization of better packaging techniques and increasing awareness regarding the composition of toxic products is crucial, since intoxication are still frequent in children, particularly in those aged 2 to 3 years old[3]. In 2017, the “35th Annual Report of the American Association of Poison Control Centers, National Poison Data System” recorded more than two million calls concerning cases of human exposure to toxic substances. Among these more than 50% were due to acute intoxications in children under 13 years of age[4].

Correspondence (İletişim): Muhterem Duyu, M.D. Istanbul Medeniyet Universitesi, Goztepe Eğitim ve Araştırma Hastanesi, Çocuk Sağlığı ve Hastalıkları, Çocuk Yögun Bakım Ünitesi, İstanbul, Turkey
Phone (Telefon): +90 555 674 56 61 E-mail (E-posta): drmuhteremduyu@gmail.com
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According to the 2008 report of the "National Poison Counseling Center (Ulusal Zehir Danışma Merkezi, UZEM)", 60.1% of the 77,988 intoxication cases in Turkey were younger than 19 years old, and 52.8% of these were recorded in children younger than 5 years[5]. Although most cases of intoxication in children are asymptomatic at admission, some may have life-threatening symptoms. In the presence of such symptoms, children should be admitted to and treated in the pediatric intensive care unit (PICU)[6]. Although a previous study by Patel et al.[7] reported that approximately 70% of the 12,021 patients who had been admitted to the PICU did not require any major medical intervention, there is currently no reliable scoring system to predict patients who will need intensive care after acute intoxication. Therefore, many cases with intoxication are admitted to the PICU even when they do not have symptoms.

The epidemiology of childhood intoxication varies from country to country. It is also well-established that regional, socio-cultural and economic characteristics within the same country are also influential on epidemiological findings[8,9]. Therefore, every country and region should carry out epidemiological investigations in order to be able to implement accurate preventive interventions.

The aim of this study is to retrospectively evaluate the demographic and epidemiological characteristics and the clinical features and prognoses of patients who received inpatient treatment in our PICU within the 5-year study period.

Materials and Methods

A total of 86 patients, aged from 1 month to 18 years old, treated for acute intoxication at the PICU of Istanbul Medeniyet University, Goztepe Training and Research Hospital in Istanbul, Turkey, between May 2015 and May 2020 were included in this study. Patient files were scanned for age, gender, Pediatric Risk of Mortality III (PRISM III) score and Glasgow Coma Scale (GCS) score (at admission), type of intoxication (suicidal purpose, accidental, substance abuse, dosage error), route of intoxication (ingestion/oral, inhalation/nasal), medical interventions related to intoxication (minor interventions, gastric lavage, activated charcoal, mechanical ventilation [MV], renal replacement treatment [RRT], plasmapheresis, cardiac pacing, extracorporeal membrane oxygenation [ECMO], hyperbaric oxygen therapy, inotrope drug administration), length of stay (LOS) in PICU, LOS in hospital, and survival.

Interventions such as continuous monitoring, intravenous fluid administration and laboratory follow-up were recorded as minor interventions. Patients with missing and/or inaccessible records and cases hospitalized in the PICU due to food intoxication were not included in the study. The agents causing intoxication were divided into two groups as pharmaceutical and non-pharmaceutical agents. The number of agents were classified as single and multiple. Pharmaceutical agents responsible for intoxication were divided into the following drug groups according to their effect spectrum: central nervous system (CNS) drugs, analgesics and antipyretics, cardiovascular and antihypertensive drugs, antihistaminics and antiemetics, immunosuppressive and oncological drugs, antimicrobials, muscle relaxants, hormones and hormone antagonists, and others. All signs of intoxication observed in the patient were recorded. Intoxication findings were classified as follows: CNS, gastrointestinal system, cardiovascular system, respiratory system, and metabolic/biochemical findings.

Approval for the study was obtained from the local ethics committee (Protocol number: 2020/0336). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Data were evaluated using SPSS version 18.0 (SPSS, Inc., Chicago, IL). Categorical variables were presented as frequency and percentage. Continuous variables were presented as mean±standard deviation, and minimum (min) and maximum (max) values.

Results

A total of 94 cases were hospitalized in our PICU between May 2015 and May 2020 due to intoxication (4 cases were excluded from the study due to lack of patient records and 4 cases due to food intoxication). Detailed clinical and demographic characteristics of the patients included in the study are presented in Table 1. The average age of the patients included in the study was 10.8±6.4 years. The majority of the cases (53.5%) were between 13–18 years old. In terms of gender, 48.8% of the cases were male, and 57.5% of the cases under 5 years of age were male. The mean PRISM III score of the cases was 4.3±4.2 and the mean GCS score was 11.7±4.0.

Among the causes of intoxication, suicide attempts were the most common (53.5%), followed by accidents (39.6%), substance abuse (4.6%) and dosage errors (2.3%). The most common cause of intoxication in cases under 5 years of age was accidental drug in-take (94.0%). Suicidal purpose was
the cause of intoxication in 89.1% of cases over the age of 13 years. Of the 46 suicide cases, 36 (78.2%) were female. The most common route of exposure to intoxication was the ingestion/oral route (91.8%). The distribution of medical interventions for intoxication are presented in Table 1. Activated charcoal was applied to 44.1% of patients and gastric lavage was applied to 41.9% of subjects. Need for MV developed in 32.6% of the patients, while 24.4% of the individuals had only received minor interventions. Of the 6 patients (7.0%) who underwent RRT, two cases were anticonvulsant drug (carbamazepine) intoxication, two were metformin intoxication, one was alcohol intoxication and one was methamphetamine intoxication. Of the 3 (3.5%) cases who underwent plasmapheresis, 2 were colchicine intoxication and 1 was isoniazid intoxication. Cardiac pacing was performed in 1 case (1.2%) due to symptomatic bradycardia caused by beta-blocker intoxication. ECMO treatment was applied to 1 case for acute respiratory distress syndrome (ARDS) that had developed due to activated charcoal aspiration. All of the cases who were treated with hyperbaric oxygen therapy (3.5%) were cases of carbon monoxide intoxication.

The average time between exposure to the agent causing intoxication and admission to the hospital was 239±423.9 minutes. In cases with suicidal purpose, the time to admission was 276.5±500.5 minutes. The mean LOS in PICU was 4.3±6.7 days, and the average LOS in the hospital was 5.8±7.1 days. Survival rate was 98.8%. Only 1 case (1.2%) died, caused by intoxication with calcium channel blocker.

Detailed analysis of the agents causing intoxication is presented in Table 2. The majority (67.4%) of the patients had single-agent intoxication and 32.6% had multiple-agent intoxication. 39.7% (23/58) of single-agent intoxication cases were under 5 years old, while 69.7% (23/33) of the patients younger than 5 years old had single-agent intoxication.

Pharmaceutical agents were responsible in 79.1% of patients. CNS drugs were responsible in 41.8% of the patients, followed by analgesics and antipyretics (16.3%), cardiovascular and antihypertensive drugs (10.5%), antihistaminics and antiemics (10.5%), immunosuppressive and oncologic drugs (9.3%) and antimicrobials (6.9%). Non-pharmaceutical intoxication was present in 20.9% of individuals with carbon monoxide being the leading cause (8.1%).

The clinical findings of intoxication are presented in Table 3. The vast majority of patients (82.6%) had some form of clinical or metabolic/biochemical findings. More than one finding was present in 20.9% of the patients. The most common among these were CNS symptoms in 54.6% of patients and the most common CNS findings was confusion/tendency to sleep seen (in 29.0% of subjects). CNS findings were followed by gastrointestinal system findings (14.0%),

### Table 1. Clinical and demographic characteristics of acute intoxication cases and distribution of treatment methods

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at admission (year), mean±SD (min-max)</td>
<td>10.8±6.4 (0.5-18)</td>
</tr>
<tr>
<td>Age distribution (year), n (%)</td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>33 (38.4)</td>
</tr>
<tr>
<td>6–12</td>
<td>7 (8.1)</td>
</tr>
<tr>
<td>13–18</td>
<td>46 (53.5)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>42 (48.8)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>44 (51.2)</td>
</tr>
<tr>
<td>PRISM III at admission to the PICU, mean±SD (min-max)</td>
<td>4.3±4.2 (1-19)</td>
</tr>
<tr>
<td>GCS at admission to the PICU, mean±SD (min-max)</td>
<td>11.7±4.0 (4-15)</td>
</tr>
<tr>
<td>Cause of poisoning, n (%)</td>
<td></td>
</tr>
<tr>
<td>Suicide purpose</td>
<td>46 (53.5)</td>
</tr>
<tr>
<td>Accidentally</td>
<td>36 (39.6)</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>4 (4.6)</td>
</tr>
<tr>
<td>Dosage error</td>
<td>2 (2.3)</td>
</tr>
<tr>
<td>Route of exposure, n (%)</td>
<td></td>
</tr>
<tr>
<td>Ingestion/oral</td>
<td>79 (91.8)</td>
</tr>
<tr>
<td>Inhalation/nasal</td>
<td>7 (8.2)</td>
</tr>
<tr>
<td>aMedical intervention, n (%)</td>
<td></td>
</tr>
<tr>
<td>Activated charcoal</td>
<td>38 (44.1)</td>
</tr>
<tr>
<td>Gastric lavage</td>
<td>36 (41.9)</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>28 (32.6)</td>
</tr>
<tr>
<td>Minor interventions</td>
<td>21 (24.4)</td>
</tr>
<tr>
<td>Renal replacement treatment</td>
<td>6 (6.9)</td>
</tr>
<tr>
<td>Plasmapheresis</td>
<td>3 (3.5)</td>
</tr>
<tr>
<td>Cardiac pacing</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Extracorporeal membrane oxygenation</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Hyperbaric oxygen therapy, n (%)</td>
<td>3 (3.5)</td>
</tr>
<tr>
<td>Inotrope drug administration, n (%)</td>
<td></td>
</tr>
<tr>
<td>Duration of time from exposure to admission the hospital (min), mean±SD (min-max)</td>
<td>239.0±423.9 (15-2880)</td>
</tr>
<tr>
<td>Length of PICU stay (day), mean±SD (min-max)</td>
<td>4.3±6.7 (1-50)</td>
</tr>
<tr>
<td>Length of hospital stay (day), mean±SD (min-max)</td>
<td>5.8±7.1 (1-50)</td>
</tr>
<tr>
<td>Survival, n (%)</td>
<td>85 (98.8)</td>
</tr>
</tbody>
</table>

PRISM: Pediatric risk of mortality, GCS: Glasgow coma score, PICU: Pediatric intensive care unit, SD: Standart derivation; a: More than one medical intervention was performed to 40 patients.
cardiovascular system findings (9.3%) and respiratory system findings (8.1%). Metabolic/biochemical findings were present in 9.3% of the cases. The most common of these were metabolic acidosis (7.0%) and lactic acidosis (3.5%).

**Discussion**

The aim of this study was to investigate the demographic and clinical characteristics of pediatric patients admitted to the PICU due to acute intoxication. The analysis of the literature showed the presence of numerous studies on this...
Intoxications can occur accidentally or with suicidal purposes. The data from studies conducted in our country have reported a frequency of accidental poisoning from 53.7% to 90.0%, and suicidal poisoning from 8.2% to 46.3%[8, 10-13]. In our study, 53.5% of intoxications had occurred due to attempted suicide, 41.9% were accidental and 4.6% were due to substance abuse. When the distribution of intoxication cases in the literature were examined based on the gender and age, it was observed that male children were more likely to suffer from accidental intoxications at a younger age, whereas a higher rate of suicidal intoxications was observed in girls of pubertal age[14-16]. Concurrently, intoxication was more common in boys under the age of 5, and girls older than 13. Similar to the literature, the cause of intoxication was mostly accidental (94.0%) in cases under 5 years of age, and mostly suicidal purposes (89.1%) in patients older than 13 years of age in our study.

The age and gender distribution of intoxication cases varies from country to country and center to center. In our study, 38.4% of the patients were under 5 years old, and 51.2% of our cases were girls. The literature shows varying levels of gender distribution with slight differences[8, 10, 11, 17, 18]. The average age of childhood intoxication cases in our country has been reported to vary between 5.2 years and 8.4 years[8, 12, 18, 19]. In our study, the average age of intoxication cases considerably higher than prior publications from our country (10.8 ± 6.4 years). It was thought that this difference could be due to the variations in the criteria for admission to the PICU, which may have favored a higher likelihood of PICU admission in older patients with suicidal intent.

In our study, the mean PRISM III score was 4.3±4.2 and the mean GCS score was 11.7±4.0 at PICU admission. In the study conducted by Keskin et al. patients were divided into two groups: those with and those without indication for intensive care admission. Patients who were admitted to intensive care were found to have higher PRISM III score and lower GCS score than the other group[18]. In a multi-center study conducted in the USA, mortality was associated with high PRISM III score in a group of 12,021 intoxication cases followed in the PICU[7]. Currently, there are no clinical tools or scales that enable the prediction of PICU requirement after acute intoxication. Usually, intoxication control centers advise PICU admission in almost all pediatric intoxication cases. However, this is not possible in the majority of pediatric clinics all over the globe. To our knowledge, there is only one single-center observational study comprised of 2,565 adult patients which found that the GCS score was the only predictor for intensive care unit admission in adults[20]. The ideal predictive model should be able to determine which children examined in the emergency room, regardless of presentation severity, are at risk for later deterioration and thus should be admitted to the PICU for observation of potentially life-threatening complications following an acute intoxication. High-risk cases can be identified by developing scoring systems and criteria for investigation in the intensive care setting with multi-center studies in children. In this way, efficient use of PICU beds can be achieved.

Turkish studies on intoxication report that the route of intoxication in the ingestion/oral route in over 90% of cases[8, 11], similar to our results. The type and distribution of childhood intoxication (pharmaceuticals vs. non-pharmaceuticals) vary according to the country, geographical region and socio-cultural and economic level. Results vary depending on whether studies are carried out in the pediatric emergency department or in the PICU. Gokalp et al., from Turkey, demonstrated that the majority of intoxication cases in the pediatric emergency department were caused by non-pharmaceutical agents –mostly household cleaning products (62.9%)[19]. In a multi-center study conducted in Italy, 59.0% of the patients were reported to have been intoxicated with non-pharmaceutical agents, and among these agents the most common were household cleaning products (49.0%)[21]. In studies conducted in PICUs, the situation was different. Intoxication with pharmaceutical agents were found at a higher frequency, with rates ranging from 60.2% to 81.7%[8,13]. Similarly, intoxication with pharmaceutical agents were observed in 79.1% of our patients.

The types of drugs that cause intoxication vary according to country, socio-economic status and cultural differences. In the study conducted by Berta et al. from Italy, the most common pharmaceutical agents causing intoxication were listed as analgesics, psychotropics and cardiovascular agents[21]. In studies conducted in Turkey, CNS drugs, analgesics and antipyretics were the leading causes[8,12,13,22], exemplified by our results. These were followed by cardiovascular and antihypertensive drugs and antihistamines and antiemetics.

Intoxication caused by non-drug substances also vary according to geographical region, socio-economic status and time of year (in relation with season). Kendirci et al. found
that 49% of their cases had carbon monoxide intoxication in their study, which was associated with the low socio-economic level of the region served by the hospital and the use of coal stoves in homes. Kızılyıldız et al. found that pesticides were the most common cause of intoxication with non-drug substances in their studies in Van, Turkey. In another study in Italy, it was reported that the most common non-drug agents were household cleaning products. In our study, the most common non-pharmaceutical agent causing intoxication was found to be carbon monoxide poisoning (8.1%).

Drug intoxication may develop due to one type of agent, or it may develop due to the intake of more than one agent. In the study by Berta et al., only 4.8% of patients had intoxication with multiple agents. In this study, patients with single-agent intoxication were found to be younger than those with multiple-agent intoxication (median, 2.1 vs. 3.5 years). Yorulmaz et al. showed that the majority (80.1%) of the intoxication cases admitted to the pediatric emergency department were due to a single agent. In our study, most of the patients (67.4%) were exposed to intoxication with one type of agent, and 39.7% of single-agent intoxication cases were in patients younger than 5 years of age. 69.7% of patients under 5 years of age were found to have single-agent intoxication.

Post-intoxication treatments can be summarized as follows: prevention or reduction of the absorption of the toxic substance from the gastrointestinal tract, skin and other routes, administration of antidotes, altering metabolism of the toxic substance, accelerating excretion, detoxification, and supportive treatments with extracorporeal methods. In the literature, gastric lavage, activated charcoal, and mechanical ventilator support are listed as the most common medical interventions in intoxication cases. In our study, gastric lavage was applied to 41.9% of the patients and activated charcoal was applied to 44.1%—similar to the literature on this topic.

Some of our patients were treated with extracorporeal management methods. RRT was applied in 6 patients in total. The agents were: anticonvulsive–drug (carbamazepine) in two, metformin in two, alcohol in one and methamphetamine in one. In metformin and alcohol intoxication, RRT can be applied for the treatment of severe metabolic acidosis. Although rare, methamphetamine intoxication has been reported to cause acute kidney failure. In severe carbamazepine intoxication, RRT was recommended due to the high binding capacity of the drug to plasma proteins. Another extracorporeal method we practiced was plasmapheresis which was utilized in three patients. Two of the patients had colchicine and 1 had isoniazid poisoning. In the case with isoniazid intoxication, plasmapheresis was required due to the development of acute liver failure. There are publications in the literature reporting that plasmapheresis therapy may have beneficial effects on colchicine intoxication. Plasmapheresis treatment was applied in these two cases because colchicine intake was at a major toxic level. In one case, cardiac pacing was performed because of hypotension that was resistant to inotropic therapy (toxic dose beta blocker intoxication). ECMO treatment was applied to one case for the treatment of ARDS that had developed due to activated charcoal aspiration. Although activated charcoal is an inert substance, it is an agent that can cause serious damage to the lung with an inflammatory effect when aspirated.

Intoxication-related findings depend on the agent causing intoxication, the amount of the agent taken and the time between intoxication and hospital admission. The frequency of the presence of intoxication-related clinical findings at the time of admission (to the emergency room) and PICU admission have been reported to be 28.7% and 72.1%. In our study, the majority of patients (82.6%) had at least one toxicity-related finding. This may be due to the lower frequency of symptoms in patients admitted to the emergency department. Another reason was the acceptance criteria to PICU, which may have caused some exaggeration of findings due to the fear of toxic effects in relation to the type and/or dosage of the agent taken. The most common finding observed in our patients were CNS findings, and 54.6% of the patients had at least one neurological finding. CNS findings were followed by gastrointestinal system findings with 14.0% of patients having at least one gastrointestinal system finding. In the literature, although the findings of the gastrointestinal tract are more frequent, CNS findings are often in second place in terms of frequency.

The period between intoxication and hospital admission is very important for decontamination procedures after intoxication and also the initiation of appropriate treatment. In our study, the average time from intoxication to hospital admission was 239 minutes. In various studies reported from our country, this time ranged from 89 to 223 minutes on average.

Studies have shown that the average duration of PICU stay in intoxication cases ranged from 20 hours to 2 days and the average hospital stay from 20 hours to 3.5 days. In our study, mean LOS at PICU was 4.3
days and mean LOS at hospital was 5.8 days. In our country, mortality rates due to intoxication vary between 0% and 5.4% in the pediatric age group. In the literature, the largest study evaluating intoxication cases in PICUs belongs to Patel et al. with 12,021 cases with a mortality rate of 0.6% [7]. In our study, the mortality rate was 1.2% (n=1). The death was associated with refractory shock by calcium channel blocker intoxication. Previous studies from our country were unable to evaluate risk factors associated with mortality, since mortality rate is low and the majority of studies were performed in a single-center with limited number of patients. There is a need for multicenter studies to reach a wide range of cases.

There were some study limitations that must be discussed. Since this was a retrospective study, the long-term results of the patients are unknown. Secondly, it is not possible to generalize our findings to the entire pediatric age group, since our study only included cases admitted to the PICU. Finally, it was not possible to evaluate mortality-related risk factors due to small sample size – as is the case in the majority of studies in this field.

Conclusions

Childhood intoxications are one of the most important causes of preventable mortality and morbidity throughout the world. Knowing the epidemiology of intoxication is of great importance for rapid and correct treatment. Multicenter comprehensive studies are needed to reveal risk factors related to mortality. The development of clinical scoring tools that can predict which patients may require intensive care will increase the efficiency of PICU utilization.

Ethics Committee Approval: Approval of the study was obtained from the local ethics committee (Protocol number: 2020/0336). The study was conducted in accordance with the principles of the Declaration of Helsinki.

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Authorship Contributions: Concept: M.D., Ş.K.A.; Design: M.D.; Data Collection or Processing: Ş.K.A.; Analysis or Interpretation: M.D.; Literature Search: M.D.; Writing: M.D.

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