



Clinical features of children with drug poisoning in a single emergency department in Goyang, Korea

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Purpose: Pediatric drug poisoning is a frequent reason for emergency department (ED) visits. Considering the increasing number of mental illnesses in adolescents, it has become a serious public health problem. We aimed to investigate the drug poisoning in the ED.

Methods: We retrospectively analyzed children aged 1-17 years with diagnostic codes related to drug poisoning who visited the ED from January 1, 2010 through October 7, 2022. Exclusion criteria were non-pharmaceutical poisoning, insufficient data, and poisoning via respiratory, dermal or ocular route. Baseline characteristics, clinical manifestations, and outcomes of drug poisoning were analyzed in the study population, according to intention of poisoning and drug category.

Results: A total of 197 cases of 161 children were analyzed. Compared with non-intentional poisoning, intentional poisoning was associated a higher age, a longer time from ingestion to visit, and higher proportions of girls, antipyretics/analgesics or psychotropic drugs, symptoms related to the gastrointestinal, neurologic or cardiopulmonary systems ($P = 0.034$), psychiatric comorbidity, multiple drug ingestion, suicide attempt, decontamination ($P = 0.017$), the use of antidote, history of drug poisoning, and hospitalization ($P = 0.004$; all other P s < 0.001). Acetaminophen, a representative of antipyretics/analgesics, was associated with a longer time from ingestion to visit and higher proportions of girls ($P = 0.004$), the presence of initial gastrointestinal symptoms, suicide attempt ($P = 0.001$), the use of antidote, and hospitalization (all other P s < 0.001). Psychotropic drug was associated with higher proportions of psychiatric comorbidity ($P < 0.001$) and multiple drug ingestion ($P = 0.012$).

Conclusion: This study will enable pediatricians or emergency physicians to obtain an overview of the management of drug poisoning in EDs.

Key words: Acetaminophen; Antidepressive Agents; Antipsychotic Agents; Histamine Antagonists; Intention; Pediatrics; Poisoning

Introduction

According to the World Health Organization, acute poisoning is associated with approximately 45,000 annual deaths among patients younger than 20 years¹. In Korea, 133,646 patients with the same

age range visited health care facilities with the Korean Classification of Disease, 8th Revision codes related to drug poisoning (T36-65) annually from 2014 through 2018^{2,3}. In addition, suicide has been the most common cause of death among teenagers since 2009, with poisoning accounting for 49.2% of their suicidal methods^{4,5}. It is important to understand the features of pediatric drug poisoning to provide appropriate emergency care. Thus, we aimed to analyze the baseline characteristics, clinical manifestations, and outcomes according to the intention of poisoning and drug category in children with drug poisoning who visited the emergency department (ED).

Received: Oct 26, 2022

Revised: Dec 6, 2022

Accepted: Dec 6, 2022

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Methods

We reviewed electronic medical records of children aged 1–17 years with the aforementioned diagnostic codes related to drug poisoning (T36–65) who visited the ED of National Health Insurance Service Ilsan Hospital (Goyang, Korea) from January 1, 2010 through October 7, 2022²⁾. The ED staff cares for approximately 7,000 children annually. We excluded cases of non-pharmaceutical poisoning (e.g., exposure to household products), insufficient data or poisoning via respiratory, dermal or ocular route. Emergency practices for drug poisoning were performed by pediatricians on duty. Decontamination, such as orogastric lavage and administration of activated charcoal, was selectively performed considering the lapse of time from the ingestion (≤ 1 –2 hours), airway protection, the degree of cooperation, and potential severity of poisoning. Two or more visits for drug poisoning of a single child were regarded as separate cases and as having history of drug poisoning from the second time. Those who ingested several types of drugs at once were regarded as multiple drug ingestion (DI). The ethics committee approval was obtained for the research on October 20, 2022 with a waiver of informed consent (IRB no. 2022–10–008).

In each case, age, sex, time from ingestion to visit (hours), intention of poisoning, drug category, initial manifestations, psychiatric comorbidities, multiple DI, suicide attempt, decontamination, antidote therapy, history of drug poisoning, and ED outcomes were investigated. The outcomes included hospitalization (overall and to the intensive care unit [ICU]), length of hospital stay (days), and in-hospital mortality. Laboratory data included aspartate and alanine aminotransferases, arterial blood gas analysis, and creatine kinase (CK).

Intentional drug poisoning was defined as an ingestion that was determined to be a willful overdose, as in a suicide attempt or gesture⁶⁾. Non-intentional poisoning included cases in which drugs were mistaken for candies by infants and toddlers, taken by older children with mental retardation without

recognition or given by caregivers without knowing the proper amounts.

The drug categories included antipyretics/analgesics, psychotropic drugs, antihistamines/cold preparations, and miscellaneous. In a case of multiple DI, the case was classified by a drug ingested at higher dose. In a category, all generic names or subcategories were recorded. In cases of acetaminophen (AAP) poisoning, N-acetylcysteine (NAC) was infused per a 21-hour intravenous (IV) protocol (a total of 300 mg/kg)⁷⁾. Hepatocellular injury was defined as an alanine aminotransferase concentration greater than 2 times the upper normal limit. In cases of psychotropic drugs, elevated CK was defined as a CK concentration greater than 5 times the upper normal limit.

For continuous variables, Mann-Whitney U tests and Kruskal-Wallis H tests were used. For categorized variables, chi-square tests were used to analyze the difference between the groups. Statistical significance was defined as $P < 0.05$. All statistical analyses were done by SPSS software package for Windows ver. 22 (IBM Corp., Armonk, NY).

Results

Among a total of 274 cases of drug poisoning, 77 were excluded (Fig. 1). Resultingly, 197 cases of 161 children were included, of which 124 (62.9%) were reported to be intentional. Seventeen patients showed 2–6 repeated episodes of poisoning, making a total of 36 cases with history of drug poisoning.

Table 1 shows that compared with non-intentional poisoning, intentional poisoning was associated with a higher age, a longer time from ingestion to visit, and higher proportions of girls, antipyretics/analgesics, psychotropic drugs, the presence of initial manifestations related to the gastrointestinal, neurologic or cardiopulmonary systems, psychiatric comorbidity, multiple DI, suicide attempt, decontamination, the use of antidote, history of drug poisoning, and hospitalization. No in-hospital mortal-

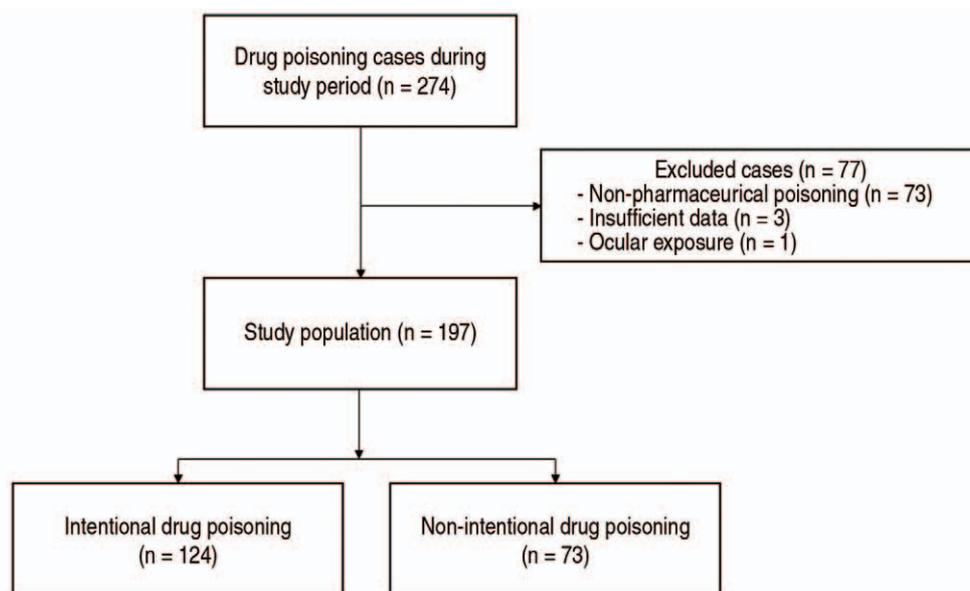


Fig. 1. Flowchart for the study population. The numbers are those of the cases, not of the children.

ity occurred in the population. In terms of the drug category, psychotropic drugs (67 [34.0%]) were most commonly taken, followed by antipyretics/analgesics (58 [29.4%]), miscellaneous (46 [23.4%]), and anti-histamines/cold preparations (26 [13.2%]).

Clinical features according to the drug category are summarized in Table 2. Among the 58 cases of antipyretics/analgesics poisoning, 54 were AAP poisonings and the other 4 were ibuprofen poisoning with a median dose of 33.5 mg/kg (therapeutic dose range, < 28 mg/kg/day). Given that the 4 cases were asymptomatic, only the AAP cases were tabulated (Table 2). Among the categories, AAP poisoning was associated with a longer median time from ingestion to visit and higher proportions of girls, the presence of initial gastrointestinal manifestation, suicide attempt, the use of antidote, and hospitalization.

In all but 6 cases of AAP poisoning, the time from ingestion to visit was 24 hours or shorter. Median ingested dose and concentration were 109.7 mg/kg (interquartile range, 70.3–195.1 mg/kg) and 35.0 $\mu\text{g}/\text{mL}$ (3.6–92.7 $\mu\text{g}/\text{mL}$), respectively. NAC was administered to 27 cases, including the ingestion of more than 150 mg/kg of AAP (n = 19), severe symptoms (n = 4), and co-ingestion of alcohol (n = 4). Two hepatocellular injuries were exclusively observed

in the AAP poisonings. A 15-year-old girl with a hepatocellular injury showed a peak concentration of alanine aminotransferase of 3,306 IU/L and an international normalized ratio of 1.6. She was discharged uneventfully after NAC therapy and observation over 1 night in the ICU.

Psychotropic drug poisoning was associated with higher proportions of psychiatric comorbidity and multiple DI (Table 2). Thirty-two cases involved 2–5 psychotropic drugs simultaneously. Because of the variability of drugs involved, ingested quantity was calculated as the total number of tablets. The median number of tablets ingested was 20.0 (interquartile range, 8.0–33.5). Some of the neurologic symptoms, including tremors (n = 2), dystonia (n = 1), drooling (n = 1), and hiccups (n = 1), were only observed in the psychotropic drug poisoning. In all rhabdomyolysis cases, concentrations of CK were rapidly normalized with IV hydration, except in the case of a 15-year-old girl undergoing continuous renal replacement therapy. Although QTc prolongations were frequently seen in the psychotropic drug poisoning, all prolonged QTc were normalized on the day after electrolyte repletion or at the first outpatient visit. L-carnitine was administered as an antidote to another 15-year-old girl with valproic acid poisoning (587 mg/kg) whose ini-

Table 1. Clinical features of the children with drug poisoning who visited the emergency department, according to intention of poisoning (N = 197)

| Variable | Intentional (N = 124) | Non-intentional (N = 73) | P value |
|--------------------------------------|--------------------------|-----------------------------|---------|
| Age, y | 15.5 (14.2-16.3) | 2.1 (1.5-2.9) | < 0.001 |
| Girls | 95 (76.6) | 33 (45.2) | < 0.001 |
| Time ingestion-visit, h | 3.1 (1.4-8.2) | 0.9 (0.5-1.7) | < 0.001 |
| Drug category | | | |
| Antipyretics/analgesics | 53 (42.7)* | 5 (6.8) | < 0.001 |
| Psychotropic drugs | 54 (43.5)* | 13 (17.8) | < 0.001 |
| Antihistamines/cold preparations | 12 (9.7)* | 14 (19.2) | 0.057 |
| Miscellaneous | 5 (4.0)* | 41 (56.2) | < 0.001 |
| Initial manifestations [†] | | | |
| Asymptomatic | 32 (25.8) | 65 (89.0) | < 0.001 |
| Gastrointestinal | 75 (60.5) | 2 (2.7) | < 0.001 |
| Neurologic | 45 (36.3) | 3 (4.1) | < 0.001 |
| Cardiopulmonary | 14 (11.3) | 2 (2.7) | 0.034 |
| Anticholinergic toxidrome | 2 (1.6) | 1 (1.4) | > 0.999 |
| Psychiatric comorbidity [†] | 102 (82.3) | 1 (1.4) | < 0.001 |
| Multiple drug ingestion | 53 (42.7) | 3 (4.1) | < 0.001 |
| Suicide attempt | 67 (54.0) | 0 (0) | < 0.001 |
| Decontamination | 16 (12.9) | 2 (2.7) | 0.017 |
| Antidote | 27 (21.8) | 1 (1.4) | < 0.001 |
| History of poisoning | 36 (29.0) | 0 (0) | < 0.001 |
| Hospitalization, overall | 28 (22.6) | 5 (6.8) | 0.004 |
| Length of stay, d | 3.0 (2.0-4.0) | 3.0 (2.0-4.0) | 0.948 |
| Intensive care unit [‡] | 2 (1.6) | 1 (1.4) | > 0.999 |
| In-hospital mortality | 0 (0) | 0 (0) | NA |

Values are expressed as medians (interquartile ranges) or numbers (%).

* The sums of proportions are not equal to 100% due to rounding.

† Mutually inclusive.

‡ Major depressive disorder (n = 49), bipolar disorder (n = 12), obsessive-compulsive disorder (n = 5), attention deficit hyperactivity disorder (n = 5), unspecified depressive disorder (n = 4), anxiety disorder (n = 3), adjustment disorders (n = 3), panic disorder (n = 3), and autistic disorder (n = 2).

§ All were discharged uneventfully.

tial concentration of valproate acid was higher than 300 µg/mL. Of the 2 ICU cases, besides the aforementioned girl undergoing continuous renal replacement therapy, a 6-year-old boy who was erroneously administered chloral hydrate of 460 mg/kg at a dental clinic developed respiratory distress with severe respiratory acidosis. He was discharged after 4-day mechanical ventilation.

Although the cases of antihistamines/cold preparations poisoning showed a higher rate of asymptomatic poisonings and lower rate of hospitalization than those of AAP poisoning, a 17-year-old girl who ingested diphenhydramine (50 mg/kg) had severe

symptoms. She underwent a 1-minute generalized tonic-clonic seizure at the ED, and showed a lactic acid concentration of 16.0 mmol/L. Electrocardiography showed sinus tachycardia with a heart rate of 150 beats/minute. After administration of a single dose of IV lorazepam, repeated doses of sodium bicarbonate, and normal saline hydration, her laboratory findings improved, and she was discharged after 5 days.

The cases of miscellaneous poisoning contained most types of drugs that can be encountered at home (Table 3). Forty-one cases involved unintentional ingestions by preschoolers with minimal doses, caus-

Table 2. Clinical features according to drug category (N = 147)

| Variable | Acetaminophen (N = 54) | Psychotropic drugs (N = 67) | Antihistamines/cold preparations (N = 26) | P value |
|--|---------------------------|--------------------------------|--|---------|
| Age, y | 15.0 (14.0-16.2) | 15.0 (13.2-16.2) | 9.0 (2.4-16.2) | 0.075 |
| Girls | 44 (81.5) | 50 (74.6) | 12 (46.2) | 0.004 |
| Time ingestion-visit, h | 4.7 (1.9-11.7) | 2.1 (1.0-5.2) | 1.5 (0.6-2.1) | < 0.001 |
| Initial manifestations* | | | | |
| Asymptomatic | 8 (14.8) | 35 (52.2) | 15 (57.7) | < 0.001 |
| Gastrointestinal [†] | 45 (83.3) | 17 (25.4) | 9 (34.6) | < 0.001 |
| Neurologic [†] | 17 (31.5) | 22 (32.8) | 4 (15.4) | 0.227 |
| Cardiopulmonary [‡] | 8 (14.8) | 6 (9.0) | 1 (3.8) | 0.285 |
| Anticholinergic toxidrome [¶] | 0 (0) | 1 (1.5) | 1 (3.8) | 0.377 |
| Laboratory abnormalities [¶] | | | | |
| Rhabdomyolysis | 0 (0) | 4 (6.0) | 0 (0) | 0.086 |
| Acidosis | 0 (0) | 1 (1.5) | 1 (3.8) | 0.377 |
| Hepatocellular injury | 2 (3.7) | 0 (0) | 0 (0) | 0.169 |
| Electrocardiographic abnormalities** | 10 (18.5) | 17 (25.4) | 6 (23.1) | 0.666 |
| Psychiatric comorbidity | 37 (68.5) | 53 (79.1) | 9 (34.6) | < 0.001 |
| Multiple drug ingestion | 18 (33.3) | 32 (47.8) | 4 (15.4) | 0.012 |
| Suicide attempt | 31 (57.4) | 29 (43.3) | 3 (11.5) | 0.001 |
| Decontamination | 3 (5.6) | 12 (17.9) | 2 (7.7) | 0.085 |
| Antidote | 27 (50.0) | 1 (1.5) | 0 (0) | < 0.001 |
| Time ingestion-therapy, h | 7.3 (4.1-10.9) | 15.2 (15.2-15.2) | NA | NA |
| Hospitalization, overall | 21 (38.9) | 7 (10.4) | 1 (3.8) | < 0.001 |
| Length of stay, d | 3.0 (2.0-3.0) | 4.0 (2.5-4.0) | 5.0 (5.0-5.0) | 0.420 |
| Intensive care unit | 1 (1.9) | 2 (3.0) | 0 (0) | 0.654 |

Values are expressed as medians (interquartile ranges) or numbers (%).

* Mutually inclusive.

[†] Nausea, vomiting, abdominal pain or dyspepsia.

[‡] In common, headache, dizziness, confusion or loss of consciousness; in psychotropic drugs, plus tremor, dystonia, drooling or hiccups; and in antihistamines/cold preparations, plus seizure.

[§] In acetaminophen and psychotropic drugs, chest pain, dyspnea or palpitation; in antihistamines/cold preparations, only palpitation.

[¶] Dry mouth or facial flushing.

[¶] Rhabdomyolysis was defined as creatine kinase > 5 times the upper normal limit; acidosis, pH < 7.30; and hepatocellular injury, alanine aminotransferase > 2 times the upper normal limit.

** In acetaminophen, sinus tachycardia or bradycardia (n = 4), nonspecific T wave abnormality (n = 3), and QTc prolongation (> 470 msec) (n = 3); in psychotropic drugs, QTc prolongation (> 470 msec) (n = 10), sinus tachycardia or bradycardia (n = 4), and nonspecific T wave abnormality (n = 3); in antihistamines/cold preparations, sinus tachycardia or bradycardia (n = 3) and nonspecific T wave abnormality (n = 3).

ing no major clinical or laboratory abnormalities in most cases.

Discussion

This study shows the following findings. First, intentional poisoning was associated with adolescence (mostly girls), delayed visits, ingestion of

antipyretics/analgesics or psychotropic drugs, symptomatic poisoning, psychiatric comorbidity, multiple DI, suicide attempt, emergency measures, history of drug poisoning, and hospitalization. Hospitalization was considered to have low severity given the absence of differences in the median length of stay, intensive care, and in-hospital mortality. Second, the features related to the intentional poisoning were also demonstrated in the poison-

Table 3. Details of the psychotropic drugs, antihistamines/cold preparations, and miscellaneous

| Psychotropic drugs (N = 67)* | Antihistamines/cold preparations (N = 26) [†] | Miscellaneous (N = 46) |
|---|--|---|
| BZDs, 37 (55.2) | First generation antihistamines, 14 (53.8) | Antihypertensive medications, 13 (28.3) |
| SSRIs, 35 (52.2) | Nasal decongestants, 8 (30.8) | Montelukast, 4 (8.7) |
| Atypical antipsychotics, 26 (38.8) | Second generation antihistamines, 7 (26.9) | Finasteride, 4 (8.7) |
| Anti-epileptic drugs, 13 (19.4) | Mucolytics, 3 (11.5) | Synthroid, 3 (6.5) |
| Anti-anxiety drugs other than BZDs, 5 (7.5) | Bronchodilators, 2 (7.7) | Antibiotics, 3 (6.5) |
| Atypical antidepressants, 4 (6.0) | Herbal cold medications, 2 (7.7) | Dyslipidemia medication, 3 (6.5) |
| Stimulants, 3 (4.5) | | Diabetes medication, 2 (4.3) |
| SNRIs, 2 (3.0) | | Antiplatelet drugs, 2 (4.3) |
| Tricyclic antidepressants, 1 (1.5) | | Vitamins, 2 (4.3) |
| Others, 5 (7.5) [‡] | | Others, 11 (23.9) [§] |

Values are expressed as numbers (%).

* The combinations of generic names or subcategories in the order of frequencies were as follows: SSRI + BZD (n = 8), SSRI + BZD + atypical antipsychotics (n = 5), and SSRI + atypical antipsychotics (n = 4); escitalopram (n = 17), alprazolam (n = 17), clonazepam (n = 14), quetiapine (n = 11), fluoxetine (n = 10), aripiprazole (n = 10), lorazepam (n = 9), divalproex (n = 6), risperidone (n = 5), and lamotrigine (n = 4).

[†] Anti-parkinsonism drugs (n = 2), hypnotics/sedatives other than BZD (n = 2), and lithium (n = 1).

[‡] Three most frequently ingested drugs with the dosages were pseudoephedrine (n = 4; dose range, 2–24 mg/kg), diphenhydramine (n = 3; 5.3–50 mg/kg), and chlorpheniramine (n = 3; 0.3–1.5 mg/kg).

[§] Anti-seasickness pills, iron complex, immunosuppressant, and caffeine, et cetera.

BZD: benzodiazepine, SSRI: selective serotonin reuptake inhibitor, SNRI: serotonin and norepinephrine reuptake inhibitor.

ing of AAP or psychotropic drugs.

Girls' predominance was noted in both comparisons according to the intention and drug category. This finding is consistent with previously reported girls' predominance in adolescent poisoning^{1,8}. Age distribution peaked at nearly 15.2 years in the intentional group and 2.1 years in the non-intentional group, which was also similar to other studies^{9,10}. The drug categories that were intentionally ingested consisted mostly of readily available or regularly taken drugs.

In this study, AAP poisoning showed the highest proportion of having gastrointestinal symptoms. In 83.3% of AAP poisoning, the children developed gastrointestinal symptoms, such as nausea and vomiting (n = 44), abdominal pain (n = 17), and dyspepsia (n = 2), which are similar to the previous study¹¹. Since the NAC therapy is well known for the prevention of hepatotoxicity in AAP poisoning¹², the rate of antidote use for AAP poisoning was higher than the other drug categories. This led to the highest hospitalization rate in AAP poisoning due to the 21-hour IV protocol of NAC. Apart from the

administration of NAC within 24 hours of ingestion, IV NAC is recommended for patients with delayed presentation (> 24 hours) or evidence of hepatic injury^{13,14}. The amount of ingested AAP and the lapse of time from the ingestion by 2 children with hepatocellular injuries were as follows: 209 mg/kg and 84 hours; and 148 mg/kg and 94 hours. Both children recovered with IV NAC despite the delayed presentation.

In the cases of psychotropic drugs poisoning, asymptomatic or discharge cases were more common compared to the cases of AAP poisoning because most of the ingested psychotropic drugs had a weak toxicity. Benzodiazepines (BZDs), selective serotonin reuptake inhibitors (SSRIs), and atypical antipsychotics were the 3 most common drugs ingested (Table 3). SSRIs have less severe toxicity than tricyclic antidepressants in overdose, and rarely result in fatality¹⁵. In this current study, a single case of tricyclic antidepressants poisoning was reported. A 1-year-old boy accidentally took the drugs within the therapeutic dose range, and remained asymptomatic. Although overdose of BZDs and atypical

antipsychotics without other co-ingestions rarely cause a severe toxicity, BZDs can sometimes lead to central nervous system depression or hemodynamic instability^{16,17}. In a case of poisoning by the psychotropic drugs, a 15-year-old girl developed loss of consciousness and respiratory distress. Flumazenil was not tried in the study population because of its short half-life, adverse effects such as convulsions¹⁸, and the on-duty pediatricians' preference for conservative therapy.

This study has a few limitations. First, as the hospital is not a tertiary care center, some children requiring ICU care might have been initially transferred to a nearby tertiary hospital. This could explain the low incidence of morbidity and mortality in this current study. Second, since this study included cases of all kinds of drug poisoning, the detailed evaluation of single drug category may be lacking.

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Conflicts of interest

No potential conflicts of interest relevant to this article were reported.

Funding sources

No funding source relevant to this article was reported.

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