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Impact of drug formulation on outcomes of pharmaceutical poisoning in children aged 7 years or younger

A retrospective observational study in South Korea

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Abstract

Pharmaceutical poisoning in children is almost unintentional and there are various types of drug out of curiosity. Understanding the attractive features and formulation of drugs related to poisoning in younger children may be helpful in treatment and prevention of poisoning. To investigate the impact of drug formulation on outcomes of pharmaceutical poisoning in young children.

We retrospectively reviewed the data of pharmaceutical exposures among children who were registered in a Korean 23-center, emergency department (ED) based registry from 2011 to 2016. Our study was conducted on preschool children aged 0 to 7 years. According to the formulation and category of the ingested drugs, the exposures were divided into the "tablet and capsule (TAC)" and "syrup" groups. In the TAC group, we additionally recorded data on the shape, color, and size of the drugs. The ED outcomes, such as hospitalization and length of stay, were compared between the 2 groups.

Among the 970 enrolled exposures, 674 (69.5%) were classified into the TAC group. In this group, hormones/hormone antagonists (18.5%) were the most commonly ingested, followed by central nervous system drugs (17.1%). In the syrup group, antihistamines (28.4%) were the most commonly ingested, followed by respiratory drugs (24.3%). The TAC group showed a higher hospitalization and transfer rate to tertiary centers than the counterpart (TAC, 18.0% vs syrup, 11.5%, $P = .03$) without a significant difference in the length of stay (TAC, 173.5 minutes [interquartile range, 95.0–304.0] vs syrup, 152.5 [77.5–272.0]; $P = .08$). No in-hospital mortality occurred in the exposures. Round-shaped and chromatic TACs, accounting for 91.7% (618) and 56.1% (378), respectively, were more commonly ingested. The median size of the TACs was less than 1.0 cm.

Young children who visited the ED ingested TACs more frequently than syrups, particularly small, round-shaped, or chromatic drugs, leading to a higher hospitalization rate. Our findings can contribute to prevention strategies and safety education on childhood drug poisoning.

Abbreviations: CNS = central nervous system, ED = emergency department, EDLOS = emergency department length of stay, ICU = intensive care unit, IQR = interquartile rage, TAC = tablet and capsule.

Keywords: child, emergency department, pharmaceuticals, poison

1. Introduction

As deaths from infectious disease have decreased, the proportion of deaths caused by injury and poisoning have increased in children.[1,2] Pharmaceutical poisoning in children has increased, and the relevant serious outcomes have been emphasized.[3] In the United States, a 33% increase in pharmaceutical poisoning was noted in children younger than 6 years from 2000 to 2010.[3] In Korea, the proportion of pharmaceutical poisoning cases increased from 14% to 17% in the 1980s to 31% to 57% in the 2000s.[4]

Poisoning in children and adolescents shows different characteristics, according to age groups.[4,5] Unlike poisoning in adolescents, which has similar features to those of adult poisoning, most poisoning cases in young children are unintentional.[4–6] Although the mortality and morbidity in pediatric poisoning are lower than in adult poisoning,[5] we noted an increase in serious outcomes attributed to drugs which have potential fatality, even in low doses, such as opioids, cardiovascular medications, and oral hypoglycemic.[7] Because younger children ingest various drugs out of curiosity, the attractive features of formulations may play an important role in poisoning.

Although the common categories of drugs related to poisoning in younger children have been reported, there is a lack of research

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on their features and formulation types. Understanding the characteristics of these drugs may be helpful in the treatment and prevention of poisoning due to their ingestion. Thus, we aimed to investigate the impact of formulation types on the outcomes of pharmaceutical poisoning in children aged 7 years or younger.

2. Methods

2.1. Study design and setting

We retrospectively reviewed the data of children with pharmaceutical poisoning registered in the emergency department (ED) based Injury In-Depth Surveillance database in Korea. This database is a nationwide, 23-center, ED-based injury registry conducted by the Korean Centers for Disease Control and Prevention. To maintain data quality, researchers from the 23 academic hospitals participating in the registry underwent continuous education and received periodic feedback. In this study, we tried to reduce selection bias using prospectively collected data from this registry instead of medical records from individual EDs without standardized formats. Based on the online registry system, information on clinical characteristics and outcomes were documented in a standardized format. The authors conducted a pilot study to explore the characteristics of poisoning among younger children from this registry[8] prior to implementing the current study with a larger number of pediatric patients. This study was approved by the institutional review board with a waiver for informed consent from patients (IRB no. MED-MDB-20-533).

2.2. Study population

The authors enrolled preschool children aged 0 to 7 years with pharmaceutical poisoning who visited the participating EDs from 2011 to 2016. Given the features of the multicenter registry, this study was based on pharmaceutical exposure rather than on clinical presentation.[3,9] An exposure was defined as a case of drug ingestion. The exclusion criteria were as follows: when the drug names or information were not known, use of parenteral drugs, coingestion of drugs, non-pharmaceutical agents, and insufficient medical records. Taking ≥2 drugs simultaneously was an exclusion criterion because it could hinder the analysis of the impact of formulation on outcomes.

2.3. Data collection and study definitions

The clinical characteristics included age (in years), sex, intentionality, and place of poisoning. We divided the data into 2 groups according to the formulation of the drug; tablet and capsule (TAC) and syrup. We obtained details of the drugs ingested, such as type of formulation and category, from a website.[10] Based on the type of formulation, the exposures were classified into the TAC and syrup groups. The categories of drugs were listed.

The ED treatment outcomes between the groups were the primary endpoints. The outcomes included the frequency of discharge from the ED, hospitalization (overall and intensive care units [ICUs]), transfer to the tertiary hospital, ED length of stay (EDLOS; in minutes), and in-hospital mortality. We further investigated the shape (round [circle or ellipse] vs angular [triangle or square]), color (chromatic vs white or ivory), and size (long and short axis in centimeter [cm]) of the TAC group. And dividing age into secondary groups, drug formulation and ED outcome was compared: an infant group (<2 years), a preschooler group (2–7 years).

2.4. Statistical analysis

The continuous variables are described as medians with interquartile ranges (IQR) and the categorical variables are presented as numbers and percentages. The outcomes were compared between the 2 groups, using chi-squared or Fisher exact tests for categorical variables, and the Mann–Whitney *U* test for continuous variables. *P* values $<.05$ were considered statistically significant. Statistical analyses were performed using Stata software, version 15 (Stata Corp. LP, TX).

3. Results

3.1. General characteristics of the exposures

A total of 1654 exposures were collected and 970 were finally analyzed (Fig. 1). The median age was 2 years (IQR, 1.0–2.0); the majority of the exposures were unintentional (97.6%) and occurred at home (98.8%). Poisoning with TACs were more common than with syrups (TAC, 69.5% vs syrup, 30.5%). Although most exposures were discharged from the EDs, 15.2%

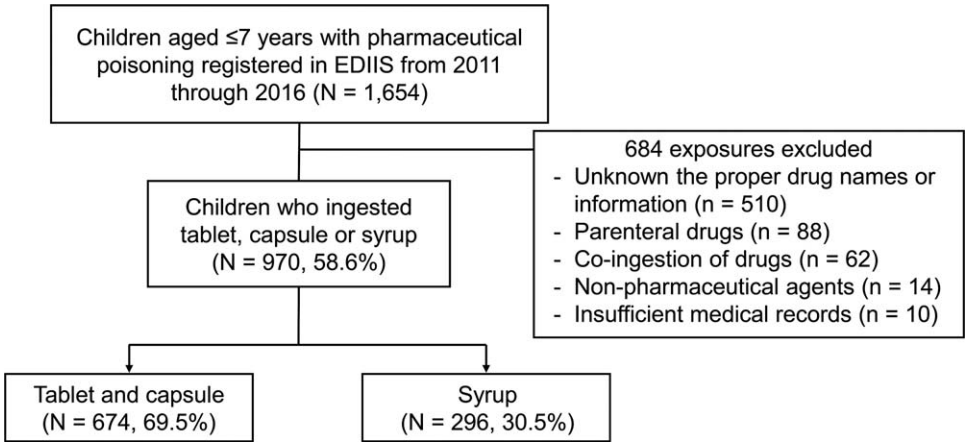

Figure 1. Flowchart for the selection of the study population. EDISS = Emergency Department Based Injury In-Depth Surveillance.

Table 1

General characteristics of the pharmaceutical exposure (N = 970).

Variable	
Age, y	2 (1–2)
Boys	499 (51.4)
Unintentional	947 (97.6)
Place of poisoning	
Home	958 (98.8)
Educational facilities	6 (0.6)
Others	6 (0.6)
Tablet and capsule	674 (69.5)
Syrup	296 (30.5)
Emergency department outcomes	
Discharge	815 (84.1)
Overall hospitalization	148 (15.2)
Intensive care units	8 (0.8)
Transfer to the tertiary hospital	7 (0.7)
Length of stay, min	170.0 (89.0–297.0)

Values are expressed as median (interquartile range) or number (%).

Table 2

Categories of drugs according to the formulations.

Category	Tablet and capsule (N = 674)	Syrup (N = 296)
Hormones/hormone antagonists	125 (18.5)	0 (0)
Central nervous system	115 (17.1)	0 (0)
Analgesics/antipyretics	103 (15.3)	60 (20.3)
Cardiovascular	96 (14.2)	3 (1.0)
Respiratory	46 (6.8)	72 (24.3)
Antihistamines	34 (5.0)	84 (28.4)
Gastrointestinal	34 (5.0)	9 (3.0)
Antimicrobials	28 (4.2)	54 (18.2)
Genitourinary	21 (3.1)	0 (0)
Anticonvulsants	12 (1.8)	6 (2.0)
Iron	10 (1.5)	6 (2.0)
Miscellaneous	50 (7.4)	2 (0.7)

Values are expressed as number (%).

required hospitalization, including 0.8% in the ICU. Median EDLOS was 170.0 minutes (IQR, 89.0–297.0 minutes) (Table 1).

3.2. Frequency of drugs ingested according to formulation

We analyzed drug categories according to the type of formulations; TAC and syrup (Table 2). Hormones/hormone antagonists and central nervous system (CNS) drugs were the most common categories in the TAC group. Regarding single-agent drugs, levothyroxine (82 exposures) was most commonly ingested as a TAC, followed by non-steroidal anti-inflammatory drugs (66 exposures), antihypertensives (63 exposures), and benzodiazepines (54 exposures) (Table 3). In the syrup group, antihistamines and respiratory drugs were the most frequently ingested.

3.3. ED outcomes according to formulation

Table 4 shows the differences in ED outcomes between the groups. Compared with the syrup group, the TAC group showed a significantly higher overall hospitalization and transfer rate to tertiary hospitals (TAC, 18.0% vs syrup, 11.5%; $P = .03$). In this group, a total of 109 (16.2%) exposures led to hospitalization in the general wards. Among them, poisoning with levothyroxine accounted for 31 cases, followed by antihypertensive drugs (18 exposures). In the syrup group, 31 exposures led to hospitalization in the general wards; of which antihistamines (11 exposures) and analgesic/antipyretic drugs (8 exposures) were the most

Table 3

Category of the tablets and capsules.

Category	Subcategory
Hormones and hormone antagonists (125)	Levothyroxine (82), oral contraceptives (25), female hormone agents (13), adrenocortical hormones (2), desmopressin (2), and methimazole (1)
Central nervous system (115)	Benzodiazepines (54), sedatives/hypnotics (20), medications for CNS diseases (e.g., Parkinson and Alzheimer disease) (17), TCA/SSRI/SNRI (9), antipsychotics (7), appetite suppressants (4), and GABAergic drugs (4)
Analgesic/antipyretics (103)	NSAIDs (66), acetaminophen (36), and sumatriptan (1)
Cardiovascular (96)	Antihypertensives (63)*, antiarrhythmics (9)†, anticoagulants (8), antihyperlipidemics (6), medications for artery obstruction (e.g., Buerger disease) (5), diuretics (3), and vasodilators (2)
Respiratory (46)	Leukotriene modulators (31) and antitussives (15)
Antihistamines (34)	NA
Gastrointestinal (34)	NA
Antimicrobials (28)	Antibiotics (14), antifungal (5), antiviral (3), anti-malarial (3), mediation for Hansen disease (2), and anti-tuberculosis (1)
Genitourinary (21)	Medications for BPH (12), medications for erectile dysfunction (7), and uterotonic agents (2)
Anticonvulsants (12)	NA
Iron (10)	NA
Miscellaneous (50)	Mineral and vitamin agents (9), oral hypoglycemics (7), medications for gout (6), medications for periodontal disease (4), medications for hair loss (4), antivertigo drugs (3), dopamine agonists (3), medications for ophthalmic diseases (3), opioids (3), immunosuppressants (2), nilotinib (1), tranexamic acid (1), Leodase (1), Salagen Tab (1), Actojenic (1), and Champix (1)

The parenthesized values refer to numbers of the exposures of drug ingestion.

BPH = benign prostatic hyperplasia, CNS = central nervous system, GABA = gamma-aminobutyric acid, NSAID = nonsteroidal anti-inflammatory drug, SNRI = serotonin–norepinephrine reuptake inhibitor, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant.

* The subcategories were as follows: calcium channel blockers (21), angiotensin receptor blockers (15), angiotensin receptor blockers + diuretics (13), calcium channel blockers + angiotensin receptor blockers (9), angiotensin-converting enzyme inhibitors (2), □-blocker (1), α-blocker (1), and angiotensin-converting enzyme inhibitor + diuretics (1).

† The subcategories were as follows: β-blockers (7), flecainide (1), and digoxin (1).

Table 4

ED outcomes according to the formulations.

	Tablet and capsule (n = 674)	Syrup (n = 296)	*P* value
Discharge	553 (82.0)	262 (88.5)	.03
Overall hospitalization	115 (17.1)	33 (11.2)	NA
Intensive care unit	6 (0.9)	2 (0.7)	NA
Transfer to the tertiary hospital	6 (0.9)	1 (0.3)	NA
Length of stay, min	173.5 (95.0–304.0)	152.5 (77.5–272.0)	.08

Values are expressed as medians (interquartile rages) or numbers (%).
ED = emergency department.

Table 5

Drug formulation and ED outcomes according to the age groups.

	Infant (n = 448)	Preschool (n = 522)	*P* value
Boys	224 (50.0)	275 (52.7)	.440
Formulation			.000
Tablet and capsule	348 (77.7)	326 (62.5)	
Syrup	100 (22.3)	196 (35.5)	
ED outcome			.007
Discharge	359 (80.1)	456 (87.3)	
Overall hospitalization	85 (19.0)	63 (12.1)	
Transfer to the tertiary hospital	4 (0.9)	3 (0.6)	
Length of stay, min	168.5 (87.0–296.0)	172.5 (90.0–303.0)	.920

Values are expressed as numbers (%) or medians (interquartile rages).
ED = emergency department.

common (Fig. 2). In respect of ICU admission cases in the TAC group, there were 3 cases of poisoning with anti-hypertensive drugs, 2 cases with levothyroxine, and 1 case with an oral hypoglycemic. In the syrup group, 1 patient with iron poisoning and 1 patient with ibuprofen poisoning were admitted to the ICU. Despite the lack of significance, the median EDLOS tended to be longer in the TAC group (TAC, 173.5 minutes vs syrup, 152.5). No in-hospital mortality occurred.

3.4. Morphologic features of TAC and data according to the age group

Because the TAC group had clinical implications in terms of higher hospitalization rates and longer stays in the ED, a sub-analysis was performed in this group (n = 674). The round shape was more common than the angular shape (91.7% vs 8.3%), and poisoning with chromatic drugs was more common than with white or ivory ones (56.1% vs 43.9%). The median sizes were 0.9 cm (IQR, 0.7–1.1) as the long axis and 0.7 (0.6–0.8) as the short axis.

We analyzed drug formulations and ED outcomes according to the age groups. Compared with the preschool age group (2–7 years), the infant group (<2 years) ingested TACs more and showed a significantly higher overall hospitalization and transfer rate to tertiary hospitals (infant, 19.9% vs preschool, 12.7%; $P = .007$). There was not significant difference in color and shape between the 2 groups (Table 5).

4. Discussion

To the best of our knowledge, this is the largest study to evaluate the characteristics of pediatric poisoning according to the details of drug formulations. This multicenter ED-based study showed that TACs were more frequently ingested than syrups in children aged 7 years or younger. Moreover, the ingestion of TACs was associated with a significantly higher hospitalization and transfer rate to tertiary hospitals, suggesting worse outcomes with these formulations. We confirmed these findings by comparing them with those of the pilot study.[8]

The median age of 2 years is similar to the 24 to 41 month age range which has the highest incidence or odds of pharmaceutical poisoning in other studies on preschoolers.[11–13] This age group has been identified as most susceptible to poisoning. The increasing susceptibility of this age group may be due to their

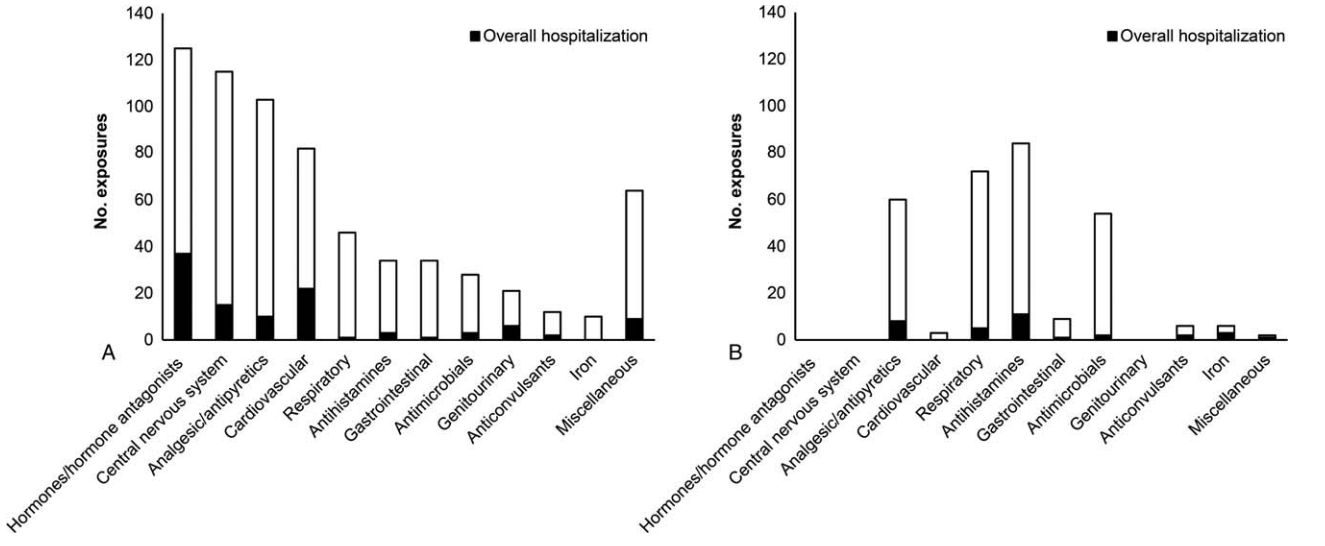

Figure 2. Comparison of overall hospitalizations between the tablet and capsule (TAC) group (A) and the syrup group (B). Shaded bars indicate the number of overall hospitalizations whereas the sum of the shaded and open bars indicates the total number of exposures.

inherent curiosity, development of hand motor skills, and increasing mobility. These developmental features can lead to drug ingestion by hand-to-mouth activity.[5,14] The hospitalization rate of 15.2% is parallel to the known equivalent rates, ranging from 12.0%[7] to 19.9%, found in other studies.[11]

In contrast to other studies, our study showed different frequencies in the drug categories. In our study, hormones and hormone antagonists were the most common category that caused poisoning, with levothyroxine being the most common single agent. Unlike our study result, neurological systemic agents were the most commonly reported in a study conducted in Taiwan,[15] anticonvulsant drug in Northeast Romania,[16] and psychotropic drugs in study from Spain[17] in the under 18 age group. In addition, Ahmed et al[18] demonstrated the analgesics and antipyretics as the most commonly ingested in age ≤14 years who visited hospitals managed under Hamad Medical Corporation in Qatar. In the USA, hormones and hormone antagonists ranked 19th amongst drug categories involved in overall exposure, and they accounted for 1.5% in single-substance exposure in children aged ≤5 years in the 2018 National Poison Data System annual report.[19] Levothyroxine poisoning is reported to be rare in children, although it is more common in children than in adults.[20,21] The high rate of levothyroxine poisoning in this study may be due to the high increases in the incidence of thyroid cancer in Korea.[22]

The drug category was different between the 2 groups. The majority of the TACs, such as hormones, CNS drugs, and cardiovascular drugs, were prescription drugs of adults who were members of the child's family. Among adult prescription drugs, oral hypoglycemics, opioids, β-blockers, calcium channel blockers, and benzodiazepines can lead to serious outcomes in young children.[3,7,9] Oral hypoglycemics accounted for the highest admission and injury rate. Opioids, sedatives, and cardiovascular drugs were associated with increased rates of hospitalization and serious outcomes.[7] Use of these drugs has been increasing in the United States[9] and Korea.[23,24] If adults take the drugs for long periods, the risk of poisoning increases among children who are curious about these drugs.[25] Because children aged approximately 2 years have a strong desire to imitate the adults around them,[26] they tend to ingest medicine unintentionally, not knowing the risks, since they see adults consuming it. This increasing risk may be worsened by the potential for life-threatening toxicity at single-pill doses.

We found that the hospitalization rate of the TAC group was higher than that of the syrup group. This might be because hormones, cardiovascular, and CNS drugs, which can be fatal to children, even in small amounts,[27] were common in the TAC group. This potential fatality could have led to more diagnostic tests or longer observation in the ED, causing a slightly longer EDLOS among these patients. In contrast, the commonly ingested categories of syrup were antihistamines and antipyretics, which were prescriptions for children. These drugs are known to have relatively wide ranges of safety dosages and benign outcomes[28,29] compared with the common categories of the TAC group. Therefore, the syrup group had a lower frequency of hospitalization.

Because the outcomes of TAC ingestion were worse than those of syrup ingestion, we analyzed the details of TAC that were attractive to younger children. We found that children were more likely to take round shapes rather than angled ones, and colored drugs rather than colorless ones. This might be because round-shaped drugs are available in higher proportions in the Korean market (see Table, Supplemental Digital Content, http://links.lww.com/MD2/A546 which lists the shape-based distribution of TACs in the Korean pharmaceutical market) and children are more attracted to colored drugs. The median size of the ingested TAC was <1.0 cm, which is assumed to be easier for young children to swallow.

Based on these characteristics, it is important to inform and pay attention to prevention and education on poisoning. The TACs that are dangerous for young children might be presumed to belong to an adult family member. Because children exhibit imitative behavior, it is necessary to educate caregivers not to take drugs in front of children.[26] In particular, storing small, round colored pills requires more attention. Drugs should be kept out of reach of children and should be stored in a safe container or in those with child-resistant closures. In addition, it is necessary to emphasize that caregivers should check the correct drug and dose of syrups prescribed to children. Our results can be used as a basis for policies on the prevention of poisoning and for preparation of treatment plans for emergency physicians who encounter pediatric poisoning cases.

This study has several limitations. First, because of the retrospective design, we could not analyze the total exposure dosage, whether antidotes were used, causes of admission, and so on. Second, in respect of the data of the multicenter registry, the outcomes might be partially affected by the lack of a standard protocol for hospitalization among the participating EDs. Third, this study was based on 23-ED registry, patients who visited the ED not registered in EDIIS or from private clinics may be excluded, and this might be potential for selection bias. However, most of childhood poisoned patients visits large EDs which are included in EDIIS due to the reality that lack of expert in child poisoning and fear for treating child poisoning. We consider that majority of the poisoning children may be included. Our study represents the results of a relatively serious form of childhood poisoning. To overcome these limitations, a prospective poisoning registry study for young children is necessary.

In conclusion, young children who visited the ED were more susceptible to poisoning with TACs prescribed to an adult family member than to poisoning with syrups prescribed to children. This feature of TAC poisoning was associated with a higher hospitalization rate. The round shape, colored features, and small size TACs were attractive to young children, leading to accidental ingestion and poisoning. These findings can be useful to physicians and caregivers for preventing and treating pharmaceutical drug poisoning among children.

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References

[1] Cunningham RM, Walton MA, Carter PM. The major causes of death in children and adolescents in the United States. N Engl J Med 2018;379:2468–75.
[2] Nagaraja J, Menkedick J, Phelan KJ, Ashley P, Zhang X, Lanphear BP. Deaths from residential injuries in US children and adolescents, 1985-1997. Pediatrics 2005;116:454–61.
[3] Spiller HA, Beuhler MC, Ryan ML, Borys DJ, Aleguas A, Bosse GM. Evaluation of changes in poisoning in young children: 2000-2010. Pediatr Emerg Care 2013;29:635–40.
[4] Woo JH, Ryoo E. Poisoning in Korean children and adolescents. Pediatr Gastroenterol Hepatol Nutr 2013;16:233–9.
[5] Lee VR, Connolly M, Calello DP. Pediatric poisoning by ingestion: developmental overview and synopsis of national trends. Pediatr Ann 2017;46:e443–8.
[6] Mintegi S, Fernández A, Alustiza J, et al. Emergency visits for childhood poisoning: a 2-year prospective multicenter survey in Spain. Pediatr Emerg Care 2006;22:334–8.
[7] Bond GR, Woodward RW, Ho M. The growing impact of pediatric pharmaceutical poisoning. J Pediatr 2012;160:265.e1–70.e1.
[8] Jang M, Ko Y, Yang HW, Lee J. Characteristics of poisoning in younger children according to different forms of the drugs. Pediatr Emerg Med J 2019;6:57–62.
[9] Burghardt LC, Ayers JW, Brownstein JS, Bronstein AC, Ewald MC, Bourgeois FT. Adult prescription drug use and pediatric medication exposures and poisonings. Pediatrics 2013;132:18–27.
[10] KIMS Online. Available at: http://www.kimsonline.co.kr. Accessed Dec 20, 2020.
[11] Chien C, Marriott JL, Ashby K, Ozanne-Smith J. Unintentional ingestion of over the counter medications in children less than 5 years old. J Paediatr Child Health 2003;39:264–9.
[12] Tyrrell EG, Orton E, Tata LJ, Kendrick D. Children at risk of medicinal and non-medicinal poisoning: a population-based case-control study in general practice. Br J Gen Pract 2012;62:e827–33.
[13] Schmertmann M, Williamson A, Black D. Unintentional poisoning in young children: does developmental stage predict the type of substance accessed and ingested? Child Care Health Dev 2014;40:50–9.
[14] MacInnes K, Stone DH. Stages of development and injury: an epidemiological survey of young children presenting to an emergency department. BMC Public Health 2008;8:120. doi: 10.1186/1471-2458-8-120.
[15] Lin YR, Liu TH, Liu TA, Chang YJ, Chou CC, Wu HP. Pharmaceutical poisoning exposure and outcome analysis in children admitted to the pediatric emergency department. Pediatr Neonatol 2011;52:11–7.
[16] Nistor N, Frasinariu OE, Rugina A, Ciomaga IM, Jitareanu C, Streanga V. Epidemiological study on accidental poisonings in children from northeast romania. Medicine (Baltimore) 2018;97:e11469. doi: 10.1097/MD.0000000000011469.
[17] Hernando JM, Nebot SS, Sánchez LM, de la Maza DV, Cubells LC. Unintentional intoxications in children: detecting risks. Emerg Med 2015;5:6. DOI: 10.4172/2165-7548.1000290.
[18] Ahmed A, AlJamal AN, Mohamed Ibrahim MI, et al. Poisoning emergency visits among children: a 3-year retrospective study in Qatar. BMC Pediatr 2015;15:104. doi: 10.1186/s12887-015-0423-7.
[19] Gummin DD, Mowry JB, Spyker DA, Brooks D, Osterthaler KM, Banner W. 2018 annual report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 36th annual report. Clin Toxicol 2019;57:1220–413.
[20] Ergul AB, Torun YA, Serbetci MC, Ozcan A, Bas VN. Clinical toxicity of acute overdoses with L-thyroxin in children. Pediatr Emerg Care 2019;35:787–90.
[21] Nygaard B, Saedder EA, Dalhoff K, Wikkelsoe M, Jurgens G. Levothyroxine poisoning - symptoms and clinical outcome. Basic Clin Pharmacol Toxicol 2015;117:280–5.
[22] Hyun MK, Kim JH, Kwon JW. Incidence of thyroid cancer and medical cost among patients with newly diagnosed thyroid nodules in Korea: a retrospective cohort study using nationwide data. J Cancer Res Ther 2019;15:676–80.
[23] Kim HC, Cho MC. Korean Society Hypertension (KSH), Hypertension Epidemiology Research Working GroupKorea hypertension fact sheet 2018. Clin Hypertens 2018;24:13. doi: 10.1186/s40885-018-0098-0.
[24] Lee MH, Choi JW, Lee J, et al. Trends in prescriptions for sedative–hypnotics among Korean adults: a nationwide prescription database study for 2011-2015. Soc Psychiatry Psychiatr Epidemiol 2019;54:477–84.
[25] Dayasiri MBKC, Jayamanne SF, Jayasinghe CY. Patterns and outcome of acute poisoning among children in rural Sri Lanka. BMC Pediatr 2018;18:274. doi.org/10.1186/s12887-018-1246-0.
[26] Rodgers GB, Franklin RL, Midgett JD. Unintentional paediatric ingestion poisonings and the role of imitative behaviour. Inj Prev 2012;18:103–8.
[27] Michael JB, Sztajnkrycer MD. Deadly pediatric poisons: nine common agents that kill at low doses. Emerg Med Clin North Am 2004;22:1019–50.
[28] Ten Eick AP, Blumer JL, Reed MD. Safety of antihistamines in children. Drug Saf 2001;24:119–47.
[29] Burillo-Putze G, Mintegui S, Munne P. Changes in pediatric toxic dose of acetaminophen. Am J Emerg Med 2004;22:323. doi: 10.1016/j.ajem.2004.04.018.