

Poisoning in Korean Children and Adolescents

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Drug intoxication in children and adolescents is not uncommon in Korea. But the tendency of intoxication is changing with some factors, such as national surveillance system, Naderism and increasing concern among physicians. But the death rate of intoxication among adolescents is increasing in spite of decreasing total death rate of intoxication among children and adolescents. Therefore the physician must be concerned about the basic management of intoxication and figure out the common toxic substance among children and adolescents.

Key Words: Poisoning, Child, Adolescent, Drug overdose, Korea

INTRODUCTION

Younger children are vulnerable to unintentional poisoning, whereas adolescence is critical age for intoxication by intentional drug ingestion. In the past, one of the confusing forms of intoxication to inexperienced physicians was the ingestion of liquid mercury from broken mercury thermometer. And the notorious toxic herbicide, 'paraquat (Gramoxone; SYNGENTA Korea, Seoul, Korea)', was a major worry to Korean physicians in emergency rooms in the past, but this concern has disappeared since its removal from the market in Korea in 2011.

The term 'toxicology' is a word derived from the Greek term, 'toxikos' and 'toxikon', which each means bow and poison into which arrowheads are dipped [1]. The term 'poisoning' usually means the

physiological state led by medicine, and the term 'intoxication' has wider meaning that it is led by a poison or other toxic substance. Drug misuse and drug abuse also has different meanings according to the purpose of drug use. The former is defined by the use of a drug against its original purpose, and the latter is defined as the repetitive misuse of an addictive drug.

This paper reviews the common intoxications that are changing, and what the recent new modalities are in the management of intoxication in children and adolescents.

EPIDEMIOLOGY

Drug poisoning in the United States (US) was a leading cause of death [2], and 429.4 poisonings per 100,000 children was treated in hospital emergency

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departments in 2004 in spite of non-fatal poisonings in children younger than 5 years of age [3]. These were similar in Korean children from the results showing a decreasing death rate of younger childhood due to poisoning.

Death from poisoning in Korean children and adolescents has decreased since 1983 according to the national data collected by the Korean Statistical Office. Of the total death rate of 530.8/100,000 population, the death rate of children and adolescents below 19 years of age was 374.9/100,000 population in 2012. Although the death rate from unintentional causes has decreased slightly, the death rate from intentional exposure has increased due to suicidal attempts during adolescence. Suicide is the most common cause of teenage deaths and it has increased from 3.5/100,000 population in 2002 to 5.5/100,000 population in 2012. The increase in the death rate of teenagers from poisoning in Korea (1.7 to 3.3/100,000 population) was similar in the US according to the Centers for Disease Control and Prevention (CDC) data in 2000 to 2009 [4,5]. These results were explained partially by intentional teen poisoning.

A nationwide study based on the database from National Health Insurance Corporation and Statistics Korea in 1997 identified a male predominance of childhood poisoning [6]. But there has been conflicting results regarding the gender differences among other studies [6-10]. The age distribution of poisoning showed a bimodal pattern with the first peak in younger children and the second peak in adolescents among above studies [6-10]. The common cause of poisoning was different in the two periods. Although accidental exposure was the most common cause in younger children, suicidal attempts was the most common cause in adolescence [7-9]. This is similar to that reported in the US. From the reports of the American Association of Poison Control Centers' National Poison Data System (NPDS), intentional exposure was common in ages, 13-19 years, and this fatal exposure was caused by suicidal attempts [11].

In 1980s, poisoning by agricultural chemicals, such as insecticides, rodenticides and herbicides,

were predominant at 37-52%, but a gradual decreasing tendency was noted [7,8]. After the year 2000, the proportion of poisonings by agricultural chemicals was only 6-23%. On the other hand, the proportion of medication poisonings increased to 31-57% compared to 14-17% in the 1980s [7-10]. These increasing rates of poisoning by medication were noted regardless of regional areas. The other common causes of intoxication were hydrocarbons and personal care products. These were also noted in our unpublished studies (Fig. 1). These causative changes according to time in Korea were explained by some reasons such as, industrialization, decreasing use of agricultural chemicals, and the introduction of the national medical insurance system with increasing opportunities to come in contact with hospitals and pharmacies. These changes may have even changed with the establishment of the national poison information center since 2012 [12].

Above 50% drug intoxication were developed in children below 6 years of age. More than 90% of toxic

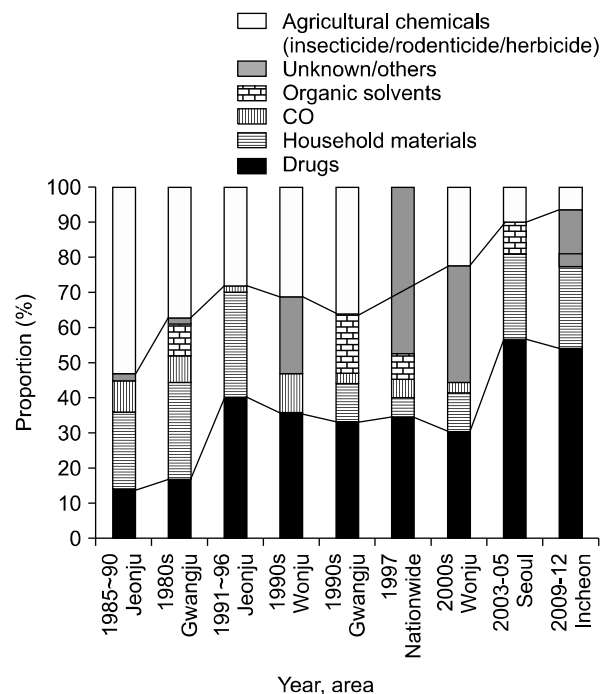


Fig 1. Proportion of causative substances of drug intoxication according to the regional areas and years. CO: carbon monoxide.

exposure in children occurred in the home. Most intoxications were caused by a single toxic substance, and the most common route was ingestion rather than via dermal, inhalational and ophthalmic exposure. Approximately 50% of intoxications were caused by nondrug substances, such as cosmetics, personal care items, cleaning solutions, plants, and foreign bodies. Common pharmacological preparations were analgesics, topical preparations, cough and cold products, and vitamins. Therefore, 85% of exposures in children younger than 6 years of age can be managed without direct medical intervention, which means that most childhood intoxications are inherently non-toxic or minimally toxic [4,13-15]. On the other hand, in adolescence, which was second peak period of pediatric toxic exposure, most intoxications were intentional and often severely toxic with a high death rate in pediatric population (44/70 poison-related pediatric death < 19 years old). The common substances of toxic exposure in adolescence are over-the-counter drugs, prescription medications and household products. According to the US reports in 2012, the proportion of poisonings by pharmaceutical agents was approximately 47% in children younger than 13 years of age [11].

TOXIC AND NONTOXIC SUBSTANCES

Table 1 lists the common nontoxic or minimally toxic substances [13,14]. Most of the substances encountered in the home are nontoxic or minimally toxic. On the other hand, some of the prescribed drugs are toxic, even at the minimal dose (Table 2) [13,14,16,17].

EVALUATION

Although problem-oriented history taking is most important for evaluating patients with poisoning, special attention should be paid to children and adolescents with intentional exposure and without a witnessed exposure. When considering the time of ingestion, it will be better to overestimate the status of the patients. Toxidromes via vital signs and physical examinations are usually valuable for an appropriate laboratory evaluation and the prediction of ingested drugs. General laboratory tests are as follows; complete blood count, liver function test, urinalysis, serum and urine electrolytes, anion gap, and osmolality, serum creatine kinase-MB (CK-MB), and coagulation time. If several types of intoxications, such as carbon monoxide (CO), acetaminophen, salicy-

Table 1. Common Nontoxic or Minimally Toxic Substances

Household products	Abrasives, candles, fabric softeners, incense
Medications	Antacid, antibiotics, antifungals, corticosteroids, calamine lotion, diaper rash cream & ointments, hydrogen peroxide (3%), iodophil disinfectants, laxatives, oral contraceptives
Personal care products	Bath oil, body conditioners, cosmetics, hand lotions & creams, soap, dish washing detergents, shampoo, shaving cream, sunscreen (zinc oxide)
Stationary	Ballpoint pen ink, chalk, clay, crayons, glow products, glues, paste, indelible markers, ink, pencil lead, water and oil colors
Others	Fertilizers, fishbowl additives, plant food, silica, warfarin rodenticides (<0.5%)

Table 2. Substances that Can Be Toxic to Children Even in Small Dose of Ingestion

Anti-malarials	Chloroquine, quinine, quinidine
Antipsychotics	Monoamine oxidase inhibitors, phenothiazines, tricyclic antidepressants
Cardiovascular agents	Atropine, β -blockers, calcium channel blockers, clonidine
Opioids	Diphenoxylate, lomotil, methadone, oxycodone, suboxone
Oral hypoglycemics	Sulfonylurea, meglitinides
Topical agents	Benzocaine, lindane
Others	Alcohol, camphor, hydrocarbon, nicotine, theophylline

Table 3. Methods for Evaluation of Toxicity and Prediction of Severity in Children and Adolescents with Poisoning

Detailed history and physical examination	Consider toxidromes: vital signs (temperature, blood pressure, and heart rate alterations, respiratory disturbances), pupillary findings, skin findings, neuromuscular abnormalities, mental status alterations Characteristic odors
Diagnostic test	Blood glucose, acid base status and anion gap with ABGA, serum electrolytes, osmolality with osmolar gap, BUN/Cr, liver function test, CPK with cardiac enzyme, coagulation test Urine dipstick test, urinalysis, pregnancy test (if needed) Quantitative drug serum concentration (e.g., acetaminophen, salicylate) Electrocardiogram Chest radiography Toxicologic screen (if needed)

ABGA: arterial blood gas analysis, BUN/Cr: Blood urea nitrogen and creatinine, CPK: creatine phosphokinase.

lates, anticonvulsants, iron, methanol, digoxin, and theophylline etc., are suspected, the quantitative blood concentrations are needed (Table 3). In addition, a toxicology screen must be done in the case of children who are neglected or abused [13,14,17,18].

MANAGEMENT

Four principles, decontamination, enhanced elimination, antidotes and supportive care, are usually used in the management of intoxication [13]. Although the gastrointestinal decontamination is controversial, it will be effective after acute ingestion. Ipecac syrup has no longer been used in the US since the policy by the American Academy of Pediatrics (AAP) was released in 2003 [15]. Activated charcoal (AC) is used widely as the initial treatment because it acts as an adsorbent of toxic substances and can delay the absorption of toxins. With the exception of some poorly adsorbed substances, such as alcohols, caustics, hydrocarbons, iron etc., AC is one of the most useful agents of acute intoxication, particularly when administered within one hour after toxin ingestion [19].

The optimal dose of AC is not known, but the United States Pharmacopeia (USP, 2003) suggests the following: children up to one year of age, 10-25 g or 0.5-1.0 g/kg; children 1 to 12 years of age, 25-50 g or 0.5-1.0 g/kg; and adolescents, 25-100 g. Recently, whole-bowel irrigation with a large volume of polyethylene glycol electrolyte solution is used to man-

age intoxication by slowly absorbing substances [20]. And this method has only minor side effects, such as transient adverse drug reactions, vomiting and abdominal pain.

To enhance the elimination of toxins, several methods, such as, multiple-dose AC, urinary alkalinization, dialysis and antidotes, are available. Multiple-dose AC is only useful for some drugs [21], and others recommend this method restrictively [22]. In the case of intoxication by several drugs, antidotes are quite useful. These antidotes are listed in Table 4 [13,14,17,18,23]. In addition, supportive care is needed for intoxicated children and adolescents. A common form of intoxication that is rarely cited and being at issue and its management in children and adolescents is described in the following:

1. Caustics (sodium or potassium hydroxide, sodium hypochlorite, sodium carbonate, hydrochloric acid): Most alkali substances, which are more commonly ingested than acidic substances, are tasteless and are common in children less than 6 years of age. Esophageal strictures develop in approximately 20% of patients, and are not related to the extent of oropharyngeal injuries despite the proportional relationship with the presence of more symptoms. Therefore, endoscopy is needed to identify the stages of injury. In children, severe long-term complications including esophageal cancer can develop [13,18,24].

2. Plants: Because of the variable toxicity of the parts of plants, time of the year, growth conditions, route of exposure and variable common names ac-

Table 4. Common Antidotes for Poisoning

Poison	Antidote
Acetaminophen	N-acetylcysteine
Anticoagulant, rodenticides	Vitamin K1
Anticholinergics	Physostigmine
Anti-malarials (chloroquine, quinine, quinidine)	Octreotide
Anti-psychotics (serotonin syndrome)	Dantrolene
Benzodiazepines	Flumazenil
β -Blocker	Glucagon
Calcium channel blocker	Glucagon, insulin, calcium salts
Carbon monoxide	Oxygen
Cyanide	Cyanide kit (amyl nitrate, sodium nitrate, sodium thiosulfate), hydroxocobalamin
Digitalis	Digoxin-specific Fab antibodies (Digibind; Digifab)
Ethylene glycol, methanol	Ethanol, fomepizole
Iron	Deferoxamine
Isoniazid	Pyridoxine
Lead and other heavy metals (arsenic, inorganic mercury)	BAL, CaNa^{2+} -EDTA, DMSA
Lipophilic drugs: local anesthetics, amitriptyline, diltiazem, bupropion, dosulepin, lamotrigine, quetiapine, and verapamil	20% lipid emulsion
Methotrexate	Folic acid, leukovorin
Methemoglobinemia	Methylene blue, 1% solution
Opioids	Naloxone
Oral hypoglycemic agents (sulfonylurea, other hyperinsulinemic agents)	Dextrose, octreotide
Organophosphates	Atropine, pralidoxime (2PAM)
Salicylates	Sodium bicarbonate
Tricyclic antidepressants	Sodium bicarbonate
Valproic acid	L-carnitine

BAL: British anti-Lewisite, EDTA: edetate calcium disodium, DMSA: 2,3-dimercaptosuccinic acid (succimer).

According to the region and countries, it is difficult to predict whether the plants would be toxic or non-toxic [25,26]. Therefore, it is important to communicate with the poison center or obtain information using smart phone applications [12,27].

3. Energy drinks: Since the introduction of energy drinks in Korea, 2010, they are becoming an object of public concern, particularly with adolescents. From the recent US data, accidental unintentional exposure in children less than 6 years of age is a major concern. In addition, almost one quarter of college students have consumed alcohol mixed with energy drinks [28]. This behavior is even more common in Korean college students with 49.3% than in the US. The mean caffeine content of 35 products in Korea is 67.94 mg, and each drink contains 30-175.8 mg of caffeine [29]. These are potentially dangerous because of the more concentrated volume of caffeine

and the regular or mixed consumption with alcohol. The major adverse effects are vomiting, seizure, tachycardia, tachypnea, dysrhythmia, hypokalemia, hyperglycemia, and death [14,30,31]. No known specific antidotes are available, but benzodiazepines, beta-adrenergic blockers and lidocaine, are used according to the symptoms.

CONCLUSION

Pediatricians and physicians related to emergency departments should be aware of the changing causative substances of intoxication according to age and time. And precise history taking, through physical examination and current knowledge about care are needed for the proper and prompt management of intoxicated children and adolescents. Furthermore, all physicians must promote ways of preventing in-

toxication and help to establish a nationwide poison control center.

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