Toxicology

Clinical analysis of Korean adult patients with acute pharmaceutical drug poisoning who visited the emergency department

Changyeob Lee[1], Sunpyo Kim[1], Sun Hyu Kim[2], Gyu Chong Cho[3], Ji Hwan Lee[4], Eun Jung Park[5], Duk Hee Lee[6]

[1]Department of Emergency Medicine, Chosun University College of Medicine, Gwangju, [2]Department of Emergency Medicine, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, [3]Department of Emergency Medicine, Kangdong Sacred Heart Hospital, Hallym University School of Medicine, Seoul, [4]Department of Emergency Medicine, Yonsei University College of Medicine, Seoul, [5]Department of Emergency Medicine, Ajou University School of Medicine, Suwon, [6]Department of Emergency Medicine, Ewha Womans Kangdong Sacred Heart Hospital, Hallym University School of Medicine, Seoul, Korea

Objective: This study classified patients with acute pharmaceutical drug poisoning who visited the emergency department (ED) to identify clinical characteristics that could be used as the foundation for poisoning prevention programs.
Methods: Adult patients aged ≥19 years who visited one of the 23 EDs in South Korea between 2011 and 2018 with pharmaceutical drug poisoning were analyzed retrospectively by sex. The data were sourced from in-depth survey data and the ED patient surveillance system managed by the Korea Disease Control and Prevention Agency.
Results: A total of 21,620 cases were analyzed. The sample had more female cases, 15,057 (69.6%); the mean age was 48.3±18.7 years for men and 44.7±17.2 years for women. The onset time was mostly between 18:00 and 24:00 hours; most patients visited the ED via 119 or private vehicles; 5,498 (83.8%) men and 13,070 (86.8%) women reported intentional poisoning; the cause being an intention to commit suicide, though most patients had no history of previous suicide attempts. The frequency of intensive care unit admission and mortality were higher in males than females. When a comparison of the type of drug by sex was carried out, it was observed that analgesic and anti-inflammatory drug poisoning were more frequent in females. On the other hand, cardiovascular drug poisoning was more frequent in males.
Conclusion: There were more women than men among patients with pharmaceutical drug poisoning. Severity was found to be higher in men than women. In most cases, the poisoning was intentional, and the cause of poisoning was a suicide attempt. Sedatives and antipsychotic drugs were the most commonly used drugs in both groups.

Keywords: Pharmaceutical; Poisoning; Sex

INTRODUCTION

Poisoning is a state in which there is an excess drug in the body, manifesting various side effects. When the patients with poisoning who visited the emergency department (ED) in South Korea were classified by toxic substances, pharmaceutical drugs account for the highest percentage with 52.6%, followed by gases (21.5%), pes-ticides, and synthetic toxic substances (10.8%). In addition, among the total number of poisoning cases, there were always more female than male patients.[1]

Among the Organization for Economic Co-operation and Development (OECD) countries, South Korea has the highest number of annual doctors' consultations per capita of 16.9, followed by Japan with 12.6, and an OECD average of 6.8. This is due to the rapid increase in the number of consultations in South Korea, combined with easy

책임저자: 김 선 표
　　　　광주광역시 동구 필문대로 365
　　　　조선대학교병원 응급의학과
　　　　Tel: 062-220-3285,　　Fax: 062-224-3501,　　E-mail: ksp93133@naver.com

Capsule Summary

What is already known in the previous study
When patients with poisoning who visited the emergency department in South Korea were classified by their consumption of toxic substances, pharmaceutical drug poisoning accounted for the highest percentage with 52.6% of the total of such patients, followed by gases (21.5%), pesticides, and synthetic toxic substances (10.8%). In addition, there were always more females than male patients in the total number of poisoning cases.

What is new in the current study
Patients with pharmaceutical drug poisoning, who account for the most cases of poisoning in the emergency department, were categorized by sex to identify their general as well as medical characteristics. An analysis was conducted by drug type and the resultant data could form the foundation for poisoning prevention programs.

access to medical services, making it easier to receive prescriptions and store a large amount of medication for oneself.[2] Furthermore, with the expansion of locations that sell over-the-counter (OTC) drugs since November 15, 2012, it became easier to access OTC drugs in daily life with increased accessibility to medication. Regardless of sex and intentionality, the number of patients with drug poisoning following self-administration of drugs is on the rise, adding to the burden of public health.[3,4]

Several studies report that the proportion of drug poisoning is higher in women than in men, but few discuss the details on the comparative analysis. In this study, the patients with pharmaceutical drug poisoning, who account for the most cases of poisoning in the ED, were categorized by sex to identify the general as well as medical characteristics and conduct analysis by drug type to use the data as the foundation for poisoning prevention programs.

METHODS

1. Study period and subjects

This study retrospectively analyzed the in-depth sample survey data and the surveillance system of ED patients managed by the Korea Disease Control and Prevention Agency (KDCPA). The in-depth survey of ED patients began in 2006, and a total of 23 hospitals are participating to date to construct a prospective data registry by collecting data on patients who visit the ED. This study analyzed the adult patients aged 19 years and older who visited the ED between 2011 and 2018 with pharmaceutical drug poisoning, excluding the variables that were not recorded under the toxic substance code.

2. Collected variables

Among the variables collected by the registry, the sex, age, season, time, the highest level of education, means for visiting the ED, source of drug, drinking, location of poisoning, intentionality, vital signs and level of consciousness at the time of ED visit, treatment outcome, and admission outcome of the patients with pharmaceutical drug poisoning were used as the variables in the survey. As for the pharmaceutical drugs, they were surveyed during the interview with the doctor of emergency medicine and categorized by sex and into analgesics-anti-inflammatory drugs, sedatives-antipsychotic drugs, antidepressants, and cardiovascular drugs as per the guidelines of the Injury Patient In-depth Survey Project.

This study was approved by Chosun University Hospital Institutional Review Board (IRB no 2021-06-003)

3. Data analysis

Statistical analysis was performed using SPSS ver. 20.0 (IBM Corp., Armonk, NY, USA). To test for severity and type of drug by sex, the chi-square test was used. Statistical significance level (significance level, α) was set to 0.05.

RESULTS

1. General characteristics of patients with acute pharmaceutical drug poisoning (Table 1)

Among 2,116,039 patients who visited the ED between 2011 and 2018 in the in-depth survey of ED patients, those who visited due to poisoning were 56,276 subjects (2.7%) in total. Among them, 29,658 patients

Table 1. General characteristics of patients with acute pharmaceutical poisoning

	Total (n=21,620)	Male (n=6,563)	Female (n=15,057)
Age (yr)	45.7 ± 17.7	48.3 ± 18.7	44.7 ± 17.2
Season of poisoning			
Spring (March-May)	5,462 (25.3)	1,648 (25.1)	3,814 (25.3)
Summer (June-August)	5,856 (27.1)	1,771 (27.0)	4,085 (27.1)
Autumn (September-November)	5,386 (24.9)	1,656 (25.2)	3,730 (24.8)
Winter (December-February)	4,916 (22.7)	1,488 (22.7)	3,428 (22.8)
Poisoning time			
00:00-06:00	4,980 (23.0)	1,348 (20.5)	3,632 (24.1)
06:00-12:00	3,673 (17.0)	1,197 (18.2)	2,476 (16.4)
12:00-18:00	5,076 (23.5)	1,631 (24.9)	3,445 (22.9)
18:00-24:00	7,626 (35.3)	2,287 (34.8)	5,339 (35.5)
Unknown	265 (1.2)	100 (1.5)	165 (1.1)
Education	n=5,941	n=1,992	n=3,949
Uneducated or elementary school	684 (11.5)	216 (10.8)	468 (11.9)
Junior high school	475 (8.0)	208 (10.4)	267 (6.8)
High school	1,744 (29.4)	585 (29.4)	1,159 (29.3)
≥College	932 (15.7)	275 (13.8)	657 (16.6)
Unknown	2,106 (35.4)	708 (35.5)	1,398 (35.4)
Mode of arrival			
119 Ambulance	13,030 (60.3)	4,144 (63.1)	8,886 (59.0)
Other ambulance	2,468 (11.4)	878 (13.4)	1,590 (10.6)
Private vehicle	5,768 (26.7)	1,421 (21.7)	4,347 (28.9)
On foot	257 (1.2)	64 (1.0)	193 (1.3)
Others	97 (0.4)	56 (0.9)	41 (0.3)
Source of the drug	n=6,517	n=1,922	n=4,595
Self-medication	5,426 (83.3)	1,576 (82.0)	3,850 (83.8)
Family-medication	318 (4.9)	92 (4.8)	226 (4.9)
Around people-medication	106 (1.6)	43 (2.2)	63 (1.4)
Buy medication	578 (8.9)	175 (9.1)	403 (8.8)
Others	28 (0.4)	9 (0.5)	19 (0.4)
Unknown	61 (0.9)	27 (1.4)	34 (0.7)
Alcohol drinking	9,058 (41.9)	2,664 (40.6)	5,394 (35.8)
Poisoning place			
Residential facility	20,161 (93.3)	5,847 (89.1)	14,314 (95.1)
Medical facility	173 (0.8)	70 (1.1)	103 (0.7)
School	24 (0.1)	9 (0.1)	15 (0.1)
Industrial facility	24 (0.1)	16 (0.2)	8 (0.1)
Public or commercial facility	592 (2.7)	290 (4.4)	302 (2.0)
Outdoor	155 (0.7)	76 (1.2)	79 (0.5)
Other	491 (2.3)	255 (3.9)	236 (1.6)
Type of insurance			
Health insurance	16,872 (78.1)	4,893 (74.6)	11,979 (79.6)
Medical aid	2,101 (9.7)	867 (13.2)	1,234 (8.2)
Self-pay	2,552 (11.8)	770 (11.7)	1,782 (11.8)
Others	95 (0.4)	33 (0.5)	62 (0.4)
Intentionality of poisoning			
Unintentionality	2,782 (12.9)	971 (14.8)	1,811 (12.0)
Intentionality	18,568 (85.9)	5,498 (83.8)	13,070 (86.8)
Suicide	17,839 (96.1)	5,259 (95.7)	12,580 (96.3)
Violence	15 (0.1)	7 (0.1)	8 (0.1)
Others	714 (3.8)	232 (4.2)	482 (3.7)
Unknown	270 (1.2)	94 (1.4)	176 (1.2)
Previous suicidal attempts	17,620	5,195	12,425
0	9,872 (56.0)	2,986 (57.5)	6,886 (55.4)
1	2,519 (14.3)	678 (13.1)	1,841 (14.8)
≥2	1,775 (10.1)	495 (9.5)	1,280 (10.3)
Unknown	3,454 (19.6)	1,036 (19.9)	2,418 (19.5)

Values are presented as mean ± SD or number (%).
SD, standard deviation.

who did not have primary pharmaceutical poisoning were excluded, along with 4,998 patients who were under the age of 19, had chronic poisoning, and had uncertain clinical value. A total of 21,620 patients were divided in 6,563 men (30.4%) and 15,057 women (69.6%) for analysis (Fig. 1). As for the sex characteristics of patients, patients in their 40s accounted for the highest percentage in both groups, while the mean age was 48.3 ± 18.7 years in men and 44.7 ± 17.2 years in women. When the onset season was compared by sex, no difference was observed, but the onset time was mostly between 18:00 and 24:00 hours. The insurance type was health insurance in most cases, and most patients visited the ED using a private vehicle or the 119. The source of the drug was self-medication in most cases for both groups, followed by the pharmacy. The location of poisoning was the patient's residence in most cases in both groups. When classified by intentionality, 5,498 men (83.8%) and 13,070 women (86.8%) responded that the poisoning was intentional. In most cases, suicide was the cause of intentionality, and most patients did not have a history of suicide attempts.

2. Medical characteristics of patients with acute pharmaceutical drug poisoning (Table 2)

In most cases, patients' vital signs upon a visit to the ED were in the normal range with clear consciousness. Glasgow Coma Scale was 12.5 ± 3.5 in men and 12.9 ± 3.1 in women. Patients with normal discharge as treatment outcome at the ED were 1,695 in men (25.8%) and 4,269 in women (28.4%). Hospitalized patients accounted for 2,544 cases in men (38.7%) and 5,025 cases in women (33.4%), with most of them being normally discharged as admission outcomes. Due to the nature of the patients, those with discharge against medical advice also accounted for a significant percentage. In terms of severity, the frequency of intensive care unit admission (21.7% vs. 15.6%, P<0.001) and mortality (1.37% vs. 0.46%, P<0.001) were significantly higher in male than female (Fig. 2).

3. Comparison of type of drug in patients with acute pharmaceutical drug poisoning (Table 3)

When classified by type of drug, sedatives-antipsychotic drugs accounted for the most cases with 4,280 in
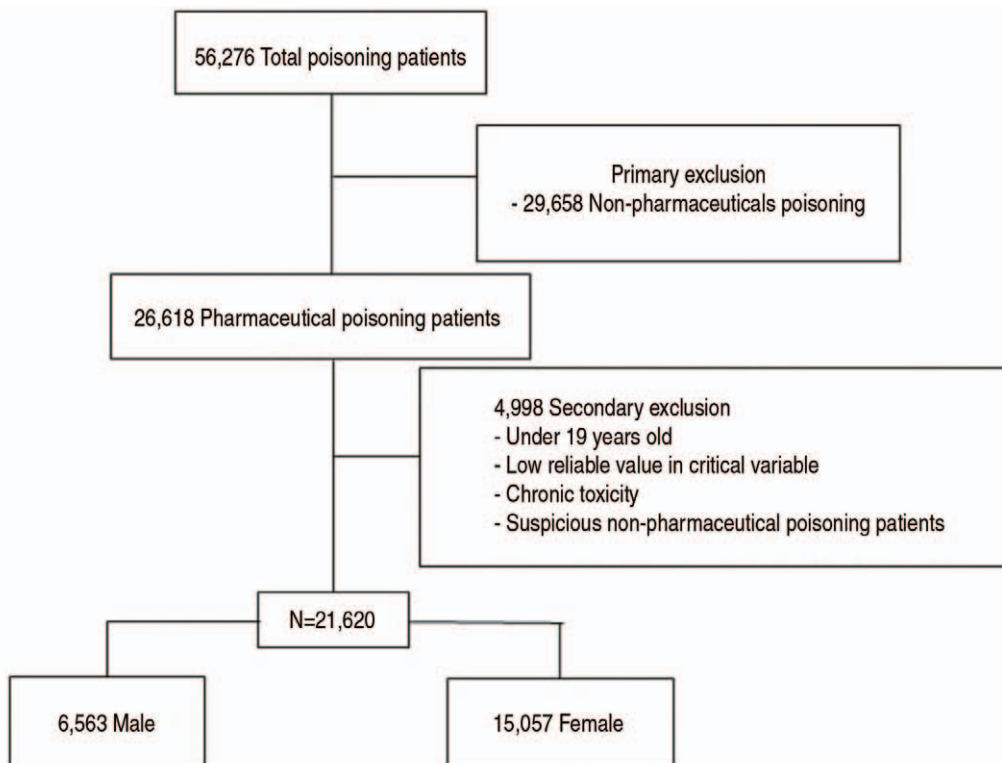

Fig. 1. Flow chart of study selection based on the inclusion and exclusion criteria.

men (65.2%) and 9,685 in women (64.3%); among these, other sedatives-antipsychotics, Zolpidem-based drugs accounted for the most cases followed by benzodi- azepines. The second was analgesics-anti-inflammatory drugs, with acetaminophen accounting for the highest number of cases for both sexes, with 285 cases in men and 1,031 cases in women. It was followed by Antidepressants and Cardiovascular drugs. When com- pared type of drug by sex, analgesic and anti-inflamma- tory drug poisoning was more frequent in female (7.1%

Table 2. Medical characteristics of patients with acute pharmaceutical drug poisoning in the ED

	Total (n=21.620)	Male (n=6,563)	Female (n=15,057)
Vital signs			
Systolic blood pressure (mmHg)	123.0±24.2	127.7±25.5	121.0±23.5
Heart rate (beats/min)	88.5±19.3	89.5±20.1	88.1±18.9
Respiratory rate (breaths/min)	19.2±2.8	19.3±3.0	19.2±2.7
Body temperature (℃)	36.4±0.5	36.5±0.6	36.5±0.5
Consciousness at ED		n=5,727	n=12,957
Alert	10,193 (54.6)	2,946 (51.4)	7,247 (55.9)
Response to verbal stimuli	5,029 (26.9)	1,514 (26.4)	3,515 (27.1)
Response to painful stimuli	3,038 (16.3)	1,084 (18.9)	1,954 (15.1)
Unresponsiveness	424 (2.2)	183 (3.2)	241 (1.9)
Glasgow coma scale	12.7±3.2 (n=13,486)	12.5±3.5 (n=4,138)	12.9±3.1 (n=9,348)
Disposition at ED			
Discharge (excluding DAMA)	5,964 (27.6)	1,695 (25.8)	4,269 (28.4)
DAMA	6,989 (32.4)	1,876 (28.6)	5,113 (34.0)
Admission (ICU)	3,777 (17.5)	1,426 (21.7)	2,351 (15.6)
Admission (general ward)	3,792 (17.5)	1,118 (17.0)	2,674 (17.8)
Transfer	937 (4.3)	357 (5.4)	580 (3.9)
Death	64 (0.3)	33 (0.5)	31 (0.2)
Others	97 (0.4)	58 (0.9)	39 (0.3)
Result of admission	n=7,569	n=2,544	n=5,025
Discharge (excluding DAMA)	5,190 (68.6)	1,679 (66.0)	3,511 (69.9)
DAMA	1,657 (21.9)	511 (20.1)	1,146 (22.8)
Transfer	585 (7.7)	276 (10.8)	309 (6.1)
Death	96 (1.3)	57 (2.2)	39 (0.8)
Escape	10 (0.1)	6 (0.2)	4 (0.1)
Others	31 (0.4)	15 (0.6)	16 (0.3)

Values are presented as mean±SD or number (%).
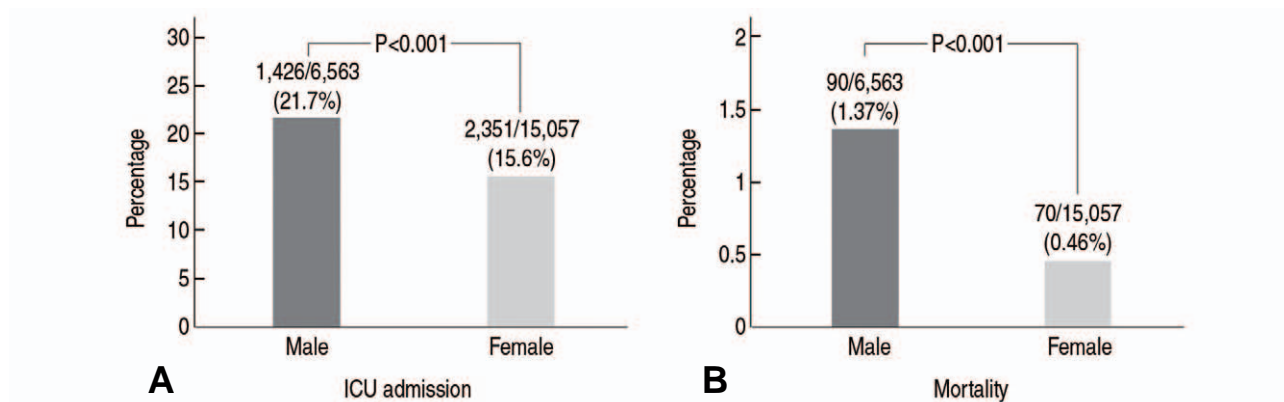ED, emergency department; DAMA, discharge against medical advice; ICU, intensive care unit; SD, standard deviation.

Fig. 2. Comparison of the frequency of intensive care unit (ICU) admission (**A**) and mortality (**B**) by sex.

Table 3. Comparison of type of drug in patients with acute pharmaceutical drug poisoning

	Total (n=21,620)	Male (n=6,563)	Female (n=15,057)	P-value
Analgesics-Anti-inflammatory drugs	1,968 (9.1)	468 (7.1)	1,500 (22.9)	<0.001
Acetaminophen	1,316 (66.9)	285 (60.9)	1,031 (68.7)	
Opioid analgesics	110 (5.6)	48 (10.3)	62 (4.1)	
Other analgesics	542 (27.5)	135 (28.8)	407 (27.1)	
Sedatives-antipsychotic drugs	13,965 (64.6)	4,280 (65.2)	9,685 (64.3)	0.056
Benzodiazepines	2,864 (20.5)	842 (19.7)	2,022 (20.9)	
Doxylamine	476 (3.4)	166 (3.9)	310 (3.2)	
Zolpidem	3,782 (27.1)	1,138 (26.6)	2,644 (27.3)	
Antipsychotics	622 (4.5)	208 (4.9)	414 (4.3)	
Other sedatives-antipsychotics	6,221 (44.5)	1,926 (45.0)	4,295 (44.3)	
Antidepressants	1,684 (7.8)	432 (6.6)	1,252 (8.3)	0.105
TCA antidepressants	359 (21.3)	104 (24.1)	255 (20.4)	
Other antidepressants	1,325 (78.7)	328 (75.9)	997 (79.6)	
Cardiovascular drugs	914 (4.2)	416 (6.3)	498 (3.3)	<0.001
Anticonvulsants	436 (2.0)	158 (2.4)	278 (1.8)	0.007
Cold and cough preparation	699 (3.2)	275 (4.2)	424 (2.8)	<0.001
Antimicrobials	31 (0.1)	10 (0.2)	21 (0.1)	0.818
Gastrointestinal preparation	212 (1.0)	52 (0.8)	160 (1.1)	0.634
Diagnostic drugs	139 (0.6)	50 (0.8)	89 (0.6)	0.149
Vitamin-dietary supplements	60 (0.3)	18 (0.3)	42 (0.3)	0.952
Bronchodilators	11 (0.1)	4 (0.1)	7 (0.0)	0.665
Other pharmaceuticals	1,132 (5.3)	291 (4.4)	841 (5.6)	<0.001
Unknown pharmaceuticals	369 (1.7)	109 (1.7)	260 (1.7)	0.731

Values are presented as number (%).
TCA, tricyclic antidepressant.

vs. 22.9%, P<0.001), on the other hand, cardiovascular drug poisoning was more frequent in male (6.3% vs. 3.3%, P<0.001).

DISCUSSION

In South Korea, 50% of patients experience poisoning due to drugs used for therapeutic purposes, and some studies reported that the percentage reaches 84% among all non-intentional poisoning.[5] As seen in many studies conducted in Korea, most of the poisoned patients are adult women, and the current research on poisoning of therapeutic medications also reports that the ratio is twice as great in women. Continued research on the cause of this higher ratio is needed.[6,7]

Poisoning is critical and essential to accumulate the information on the substances exposed and the data related to the poisoning, including demographic characteristics, the use of antidote, and the prognosis of the patients with acute poisoning.[1] In the United States, the poison

control center follows up on the causative substance, initial symptoms, and the outcome of ED treatment for acute poisoning patients to accumulate data in the National Poison Data System; the results are published as an annual report to provide emergency treatment guidelines as a preventive measure to reduce patients with poisoning injury.[8,9] In South Korea, a nationwide data collection on poisoning patients is not yet being conducted. Although various injury surveillance systems are running based on demographic surveys and by medical institutions under the supervision of the KDCPA while toxin provides information on toxic substances, a customized prevention strategy, and the system must be prepared to reduce the risk number of poisoning injury patients.[1,10,11]

The reason for acute pharmaceutical drugs accounting for the highest percentage of poisoning vary by region, but it is mostly because of the increase in the number of people abusing drugs with easy access to OTC drugs which are available at convenience stores and even on the internet.[3,10] However, safety regulations are often vio-

lated for practical reasons, and anyone can purchase OTC drugs multiple times at any location. As such, it was difficult to clearly identify the location of the drug purchase and the sex or age of the buyer in this study.

In South Korea, it was found that 90% of acute pharmaceutical drug poisoning occurs in residential areas, with the source of the drug being self-medication; this is similar to the findings from overseas studies.[12,13] Jo et al.[5] also reported residential areas are 95.3%. This is similar results to our study.

According to the treatment results of poisoning of therapeutic medications in the ED, discharge rate was the highest in both men and women, more men were admitted or died, and death after admission was 57 men (2.2%) and 39 women (0.8%). This suggests that while the number of poisoning was higher in women, severity was higher in men, demonstrating similar sex characteristics as intentional poisoning.[14,15] In addition, the severity and mortality rate are lower in patients poisoned to acute pharmaceutical drug than the severity of patients poisoned to various pesticides.[16,17] Although the mortality rate is not high for patients with acute pharmaceutical drug poisoning, the cases of using drugs as a means for suicide and self-harm are steadily increasing in South Korea, where suicide rates are high.[18] In studies on EDs, poisoning as a means of suicide attempt accounted for the highest percentage with 55.8%, and overseas studies also showed a high proportion of patients with intentional poisoning, with the cause being suicide. In this study, 83.8% of men and 86.8% of women exhibited intentional poisoning, 96.1% committed suicide, and 56% have never attempted suicide before, indicating similar results to Kim et al.[19] They studies have derived similar results. The rate of intentional poisoning is high, with most cases being attempted suicide among acute pharmaceutical drug poisoning patients in South Korea.[14,15]

As for the drug used, poisoning due to analgesics-anti-inflammatory drugs accounted for the most cases, while sedatives-antipsychotic drugs accounted for the most in this study, followed by analgesics-anti-inflammatory drugs, which was different from the results of other countries.[1,14] In the United States and the United Kingdom, regardless of intentionality, analgesics-anti-inflammatory drugs were the most common drug for poisoning, followed by sedatives-antipsychotic drugs.[20] In Japan, sedatives-hypnotics and antipsychotics accounted for the most cases.[21]

This study found that poisoning due to sedatives-antipsychotic drugs accounted for the most cases; among these in both males and females. The change in patients with drug poisoning can be related to the change in prescription frequency. According to the Health Insurance Review & Assessment Service of Korea, it can be seen that treatments at hospitals increased annually between 2010 and 2016, with the prescription for sedatives-antipsychotic drugs also increasing as well.[22] Zolpidem with hypnotic effects as a treatment for insomnia accounted for the most cases. This is because zolpidem misuse or abuse cases frequently occur as it is known for rapid action, short half-life, and easy excretion from the body as the most stable hypnotic, which is relatively easily prescribed in South Korea.[23] In addition, benzodiazepines requiring doctor's prescription was also found to be a toxic substance. This is probably because it is relatively easily prescribed in South Korea compared to other countries. Patients usually keep a large dose at home, resulting in sedatives-antipsychotic drugs being the most common substance for poisoning.[24]

Although the proportion of men and women in this study is similar, the largest difference among sexes is shown in those poisoned to acetaminophen, where the number of women is 3.6 times more than that of men. This difference can be explained by the fact that women purchase more OTC drugs than men. The poisoning of benzodiazepines, zolpidem, and antidepressants was twice as high in women as men, and this is due to the common prescription of these drugs to women in Korea.[24,25]

The limitations of this study are: first, it is a retrospective study with only 23 medical institutions with sample surveillance data; there is a limitation in collecting detailed data on acute pharmaceutical drug poisoning in overall injured patients. Second, the drug for poisoning was classified based on the statements from the patients, caregivers, or witnesses. For prescription drugs, the prescription was verified, or the hospital that issued the prescription was contacted for verification; for non-prescription drugs, the packaging was checked. Despite the attempts, there were cases in which the type of drug could not be verified. Third, when patients took multiple drugs at once, the patient was classified as the most representative drug, and many cases were classified as unknown or other as the drug type was not verified dur-

ing the interview.

In this study, although there were more cases of pharmaceutical drug poisoning in females than in males. Further research on why there are more female patients than males that are poisoned to drugs, and the interaction differences between drugs need to be conducted. Pharmaceutical drugs should be further managed to reduce the number of poisoning patients through prospective, specialized research in the future.

ORCID

Changyeob Lee (https://orcid.org/0000-0002-2362-7821)
Sunpyo Kim (https://orcid.org/0000-0001-6802-0807)
Sun Hyu Kim (https://orcid.org/0000-0002-4836-0940)
Gyu Chong Cho (https://orcid.org/0000-0001-9228-3674)
Ji Hwan Lee (https://orcid.org/0000-0002-6908-9459)
Eun Jung Park (https://orcid.org/0000-0001-7854-0961)
Duk Hee Lee (https://orcid.org/0000-0001-5992-5284)

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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