

## ORIGINAL RESEARCH

# Trends in drug poisoning of youth patients after the deregulation of over the counter drug sales

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**Abstract**

Since 15 November 2012, the South Korean government amended the law to make some medicines available at 24-hour convenient stores that had previously been sold at pharmacies only. The aim of this study was to evaluate the impact of this legislation on drug poisoning in youth patients, who may be affected by increased access. This study retrospectively analyzed data registered in the Emergency Department-based Injury In-depth Surveillance (EDIIS) database from January 2007 to December 2018. Patients aged 15 to 24 years old were selected to analyze the incidence and outcomes of acetaminophen (AAP) poisoning in youth patients. Before the deregulation of over-the-counter (OTC) medication sales, 1994 youth patients visited the emergency department (ED) from 2007–2012. By contrast, 5440 youth visited the ED from 2013–2018 after deregulation. In particular, there were 263 (13.2%) and 820 (15.1%) cases of AAP poisoning intentionally before and after deregulation, respectively, which was not significantly different ( $p = 0.085$ ). However, the number of patients who were admitted to the general ward (GW) due to AAP poisoning significantly increased from 93 (35.4%) to 339 (41.3%) ( $p = 0.041$ ). Furthermore, the number of patients who were admitted to the intensive care unit (ICU) after ingesting AAP significantly increased from 9 (3.4%) to 93 (11.3%) ( $p < 0.001$ ). There was no significant difference in intentional AAP poisoning ratios following the deregulation of OTC drug sales; however, GW and ICU admission rates significantly increased. This study demonstrated that there is positive relationship between intentional AAP poisoning and severity in youth patients after the deregulation legislation.

**Keywords**

Acetaminophen; Adolescent; Emergency department; Nonprescription drug; Poisoning

## 1. Introduction

Since 15 November 2012, the South Korean government amended the law to make some medicines available at 24-hour convenient stores (CVS), which had previously been sold at pharmacies alone. The drugs available at the CVS are as follows: antipyrine acetaminophen and ibuprofen syrup, cold medicine, digestive medicine and pain relief patches. The proportion of youth who attempt suicide by drug poisoning with non-prescription drugs, such as acetaminophen (AAP) and non-steroidal anti-inflammatory drugs (NSAIDs) is large [1]. Therefore, any increase in drug accessibility to the drug may influence in drug poisoning patterns and outcome severity [2, 3].

Youth suicide is a worldwide phenomenon and a serious health issue [4, 5]. Suicide is the second leading cause of death in individuals aged between 15–29, which is defined as youth [6]. The proportion of youth attempting suicide is continually increasing. From 2014–2017, the suicide rate among youth in the United States increased by an annual average of 10%

[7]. The suicide rate among South Korean youth is 8.2 per 100,000, which is 1.4 times higher than the Organisation for Economic Cooperation and Development (OECD) average [8]. Furthermore, the primary cause of death in individuals between 9 and 24 years of age from 2011–2018 was suicide. In 2018, the percentage deaths caused by suicide increased approximately 4% compared with the previous year [9].

When classifying suicide in Korea according to the methods, the report shows that 51.3 percent of deaths are by hanging, 16.5 percent of fell down, and 16.5 percent by gas intoxication [10]. However, in the study by Kim *et al.* [11], based on the emergency department (ED), 55.8 percent of suicide attempts were drug poisoning. The study by Min *et al.* [12] also reports that 48.6 percent of suicide attempts were by drug poisoning. As a method of suicide attempts, it has been reported that poison is used by 70 percent up to 96.5 percent [13, 14]. Although there are not many studies on adolescents' drug poisoning, according to the previous studies, the largest portion of adolescents choose drug poisoning as a suicide attempt method. Therefore, a characteristic analysis of poisoning-

related suicide attempts in the youth and an evaluation of differences with adults is important to establish countermeasures that will prevent deaths from poisoning. However, investigation into suicide by poisoning in youths is sparse.

Few reports have studied the impact of legislation, and the results are controversial [15–17]. Furthermore, no specific data have been reported on youth drug intoxication. Therefore, the aim of this study was to evaluate the impact of legislation on youth patients who are admitted to hospital following drug intoxication.

## 2. Methods

### 2.1 Study design and population

This study retrospectively reviewed data registered in the Emergency Department-based Injury In-depth Surveillance (EDIIS) database in South Korea from January 2007 to December 2018. This database has been developed and operated by the Korea Centers for Disease Control and Prevention (KCDC).

Since 2006, 23 emergency centers have participated in EIDS implementation to proactively collect demographic features and injury-related factors for patients visiting the ED. Hospitals participating in this research were tertiary university hospitals, where the final treatment for severe emergency patients is provided for over 30,000 patients per year and over six specialized emergency department specialists. Participating emergency centers are prospectively investigating and entering 58 common items as damage-related items (If the damage is poisoning, the poisoning substance code must be entered). Moreover, the participating institutions were subdivided into six in-depth investigation divisions, and six emergency centers participated in the poisoning department to investigate three additional in-depth investigation items: the amount of poisoning substances, the reason for poisoning, and the source of poisoning substances.

The inclusion criteria of this study were (1) patients who were admitted due to poisoning intentionally; and (2) aged between 15 and 24 years. Exclusion criteria were (1) poisoning from non-drug sources, such as pesticides, carbon monoxide, herbicides, and corrosive agents. The flow chart of our study is presented in Fig. 1.

### 2.2 Data collection and outcome measurement

Comparisons were made between 2007 and 2012 (before the sale of drugs at CVS) and between 2013 and 2018 after the new legislation was passed permitting drug sales at CVS.

This study examined age and gender as demographic variables and collected the type of poison, intentionality, drinking status, and emergency department (ED) care results as the poisoning characteristics. Poisoning medicines were classified as AAP, NSAID, cold medicine, digestive, tranquilizer, antidepressant, antiepileptic, and cardiovascular medicine. And results of ED treatment were defined as general ward (GW) admission, intensive care unit (ICU) admission, discharge, in-hospital death and unknown. Lastly, poisoning intentionality

was segregated as accidental, self-harm, harm, and unknown.

In this study, the primary outcome was the number and percentage of patients who visited the ED following drug poisoning intentionally. The percentage of patients poisoned by AAP was compared before and after 2013. The second outcome was the admission and mortality rates in hospitals after AAP drug poisoning intentionally.

### 2.3 Statistical analyses

Continuous variables are presented as mean  $\pm$  SD (standard deviation), while categorical variables are presented as count (percentage). Categorical variables were analyzed using a *t*-test. A *p*-value of  $< 0.05$  was considered statistically significant. All analyses were performed using STATA version 17 (StataCorp., LLC, TX, USA).

## 3. Result

### 3.1 Demographic and clinical characteristics before and after legislation (Table 1)

Before the sale of safety-related drugs in CVS, 1994 youth patients visited the ED from 2007–2012 and 5440 youth patients visited the ED from 2013–2018 after the legislation was passed. Before legislation, 680 (34.1%) males were recorded visiting the ED compared with a significant increase in 2022 males (37.2%) visiting the ED after legislation. The average age of acute drug poisoning before and after deregulation of over-the-counter (OTC) drug sales was  $19.5 \pm 2.94$  and  $20.0 \pm 2.78$  years, respectively ( $p = 0.189$ ). Before OTC medication sales in CVS, there were 1411 cases (70.8%) of intentional acute poisoning. This increased to 3962 cases (72.9%) after OTC medication was sold in CVS ( $p = 0.887$ ).

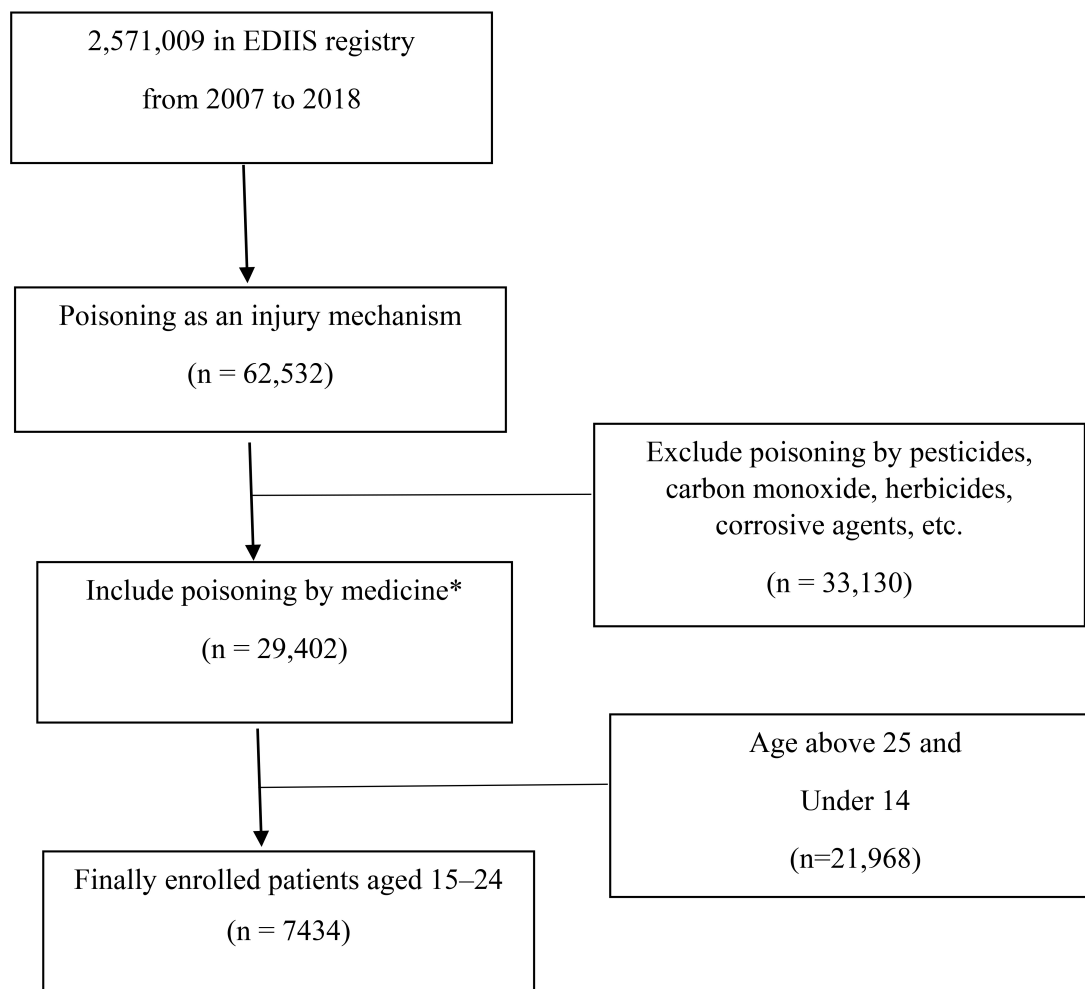
Additionally, before OTC medication sales in CVS, 379 people (19.0%) visited the ED related to alcohol consumption. This increased to 1253 people (23.0%) after selling OTC in CVS, which was significant ( $p = 0.016$ ).

### 3.2 Medication usage among the youth before and after legislative change (Table 2)

There were 263 (13.2%) and 820 (15.1%) cases of AAP poisoning before and after the deregulation of OTC medication, respectively, which was not significant ( $p = 0.085$ ). Moreover, poisoning with cold medicine, NSAIDs, digestives, and cardiovascular medicine were not significantly difference before and after OTC medication sales in CVS. However, there was a significant increase in tranquilizer poisoning from 326 cases (16.3%) to 1552 (28.5%) ( $p = 0.009$ ). Antidepressant poisoning increased from 81 (4.1%) to 382 (7.0%). Additionally, antiepileptic poisoning was significantly increased from 16 (0.8%) to 80 (1.5%) ( $p = 0.032$ ).

### 3.3 Clinical outcomes before and after the legislative change (Table 3)

The number of patients who were admitted to the GW after ED treatment due to AAP poisoning significantly increased from 93 (35.4%) to 339 (41.3%) ( $p = 0.041$ ). Furthermore, the number of patients who were admitted to the ICU after



**FIGURE 1. Study flow diagram.** EDIIS: Emergency Department-based Injury In-depth Surveillance. \*Medicine includes prescription drugs and non-prescription drugs. Medicine included acetaminophen, non-steroidal anti-inflammatory drugs, cold medicine, digestives, tranquilizer, antidepressants, antiepileptics and cardiovascular medicine.

**TABLE 1. Demographic characteristics of patients who ingested drugs before and after legislative change.**

	Before Legislation n = 1994	After Legislation n = 5440	p-value
Sex = male (%)	680 (34.1)	2022 (37.2)	0.016
Age	19.5 ± 2.94	20.0 ± 2.78	0.189
Intention (%)			
Accidental	488 (24.5)	1300 (23.9)	0.357
Self-harm	1411 (70.8)	3962 (72.9)	0.887
Harm	4 (0.2)	7 (0.1)	0.983
Unknown	91 (4.5)	171 (3.1)	0.059
Alcohol related (%)	379 (19.0)	1253 (23.0)	0.016

**TABLE 2. The amount and proportion of medication usage among youth patients before and after legislative change.**

Medication	Before Legislation		After Legislation		p-value
	n	%	n	%	
Acetaminophen	263	13.2	820	15.1	0.085
Cold medicine	51	2.6	59	1.1	0.279
NSAID	67	3.4	175	3.2	0.174
Digestives	17	0.9	30	0.6	0.479
Tranquilizer	326	16.3	1552	28.5	0.009
Antidepressant	81	4.1	382	7.0	0.010
Antiepileptic	16	0.8	80	1.5	0.032
Cadiovascular	24	1.2	93	1.7	0.682
Others	1149	57.6	2249	41.3	0.030

NSAID: Nonsteroidal anti-inflammatory drug; Others: hypertension medication, diabetes medication, or other drugs for own disease.

**TABLE 3. Clinical outcomes before and after legislative change.**

Medication	Clinical outcome	Before Legislation		After Legislation		p-value
		n	%	n	%	
Acetaminophen						
	Discharge	161	61.2	384	46.8	0.252
	GW admission	93	35.4	339	41.3	0.041
	ICU admission	9	3.4	93	11.3	<0.001
	Death	0	0.0	0	0.0	-
	Other	3	1.1	4	0.5	0.803
Cold medicine						
	Discharge	38	74.5	45	76.3	0.349
	GW admission	9	17.6	10	16.9	0.546
	ICU admission	2	3.9	3	5.1	0.836
	Death	0	0.0	0	0.0	-
	Other	2	3.9	1	1.7	0.445
NSAID						
	Discharge	49	73.1	113	64.6	0.273
	GW admission	11	16.4	42	24.0	0.084
	ICU admission	4	6.0	18	10.3	0.018
	Death	0	0.0	0	0.0	-
	Other	3	4.5	2	1.1	0.652
Digestive						
	Discharge	15	88.2	26	86.7	0.506
	GW admission	2	11.8	4	13.3	0.504
	ICU admission	0	0.0	0	0.0	-
	Death	0	0.0	0	0.0	-
	Other	0	0.0	0	0.0	-

TABLE 3. Continued.

Medication	Clinical outcome	Before Legislation		After Legislation		<i>p</i> -value
		n	%	n	%	
<b>Tranquilizer</b>						
	Discharge	212	65.0	997	64.2	0.010
	GW admission	84	25.8	340	21.9	0.023
	ICU admission	26	8.0	199	12.8	0.001
	Death	0	0.0	0	0.0	-
	Other	4	1.2	16	1.0	0.133
<b>Antidepressant</b>						
	Discharge	40	49.4	227	59.4	0.010
	GW admission	28	34.6	83	21.7	0.004
	ICU admission	13	16.0	69	18.1	0.128
	Death	0	0.0	0	0.0	0.003
	Other	0	0.0	3	0.8	-
<b>Antiepileptic</b>						
	Discharge	11	68.8	41	51.3	0.166
	GW admission	3	18.8	22	27.5	0.015
	ICU admission	2	12.5	17	21.3	0.004
	Death	0	0.0	0	0.0	-
	Other	0	0.0	0	0.0	-
<b>Cardiovascular</b>						
	Discharge	16	66.7	36	38.7	0.625
	GW admission	3	12.5	19	20.4	0.338
	ICU admission	4	16.7	37	39.8	0.214
	Death	0	0.0	0	0.0	-
	Other	1	4.2	1	1.1	0.635
<b>Others</b>						
	Discharge	767	66.8	1464	65.1	0.029
	GW admission	247	21.5	491	21.8	0.053
	ICU admission	96	8.4	248	11.0	0.162
	Death	3	0.3	18	0.8	0.161
	Other	36	3.1	28	1.2	0.012

*NSAID: nonsteroidal anti-inflammatory drug; Others: hypertension medication, diabetes medication, or other drugs for own disease; GW: General Ward; ICU: Intensive Care Unit.*

ingesting AAP significantly increased from 9 (3.4%) to 93 (11.3%) ( $p < 0.001$ ). There was a significant increase in patients who were admitted to the ICU in patients who ingested NSAIDs after the legislative change. Interestingly, the rate of discharge and GW admission decreased in patients who ingested tranquilizers after the legislative change, while ICU admission rates significantly increased.

In patients who ingested antidepressants, the discharge rate increased from 49.4% to 59.4% and GW admission rate dropped from 34.6% to 21.7%. In patients who ingested antiepileptics, the GW and ICU admission rates increased significantly.

## 4. Discussion

This study is a retrospective analysis of intentional drug poisoning trends among the youth over six years (2007–2012, 2013–2018) before and after the implementation of the CVS OTC sales on 15 November 2012 in South Korea. We demonstrated that there is positive relationship between intentional AAP poisoning and severity after legislation.

Youth patients who visited the ED after ingesting drugs for self-harm are present in both periods. The number of patients who ingested AAPs increased after OTC CVS drug sales were available; however, the percentage of total drug poisonings remained statistically unchanged. The differences in ingestion of other OTCs, such as cold medicines, NSAIDs, and digestive drugs, were not significant; however, their rates decreased. Interestingly, the use of drugs before and after legislation were significantly increased in tranquilizers, antidepressants, and antiepileptics. Previous studies have shown that intentional AAP poison rates in youth patients is high [18–20]. Furthermore, the rate of prescription drugs in youth patients has increased. Table 3 showed increased ICU admission rates due to tranquilizer ingestion and increased GW and ICU admission rates due to antiepileptic ingestion in youth patients.

OTC sales in non-pharmacy stores have been shown in several studies. In Sweden, AAP has been sold in non-pharmacy outlets since 2009. This was associated with an increased frequency of AAP poisoning, which verified it was closely related to accessibility [21]. In Canada, AAP availability increased for 1.5 years after a nonpharmacy locations law was enforced in 1999 and the admission rate due to AAP overdose toxicity did not increase [22]. Kim *et al.* [23] have conducted a study using intentional poisoned patient data collected from a single hospital from 2008 to 2016. They reported that AAP poisonings decrease after OTC sales begin. Additionally, Kim *et al.* [24] have utilized EDIIS collected data from 2011 to 2014 to show that the deregulation of OTC sales was associated in increase drug poisonings overall; however, AAP poisoning decreased.

Previous studies have shown a difference in the sales of AAP; however, no significant differences were shown in admission rate or toxicity by overdose. By contrast, this study demonstrated an increase in GW and ICU admission rates in youth patients. Increased access to AAP did not affect the number of addictions; however, the severity of drug poisoning outcomes increased. In particular, in youth who are underweight, toxicity can occur with a smaller ingestion of

AAP than adults. AAP is an antidote drug that can cause permanent liver injury; it is the most common cause of liver failure in children [25]. Therefore, more attention should be paid to the increase in severity and preventive measures should be taken. In the case of other drugs, prescription care should be managed. Additionally, research to prevent poisoning should be considered, such as shortening the number of days of prescription for psychiatric disorders. Some reports have shown that the proportion of non-pharmacist APP sales has been steadily increasing since 2018 [26]. Therefore, the sales system should be considered, and policies should be conducted, such as reducing the number of purchases per day or the number of drugs within packages. Furthermore, education should be implemented for the youth and sellers. This includes public relations and campaigns at the national level, regular and systematic education, and the adoption of an electronic system for drug purchases.

This study has several limitations. First, this study uses the data of patients visiting 23 EDs nationwide; however, there it does not represent all patients in South Korea due to sampling bias. However, this study minimized selection bias because it used a large dataset with over 360,000 in 12 years. This is the longest period found in the current published studies. Second, this study is based on medical records; therefore, there may be omissions and errors in the impairment period. In particular, the data relates to youths; therefore, they or their guardian may provide false information. Third, the exact dosage, number of doses, presence of polydrug, or blood concentration are unknown. These data should be collected to determine the exact drug severity because each hospital may different ICU or GW admission standards. However, the admission standard is set for AAP intake; therefore, severity can be partially reflected as the admission rate. Fourth, the database did not collect patients' underlying diseases, especially the presence or absence of mental disease in detail. If the underlying disease is not corrected, interpretation bias may occur. Lastly, the database is not designed to classify medication sold at CVS; therefore, further prospective studies should be constructed to determine medicines by ingredient.

## 5. Conclusions

There is no statistical change in the intentional AAP poisoning ratio since OTC drug sales were introduced; however, GW and ICU admission rates increased significantly. This study demonstrated that there is positive relationship between intentional AAP poisoning and severity in youth after the introduction of new legislation.

### AVAILABILITY OF DATA AND MATERIALS

The data used to support the findings of this study are available from the corresponding author upon request.

### AUTHOR CONTRIBUTIONS

JYL—designed the research study. SHL and DHL—performed the research. SHL—analyzed the data. JYL and

SHL—wrote the manuscript. All authors read and approved the final manuscript.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the institutional review board of Ewha Womans University Seoul Hospital, and the requirement for written informed consent was waived (IRB No: EUMC-015-002).

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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