http://dx.doi.org/10.22537/jksct.16.2.141
pISSN: 1738-1320 / eISSN: 2508-6332

Journal of The Korean Society of Clinical Toxicology

원 저

편의점 안전상비의약품 판매 허용 이후 치료 약물 중독

인제대학교 일산백병원 응급의학과[1], 아주대학교 의과대학 응급의학교실[2]

김성호[1] · 김현종[1] · 이지숙[2] · 박준석[1] · 김경환[1] · 신동운[1] · 김 훈[1] · 박준민[1] · 전우찬[1]

Pharmaceutical Drug Poisoning after Deregulation of Over the Counter Drug Sales: Emergency Department Based In-depth Injury Surveillance

Sung Ho Kim, M.D.[1], Hyunjong Kim, M.D.[1], Ji Sook Lee, M.D.[2], Junseok Park, M.D.[1], Kyung Hwan Kim, M.D.[1], Dong Wun Shin, M.D.[1], Hoon Kim, M.D.[1], Joon Min Park, M.D.[1], Woochan Jeon, M.D.[1]

Department of Emergency Medicine, Inje University, Ilsanpaik Hospital, Goyang[1], Department of Emergency Medicine, Ajou University, School of Medicine, Suwon[2], Korea

Purpose: The Korean government approved selected nonprescription drugs (Over-The-Counter drug; OTC drug) to be distributed in convenience stores from 15. Nov. 2012. This study examined the changes in the incidence and the clinical outcome of acute pharmaceutical drug poisoning after the deregulation of OTC drug sales.

Methods: This study analyzed the data of Emergency Department based Injury In-depth Injury Surveillance (EDIIS), Korea Centers for Disease Control and Prevention, from 2011 to 2014. The following items were examined: age, gender, intention, alcohol association, pharmaceutical drugs resulting acute poisoning, the clinical outcomes in emergency department, and the admission rate of intensive care unit (ICU). This is a retrospective cross section observational study.

Results: A total of 10,162 patients were subject to pharmaceutical drug poisoning. Acute poisoning by acetaminophen and other drugs were 1,015 (10.0%) and 9,147 (90.0%) patients, respectively. After the deregulation of OTC drug sales, acute poisoning by other drugs increased from 4,385 to 4,762 patients but acute poisoning by acetaminophen decreased from 538 to 477 patients (p<0.05). The rate of admission of acetaminophen poisoning increased from 36.1% (194/538) to 46.8% (223/477). The admission rate to the ICU by acetaminophen poisoning increased from 4.6% (25/538) to 11.3% (54/477) after the deregulation of OTC drug sales (p<0.05).

Conclusion: Since the deregulation of OTC drugs sales, pharmaceutical drug poisoning has increased but acetaminophen poisoning has decreased. The rate of hospitalization and ICU admission by pharmaceutical drug poisoning with or without acetaminophen has also increased.

Key Words: Nonprescription drug, Acetaminophen, Poisoning, Drug overdose

책임저자: 전 우 찬
경기도 고양시 일산서구 주화로 170
인제대학교 일산백병원 응급의학과
Tel: 031) 910-9781 Fax: 031) 910-7188
E-mail: woowoochan@gmail.com, wcjeon@paik.ac.kr

투고일: 2018년 8월 6일 1차 심사일: 2018년 8월 6일
게재 승인일: 2018년 9월 5일

INTRODUCTION

An over-the-counter (OTC) drug is available to the public without a prescription[1)]. Despite concerns of potential drug abuse and acute poisoning with OTC drugs, they are advantageous in terms of medical economics. In the United States (US), the cost-effectiveness of OTC

drugs in medical expenses was reported to be 10 billion dollars, and according to a survey on the safety of OTC drugs, more than 90% of doctors considered OTC drugs to be safe and effective[2,3]. Based on such advantages, many countries allow sales of OTC drugs.

Classification and sales methods of OTC drugs vary by country. The drug classification of the US separates prescription drugs, which are available at pharmacies and require doctor' s prescription and pharmacist' s medication counselling, and OTC drugs, which are available at stores other than pharmacies and do not require prescription or medication counselling. Meanwhile in the United Kingdom (UK), drugs are classified as prescription-only medicine, pharmacist supervised sale, and general sales list[4]. In Japan, drugs are classified as prescription and OTC drugs, and certain types of OTC drugs may be sold in stores other than pharmacies without medication counselling (Table 1)[4]. Korea' s drug classifications are prescription and nonprescription drugs, which are solely sold at pharmacies with pharmacist' s

Table 1. Classification of medicine for supply of the nation

Nation	Prescription	Non-prescription	
		With supervision by pharmacist	Without supervision by pharmacist
US	POM		Over The Counter drug
UK	POM	Pharmacist Supervised Sale	General sale
Japan	POM	General medicine (Class I, II, III)	General medicine (Class II, III)

US: United States, POM: Prescription Only Medicine, UK: United Kingdom

Table 2. The list of oral medicines available at convenience stores without medication counselling by pharmacists

Classification	Product name/ Formulation	Ingredient	Package
Antipyretics-analgesics	Tylenol 500 mg®/ Tablet	Acetaminophen 500 mg, 160 mg	8 tablets by strip
	Tylenol 160 mg®/ Tablet	Acetaminophen 160 mg	8 tablets by strip
	Tylenol for children®/ Tablet	Acetaminophen 80 mg	10 tablets by strip
	Tylenol suspension®/ Syrup	Acetaminophen 3200 mg/ 100 mL	Syrup by bottle
	Ibuprofen syrup®	Ibuprofen 80 mL	
Cold medicine	Pancol A- solution® /30 ml pack	Acetaminophen 300 mg, Guaifenesin 80 mg, Carbetapentane Citrate 15 mg, Caffeine anhydrous 30 mg, Chloropheniramine maleate 2.5 mg, Phenylephrine HCl 10 mg	3 pack
	Panpyrin-T®/ Tablet	Acetaminophen 300 mg, Caffeine anhydrous 30 mg, Chloropheniramine maleate 2 mg	3 tablet by strip
Digestive medicine	Bearse.®/ Tablet	Lipase100 15 mg, Biodiastase2000 50 mg, Simethicone 40 mg, Ursodeoxycholic Acid 10 mg, Pancellase SS 30 mg, Pancreatin Enteric Gr. 78.6 mg, Panprosin SS 20 mg	3 tablet by strip
	Dr. Bearse.®/ Tablet	Dizet 100 10 mg, Lipase II 30 mg, Bromelain 10 mg, Biodiastase2000 III 50 mg, Simethicone Powder 70 mg, Ursodeoxycholic Acid 10 mg, Pancellase 30 mg, Panprosin 20 mg	3 tablet by strip
	Festal Gold®/ Tablet	Lipase I 15 mg, Biodiastase2000 IV 10 mg, Cellulase AP3 II 9 mg, Simethicone 60 mg, Ursodeoxycholic Acid 20 mg, Pancreatin 150 mg, Prozyme 6 10 mg	3 tablet by strip
	Festal Plus.®/ Tablet	Cellulase AP3 10 mg, Simethicone 30 mg, Ursodeoxycholic Acid 10 mg, Pancreatin 315 mg	3 tablet by strip

medication counselling. However, to resolve the issue of restricted access during holidays and night-times when pharmacies close, 13 OTC medications have been selected to be sold at convenience stores without medication counselling by pharmacists since November 15, 2012 (Table 2)[5,6]. According to a survey conducted in 2013 by Korea Institute for Health and Social Affairs[7], over 30,000 OTC drugs were sold daily since the deregulation of off-pharmacy OTC drug sales. Initially, 11,538 convenience stores registered for sales registration, which increased to 19,944 stores after 4 months[7]. Average daily sales also increased 30%, indicating increased purchase of pharmaceutical drugs[8]. In addition, 83% of the population are aware of off-pharmacy OTC drug sales, and 56.9% of people have purchased OTC drugs from convenience stores during national holidays or night-times when pharmacies were closed[9]. Such reports and the sales analysis of the 13 OTC drugs indicate that deregulation of OTC drugs sales have increased the accessibility and convenience of OTC drugs for Korean people[8,9].

Accurate report on overall acute poisoning in Korea is insufficient, but according to studies based on emergency room treatment, about 0.5-0.6% of admitted patients had acute poisoning, and the statistics show that death due to acute poisoning accounts for about 0.5% of all causes of death[9,10]. According to the emergency room based report, 38.1% of acute poisonings were caused by pharmaceutical drugs such as sedatives, sleeping pills, psychotropic drugs, pain killers, and gastrointestinal drugs, followed by 26.3% by pesticides and herbicides[11].

Considering the high ratio of pharmaceutical drug in acute poisoning in Korea, deregulation of OTC drugs sales is likely to increase the incidence and severity of acute pharmaceutical drug poisoning. Therefore, we compared the overall frequency of pharmaceutical drugs poisoning observed at emergency rooms, admission rates, and intensive care unit admission rates before and after deregulation of OTC drugs sales. Further, many of the 13 OTC drugs include acetaminophen as the active ingredient; when acute poisoning occurs from overdose[12,13], the patient requires hospitalization for antidote treatment with N-acetyl cysteine. Thus, we also surveyed the incidence, the rate of hospitalization and intensive care unit (ICU) admission of acute acetaminophen poisoning to indirectly investigate that the deregulation by OTC drugs is causing increase of acute pharmaceutical drug poisoning.

METHOD

1. Study design

For this study, we retrospectively analysed Emergency Department Injury In-depth Surveillance (EDIIS) data collected from the emergency rooms of 20 hospitals designated as local or regional emergency medical centres during the four-year period from January 1, 2011, to December 31, 2014. Deregulation of off-pharmacy OTC drug sales began in November 15, 2012. However, due to initial marketing of the system and an adjustment period, we considered January 1, 2013, as the date for before and after off-pharmacy OTC drug sales because more than 20,000 convenience stores began selling more than 40,000 package of off-pharmacy OTC drugs[8].

2. Study subjects and method

We selected patients who had acute pharmaceutical drugs poisoning as the injury mechanism based on EDIIS data. We excluded cases of unknown drugs, unknown time of acute poisoning, and poisoning accompanied with non-pharmaceutical drugs like pesticides, herbicide, household product or toxic substances. We collected sex, age, and date of acute poisoning. We investigated intentionality, consumption of alcohol, name of drug causing acute poisoning, clinical outcomes of emergency treatment, presence of hospitalization and ICU admission.

We defined acute poisoning cases that occurred between January 1, 2011, and December 31, 2012, as before sales of OTC drugs at convenience stores and cases that occurred between January 1, 2013, and December 31, 2014, as after sales of OTC drugs at convenience stores. We classified intentionality as non-intentional and intentional poisoning and consumption of alcohol as confirmed or suspected alcohol con-

sumption at the time of admission to the emergency room. The pharmaceutical drugs that caused acute poisoning were classified as with or without acetaminophen. We classified the clinical outcome of acute poisoning patients into three groups; "Discharge" for normal or voluntary discharge from the emergency department, "General ward admission" for admission or transfer to general ward and "ICU admission" for admission to ICU or death in emergency department who should have managed in ICU.

3. Statistical analysis

Categorical variables like sex, results of emergency room examination, intentionality, association with alcohol consumption, and inclusion of acetaminophen are presented as number of cases and frequency (%), while continuous variables like age were analysed with Kolmogorov-Smirnov test and those showing normal distribution are presented as mean with standard deviation. Comparison analysis of before and after allowing sales of 13 OTC drugs in convenience stores other than pharmacies was done with chai-square and independent t test. Statistical analysis was performed with SPSS 21.0 (SPSS. Inc., Chicago, IL, USA) and results with $p<0.05$ were considered statistically significant.

4. Ethics approval

This study was reviewed and approved by the Institutional Review Board (Reference: ISPAIK 2017-01-005-001) and satisfied requirements specified under the Ministerial Decree of Health and Welfare and passed by the National Bioethics Committee. Informed consent was waived by the board.

RESULTS

1. General characteristics of acute pharmaceutical drug poisoning

We initially identified 10,403 patients as having acute pharmaceutical drug poisoning. We excluded 241 patients that presented with acute poisoning from other substances, had ingested unknown drugs, or had an unknown time of development. Of the 10,162 patients with acute pharmaceutical drug poisoning, 3,031 patients (29.8%) were males, and 7,131 patients (70.2%) were females, and the average age was 37.59 years old±21.05. For intentionality, 2,250 patients (22.1%) were unintentionally poisoned while 7,912 patients (77.9%) were intentionally poisoned (Table 3). For alcohol consumption, 3,048 patients (30.0%) showed association while 7,114 patients (70.0%) did not show association (Table 3). For the clinical outcome of acute poisoning, 6,489 patients (63.8%) were

Table 3. Characteristics of acute pharmarceutical drug poisoning before and after the deregulation of over-the-counter drugs sales

	Before (N=4923)	After (N=5239)	Total	*p*-value
Age (Mean±SD)	36.8±20.8	38.4±21.3		0.068
Gender				
Male	1,404 (28.5%)	1,627 (31.1%)	3,031 (29.8%)	0.005
Female	3,519 (71.5%)	3,612 (68.9%)	7,131 (70.2%)	
Intention				
Unintentional	1,109 (22.5%)	1,141 (21.8%)	2,250 (22.1%)	0.364
Intentional	3,814 (77.5%)	4,098 (78.2%)	7,912 (77.9%)	
Alcohol association				
No	3,487 (70.8%)	3,627 (69.2%)	7,114 (70.0%)	0.079
Yes	1,436 (29.2%)	1,612 (30.8%)	3,048 (30.0%)	
Clinical outcome				
Discharge	3,253 (66.1%)	3,236 (61.8%)	6,489 (63.8%)	<0.001
Adm. (GW & ICU)	1,670 (33.9%)	2,003 (38.2%)	3,673 (36.2%)	

SD: standard deviation, Adm: admission, GW: general ward, ICU: intensive care unit

discharged, and 3,673 patients (36.2%) were general ward and ICU admission, including 16 patients (0.2%) died in emergency room (Table 3).

2. Acute pharmaceutical drug poisoning after deregulation of OTC drugs sales

4,923 patients (48.4%) and 5,239 patients (51.6%) had acute pharmaceutical drug poisoning before and after deregulation of OTC drug sales (Table 3). The mean age of acute pharmaceutical drug poisoning patients before and after the deregulation of OTC drug sales were 36.8±20.8 and 38.4±21.3 years old, respectively (p=0.068) (Table 3). Sex distribution was 1,404 males (28.5%) and 3,519 females (71.5%) before off-pharmacy OTC drug sales and 1,627 males (31.1%) and 3,612 females (68.9%) after off-pharmacy OTC drug sales; male distribution showed a statistically significant increase (p=0.005) (Table 3). Intentional acute poisoning occurred in 3,814 cases (77.5%) before off-pharmacy OTC drug sales and in 4,098 cases (78.2%) after off-pharmacy OTC drug sales, which did not hold statistical significance (p=0.364) (Table 3). Before off-pharmacy OTC drug sales, 1,436 acute poisoning patients (29.2%) had association with alcohol consumption and 1,612 patients (30.8%) had after off-pharmacy OTC drug sales, which did not have statistical significance (p=0.079) (Table 3). Before off-pharmacy OTC drug sales, 1,670 cases (33.9%) were general ward and ICU admission; after off-pharmacy OTC drug sales, the number of patients increased to 2,003 (38.2%), which was statistically significant (p<0.001) (Table 3).

3. Acetaminophen poisoning after deregulation of OTC drug sales

Of the total, 1,015 patients (10.0%) had acute acetaminophen poisoning, and 9,147 patients (90.0%) had acute pharmaceutical drugs poisoning from drugs other than acetaminophen. The mean age of acute acetaminophen poisoning patients before and after off-pharmacy OTC drug sales were 24.7±14.2 and 24.7±21.2 years of age, respectively, which did not have statistical significance (p=0.768) (Table 4). The sex distribution of acetaminophen acute poisoning patients before off-pharmacy OTC drug sales was 99 males (18.4%) and 439 females (81.6%), and 101 males (21.2%) and 376 females (68.9%) after; male distribution increased but without statistical difference (p=0.268) (Table 4). Intentional acute poisoning before off-pharmacy OTC drug sales occurred in 448 cases (83.3%) and 398 (83.4%) after but without statistical difference (p=0.943) (Table 4). Before off-pharmacy OTC drug sales, acute poisoning associated with alcohol consumption occurred in 122 patients (22.7%) and in 130 patients (27.3%) after, but there was no statistical significance (p=0.092) (Table 4). Despite increased acute pharma-

Table 4. Characteristics of acute acetaminophen poisoning before and after the deregulation of Over-The-Counter drugs sales

	Before (N=538)	After (N=477)	p-value
Age (Mean±SD)	24.7±14.2	24.7±21.2	0.768
Gender			
Male	99 (18.4%)	101 (21.2%)	0.268
Female	439 (81.6%)	376 (68.9%)	
Intention			
Unintentional	90 (16.7%)	79 (16.6%)	0.943
Intentional	448 (83.3%)	398 (83.4%)	
Alcohol association			
No	416 (77.3%)	347 (72.7%)	0.092
Yes	122 (22.7%)	130 (27.3%)	
Clinical outcome			
Discharge	344 (63.9%)	254 (53.2%)	0.001
Adm. (GW & ICU)	194 (36.1%)	223 (46.8%)	

SD: standard deviation, Adm: admission, GW: general ward, ICU: intensive care unit

ceutical drug poisoning, acute acetaminophen poisoning decreased from 538 to 477 patients after deregulation of OTC drugs sales (Table 4). Before off-pharmacy OTC drug sales, General ward and ICU admission by acetaminophen poisoning occurred in 194 cases (36.1%) but statistically increased to 223 cases (46.8%) after (p=0.001) (Table 4). Among acetaminophen poisoning patients, death occurred in one case before off-pharmacy OTC drug sales as a result of overdosing on tramadol hydrochloride and acetaminophen. ICU admission by acetaminophen occurred in 4.6% (25/538) before but statistically increased to 11.3% (54/477) after off-pharmacy OTC drug sales (p<0.001) (Table 5). Also, ICU admission by other pharmaceutical drugs except acetaminophen occurred in 10.7% (470/4,385) before off-pharmacy OTC drug sales, and that increased to 14.6% (695/4,762) after off-pharmacy OTC drug sales, which was statistically significant (p<0.001) (Table 5).

DISCUSSION

In terms of abuse of OTC drugs, a study conducted in the United Kingdom which allowed off-pharmacy OTC drugs reported that the abuse rate of ibuprofen since deregulation had increased but had no influence on toxicity when compared to prescription use[14]. Among the overall abuse cases, poisoning by OTC drugs accounts for 40.1%, among which acetaminophen was most common with 36%, and 62.2% of those cases were reported as mild with dosages less than 32 tablets[15]. In this study, the frequency of acute pharmaceutical drugs poisoning was reported to have increased from 4,923 cases to 5,239 cases since deregulation of off-pharmacy OTC drug sales on January 1, 2013. However, acetaminophen poisoning decreased from 538 cases to 477 cases, and the ratio of acetaminophen poisoning to overall therapeutic drug poisoning significantly decreased from 10.3% to 8.6% (p=0.005). This result is believed to be an outcome of various sales regulations set up to decrease abuse of OTC drugs. According to a study reported by Hawkins et al.[16], death and hospitalization due to acetaminophen poisoning have decreased through policies restricting dosages of OTC drugs. Furthermore, a study by Chan et al.[17] reported decrease of acute poisoning even with the same dosage when strip packaging is used instead of a bag or container. In Korea, sales regulatory policy is in effect to prevent abuse of off-pharmacy OTC drugs. Considering the adult maximum dosage of 3,000 mg per day of acetaminophen, one pack consists of six 500 mg acetaminophen pills in a strip to prevent exceeding the daily maximum dosage. Also, sales are regulated so that one person can buy only one pack of acetaminophen[18]. As such, we can presume that the regulatory policy for off-pharmacy OTC drug sales has prevented the increase of acetaminophen acute poisoning occurrences after deregulation. Furthermore, we can presume deregulation of OTC drug sales has no correlation with the increase of acute therapeutic drug poisoning.

According to the results of this study, general ward and ICU admission occurred in 1,670 cases (33.9%) before deregulation of off-pharmacy OTC drug sales and in 1,996 cases (38.2%) after; the rates for ICU admission before and after were 34.9% (495/1,418) and

Table 5. Comparison of clinical outcome of pharmaceutical drugs poisoning with or without acetaminophen after the deregulation of Over-The-Counter drugs sales

Clinical outcome of acute poisoning	Before	After	p-value
Pharmaceutical drugs without acetaminophen	n=4,385	n=4,762	
Discharge	2,909 (66.3%)	2,982 (62.6%)	<0.001
General Ward admission	1,006 (33.0%)	1,085 (22.8%)	
Intensive care unit admission	470 (10.7%)	695 (14.6%)	
Pharmaceutical drugs with acetaminophen	n=538	n=477	
Discharge	344 (63.9%)	254 (53.2%)	<0.001
General Ward admission	169 (31.5%)	169 (35.5%)	
Intensive care unit admission	25 (4.6%)	54 (11.3%)	

41.2% (749/1,817), respectively, showing a statistically significant increase ($p<0.05$). In addition, the frequency and ratio of acetaminophen poisoning decreased, but general ward and ICU admission after deregulation of off-pharmacy OTC drug increased from 194 patients (36.1%) to 223 patients (46.8%), and ICU admission from 4.6% (25/179) to 11.3% (54/208) ($p<0.001$). There could be some reasons for increase of the rates for ICU admission by poisoning. Some hospitals could have made more ICU beds, and that could have made possible for the patients to be admitted to ICU more easily. Also, more physicians could have tried to manage acute poisoning patients in ICU for close observation, although in small amount. However in general, discharge, admission, or transfer for acetaminophen acute poisoning is decided based on the administered dosage, increased dosage can be presumed to be one of the major reasons. Many factors may be present for the increased dosage, but concomitant duplication of medication with prescription drug and multiple purchases of OTC drugs from several stores can result in increased OTC drugs in households. To reduce the severity of acute poisoning from OTC drugs, we recommend additional regulations to prevent duplicate purchases of OTC drugs, increased marketing communication about appropriate OTC drug administration, and expanding a drug utilization review system that allows individuals or physicians to review complete prescription drug history.

Most countries that allow sales of OTC drugs classify acetaminophen as an OTC drug, and acetaminophen poisoning requires hospital appointments or hospitalization for symptom observation or antidote treatment. According to the results of this study, deregulation of OTC drugs in Korea did not affect the occurrence of acute therapeutic drug poisoning but has had an influence on the severity considering the rise of admission and intensive care unit admission rates. Therefore, we believe that future investigation about the frequency, purchase route and dosage, admission rate, intensive care unit admission rate, and use of antidote of acetaminophen poisoning consider as potential useful indirect markers that use to identify acute OTC drug poisoning as a result of the deregulation of OTC drugs.

There are some limitations in this study. First, we could not identify how acute poisoning patients had purchased the pharmaceutical drugs based on EDIIS data. In Korea, The pharmaceutical drugs can be purchased in three ways: prescription issued by a medical institution, medication counselling offered by pharmacist, or OTC drugs available at convenience stores. However, our study could not identify the route of purchase. Second, the serologic test results of acute poisoning patients and the use of antidote were not available; therefore, we reviewed the status of discharge, hospitalization and ICU admissions. However, we could not accurately reflect the severity of acute poisoning patients for several reasons. We could not know patient information such as vital signs or laboratory findings by EDIIS data. Some acute poisoning patients are admitted for psychological treatment. Others seek treatment for preexisting conditions or exposure of other pharmaceutical drugs and toxins. Additionally, because we classified acute poisoning based on discharge, transfer, hospitalization or ICU admission, it was difficult to determine the actual severity of patients at the time of acute poisoning. Third, because we conducted this study as a retrospective cross-sectional observational study, there may be selection bias because we only included twenty regional emergency medical centres in Korea.

CONCLUSION

Since the deregulation of OTC drugs sales, pharmaceutical drug poisoning increased but acetaminophen poisoning had been decreased. The rate of hospitalization and ICU admission by pharmaceutical drug poisoning with or without acetaminophen had been also increased. Despite decline of acute acetaminophen poisoning, the rate for ICU admission of acute acetaminophen poisoning maybe increased.

ORCID

Sung Ho Kim (https://orcid.org/0000-0002-7508-3707)
Woochan Jeon (https://orcid.org/0000-0003-2674-3593)

REFERENCES

1. Association CHP. The value of OTC medicine to the United States. Washington, DC: Consumer Healthcare Products Association 2012.
2. Available at: https://www.chpa.org/OTCResearch.aspx Accessed August 1, 2018.
3. Dudley JW. OTC distribution in Europe. Worcestershire: James Dudley International Ltd; 2010.
4. Domestic and international cases of improvement in regulations concerning general pharmaceuticals. Seoul: Korea Chamber of Commerce and Industry; 2009.
5. Park HW. Reform of OTC distribution in Korea. J Korean Med Assoc 2012;55:843-51.
6. Pre-Announcement of Legislation of Enforcement Ordinances and Enforcement Regulations of Pharmaceutical Law. In. The Press Release of the Minister of Health and Welfare; May 22, 2012.
7. Kim EH, Bang JS. Changes in Perception of Consumers for Non-prescription Drug Policy since Sales Begins at the Outside of Pharmacy. Korean J Clin Pharm 2014;24:183-92.
8. Kim HH. An analysis on the change of OTC drugs sales in pharmacies after the implementation of selling OTC drugs outside of pharmacies. Department of Industrial Pharmaceutical Science The Graduate School, Sungkunkwan University 2014.
9. Lee KH, Kim KH. Clinical analysis of acute drug intoxication in the emergency department. J Korean Soc Emerg Med 1996;7:398-404.
10. Kang JH, Lee HN, Jin YH, Lee JB. A clinical analysis of acute drug intoxication in emergency department setting. J Korean Soc Emerg Med 1999;10:431-40.
11. Sung AJ, Lee WL, So BH, Lee MJ, Kim H, Park KH et al. Multicenter Survey of Intoxication Cases in Korean Emergency Departments: 2nd Annual Report. J Korean Soc Clin Toxicol 2012;10:22-32.
12. Smilkstein MJ, Knapp GL, Kulig KW, Rumack BH. Efficacy of oral N-acetylcysteine in the treatment of acetaminophen overdose. New England Journal of Medicine 1988;319:1557-62
13. Chung SP, Kim SH, Lee HS. Acetaminophen poisoning. J Korean Soc Clin Toxicol 2008;6:1-8.
14. Perry S, Streete P, Volans G. Ibuprofen overdose: the first two years of over-the-counter sales. Human Toxicology 1987; 6:173-8.
15. Wazaify M, Kennedy S, Hughes CM, McElnay JC. Prevalence of over-the-counter drug-related overdoses at Accident and Emergency departments in Northern Ireland-a retrospective evaluation. Journal of clinical pharmacy and therapeutics 2005;30:39-44.
16. Hawkins MLC, Edwards JN, Dargan PI. Impact of restricting paracetamol pack sizes on paracetamol poisoning in the United Kingdom. Drug safety 2007;30:465-79.
17. Chan TY. Safety packaging of acetaminophen combination preparations and severity of adult poisoning. Journal of Toxicology: Clinical Toxicology 1996;34:747-9.
18. Article 44-4 of Pharmaceutical Affairs Act (May 14, 2012).