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ANALYSIS OF DEATHS DUE TO ACUTE INTOXICATION IN THE REPUBLIC OF KOREA: AN AUTOPSY-BASED STUDY

Joo-Young Na*

Pusan National University, Yangsan Hospital, Department of Pathology, Yangsan, Republic of Korea

Abstract: Due to its high reliability, forensic autopsy data are useful for determining cause of death and studying deaths. This study aimed to analyze deaths resulting from acute intoxication in the Republic of Korea. This study analyzed 448 deaths resulting from acute intoxication using forensic autopsy data. This study analyzed a demographic characteristics, cause and manner of death, and type and blood concentration of the toxic substance. The most common manner of death was a suicide. The most common type of toxic substance was gas, followed by drugs and agrochemicals. The mean blood concentration was 0.417% among acute intoxication deaths due to ethyl alcohol, which was the most common toxic alcohol. Among acute intoxication deaths due to chemicals, nicotine and cyanide were the most common. Among insecticides, organophosphates and carbamates were the most common and, among herbicides, organophosphates were the most common. The most common intoxication drug was zolpidem and, in cases of acute multi-drug intoxication, an average of 2.7 drugs were detected at a blood concentration above the therapeutic range. The mean blood concentration was 68.6% for deaths due to carbon monoxide intoxication. This is the first nationwide study to analyze acute intoxication deaths in the Republic of Korea using autopsy data and shows several points to consider in forensic aspect.

Key words: autopsy, cause of death, epidemiology, poisoning, Republic of Korea.

INTRODUCTION

Various substances can cause an intoxication, including drugs and agrochemicals, and acute or chronic intoxication can be fatal. In the Republic of Korea (RoK), deaths considered to be due to unnatural causes, including acute intoxication, are reported to police investigators who then perform a postmortem examination, including a postmortem inspection. Based on this process, a forensic autopsy may be performed under a court warrant. In 2015, 6,610 forensic autopsies were performed in the RoK, of which 566 forensic autopsies involved acute intoxication deaths. This was the third most common cause of death (COD) among 3,326 cases of unnatural death, behind 1,330 cases of trauma and 588 cases of asphyxia [1]. Forensic autopsy data are based not only on postmortem information investigated by the police, but also on postmortem data from comprehensive studies, including autopsy and laboratory tests using postmortem samples collected during autopsy. Therefore, forensic autopsy data are useful when investigating the cause of death due to high reliability. While some previous reports have analyzed intoxication deaths using forensic autopsy data, these studies have been limited to specific regions of the RoK [2-3]. This study aimed to analyze acute intoxication deaths in the RoK using nationwide forensic autopsy data. To our knowledge, this is the first nationwide study to analyze acute intoxication deaths in the RoK.

MATERIALS AND METHODS

Subjects and ethics

Of 6,610 forensic autopsies performed in the RoK in 2015, 566 deaths were due to acute intoxication. Of these, 448 cases of death due to acute intoxication were analyzed. All data used in this study were obtained from forensic autopsies, which with performed following authorization with a court-issued warrant at the request of the public prosecutor. This study was confirmed as a research activity using anonymously treated postmortem data.

*Correspondence to: Joo-Young Na, M.D., Ph.D., Pusan National University, Yangsan Hospital, Department of Pathology, 20, Geumo-ro, Mulgeum-eup, Yangsan, 50612, Republic of Korea, Fax: +82-55-360-1865, Tel.: +82-55-360-1864, E-mail: pdrdream@gmail.com

Study design and data

Concerning those who died of acute intoxication who were included in this study, demographic characteristics such as age, sex, and region were analyzed, and the regions in which the deaths occurred were categorized as either the capital city, metropolitan cities, or other regions. The manner of death (MOD) was categorized as either natural death, unnatural death, or unknown. Unnatural deaths were further categorized as either suicide, homicide, accident, or undetermined [1]. An undetermined MOD category was used for cases in which a death had been deemed unnatural but it was unclear whether the death was due to suicide or homicide. During the autopsy, gastric contents and blood samples were collected and used for toxicology tests. Toxicological testing was performed using gas and/or liquid chromatography and mass spectrometry according to the relevant scope of testing, and additional tests were performed according to information available concerning each case. The venous blood was obtained from the external iliac vein for analysis and the type and blood concentration of each toxic substance was analyzed.

Data collection

In each case of death due to acute intoxication, the substance responsible for the death was analyzed. In this study, substances determined as COD were confirmed based on the final assessment of the forensic pathologist who referred to postmortem investigation records and the results of postmortem examination and laboratory tests. Toxic substances were categorized as toxic alcohol, chemicals, agrochemicals, drugs, gases, and natural toxins. In cases involving drugs as the COD, blood concentration levels were determined in terms of therapeutic, toxic, and lethal concentrations. Cases of chronic alcoholism in which the COD was confirmed as a natural disease were excluded in this study.

RESULTS

Of 448 deaths (males, 296; females, 151; unknown, 1) due to acute intoxication analyzed in this study, most individuals were aged between 50 and 59 years (n = 122 cases) and between 40 and 49 years (n = 111 cases). In 1 case, extensive decomposition was in progress; however, endosulfan was detected in a muscle tissue sample taken for a toxicology test. In the capital city, metropolitan cities, and other regions, there were 49, 93, and 306 deaths due to acute intoxication, respectively. In term of the MOD, most cases (n = 442 cases) involved an unnatural death, while the remaining cases were unknown. Of 442 unnatural deaths, 302, 4, and 64 deaths were due to suicide, homicide, and accidents, respectively. There were 72 cases of undetermined death (Table 1). Table 2 shows the MOD according to the intoxicating substance. In total, 137, 94, 100, and 117 deaths due to acute intoxication occurred in the spring, summer, fall, and winter, respectively (data is not shown).

There were 55 cases of death due to toxic alcohols, of which, most (n = 52 cases) were due to acute ethyl alcohol intoxication and most were

Table 1. Manner of death according to the basic characteristics

	Unnatural	Suicide	Homicide	Accidental	Undetermined	Unknown	Natural	Total
Age (years)								
≤ 9	2	0	2	0	0	0	0	2
10-19	3	1	2	0	0	0	0	3
20-29	39	32	0	3	4	0	0	39
30-39	67	49	0	5	13	0	0	67
40-49	109	72	0	16	21	2	0	111
50-59	118	73	0	24	21	4	0	122
60-69	43	27	0	11	5	0	0	43
70-79	45	37	0	0	8	0	0	45
≥ 80	11	10	0	1	0	0	0	11
Unknown	5	1	0	4	0	0	0	5
Sex								
Male	291	192	3	49	47	5	0	296
Female	150	110	1	15	24	1	0	151
Unknown	1	0	0	0	1	0	0	1
Region								
Capital	49	36	0	7	6	0	0	49
Metropolitan	92	64	0	14	14	1	0	93
Others	301	202	4	43	52	5	0	306
Total	442	302	4	64	72	6	0	448

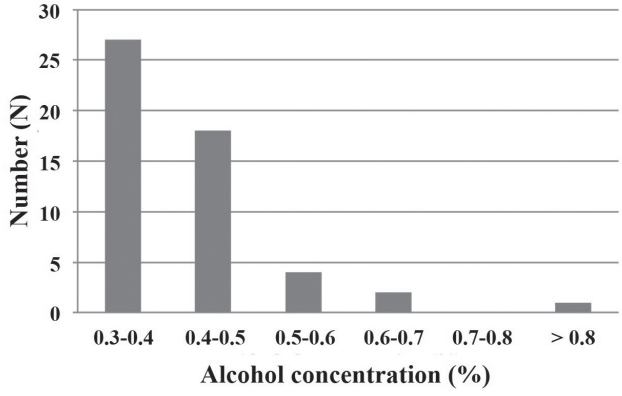

Figure 1. Number of deaths due to acute alcohol intoxication according to blood alcohol concentration.

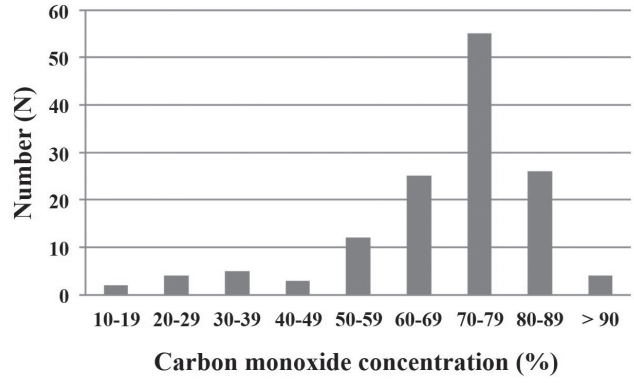

Figure 2. Number of deaths due to carbon monoxide intoxication according to blood carbon monoxide concentration.

Table 2. Specific cause and manner of death in cases wherein death occurred due to acute intoxication

		Unnatural	Suicide	Homicide	Accidental	Undetermined	Unknown	Natural	Total
Toxic alcohol	Ethyl alcohol	50	0	0	40	10	2	0	52
	Ethylene glycol	2	2	0	0	0	0	0	2
	Methyl alcohol	1	1	0	0	0	0	0	1
Chemical	Cyanide	29	25	1	1	2	0	0	29
	Nicotine	11	7	0	0	4	0	0	11
	Others	9	6	0	1	2	0	0	9
Agrochemical	Insecticide	39	35	0	0	4	0	0	39
	Herbicide	37	30	0	0	7	1	0	38
	Others	2	2	0	0	0	0	0	2
Drug	Mono-drug	43	30	0	2	11	0	0	43
	Multi-drug	76	60	0	1	15	2	0	78
Gas	Carbon monoxide	135	104	3	11	17	1	0	136
	Others	3	0	0	3	0	0	0	3
Natural toxin	Tetrodotoxin	4	0	0	4	0	0	0	4
	Others	1	0	0	1	0	0	0	1

accidental. There were 2 cases of death due to ethylene glycol intoxication and 1 case of death due to methyl alcohol intoxication, in which the blood concentration of methyl alcohol was 0.31%. The mean blood concentration in individuals who died from acute ethyl alcohol intoxication was 0.417 ± 0.11% (range, 0.30–0.981%) (Fig. 1).

There were 49 cases of acute intoxication deaths due to chemicals, and the most common chemicals involved cyanide (n = 29 cases) and nicotine (n = 11 cases). Among deaths due to acute cyanide intoxication, the mean blood cyanide concentration was 19.2 mg/L (range, 0.1 - 84 mg/L). Concerning deaths due to acute nicotine intoxication, the mean blood nicotine concentration was 58.9 mg/L (range, 1.8 – 201.1 mg/L). Among deaths due to cyanide intoxication, 1 person was 19 years old (homicide), 1 person was aged between 20 and 29 years, and the remainder were more than 30 years old. Of the nicotine intoxication cases, 1 person was 60 years old, 1 person was 70 years old, and the remainder were all aged between 20 and 39 years.

There were 79 deaths due to acute intoxication involving agrochemicals, and a total of 93 agrochemicals were detected in these cases. Most cases occurred in the provinces classified as 'other' regions. Among agrochemicals, we detected 46 insecticides and 46 herbicides. Among insecticides, organophosphates and carbamates were identified as the most common (15 cases each); the organophosphates included phosphamidon, dichlorvos, and diazinon; and methomyl was the most common carbamate (n = 9 cases). Among herbicides, organophosphates were detected in most cases (n = 24 cases), including glyphosate (n = 20 cases) and glufosinate (n = 4 cases) (Table 3).

Table 3. Toxic substances found in fatal agrochemical intoxication cases

Group		Capital	Metropolitan	Others	Total
Insecticide	Organophosphate	1	4	10	15
	Carbamate	2	2	11	15
	Pyrethroid	0	2	5	7
	Organochloride	0	0	4	4
	Others	0	5	0	5
Herbicide	Organophosphate	1	4	19	24
	Paraquat	1	0	10	11
	Phenoxy	0	3	1	4
	Others	1	0	6	7
Microbiocide	Acyl alanine	0	1	0	1
Total		6	21	66	93

There were 121 deaths due to acute intoxication involving drugs, of which 43 and 78 cases involved mono-drug and multi-drug intoxication, respectively. Among mono-drug intoxication cases, a sedative hypnotic (n = 20) was the most common drug and zolpidem (n = 16) was responsible for most deaths. Concerning deaths due to acute zolpidem intoxication, the mean blood zolpidem concentration was 1.81 ug/mL (range, 0.29–6.20 ug/mL). In 78 cases of death due to acute multi-drug intoxication, an average of 2.7 (range, 2–7) drugs was detected in the blood at levels above the therapeutic dose. Of these, psychotropic agents (29 types) were the most common. The most commonly detected substance in multi-drug intoxication cases was zolpidem. There were 10 deaths due to acute intoxication of illegal drugs, and methamphetamine (5 cases) was found to be the most common substance (Table 4).

Among deaths due to acute gas intoxication, most deaths were due to carbon monoxide (136 cases), and the mean blood carbon monoxide concentration was 68.6% (range, 10–93%) (Fig. 2). Most cases (n = 104 cases) were suicides, while 3 cases were homicides and the victims in these 3 cases were minors. Acute intoxication deaths due to other gases included accidental deaths due to hydrogen sulfide or ammonium during excreta and waste treatment processes.

There were 5 deaths due to acute intoxication from a natural toxin; of these, 4 cases were due to tetrodotoxin and 1 case was due to *Aconitum jaluense*; and all 5 deaths were accidental.

DISCUSSION

Acute intoxication is of clinical and forensic importance. In a previous study by Yoon et al. [4] involving acutely intoxicated patients who visited an emergency room, male and female numbers were reported to be similar; however, in the present study, there were twice as many males as females. It has previously been suggested that forensic autopsies are performed more frequently on males than females, and age and sex distribution data concerning death due to acute intoxication show a pattern similar to that of statistical data for forensic autopsies [1]. In Yoon et al.'s study, most acute intoxication patients had been admitted in August and September. It was suggested that this finding resulted from food intoxication due to fish and shellfish consumed during the summer season [4]. However, in this study, the highest number of acute intoxication deaths was observed in the spring and winter. This study showed differences between clinical and forensic data concerning acute intoxication, and these differences appear to show a forensic trend involving unnatural deaths due to acute intoxication compared to the clinical data in the RoK.

The most common substances that resulted in death due to acute intoxication were gases (139 cases), followed by drugs (121 cases), agrochemicals (79 cases), toxic alcohols (55 cases), and chemicals (49 cases). These results differed from those of a similar study in another country [5] and differed from clinical data. In relation to Yoon et al.'s study, this discrepancy may be because the substance responsible for acute intoxication could not be identified clearly in many clinical cases [4]. Among acute intoxication deaths, blood alcohol concentration was at least 0.05% in 193 cases (43.1%), and ethyl alcohol was the most commonly detected toxic substance in the RoK. Ethyl alcohol requires particular consideration due to its potential to interact with various other toxic substances; therefore, it is essential to determine the blood alcohol concentration in all suspected acute intoxication cases and to evaluate its clinical and forensic significance [6]. Among cases of acute chemical intoxication deaths, cyanide and nicotine were the most common substances, and the most common age groups comprised middle-aged individuals of > 40 years old and young adults between 20 and 39 years old,

Table 4. Toxic substances and their blood concentration in fatal drug intoxication cases

Group			Number	Blood concentration (mean, ug/mL)
Mono-drug	Sedative hypnotics	Doxylamine	1	9.80
		Flunitrazepam	2	0.13-3.41 (1.77)
		Diphenhydramine	1	7.90
		Zolpidem	16	0.29-6.20 (1.81)
	Anti-epileptics	Carbamazepine	2	75.10-142.60 (108.85)
		Lamotrigine	2	4.13-72.0 (38.07)
		Phenytoin	1	30.30
	Anti-pyretics, analgesics and anti-inflammatory drugs	Diclofenac	1	16.00
		Tramadole	3	1.82-32.14 (18.75)
	Drugs for psycho-nervous system	Citalopram	2	0.47-2.43 (1.90)
		Imipramine	1	4.92
		Trazodone	1	6.60
	Other central nervous agents	Amantadine	1	7.78
	Musculoskeletal relaxants	Rocuronium	1	29.20
	Autonomic drugs	Phentermine	2	17-20 (18.50)
	Other circulating system agents	Salicylate	1	71.84
	Designer drug	Methamphetamine	4	1.07-4.76 (2.46)
		Oxicodone	1	1.10
	General anesthetics	Ketamine	3	0.21
		Propofol	1	Liver
Multi-drugs	Sedative hypnotics	Diphenhydramine	12	1.5-91.4 (16.14)
		Doxylamine	15	0.24-34.5 (10.67)
		Flunitrazepam	6	0.05-0.19 (0.11)
		Flurazepam	2	0.42-0.62 (0.52)
		Midazolam	1	Liver
		Triazolam	3	0.005-0.02 (0.01)
		Zolpidem	21	0.15-12.8 (1.99)
	Anti-epileptics	Clonazepam	1	Liver
		Lamotrigine	1	159.09
		Topiramate	1	4.22
		Valproic acid	1	143.80
	Anti-pyretics, analgesics and anti-inflammatory drugs	Acetaminophen	5	65.0-339.0 (219.14)
		Tramadole	3	2.94-22.7 (15.74)
	Drugs for the psycho-nervous system	Alprazolam	16	0.04-2.98 (0.57)
		Amisulpride	1	38.60
		Amitriptyline	6	0.38-2.17 (1.14)
		Bromazepam	1	1.71
		Buspirone	2	1.00
		Chlorpromazine	2	0.87-4.55 (2.71)
		Citalopram	7	0.35-3.37 (1.82)
		Clobazam	1	0.60
		Clozapine	3	2.79-57.87 (21.20)
		Diazepam	1	10.80
		Escitalopram	2	1.27-4.53 (2.90)
		Etizolam	1	0.06
		Fluoxetine	2	0.48-1.4 (0.94)
		Haloperidol	1	0.07
		Hydroxyzine	2	0.28-0.81 (0.54)
		Imipramine	5	0.43-3.57 (1.30)
		Lorazepam	3	0.39-1.51 (0.95)
		Mirtazapine	8	0.44-2.41 (1.10)
		Nortriptyline	4	0.14-8.88 (3.95)
		Olanzapine	2	0.29-1.12 (0.71)
		Paroxetine	3	0.14-0.78 (0.47)
		Perphenazine	1	0.18
		Quetiapine	11	1.08-40.38 (7.72)
		Risperidone	2	0.15-0.45 (0.30)
		Sulpiride	1	19.95
		Tianeptine	2	0.4-2.5 (1.45)
		Trazodone	5	1.73-8.2 (5.07)
		Trazodone	5	1.73-8.2 (5.16)
		Venlafaxine	2	1.04-23.6 (12.32)
	Other central nervous agents	Benztropine	6	0.09-6.57 (1.56)
		Procyclidine	2	1.91-2.24 (2.07)
	Autonomic drugs	Phentermine	2	0.72-3.3 (2.01)
	Arrhythmic agents	Propranolol	3	0.95-36.11 (12.78)
	Anti-hypertensive	Amlodipine	4	0.07-0.10 (0.08)
	Other circulating system agents	Salicylic Acid	1	713.00
	Anti-leprotics	Dapsone	1	30.00
	Anti-protozoal	Hydroxychloroquine	1	10.50
	Designer drug	Fentanyl	2	0.003-0.12 (0.06)
		Methamphetamine	1	0.27
		Oxycodone	2	0.21-0.83 (0.52)
		Paramethoxyamphetamine	1	0.57

respectively. In 2014, it was reported that a relatively young individual had been intoxicated due to nicotine, and that nicotine intoxication had increased in the RoK [7]. This trend in nicotine intoxication has been considered to be associated with the use of e-cigarettes. A more thorough awareness of the dangers of nicotine intoxication is necessary, especially among young adults. In acute agrochemical intoxication deaths, this study detected a number of fatal agrochemicals whose production and sales have been prohibited since 2012 in the RoK, but which had been used for intoxication, such as paraquat (11 cases), dichlorvos (3 cases), methomyl (9 cases), and endosulfan (4 cases). Among deaths due to acute drug intoxication, cases of multi-drug intoxication occurred 1.8 times more frequently than those due to mono-drug intoxication and, among cases of multi-drug intoxication there was an average use of 2.7 drugs. And these findings are similar to those of previous report [5]. The drug most commonly responsible for acute intoxication deaths was zolpidem (mean, 1.81 ug/mL). This sedative hypnotic is taken orally and is frequently prescribed in the RoK. Drugs for the psycho-nervous system and sedative hypnotics were most commonly found in cases of acute drug intoxication death. Antidepressants and antipsychotics have been reported to widely used in cases of suicide [5]. Therefore, it is considered that these drugs should be more carefully controlled for patients with sleep or mental health disorders.

Blood toxic substance concentrations concerning the toxic substances reported in this study require careful interpretation. For example, in cases in which hospital treatment was provided after acute intoxication and prior to death, the blood toxic substance concentrations could have been below lethal concentrations. Nevertheless, because the CODs in this study were determined based on a forensic pathologist's assessment and through combining investigation records and autopsy and post-mortem test results, we consider the analysis of toxic substances as the COD to be reliable.

In the United States, extensive data concerning intoxication are collected and analyzed through the Toxic Exposure Surveillance System, which is an intoxication database operated by the American Association of Poison Control Center. These important basic data are used to develop poison-related policies and in the prevention and treatment of intoxication. However, in the RoK, there is no organization responsible for managing clinical and forensic information concerning acute intoxication for preventing and treating acute intoxication. It is recommended to establish an organization for collection, integration, and management of clinical and forensic data on acute intoxication. To our knowledge, this was the first nationwide study to analyze acute intoxication deaths in the RoK.

Conflict of interest

The author declares that there is no conflict of interest.

Ethics

This study underwent using forensic autopsy data with court's warrant requested by the public prosecutor. The study was confirmed as a research activity qualifies as non-human participant and as all data were analyzed anonymously.

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