The experience of intoxication analysis center service linked to the National Forensic Service in the emergency room of one tertiary hospital and its effect on the treatment of acute intoxication patients

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The experience of intoxication analysis center service linked to the National Forensic Service in the emergency room of one tertiary hospital and its effect on the treatment of acute intoxication patients

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감사의 글

본 논문의 계획부터 완성에 이르기까지 방향을 잡아주시고 자애로운 가르침으로 지도해주신 김현 지도 교수님께 진심으로 감사드립니다. 또한 바쁘신 업무 중에도 논문 작성에 아낌없는 조언을 해주시고 올바른 방향으로 격려를 해주신 이강현 교수님과 차경철 교수님께도 깊은 감사드립니다.

또한 현재의 제가 있을 수 있도록 소중한 가르침을 주신 저희 응급의학교실의 황성오 교수님, 차용성 교수님, 김오현 교수님, 정우진 교수님, 박경혜 교수님께도 감사드립니다.

더불어 함께 수련을 하며 힘을 주고 의지할 수 있었던 동기 김태윤 선생님, 김진혁 선생님, 강희승 선생님 감사드립니다.

무엇보다도 항상 제가 걷는 길을 조건 없이 응원해주시는 제 아버지, 어머니, 형에게 다시 한번 큰 감사의 말씀을 올리며, 함께하는 것만으로 큰 지지가 되어준 아내와 두 아들에게 감사의 말을 전하고 싶습니다.

2021년 2월

이 제 섭 드림

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Abstract

The experience of intoxication analysis center service linked to the National Forensic Service in the emergency room of one tertiary hospital and its effect on the treatment of acute intoxication patients

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(Directed by Professor Hyun Kim)

Objective : It is difficult to diagnose poisoned patients and determine the causative agent in the emergency room. Usually, the diagnosis of such patients is made based on their medical history and physical examination findings. The “Intoxication Analysis Service” was launched in June 2017 at our hospital with the “National

Forensic Service" to diagnose intoxication and identify the types of toxic substances by using systematic toxicological analysis (STA). We confirmed the clinical diagnosis using STA and investigated changes in the diagnosis of poisoned patients.

Methods : For drug analysis, gas chromatography–mass spectrometry or liquid chromatography–tandem mass spectrometry was used. Data were collected from patients hospitalized in the emergency room between June 2014 and May 2020. Data were collected and compared between two time periods: before the initiation of the service i.e. from June 2014 to May 2017 and from June 2017 to May 2020.

Results : A total of 492 and 588 patients were enrolled before and after the service, respectively. Among the 588 after-service patients, 446 received STA. Among the 492 before-service patients, 113 could be diagnosed through hospital available toxicological analysis. However, 69.9% of patients were diagnosed clinically, and 35 patients could not find the causative agent. After the start of the project, confirmed diagnosis was established in 84.4% of patients through hospital available toxicological analysis or STA. Among the patients with known toxins based on medical history, 83.6% matched with the STA results, and 8.4% did not report any poison, including known toxins. The accuracy of the substance suspected by the emergency physician was 49.3%, and 12% were not actually poisoned. In 13.4% of patients who visited the emergency room because of poisoning of unknown causes,

poisoning could be excluded after STA. It was found that poisoning was the cause of altered mental status in 31.4% of patients who were unable to find a cause in the emergency room.

Conclusions : Diagnosis may change depending on the STA results of the intoxicated patient. Therefore, an appropriate STA can increase the accuracy of diagnosis and help in making appropriate treatment decisions.

Keywords: Toxicology, Poisoning, Laboratory diagnosis, Forensic Toxicology

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I. Introduction

Poisoning is one of the leading causes of morbidity and mortality in the United States.[1] According to an annual report by the American Association of Poison

Control Centers' National Poison Data System, more than 2.0 million poisonings occurred in 2018 alone, which resulted in approximately 1300 poisoning-related deaths.[2] The in-hospital mortality rate of poisoned patients is known to be approximately 0.5%.[3] However, the deaths from poisoning reported to the Poison Control Center in the United States account for only 5% of the actual deaths.[4] In the Republic of Korea, the number of poisoned patients is gradually increasing; in 2015, more than 32,000 patients visited the emergency room (ER) for poisoning.[5] It is also known that the in-hospital mortality rate of poisoned patients is 1.6%–7.9%.[5-7]

The identification of the substance causing the poisoning and the time taken to reach the hospital after exposure are related to the patient's prognosis.[8] For certain substances, the proper use of burdensome treatments such as antidote or decontamination therapy can be important. In addition, even if a substance turns out to not affect treatment, it can help doctors determine the treatment directions for patients with unclear diagnosis.[9]

It is difficult to determine whether a patient has been poisoned and what toxins are causing the poisoning. This is usually determined through medical history and physical examination. However, poisoning can present a variety of clinical signs and symptoms, which may be the only indication of poisoning.[8] Therefore, it is

often difficult to differentiate poisoning from other diseases on the basis of clinical symptoms alone, and there are other types of toxic substances that show similar clinical manifestations. In particular, the diagnosis of herbicide poisoning relies mostly on medical history.[10] Furthermore, many patients tend to withhold details about their poisoning. In such cases, additional unnecessary tests may be performed, adequate treatment time may be missed, and ER stay time may increase.

Given the wide variety of toxins in poisoned patients who present to the ER, it is difficult to maintain a toxicology laboratory in one hospital owing to problems of time, manpower, and cost.[11] Although toxicology screening tests have been developed and used to differentiate poisoned patients, their use is limited. The "Intoxication Analysis Service," which was started in June 2017, is a cooperative project between the hospital and the Forensic Toxicology Division of the National Forensic Service, Republic of Korea. This project uses systematic toxicological analysis (STA) and was initiated with the aim of improving the quality of treatment for intoxication by confirming the presence of poisoning in a patient and detecting the type of toxin. We collected clinical diagnosis and toxicology laboratory results and compared whether changes have occurred in the patient treatment and physician's decision after the initiation of the Intoxication Analysis Service.

II. Methods

A. Intoxication analysis service process

The “Intoxication Analysis Service” was established in our hospital in cooperation with the National Forensic Service to improve problems arising from the diagnosis and treatment of intoxicated patients. If it is determined that STA is necessary, the test is performed after providing an explanation to patients and obtaining their consent. Furthermore, the test is performed at no cost to the patient. The patient’s blood or urine, gastric lavage, or a suspected substance is obtained when performing a blood test in the ER. The emergency physician notifies the request for toxicology via the social network system (SNS) and shares the encrypted patient information, the reason for the analysis request, and the information on the toxic substances and patient’s conditions. Thereafter, the documented patient information and specimens are sent to the National Forensic Service, which is 15minutes, 4.6km away from the hospital. Whole blood sample is transferred after injecting it into a vacuum tube, and other samples are transferred into a sealed container. Gas chromatography–mass spectrometry (GC/MS) or liquid chromatography–tandem mass spectrometry (LC-MS/MS) is used to analyze drug or poison components in the blood and, if necessary, perform quantitative analysis.

The results of the analysis can be reported by using the SNS and documents. From April 2019, information exchange via the internet has enabled faster sample requests and result reception, and physicians can check the results by visiting the website of the National Emergency Medical Center. (www.e-gen.or.kr)

B. Systematic toxicological analysis

Sample preparation and detection were performed on the basis of the chemical structure and properties of the target substance. The following substances are used in the classification by chemical structure and property: liphophilic–basic compounds such as typical antipsychotic drugs and synthetic pyrethroids; hydrophilic or ionic moiety compounds such as paraquat, glyphosate, and glufosinate; and volatile solvents such as methanol, xylene, and toluene. When analyzing liphophilic–basic compounds, 1 mL of blood and urine samples were taken and introduced in a solid-phase extraction system. The eluted samples were concentrated and injected into the GC/MS and LC-MS/MS systems. In the hydrophilic or ionic moiety compound, 0.1 mL of blood and urine samples were taken and 0.2 mL of acetonitrile was added, next the samples were homogenized via sonication and finally centrifuged. The supernatants were then injected into the GC/MS and LC-MS/MS systems. Next, 0.5 mL of blood and urine samples required for volatile solvent analysis were injected into GC/MS directly with solid-phase

microextraction.

C. Study design and population

To determine the changes in management for poisoned patients before and after the implementation of the “Intoxication Analysis Service,” we collected data of poisoned patients who were admitted to the ER of Wonju Severance Christian Hospital from June 2014 to May 2020, which is a tertiary university hospital. Patients were compared by dividing them into two groups from June 2014 to May 2017 and June 2017 to May 2020 on the basis of the time of the service.

Some of the patients were excluded on the basis of the following criteria: (1) patients who were discharged against medical advice, (2) those who were transferred to another hospital, (3) those who arrived at the ER in arrest status, (4) those who were discharged from the ER without hospitalization owing to mild symptoms, and (5) those who presented to the ER owing to CO poisoning, insect bites, or snake bites that do not require poisoning analysis.

STA was conducted on patients who visited the hospital between June 2017 and May 2020. The inclusion criteria for the STA are as follows: (1) Patients were included when they directly mention a toxic substance or when the substance is found with the patient, this was confirmed by toxicity analysis. (2) The purpose of

confirming if there is a substance suspected by medical staff after physical examination is because toxic substances could not be identified by medical history. (3) The patient's symptoms appear to be due to exposure to a specific substance, but the type of toxic substance was not known. (4) If the reason for the altered mental status was not known after evaluating laboratory test findings, brain evaluation, and spinal tapping, a test was requested to determine whether it was due to intoxication.

Some of the patients were not analyzed (1) when the exposed toxins can be analyzed in a hospital and (2) when it was judged that STA was unnecessary because conservative treatment was possible owing to minor symptoms. The institutional review board of Wonju Severance Christian Hospital approved this study (approval number: CR320113). Owing to the retrospective and observational nature of the study, the need for informed consent was waived.

D. Data collection

Patient data were collected retrospectively by a board-certified emergency physician. The patient's age, sex, history, physical examination, patient prognosis, and toxicity analysis results were assessed. The results of the STA were recorded in the electronic medical records. On the basis of these results, the reason for the

analysis, the time to report the results, and the results of the STA were collected. Intoxication analysis results were classified as medical drugs, agrochemicals, and other natural poisons such as mushrooms and plant roots.

F. Statistical analysis

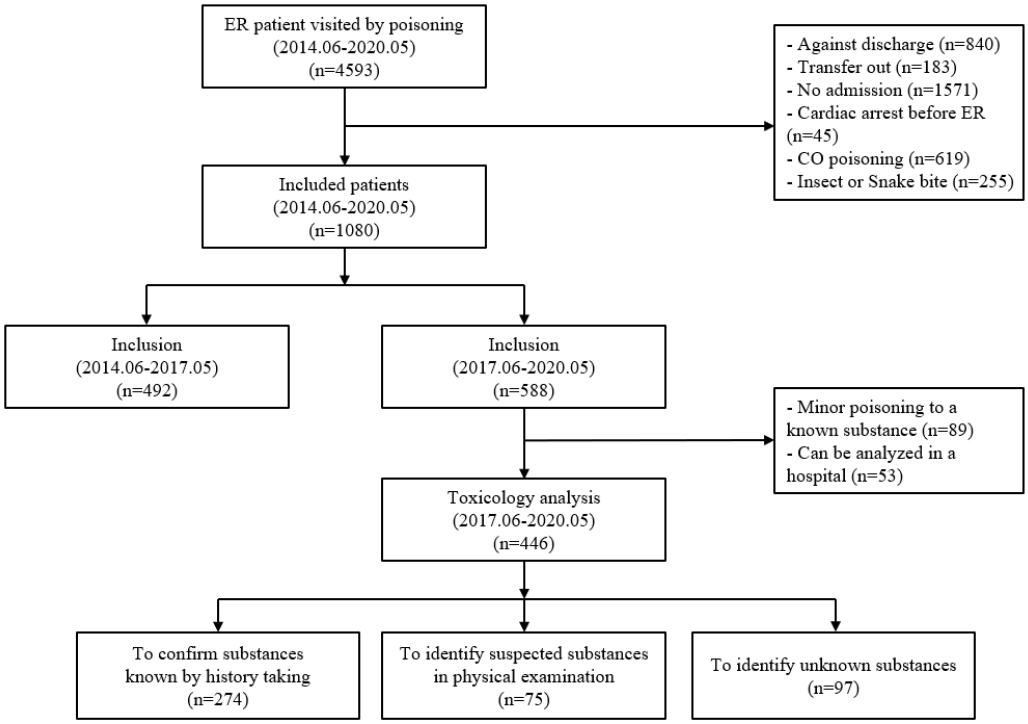
The general characteristics of the participants, laboratory findings, and clinical parameters were presented as mean (standard deviation) or median (interquartile range) for continuous variables and as frequencies (percentages) for categorical variables. The differences between the poisoning patients before and after analysis service were assessed using an independent t-test for continuous variables and a chi-square test and Fisher's exact test for categorical variables. All statistical analyses were performed using IBM Statistical Package for the Social Sciences Statistics for Windows version 25.0 (IBM Corp., Armonk, NY), and the significance level was set at 0.05.

III. Results

A. General characteristics

During the study period, a total of 4593 ER patients were admitted for poisoning. Among them, 1080 patients were included in the analysis, and 3513 patients were excluded according to the exclusion criteria. A total of 492 patients were admitted in the ER for 3 years before the start of the service. Among the 588 patients who presented to the ER during the period after the service, 446 (%) were subjected to STA as needed. Among these, 274 patients (61.4%) were referred for analysis to confirm their exposure to known toxins via history taking. A total of 75 patients (16.8%) were referred for the purpose of confirming the substances suspected on the basis of symptom and physical examinations. A total of 97 patients (21.7%) visited the ER due to poisoning, but the intoxication substance could not be identified. Given that no substance was suspected, an STA was performed. The other 54 patients visited the ER with altered mental status, and STA was requested when the cause of the decreased mental status was not identified after brain imaging, laboratory study, and tapping.

Figure 1. Flowchart of the study. ER = emergency room; CO = carbon monoxide.



Changes before and after the project were analyzed by comparing the patients hospitalized for poisoning in the ER. Table 1 shows a comparison of the patients' characteristics and laboratory results. The baseline characteristics of the two groups showed that there were no statistically significant differences, except for age (median: 51 vs. 56 years) and body temperature (median: 36.3 versus 36.5). A total of 44.9% and 46.9% of the before and after groups were men, respectively. Psychiatric diseases (28.9% and 29.3%) were the most common diseases in the medical history of the patients, and depressive diseases accounted for the majority.

Intentional poisoning occurred in 80.9% and 77.6% of patients in the before and after groups, respectively. There were 17 and 28 deaths in the hospital for the before and after groups, respectively; however, the findings were not statistically different.

Table 1. Baseline characteristics, past medical histories, and clinical parameters of patients with poisoning

Variable	Before (*n* = 492)	After (*n* = 588)	P value
Age (yr)	51 (35–67)	56 (38–72)	0.001
Sex (male)	221 (44.9)	276 (46.9)	0.507
Medical history			
Hypertension	110 (22.4)	152 (25.9)	0.182
Diabetes mellitus	55 (11.2)	66 (11.2)	0.981
Chronic lung disease	11 (2.2)	18 (3.1)	0.403
Congestive heart failure	26 (5.3)	48 (8.2)	0.062
Liver disease	12 (2.4)	16 (2.7)	0.771
Chronic renal failure	4 (0.8)	10 (1.7)	0.281
Stroke	25 (5.1)	28 (4.8)	0.809
Cancer	15 (3.0)	28 (4.8)	0.152
Psychiatric disease	142 (28.9)	172 (29.3)	0.888
Depressive disorder	114 (23.2)	140 (23.8)	0.805
Panic disorder	6 (1.2)	14 (2.4)	0.159
Bipolar disorder	6 (1.2)	8 (1.4)	0.838
Schizophrenia	7 (1.4)	10 (1.7)	0.715
Anxiety disorder	8 (1.6)	3 (0.5)	0.124
Suicide attempt	398 (80.9)	456 (77.6)	0.179
Initial vital sign			
Systolic blood pressure (mmHg)	130 ± 27.4	128 ± 29.6	0.177
Diastolic blood pressure (mmHg)	76 ± 17.7	78 ± 19.3	0.488
Heart rate (/min)	88 (76–102)	88 (74–102)	0.975
Body temperature (℃)	36.3 (36.0–36.7)	36.5 (36–36.8)	<0.001
GCS at the ED	14 (10–15)	13 (10–15)	0.795

Total admission days	3 (2–7)	3 (2–7)	0.142
Days in ICU	3 (1–6)	3 (1–6)	0.585
In-hospital mortality	17 (3.5)	28 (4.8)	0.285

Data were expressed as frequency (percentage), mean ± standard deviation, or median (interquartile range).

GCS, glasgow coma scale, ED, emergency department, ICU, intensive care units

B. The comparison of patient diagnosis and type of toxic materials

Before the service, most diagnoses of poisoning were clinical diagnoses. There were 113 cases that could be diagnosed by the hospital available toxicological analysis. However, most poisonings (69.9%) were caused by toxins that could not be tested by the hospital available toxicological analysis, and in 35 patients the substance that caused the poisoning could not be determined until discharge. After the start of the service, 50 cases could be diagnosed only by hospital available toxicological analysis, and 446 patients could be diagnosed through STA at the National Forensic Service. A total of 84.4% of patients could confirm the diagnosis. As a result, no intoxication could be identified. In the before group, 47.2% of the patients were poisoned by medical drugs, 39.4% were affected by agrochemical poisoning, and 1.8% were exposed to natural poisons. After the service, the proportions of the toxic substances are as follows: 51.7% were medical drugs, 30.4% were agrochemicals, and 3.7% were natural poisons (Table 2).

Table 2. Diagnosis results of patients who visited the emergency room due to poisoning

Variable	Before (*n* = 492)	After (*n* = 588)
Diagnosis		
Clinical diagnosis	344 (69.9)	92 (15.6)
Diagnosis by hospital available analysis	113 (23.0)	50 (8.5)
Diagnosis by 'intoxication analysis service'		446 (75.9)
With hospital available analysis		52 (8.8)
Without hospital available analysis		394 (67.0)
Unknown toxic substance until discharge	35 (7.1)	0 (0)
Time to result of hospital available analysis	125 (92-159)	122.5 (102-144)
Time to result of 'intoxication analysis service'		4.0 (3-5)
Type of toxic substance		
Medical drug	232 (47.2)	304 (51.7)
Agrochemical	194 (39.4)	179 (30.4)
Herbicide	108 (22.0)	110 (18.7)
Insecticide	75 (15.2)	62 (10.5)
Fungicide	2 (0.4)	3 (0.5)
Rodenticide	9 (1.8)	3 (0.5)
Natural poison	9 (1.8)	22 (3.7)
Others	45 (9.1)	52 (8.8)

Before and after the analysis service, 194 and 179 agrochemical poisoning patients were hospitalized. Of these, herbicides accounted for 55.7% and 61.5%, respectively, and insecticides accounted for 38.7% and 34.6%. The types of herbicides that accounted for the largest number in 6 years were glufosinate, glyphosate, and paraquat. The number of glufosinate intoxication patients increased from 42 to 55, and glyphosate increased from 28 to 33, but paraquat poisoning

decreased from 14 to 9. Except for these three herbicides, there was a change from 8 to 15 patients who consumed other herbicide. Organophosphate and pyrethroid poisoning accounted for the largest number of pesticide poisoning patients. However, the third most poisoned insecticides was carbamate in the previous three years, but it has recently been changed to a neonicotinoid. In the case of pesticide poisoning, all of the herbicide poisoning and pesticide poisoning, whose ingredients were unknown, disappeared as the analysis service was conducted. (Table 3)

Table 3. Changes in agrochemical poisoning

Variable	**Before (n = 194)**	**After (n = 179)**
Herbicide	108 (55.7)	110 (61.5)
Glufosinate	42 (21.6)	55 (30.7)
Glyphosate	28 (14.4)	33 (18.4)
Paraquat	14 (7.2)	9 (5.0)
Other herbicide	8 (4.1)	15 (8.4)
Unknown type of herbicide	18 (9.3)	0 (0)
Insecticide	75 (38.7)	62 (34.6)
Organophosphate	32 (16.5)	21 (11.7)
Pyrethroid	23 (11.9)	13 (7.3)
Carbamate	6 (3.1)	5 (2.8)
Neonicotinoid	4 (2.1)	7 (3.9)
Other insecticide	8 (4.1)	18 (10.1)
Unknown type of insecticide	4 (2.1)	0 (0)
Fungicide	2 (1.0)	3 (1.7)
Rodenticide	9 (4.6)	3 (1.7)

All poisonings of natural toxin were clinically diagnosed, but after the service, all toxins were diagnosed through laboratory analysis results. Only 9 patients were identified for natural poisoning in the previous 3 years. However, as the diagnosis of various natural poisons including aconitine (7 patients) and veratramine (5 patients) became possible, the number of patients increased to 22. (Table 4)

Table 4. Changes in natural toxin poisoning

Variable	**Before (n = 9)**	**After (n = 22)**
Veratramine	4 (44.4)	5 (22.7)
Aconitine	1 (11.1)	7 (31.8)
Esculentoside	0 (0)	3 (13.6)
Tetrodotoxin	0 (0)	3 (13.6)
Araceae	2 (22.2)	0 (0)
Ricinine	0 (0)	2 (9.1)
Nerium	1 (11.1)	0 (0)
Grayanotoxin	0 (0)	1 (4.5)
Amanita virosa	1 (11.1)	0 (0)
Clitocybe nebularis	0 (0)	1 (4.5)

C. The comparison of patient characteristics and results according to the reason for analysis

The STA results of the patients who were referred were consistent with the drugs identified in the history taking in 83.6% of the patients. In addition, 20 patients (7.3%) were found to have additional toxic substances other than the requested substance, and 2 patients (1.1%) did not find the requested substance, but a completely different substance was identified as the cause of the patient's poisoning. A total of 23 patients (8.4%) presented to the hospital for intoxication, but it was found that they were not actually poisoned. The majority of patients (42.7%) with poisoning visited the hospital after medical drugs exposure, followed by agrochemicals (42.3%). Compared with the results of the toxicity analysis, the accuracy of the clinically suspected substance reached 49.3%. In addition to the suspicious substance, 30.7% of patients were found to have additional substances, 8% patients were found to have other causes of poisoning, and 12% of patients had no toxic substances found on STA. In the case of 97 intoxication patients whose causative agent was unknown, 13.4% of patients were confirmed to be not actually poisoned, and they were discharged alive. In addition, 86.6% of patients were able to identify toxic substances via the STA, with medical drugs, agrochemicals, and natural poisons accounting for 61.9%, 16.5%, and 8.2% of the toxic substances,

respectively. Three of these patients died in the hospital. In all patients who underwent STA, a median of 4 hours was required to confirm the results in a document, and the results were obtained in a median of 3.5 hours via the SNS (Table 5).

Table 5. Characteristics of patients with systematic toxicological analysis

Variable	Total (*n* = 446)	Known toxin (*n* = 274, 61.4%)	Suspected toxin (*n* = 75, 16.8%)	Unknown toxin (*n* = 97, 21.7%)
Age (yr)	58 (44–74)	55 (40–67)	75 (58–82)	57 (45–72)
Sex (male)	224 (50.2)	139 (50.7)	38 (50.7)	47 (48.5)
Suicide attempt	352 (78.9)	239 (87.2)	40 (53.3)	73 (75.3)
Request to SNS report (hr)	3.5 (1.8–4.5)	3.5 (2–4.6)	3.2 (2–4.3)	3.5 (1–4.8)
Request to documented report (hr)	4.0 (3–5)	4.0 (3–5)	4.1 (3.5–5.3)	4.2 (3–35)
Accuracy of initial diagnosis				
Intoxication	401 (89.9)			84 (86.6)
Correct		229 (83.6)	37 (49.3)	
Additional substance		20 (7.3)	23 (30.7)	
Other substance		2 (0.7)	6 (8.0)	
All substance ruled out	45 (10.1)	23 (8.4)	9 (12.0)	13 (13.4)
Classification of toxin				
Medical drug	228 (50.7)	117 (42.7)	51 (68.0)	60 (61.9)
Agrochemical	143 (32.1)	116 (42.3)	11 (14.7)	16 (16.5)
Herbicide	87 (19.5)	77 (28.1)	4 (5.3)	6 (6.2)
Insecticide	50 (11.2)	35 (12.8)	7 (9.3)	8 (8.2)
Fungicide	5 (1.1)	3 (1.1)	1 (1.3)	1 (1.0)
Rodenticide	2 (0.4)	2 (0.7)	0 (0)	0 (0)
Natural poison	20 (4.5)	8 (2.9)	4 (5.3)	8 (8.2)
Others	12 (2.7)	10 (3.6)	0 (0)	2 (2.1)
In-hospital mortality	24 (5.4)	14 (5.1)	7 (9.3)	3 (3.1)

D. Results of systematic toxicological analysis of altered mental status

Among the 54 patients in whom altered mental status due to unknown cause was analyzed, it was found that poisoning altered the mental status in 17 patients (31.4%). Among these patients, four cases were confirmed to have had intentional intoxication after their consciousness improved. Intoxication was ruled out in 37 patients (68.5%), and only 4 cases of in-hospital death occurred. Among the 17 patients in whom the cause of altered mental status was found to be poison, 14 cases were caused by medical drug intoxication, 1 case was caused by herbicides, and 2 cases were caused by insecticides (Table 6).

Table 6. Characteristics of patients with toxicology laboratory analysis for the purpose of identification of the cause of altered mental status

Variable	Total (*n* = 54)
Age (yr)	70 (57-81))
Sex (male)	30 (55.6)
Medical history	
Hypertension	24 (44.4)
Diabetes mellitus	17 (31.5)
Chronic lung disease	4 (7.4)
Congestive heart failure	7 (13.0)
Liver disease	2 (3.7)
Chronic renal failure	6 (11.1)
Stroke	5 (9.3)
Cancer	1 (1.9)
Psychiatric disease	9 (16.7)
Suicide attempt	4 (7.4)
Initial vital sign	
Systolic blood pressure (mmHg)	137 ± 37.7
Diastolic blood pressure (mmHg)	78 ± 19.6
Heart rate (/min)	90 (71–107)
Body temperature (℃)	36.5 (36.0–37.0)
GCS at the ED	7 (5–10)
Total admission days	10 (3–17)
Days in ICU	7 (2–14)
Request to SNS report (hr)	3.8 (1.8–5)
Request to documented report (hr)	4 (3–5.2)
Confirmation of intoxication	
Intoxication	17 (31.4)
Medical drug	14 (25.9)
Agrochemical	3 (5.6)
Herbicide	1 (1.9)
Insecticide	2 (3.7)
All substances ruled out	37 (68.5)
In-hospital mortality	4 (7.4)

IV. Discussion

This project is a new system in the Republic of Korea and allows a national institution and a hospital request toxicity analysis via the SNS and the internet. Quick and easy information sharing is possible by using SNS, web pages, and documented records. The National Forensic Service, which is in charge of criminal investigations and autopsies, can conduct toxicological analysis by using their vast amounts of toxicology data, thus enabling more accurate and wider analysis than toxicological analysis in other laboratories. In particular, it was possible to use toxicological analysis tests for natural poisons and industrial substances, including information on various pesticides marketed in the Republic of Korea. On the other hand, the National Forensic Service was able to obtain the clinical information of patients by analyzing samples from actual clinical patients. By comparing the results of qualitative and quantitative plasma analysis with patient information, it was able to accumulate valuable data on toxic substances with insufficient information. Furthermore, this allowed doctors to make quick and accurate treatment decisions and obtain information on poisoning trends in the community.

In the past, the clinical effectiveness of toxicology laboratory analysis has been underestimated because of the following reasons. First, intoxication patients have been diagnosed only with clinical information. Second, conservative treatment is

sufficient for the treatment of intoxication; therefore, even if toxic substances were identified by laboratory analysis, the treatment direction usually did not change clinically. Third, comprehensive analysis results are usually reported after initial critical treatment, and screening tests with short report times are limited in confirmation. Lastly, the costs associated with equipment, specialists, and training for maintaining the STA are large and are often overused; therefore, the gain versus loss is not significant.[11-14] However, given that many changes have been made in the diagnosis and treatment of intoxication patients, the perception of STA is also changing.

Medical history documentation in the ER is often inaccurate because of the urgency of the situation, the patient's condition, and the hospital is not familiar with the patient. In particular, it is known that the history documentation of cardiac medications, neuropsychiatric agents, analgesics, and hypnotics is often inaccurate.[15-17] In addition, a report has stated that the accuracy of medication history from patients in the ER is 13%–36.3%.[16-18] In several previous studies, drugs other than those identified by medical history were found in the laboratory analyses of 20%–25% of poisoning patients, and the drug components stated in the medical history were not detected in 16%–23% of patients.[19,20] Therefore, it is difficult to determine the exact cause of intoxication via medical history taking or

a doctor's examination. In the case of multidrug coingestion, there is a possibility that one drug masks another drug. Therefore, for intoxication patients, it is possible to obtain accurate information about the toxic substances by conducting a toxicology laboratory analysis rather than by performing history taking only.[20,21]

In the results of this study, prior to service, 69.9% of intoxication patients were diagnosed by clinical diagnosis. In addition, 7.1% of cases in which toxic substances were not identified until discharge. On the other hand, after starting the service, 84.4% of patients were diagnosed by laboratory analysis, excluding 15.6% of patients who were judged to not need STA. There was also a difference between the clinical diagnosis of poisoned patients and the substances identified by comprehensive STA. In 13.4% of the patients who visited the ER for intoxication with an unknown substance according to history taking, poisoning was ruled out as a result of STA. And it was possible to find out the causative agent in 86.6% of patients, which would have been difficult to know the toxic substance without STA. When there was a substance suspected by the physician's examination but could not be identified in the history taking, only 49.3% of the actual analysis results were matched. Among these cases, other additional substances were identified in 30.7% of cases, 8% of cases were caused by completely different substances, and 12% of cases had no identifiable toxic substances. Even in cases where toxic substances

were identified in the history taking, 83.6% matched the actual toxic substances, 7.3% were found with other additional substances, 0.7% confirmed completely different substances, and 8.4% excluded poisoning. These patients would have been treated for an incorrect clinical diagnosis if the STA had not been performed. The diagnostic usefulness of STA also appears in the comparison before and after the service of our institute. When comparing these two patient groups, cases in which the cause of poisoning could not identified disappeared. Additional substances that may have been masked could be discovered and the causes of unknown poisoning patients were also identified. In addition, in this study, it is possible to see how the agrochemical or natural toxin poisoning ratio changed over time. Through this information, we were able to find out the exact types of toxin that patients are mainly poisoned, and this is certainly a valuable fact for medical staff's treatment decisions or the purpose of preventing recurrence of patients. Accurate toxicologic analysis will prevent patients in need of an antidote from missing appropriate treatment owing to an incorrect diagnosis. Some antidotes may not be helpful in treating patients if they are used incorrectly and can even be harmful.[22] Discriminating poisoning and determining plasma concentrations can help clinicians determine whether a patient will need further treatment or observation.[9,20] In a previous study, it was known that conducting a toxicological analysis on patients with suspected intoxication reduces unnecessary

hospitalization by 21.7% and unnecessary intensive care unit admission by 53.3%.[23]

Table 6 shows the results of patients with altered mental status in whom the cause could not be determined via the blood and imaging tests and 31.4% of these patients were found to be caused by poisoning. This is similar to that in a previous study where 19%–31% of patients visited the ER for altered mental status due to poisoning.[24-26] In this way, if other causes are excluded for patients with altered mental status, it will be helpful in determining the treatment policy of the physician to proceed with the STA. It will help physicians easily gather opinions in deciding whether a patient is admitted or discharged and will help prevent wasting medical resources. In addition, identifying the causative agent that causes the altered mental status helps prevent recurrence. It will provide information on which drugs are prone to the lowering of consciousness and which drugs are associated with a higher rate of changing mental status, and these data will be valuable not only for medical staff but also for health authorities.[27]

There are several methods of testing for drug analysis. However, according to each method, the range of materials that can be analyzed varies and the time to the result is different.[28] Among these methods, spot tests, thin layer chromatography, and immunoassays are easily used as toxicity screening tests in hospitals. These

screening methods are simpler to perform and can obtain quicker results than comprehensive tests, but they have some limitations.[29,30] Screening is usually aimed at quickly discriminating against a specific intoxication that occurs frequently. In other words, extensive testing for unknown poisonous substances is impossible. This means that intoxication cannot be ruled out even if a negative result is obtained from the screening test. In addition, given that screening is not intended to be a quantitative test, it cannot be confirmed whether the result was at a concentration that could cause the patient's symptoms even if the test was positive.[31] The screening test alone can lead to false negatives and false positives in the diagnosis of poisoned patients; therefore, there may be errors in interpretation without confirmation tests.[30] Furthermore, comprehensive toxicology laboratory analysis is not only useful for diagnosis and treatment but also may be helpful in developing toxicology screening tests that are applicable to patients with poisoning or altered mental status. Considering that the main cause of poisoning is different depending on the region, it is difficult to apply a uniform screening test. On the basis of comprehensive test results, data on the main toxins in the region can be collected. This could be the basis for the development of reliable screening tests that can be used in other hospitals and areas where a comprehensive toxicology analysis cannot be requested.

In general, it is recommended that quantitative serum toxicology tests should be reported within one hour.[28] It is also recommended to administer multiple antidotes within one hour.[32] However, studies on the time of antidote administration are lacking, and there are some antidotes that can be helpful even after a period of time.[22] In the analysis of the results of this project, it took a median of 3.5 hours from the time of requesting the analysis to the result via SNS. This seems to have increased the time owing to some extremes, and it may be the reason that no sample analysis was performed on weekends, holidays, or at night. This is because the analysis was performed outside the hospital, so it was difficult to perform on holidays or at night unless the sample was specifically requested. Furthermore, it took time for the sample to be transferred to the analysis center after the request. It could be inferred from that the time from the analysis request to the documented result was a median of 4 hours. The STA methods performed in this study are liquid chromatography and gas chromatography, which are relatively complicated and time consuming compared with screening tests.

As mentioned above, if the test is performed in a hospital, quick results can be obtained, but there are limitations to maintaining the toxicology laboratory in the hospital. Therefore, national support for the analysis of patients with acute poisoning is required. Furthermore, specialized STA tools for clinical use, such as

an analysis center that can always be used for testing, will be needed.

This study has several limitations. First, the study was conducted using chart review as a retrospective study. There are errors or missing data that occur during this process. Second, the request for samples to the National Forensic Service was decided by other emergency medical doctors according to the schedule. Therefore, there is a possibility that the consistency was inferior for the purpose of analysis. Third, if the patient's symptoms were mild or if the cause of the change in mental status was clear, the test will not be performed. Therefore, the characteristics of the intoxicated patients suggested in the results may not represent all intoxicated patients. Fourth, most of the patients blood and urine samples were analyzed, but there were various types of samples, such as actual substances or lavage fluid. Furthermore, the time from poisoning to sample collection is different. This may have had some effect on the STA results. Finally, it was not studied and used together with toxicology screening tests. A study on the effectiveness of a comprehensive test for patients who confirmed positive results via a screening test may be conducted. If the toxicity data of the region are accumulated in the future, a study that performs a screening test and a comprehensive test together will be needed.

V. Conclusions

The STA results of poisoned patients may differ from those of clinical diagnosis. It is also helpful in the differential diagnosis of intoxication in patients with altered mental status. Therefore, the proper use of STA by emergency physicians can increase the accuracy of the diagnosis of intoxication and help in making treatment decisions.

Declaration of conflicting interests

The authors declare that they have nothing to disclose.

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국 문 요 약

일개 삼차 병원 응급실에서 국립과학수사연구원 연계 중독분석센터 운영사업의 경험과 급성 중독 환자 치료에 미치는 영향

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이 제 섭

목적 : 응급실에서 중독 환자를 진단하고 원인 물질을 파악하는 것은 어려운 경우가 많다. 일반적으로 중독 환자의 진단은 병력 청취와 면밀한 신체 검사에 의존한다. 2017년 6월부터 '국립과학수사연구원'과 본원이 함께 체계적 독성 분석(STA)을 통해서 중독 환자의 진단과 독성 물질 판별을 목적으로 '중독 분석 서비스'를 시작하였다.

대상 및 방법 : 독성 분석을 위해 Gas chromatography-mass spectrometry 또는 Liquid chromatography-tandem mass spectrometry 방법을 사용하였다. 2014년 6월부터 2020년 5월까지 응급실을 통해 입원한 중독 환자로부터 데이터를 수집했다. 서비스 시작을 기준으로 2014년 6월부터 2017년 5월까지, 2017년 6월부터 2020년 5월까지의 환자 데이터를 비교하였다.

결과 : 사업 전과 후, 492명과 588명의 환자가 각각 분석에 포함되었다. 이 중 446명의 환자를 대상으로 STA를 시행하였다. 사업 시작

전의 환자들 중 113명은 원내의 독성 분석을 통해 진단할 수 있었지만 69.9%의 환자는 임상 진단만이 가능하였으며, 35명의 환자는 퇴원할 때까지 중독 원인 물질을 파악하지 못했다. 사업 시작 이후의 중독 환자들의 84.4%가 원내 독성 분석이나 STA를 통해 확정 진단을 내릴 수 있었다. 병력 청취를 통해서 중독 원인 물질이 알려진 환자들 중 83.6%가 STA 결과와 일치했으며 다른 8.4%의 환자는 병력 청취를 통해 알려진 물질을 포함한 어떠한 중독 물질도 발견되지 않았다. 응급의학과 의사가 진찰 후에 중동 원인일 것으로 추정한 물질과 STA 결과를 비교하였을 때 그 일치도는 49.3%였으며 12%의 환자는 실제 중독은 아닌 것으로 확인되었다. 원인 물질을 알 수 없었던 중독 환자의 13.4 %는 STA 결과 이후 중독을 배제할 수 있었다. 응급실 진료 후에도 의식 저하의 원인이 파악되지 않았던 환자 중 31.4 %는 STA를 통해 중독이 의식 변화의 원인인 것으로 밝혀졌다.

결론 : 중독 환자의 진단은 STA 결과에 따라 달라질 수 있다. 따라서 응급실에서의 적절한 체계적 독성 분석은 진단의 정확성을 높이고 치료 결정에 도움을 줄 수 있습니다.

핵심되는 말 : 독성학, 중독, 실험실 진단, 법의독물학