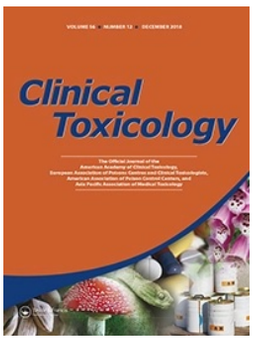

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CLINICAL RESEARCH

The usefulness of non-contrast abdominal computed tomography for detection of residual drugs in the stomach of patients with acute drug overdose

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ABSTRACT

Objectives: If clinicians can know that there are many life-threatening drugs left in the stomach through a non-invasive method over 60 min after drugs ingestion, it may be preferable to minimize absorption of remnant drugs through various methods according to the characteristic of the drug. Computed tomography (CT) has gained wide acceptance in the detection of drug mules. Therefore, we evaluated the prevalence of drugs in the gastric lumen using abdominal non-contrast CT, performed over 60 min after acute drug poisoning.

Materials and methods: This was a prospective cohort study of patients with acute drug poisoning who were admitted to the emergency department (ED) between March 2017 and February 2018. If the patient visited the ED over 60 min after ingestion of life-threatening or unknown drugs, non-contrast CT scan was performed. "Presence of drugs" was defined in the non-contrast CT as a round-shaped lesion with higher density than the gastric mucosa. In addition, "positive radiodense image" was defined as that with higher density than the gastric mucosa regardless of drug appearance in the non-contrast CT scan.

Results: Among a total of 482 patients with drug poisoning, 140 were finally included in the study. Residual drugs were detected in 36 patients (25.7%). Further, regardless of the presence of drugs, 58 patients (41.4%) showed positive radiodense image in the stomach. The median Hounsfield unit of drugs was 131.5 and that of food materials in the stomach was 34.5. Total duration of hospital stay was significantly longer in the "absence of drug" group and sustained-release drugs were detected more frequently in the "presence of drugs" group.

Conclusions: Detection rate of drugs and presence of positive radiodense image, regardless of drug appearance, were as high as 25.7% and 41.4%, respectively. Sustained-release drugs were detected more frequently in the "presence of drugs" group.

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Imaging; drug; study

Introduction

In early treatment of acute drug poisoning, inhibition of drug absorption and promotion of drug elimination are important aspects to be considered. The original position statement from the American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists concluded that, although gastric lavage should not be performed routinely, it should be considered in cases of life-threatening poisoning when the patient reports to the hospital within 60 min [1]. In many cases, drug-poisoned patients may not arrive at the hospital within 60 min. A non-invasive technique that can detect residual life-threatening drugs in the stomach, in delayed presentation cases (more than 60 min after drug ingestion), may aid clinicians in treatment planning to minimize absorption and promote elimination of the remaining drugs. The various therapeutic methods that may be used include gastric lavage, whole bowel irrigation (WBI), or esophagogastroduodenoscopy (EGD), based on the characteristic of each drug [1–8].

Computed tomography (CT) has become widely accepted as an accurate imaging technique that shows high sensitivity and specificity in the detection of drug mules [9, 10]. Abdominal CT examinations for the detection of illegal drugs in the gastrointestinal tract are usually performed based on the differences in the density of the drugs in the gastric lumen or between drugs and coverings of drugs [10]. We hypothesized that CT could be used to determine remnants of drugs in the stomach, similar to the detection of illicit drugs in the gastrointestinal tract; however, there is limited literature on the subject [2–4]. Therefore, we evaluated the prevalence of drugs in the gastric lumen using abdominal non-contrast CT, performed over 60 min after drug poisoning.

Materials and method

Study design and setting

This was a prospective cohort study of patients with drug poisoning who were admitted to the emergency department

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(ED) between March 2017 and February 2018. The ED was located in a single, suburban, tertiary university hospital (Wonju, Republic of Korea), with more than 46,000 annual visits and staffed 24 h a day by board-certified emergency physicians (EPs). This study was approved by the Institutional Review Board at Wonju Severance Christian Hospital (approval number: CR318027).

Acute drug poisoning was confirmed by statements obtained from patients or their guardians, and an emergency physician verified the agent and transcribed the names of drugs to the patient's record. Emergency physicians verified ingested agents by the following methods: (1) if the patient's prescription was available, ingested drug was confirmed through the prescription. (2) if ingested drugs were brought to the ED, drug classification was confirmed through the form and shape of drugs using the official drug search site. Upon patient arrival at the ED, intubation and mechanical ventilator care were performed in the following situations: (1) poisoned patient with an unprotected airway, such as in a patient with depressed level of consciousness and (2) patient with respiratory failure, which was defined as hypoxia (partial pressure of arterial oxygen $<$70 mmHg) or hypercapnia (partial pressure of arterial carbon dioxide $>$60 mmHg).

In situations where the patient arrived at the ED later than 60 min after drug ingestion, non-contrast CT scanning was performed at the ED as part of the standard management strategy followed at our facility for ingestion of life-threatening or unknown drugs, after obtaining consent from the patient or guardian. The definition of life-threatening or unknown drugs, as followed at our institution, is based on the following criteria: (1) ingestion of more than three times the therapeutic dose of a drug with signs and symptoms such as, shock and/or decreased mental alertness, (2) known or reported life-threatening drugs, such as lithium, anti-hypertensive agents, or salicylate, (3) overdose of multiple classification drugs or sustained release drugs, and (4) unknown type of ingested drug, but with symptoms and/or signs, or known type of drug but no information about amount ingested, with symptoms and/or signs.

Minimal sedation using intravenous etomidate (0.1–0.15 mg/kg) was performed in uncooperative, irritable patients. Etomidate has immediate onset of action and short duration of effect (5–15 min) [11]. We performed an airway assessment before procedural sedation. If it was judged that airway protection was needed, the head-tilt/chin-lift method or an airway device, such as a supraglottic airway device was used and EPs monitored the patients carefully during the CT scan. The total time required for the CT scan is usually $\leq$5 min and the scan time is only approximately 5 s. If large drug quantities, which was defined as more than five tablets or capsules, were detected in the stomach in non-contrast CT, therapeutic methods, including gastric lavage, WBI, or EGD were considered, to minimize absorption and enhance elimination of the residual drug based on the characteristic of each drug. Gastric lavage was considered in cases of life-threatening drug or dose ingestion with positive radiodense lesion or drug appearance in stomach in CT [2–6, 12]. WBI was considered in cases with potentially toxic ingestions of sustained-release drugs and/or substantial amounts of metals, and when the ingested drug was not adsorbed by activated charcoal [7, 12]. We considered endoscopic removal of tablets, which were not adsorbed by activated charcoal, or pharmacobezoars from the stomach [8, 12]. Further, activated charcoal was used in all patients with drug poisoning if the drug was adsorbable. Included patients were classified into two groups (absence of drug vs. presence of drugs) based on the presence of remnant drugs in the stomach in the CT.

Participants

We included consecutive adult patients diagnosed with acute drug poisoning in the ED. The study exclusion criteria were: (1) age less than 19 years, (2) poisoning due to non-solid drug, (3) non-life-threatening drug ingestion, (4) arrival at ED within 60 min of drug ingestion, (5) arrival at ED over 12 h after drug ingestion, (6) CT not performed, and (7) insufficient data. The patient records and information were anonymously processed prior to analysis.

Study variables

The following clinical variables were evaluated: age, sex, ingested amounts (tablets or capsules), time elapsed from ingestion to CT scan (hours), presence of known gastrointestinal disease, total duration of hospital stay, morbidity, in-hospital mortality, and drug classification. Ingested drugs were classified into: benzodiazepine, other hypnosedatives, anti-convulsant (barbiturate), anti-psychotic (atypical and typical), anti-depressant (selective serotonin reuptake inhibitor, serotonin and norepinephrine reuptake inhibitor, or tricyclic anti-depressant), lithium, monoamine oxidase inhibitor, anti-hypertensive drug (β-blockers, calcium channel blockers, diuretics, or angiotensin receptor blockers), opioid, salicylate, acetaminophen, anti-histamine, non-steroidal anti-inflammatory drug, drug for diabetes mellitus, anticholinergic, and unknown drugs. Ingested drug was also investigated for type, e.g., sustained-release.

Brilliance CT 64 Channel (Philips, Cleveland, OH) was used to evaluate the status of the stomach over 60 min after acute drug poisoning. Axial images with 5 mm reconstruction thickness and coronal reformat images with 3 mm thickness were acquired. Intravenous or oral contrast media was not used. The following parameters were evaluated using CT: (1) presence and Hounsfield units (HU) of drugs; (2) presence of positive radiodense image, regardless of drug appearance; and (3) presence and HU of gastric material. "Presence of drugs" was defined in the non-contrast CT as a round-shaped lesion with higher density than gastric mucosa. In addition, "positive radiodense image" was defined as that with higher density than the gastric mucosa, regardless of the drug appearance on non-contrast CT scan. The rationale for defining positive radiodense image was as follows [13]: (1) if lesion was not dense when compared to the gastric mucosa, it could not be detected with CT screening. (2) These lesions are within gastric lumen, so gastric mucosa is an appropriate

dense criterion for interpretation, because it (gastric mucosa) is adjacent structure of drugs.

A single radiologist specializing in gastroenterology, with more than 20 years of experience (C.S.W.), analyzed CT images acquired in this study, while blinded to clinical data. During analysis, the window settings for the abdomen and lung were used simultaneously. The region of interest used for HU determination of drugs was round shaped and 0.5 cm in diameter.

Study endpoint

The primary aim of this study was to investigate the prevalence of remnant drugs in the stomach using non-contrast CT, performed over 60 min after acute drug poisoning. The secondary aim was to compare the rate of drug detection by CT depending on the classification of ingested drug.

Statistical analysis

Data were analyzed based on the properties of the variables. Continuous variables were presented as mean and standard deviation or median and range. Categorical variables were shown as frequency and percentage. Chi-squared and Fisher's exact test were used to compare the categorical variables, and the independent *t* or Mann–Whitney *U*-tests were used to compare the continuous variables. Normality was assessed using the Shapiro-Wilk test. A *p* value less than .05 was considered statistically significant, and all statistical analyses were conducted using SPSS version 23 (IBM Inc., Chicago, IL).

Results

Characteristics of study participants

Among a total of 482 patients with drug poisoning, 140 were finally included in the study. Three hundred and forty-two patients were excluded based on the following reasons: (1) age less than 19 years (15 patients); (2) poisoning due to liquid drug (163 patients); (3) non-life-threatening drug ingestion (34 patients); (4) arrival at ED within 60 min of drug ingestion (62 patients); (5) arrival at ED over 12 h after drug ingestion (46 patients); (6) CT not performed because of lack of consent from patients or their guardians or because of unstable vital signs (19 patients); and (7) insufficient data (3 patients).

The median age of the study population was 44 years, and 37.1% of the patients were men. The median ingested drug amounts were 28 tablets or capsules. The median time until CT scan was performed after drug ingestion was 4 h; the most frequent category being 1–4 h (54.3%). Three patients presented with gastrointestinal diseases (duodenal ulcer, irritable bowel syndrome, and colon cancer). Benzodiazepine (54.3%) and anti-depressant (30.0%) were the most commonly ingested drugs. Seventy-five patients (53.6%) ingested multiple types of drugs and 24 patients (17.1%) ingested sustained-release drug. Gastric lavage and WBI were performed on 46 patients (32.9%) and 1 patient (0.7%), respectively. Two patients died during admission: one due to refractory shock by anti-hypertensive drug (calcium channel blockers and angiotensin receptor blockers) overdose and the other due to pneumonia by ingestion of multiple classification drugs including benzodiazepine, selective serotonin reuptake inhibitor, and barbiturate (Table 1).

Table 1. Baseline characteristics of patients with acute life-threatening drug overdose.

Variables	Total (*n*= 140)
Age (years)	44.0 (32.5–52.0)
Male (%)	52 (37.1)
Drug amount (number of tables or capsules)	28.0 (17.0–50.0)
Time elapsed after drug ingestion until CT scan was performed (h)	4.0 (2.0–8.8)
1–4 h (%)	76 (54.3)
4–8 h (%)	29 (20.7)
8–12 h (%)	35 (25.0)
Presence of known gastrointestinal diseases (%)	3 (2.1)
Classification of ingested drug (%)	
Benzodiazepine	76 (54.3)
Other hypnosedative drugs	27 (19.3)
Anti-convulsant	18 (12.9)
Anti-psychotic	18 (12.9)
Anti-depressant	42 (30.0)
Lithium	3 (2.1)
MAO inhibitor	1 (0.7)
Anti-hypertensive	24 (17.1)
Opioid	3 (2.1)
Salicylate	3 (2.1)
Acetaminophen	13 (9.3)
Anti-histamine	13 (9.3)
NSAID	6 (4.3)
Drug for DM	2 (1.4)
Anti-cholinergic	3 (2.1)
Other or unknown drugs	20 (14.3)
Multiple classification drugs (%)	75 (53.6)
Sustained-release drugs	24 (17.1)
Benzodiazepine	4 (2.9)
Other hypnosedative drugs	1 (0.7)
Anti-psychotics	5 (3.6)
Anti-depressants	4 (2.9)
Anti-hypertensive	5 (3.6)
Acetaminophen	4 (2.9)
Drugs for DM	1 (0.7)
Elimination techniques	
Gastric lavage	46 (32.9)
Whole bowel irrigation	1 (0.7%)
Outcome	
Total admission days	2.0 (2.0–4.0)
Morbidity	0 (0)
In-hospital mortality	2 (1.4)

CT: computed tomography; MAO: monoamine oxidase; NSAIDs: non-steroidal anti-inflammatory drugs; DM: diabetes mellitus.
Data have been expressed as median (interquartile range) and frequency (percentile).

Detection of drugs in the stomach

Drugs were detected in 36 patients (25.7%) in the non-contrast CT scan performed over 60 min after ingestion. The time category of 1–4 h was most common, including 61.1% of the patients in whom drugs were detected. The median HU of drugs was 131.5 and that of food materials in the stomach were 34.5 (Figure 1). Further, regardless of the presence of drugs, 58 patients (41.4%) showed positive radiodense image in the stomach (Table 2).

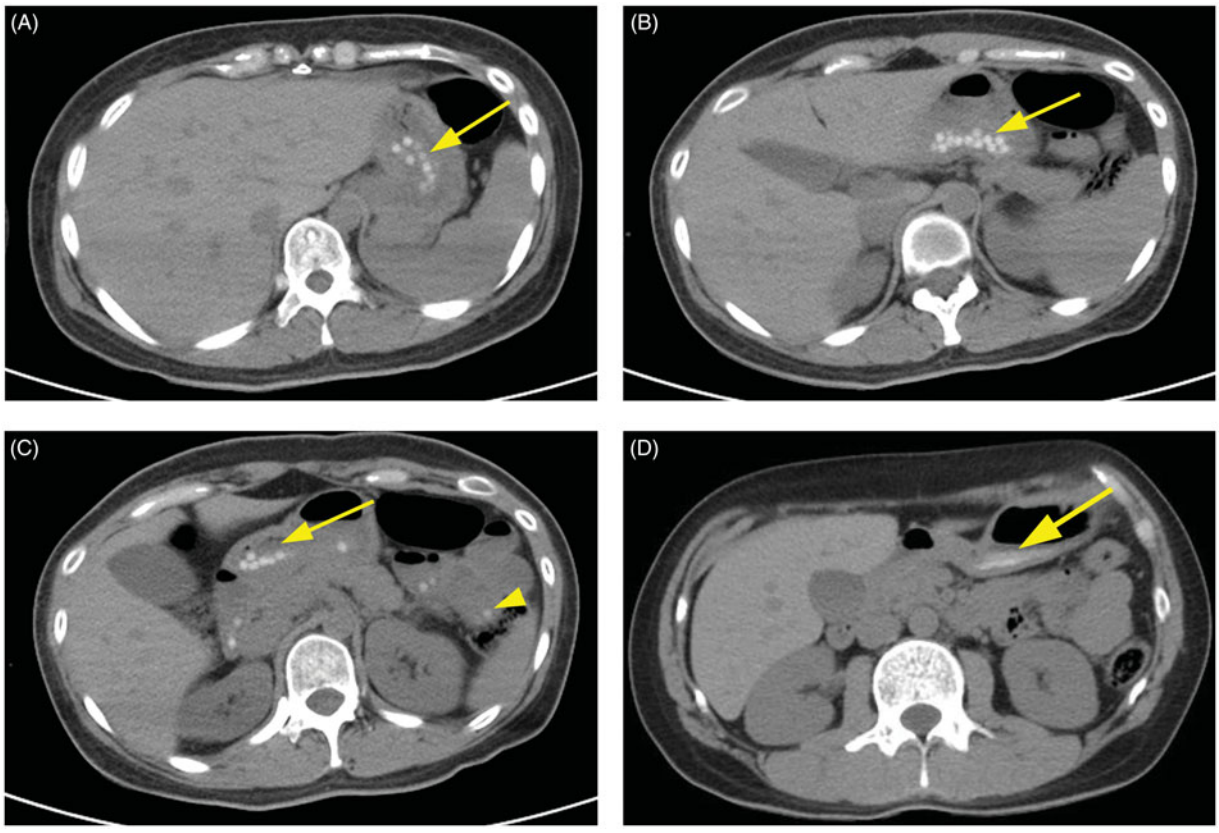

Figure 1. Typical computed tomography findings indicating presence of drug or positive radiodense image without drug appearance in the stomach lumen. (A–C) Arrows indicate drugs remaining in the stomach. (C) Arrowhead indicates drugs in the small bowel. (D) Arrows indicate positive radiodense image without drug appearance remaining in the stomach.

Table 2. Results of non-contrast computed tomography scan.

Variables	Total (n= 140)
Presence of drug appearance (%)	36 (25.7)
1–4 h (%)	22 (61.1)
4–8 h (%)	7 (19.4)
8–12 h (%)	7 (19.4)
HU of drug	131.5 (78.0–223.0)
HU of food contents	34.5 (16.5–44.8)
Presence of positive radiodense image regardless of drug appearance (%)	58 (41.4)
Presence of gastric food contents (%)	119 (85.0)

HU: Hounsfield units.
Data have been expressed as median (interquartile range) and frequency (percentile).

There were no significant difference in the amount of drug ingested, time until CT scan was performed, classification of the drugs ingested, multiple classification drugs, and in-hospital mortality in the detection of drugs based on CT. Total duration of hospital stay was significantly longer in the "absence of drug" group (p = .024) and there were significantly more sustained-release drugs in the "presence of drugs" group than in the "absence of drug" group (odds ratio 4.779, 95% confidence interval 1.898–12.034, p = .001) (Table 3).

Discussion

To the best of our knowledge, this is the first study performed using non-contrast CT to confirm the presence of remnant drugs in the stomach in patients presenting over 60 min after acute drug poisoning. Although the situation is slightly different from general acute drug poisoning, CT has become widely accepted as an accurate imaging modality, with high sensitivity and specificity, in the detection of drug mules. Therefore, in the context of acute life-threatening drug poisoning, our results demonstrating the utility of CT for the detection of residual drugs may not be surprising [14–18]. In the present study, despite food materials being detected in the stomach in most patients (85.0%), the presence of remnant drugs was confirmed in 36 (25.7%) patients using non-contrast CT scan, performed over 60 min after drug ingestion. Significant difference was observed in the HU of food materials and ingested drugs. We think that many drug appearance or positive radiodense image could be confirmed because we made a decision by comparing lesion density to gastric mucosa. Further, we detected drugs that had passed into the small intestine, and were able to discern the number of remnant drugs (Figure 1(C)). However, detection of drugs was more challenging, if the drugs appeared as iso-dense signal in the CT. In such situations, we think that manipulation of the image windowing during CT can help in the detection of remnant drugs in the stomach, as demonstrated in this study [10]. Furthermore, we suggest that it may be helpful to search for other positive radiodense image that markedly differ in their HU from that of food materials, even if drugs are not clearly detectable.

The present study did not observe any statistical difference in the rate of detection of drugs in non-contrast CT, depending on the classification of the drugs. This may be

Table 3. Comparisons of baseline characteristics according to presence/absence of drug, as indicated by non-contrast computed tomography.

Variables	Absence of drug (*n*=104, 74.3%)	Presence of drugs (*n*=36, 25.7%)	*p* value
Age (years)	46.0 (34.0–59.5)	48.0 (37.0–54.8)	.852
Male (%)	36 (34.6)	16 (44.4)	.293
Drug amounts (number of tablets or capsules)	27.0 (17.0–50.0)	30.0 (17.0–50.0)	.449
Time elapsed after drug ingestion until CT scan was performed (hours)	4.0 (2.0–9.0)	3.5 (2.0–6.8)	.624
1–4 h (%)	54 (51.9)	22 (61.1)	
4–8 h (%)	22 (21.2)	7 (19.4)	.591
8–12 h (%)	28 (26.9)	7 (19.4)	
Presence of known GI diseases (%)	2 (1.9)	1 (2.8)	1.000
Classification of ingested drug (%)			
Benzodiazepine	53 (51.0)	23 (63.9)	.180
Other sedative drugs	24 (23.1)	3 (8.3)	.053
Anti-convulsants	12 (11.5)	6 (16.7)	.403
Anti-psychotics	10 (9.6)	8 (22.2)	.079
Anti-depressants	31 (29.8)	11 (30.6)	.933
Lithium	1 (1.0)	2 (5.6)	.162
MAO inhibitor	1 (1.0)	0 (0)	1.000
Anti-hypertensive	17 (16.3)	7 (19.4)	.671
Opioid	3 (2.9)	0 (0)	.569
Salicylate	2 (1.9)	1 (2.8)	1.000
Acetaminophen	10 (9.6)	3 (8.3)	1.000
Anti-histamine	11 (10.6)	2 (5.6)	.515
NSAIDs	5 (4.8)	1 (2.8)	1.000
Drugs for DM	0 (0)	2 (5.6)	.065
Anti-cholinergics	1 (1.0)	2 (5.6)	.162
Other or unknown drugs	13 (12.5)	7 (19.4)	.305
Multiple classification drugs (%)	54 (51.9)	21 (58.3)	.506
Sustained-release drugs	11 (10.6)	13 (36.1)	< .001
Outcome			
Total admission days	3.0 (2.0–4.0)	2.0 (2.0–4.0)	.024
In-hospital mortality	2 (1.9)	0 (0)	1.000

CT: computed tomography; GI: gastrointestinal; MAO: monoamine oxidase; NSAIDs: non-steroidal anti-inflammatory drugs; DM: diabetes mellitus.
Data have been expressed as median (interquartile range) and frequency (percentile).

the reason for drugs of the same category being manufactured and commercialized in various forms, depending on the company. Sustained-release drugs were detected more frequently in the "presence of drugs" group than in the "absence of drug" group. We think that this is likely to be due to differences in the release times of the drug component contained within the sustained-release drug in the stomach. Non-contrast CT may help to plan treatment procedures to minimize absorption or enhance elimination of remnant drugs in cases of acute life-threatening drug poisoning. Additionally, the non-contrast CT technique may allow monitoring of the condition of the patient in the intensive care unit, wherein deterioration may occur due to continual drug absorption owing to the presence of remnant drugs in the stomach. Total duration of hospital stay were significantly longer in the "presence of drugs" group and in-hospital mortality occurred in the "absence of drug" group; however, the observations were not statistically significant. The non-contrast CT technique prevented further absorption of the remnant drugs by allowing detection and initiation of therapeutic modalities.

Radiation exposure is of chief concern during CT scanning; however, if the severity of the drug poisoning is high or the patient is exposed to life-threatening drugs, the benefits of non-contrast CT imaging may outweigh the risks of radiation exposure. Contrast media was not used in the present study, unlike the studies on the detection of illicit drug packing within the body. The advantage of non-contrast CT is that it can be applied to patients with decreased renal function or hypersensitivity reaction to contrast media.

The present study is associated with certain limitations. First, we could not detect the remnant drugs (false-negative) that are actually present in the stomach but are not visible on CT image, through EGD. Further research should be conducted to assess the utility of CT in detection of remnant drugs in the stomach. Second, there may be complications related to radiation-exposure during CT; thus, studies on the effectiveness of low-dose CT for remnant drug detection should be considered. Third, as this study was conducted at the ED of a single hospital, the sample size was small and not all types of drugs were evaluated. However, in order to reduce possible bias, we investigated all patients with acute life-threatening drug poisoning and performed non-contrast CT scan in all suitable cases. Fourth, the effect of CT on prognosis of drug poisoning is unknown; therefore, further studies are necessary to establish the effects.

In summary, detection rate of drugs and presence of positive radiodense image, regardless of presence of drugs, were found to be as high as 25.7% and 41.4%, respectively, in the non-contrast CT scan, performed over 60 min after acute drug ingestion. No significant difference was observed in the type of the drug ingested in detection based on CT; however, sustained-release drugs were detected more frequently in the "presence of drugs" group.

Disclosure statement

No potential conflict of interests was reported by the author(s).

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