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Original Article

Usefulness of Computed Tomography in the Diagnosis of an Overdose

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Computed tomography (CT) is superior for the detection of substances with low radiolucency in comparison with abdominal roentgenograms. In the present study, medical chart review was retrospectively performed for patients who were admitted and underwent plain CT including the stomach on arrival to investigate whether CT is useful for diagnosing overdose (OD). The subjects were divided into patients with OD who did not undergo gastric lavage (OD group) and those without OD (Control group). The presence of a radiopaque area (Hounsfield number over 100 on a range of interest of 3 mm^2) in the stomach on CT was defined as a positive finding. The average Glasgow Coma Scale in the OD group (n = 11) was significantly lower than that in the Control group (n = 137). Positive findings on CT were found more frequently in the OD group than in the Control group (100 vs. 19.7%, $p < 0.0001$). Based on the finding of a high-density deposition in the bottom of the stomach, the CT predicted OD with 98.5% specificity. Accordingly, CT findings of a high-density deposition in the stomach of a patient with a diminished consciousness may suggest the presence of a recent overdose.

Key words: overdose, diagnosis, CT

A large number of chemical substances or drugs can be detected in the gastrointestinal tract by a plain abdominal roentgen or computed tomography (CT) [1-4]. CT is superior to a plan roentgen for the detection of materials with low radiolucency due to the absence of the superimposition of lesions in transaxial CT views and high-contrast resolution [5, 6]. A patient with an overdose (OD) has ingested a large amount psychotropic drugs [7]. The diagnosis of an OD is usually based on the patient's complaint or a situation with a comatose patient who has a psychiatric disease. Drug screening tests such as Triage[R] (Biosite: San Diego, CA, USA) may be useful for detecting patients with OD among unconsciousness patients. However, patients with OD may take psychotropic drugs regularly so that it is difficult to diagnose OD correctly based on the results of screening tests. Drug screening tests also cannot accurately detect a patient with OD of a major tranquilizer and/or selective serotonin reuptake inhibitor. In addition, OD is difficult to diagnose in a comatose patient, one who cannot talk, or one who presents without evidence of OD. A diagnosis of an OD can also be based on physical findings that suggest the occurrence of toxidrome, but they are often variable or obscured by the co-ingestion of multiple drugs [8]. For example, we recently treated a male case that presented with sudden unconsciousness which occurred at a book store

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[9]. On arrival, he was in a deep coma state with bilateral pinpoint pupils, which suggested either morphine or organic phosphate poisoning. However, neuroradiological and biochemical analyses, including a urinary drug screening test, failed to disclose the etiology. On the third hospital day, a drug overdose including trazodone was finally made after the patient regained consciousness. In the present study we therefore investigated whether CT can be useful for making a diagnosis of OD by detecting high-density areas in the gastrointestinal tract, which suggest the presence of residual unabsorbed drugs.

Materials and Methods

Our institutional review board approved this retrospective study and waived the requirement of informed consent.

A medical chart review was retrospectively performed for patients admitted between January 2009 and December 2009 whoe did not undergo gastric lavage or the administration of activated charcoal, and who underwent plain CT including the stomach on arrival. The subjects were divided into patients with OD (OD group) and those without OD (Control group). The presence of OD was confirmed by interviewing the patients after they regained consciousness. The Control group consisted of the patients who were unconsciousness and had been diagnosed into other categories based on the results of radiological and biochemical analyses. The patients' age, sex ratio, physical data on arrival (GCS, systolic blood pressure, and heart rate), ratio of regular medication for any underlying diseases, the positive ratio on CT, and the survival rate were all compared between the 2 groups. The presence of a radiopaque area (Hounsfield number over 100 on a range of interest of 3 mm^2) in the stomach on CT was defined as a positive finding. To detect the presence of drugs by CT, the range of interest area was reduced to an area measuring 3 mm^2 in size because the diameter of a tablet is usually more than several mm. As for the Control group, the cause of admission was investigated in each case. The underlying psychiatric disease, name of drug, estimated ingested volume of the drug, and the duration from ingestion until undergoing CT were investigated in the OD group. In addition, the hemoglobin value on arrival and on the second hospital day in the OD group were investigated in order to identify any possible asymptomatic intestinal bleeding.

The statistical analysis was performed using the unpaired Student's t-test and the χ^2 analysis. A p value of less than 0.05 was considered to indicate a statistically significant difference.

Results

During the investigation period, 121 patients were admitted for treatment of OD and 405 patients without OD. Among them, there were 11 subjects in the OD group and 137 in the Control group. There were 3 subjects in the Control group with a past history of psychiatric disease and taking psychotropic drugs. CT was performed with a 64-raw multislice CT scan device (Aquilion 64, Toshiba, Tokyo, Japan). CT was performed in the OD group to diagnose aspiration pneumonia in 7 cases and trauma in 1 case, and to make a differential diagnosis of unconsciousness with hypotension in 3 cases. The cause of admission in the Control group was trauma in 101 cases, respiratory

Table 1 Backgrounds of the overdose (OD) and control groups

Number	OD group n = 11	Control group n = 137	*p* value
Averaged age (Year)	46.5+5.3	50.2+1.8	n.s.
Sex (Male/Female)	4/7	99/38	0.03
Glasgow Coma Scale	6.9+1.2	12.1+0.3	<0.0001
Systolic BP (mmHg)	115.6+8.1	113.5+2.9	n.s.
Heart Rate (/minute)	106.0+5.7	87.8+2.2	0.04
Medication rate (%)	11 (100)	53 (38.6)	0.0001
Survival rate (%)	11 (100)	123 (89.7)	n.s.

BP, blood pressure; n.s., not significant. (Mean + standard error) failure in 13 cases, shock in 8 cases, sepsis in 6 cases, aortic disease in 5 cases, gastrointestinal bleeding in 2 cases, and acute abdomen in 2 cases.

The backgrounds of the 2 groups are summarized in Table 1. The average age, average systolic blood pressure, and survival rate were not significantly different between the 2 groups. The GCS in the OD group was significantly lower than that in the Control group. The average heart rate in the OD group was significantly greater than that in the Control group. A female sex and a history of regularly taking medication were more frequently observed in the OD group than in the Control group.

All cases with the presence of a high-density area in the stomach of a patient with OD confirmed by CT are shown in Fig. 1. The results of the CT analysis are demonstrated in Table 2. The OD group showed a higher frequency of positive findings by CT in comparison to the Control group (100 vs. 19.7%, $p < 0.0001$). Positive findings classified into 4 categories included: surface, diffuse, deposition, and other types of high-density areas. One case was classified as surface, one as diffuse, 8 as deposition, and 1 as an other type among the OD group (Fig. 1). In contrast, 17 cases were classified as surface, 7 as diffuse, and 2 as deposition among the OD group. Both cases of

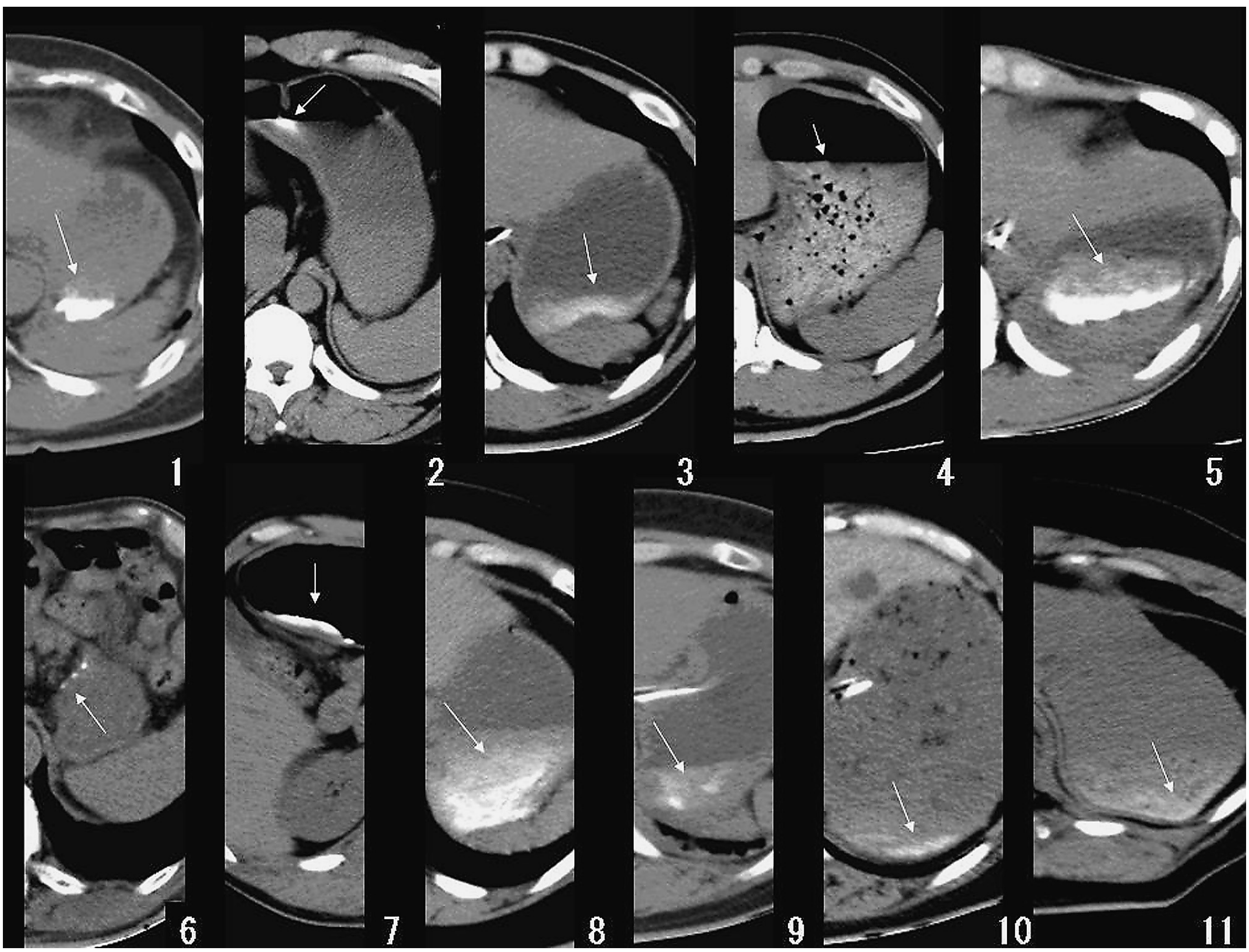

Fig. 1 All cases with a high-density area in the stomach confirmed by computed tomography (CT) in the OD group. All cases in the OD group demonstrate a high-density area in the stomach (white arrow). Eight of the 11 cases (Case numbers 1, 3, 5, 7, 8, 9, 10, 11) indicate high-density (HD) deposition in the gastric inner wall in the bottom of the stomach. Case number 2 is classified as surface-type HD that is floating at the level of gastric juice. Case number 4 is classified as diffuse-type HD that is mingling in the gastric contents, and Case number 6 is classified as an other type HD.

active gastrointestinal bleeding in the Control group, which were confirmed by gastroscopy, showed negative findings. Concerning the presence or absence of deposition, 8 out of the 11 cases in the OD group showed a high-density deposition in the gastric inner wall. However, there were only 2 subjects in the Control group that demonstrated such findings. This difference was also significant ($p < 0.0001$).

Table 3 shows the underlying psychiatric diseases, the name of the drug involved in the OD, the estimated ingested volume of the drug, and the duration from ingestion to the CT. The case numbers are the same as the numbers shown in Fig. 1. There was no consistency regarding the underlying psychiatric diseases, the name of the drug, and the estimated ingested volume. The time from ingestion to CT ranged from 4 to 12 h, with an average of 8.4 h.

Concerning the hemoglobin values on arrival and the second hospital day in the OD group, no significant changes were observed between the 2 values (on

Table 2 Results of an analysis of abdominal computed tomography between the overdose (OD) and control groups

Number	OD group n = 11	Control group n = 137	*p* value
Positive rate (%)	11 (100)	27 (19.7)	<0.0001
Deposition (%)	8 (72.7)	2 (1.4)	<0.0001
Surface (%)	1 (9.0)	17 (12.4)	n.s.
Diffuse (%)	1 (9.0)	7 (5.1)	n.s.
Others (%)	1 (9.0)	0	n.s.

n.s.: not significant

Table 3 Drug name, estimated ingested volume, and duration from ingestion to CT examination in the overdose group

Drug name		Estimated ingested volume (mg)	Duration from ingestion to CT examination (hour)	Psychiatric disease
Case 1	Fenobarbital	80	8	Borderline
	Chlorpromazine		500	
	Promethazine	250		
	Etizolam	10		
Case 2	Zopiclone	240	10	Depression
	Mirtazapine	180		
Case 3	Brotizolam	12	8	Depression
Case 4	Olanzapine	115	6	Psyzophrenia
	Clonazepam	7		
	Valproate	3,200		
	Paroxetine	160		
Case 5	Etizolam	22	12	Depression
	Loflazepate	18		
	Paroxetine	?		
	Haloperidol	?		
	Flunitrazepam	?		
	Lithium	?		
Case 6	Triazolam	7	7	Sleeping disturbance
Case 7	Amobarbital	1,100	8	Psyzophrenia
	Loflazepate	22		
Case 8	Biperiden	40	9	Psyzophrenia
	Loflazepate	42		
	Risperidone	?		
	Promethazine	?		
	Levomepromazine		?	
Case 9	Nitrazepam	218	12	Depression
	Quazepam	1,635		
	Flunitrazepam	108		
	Promethazine	950		
Case 10	Nitrazepam	130	4	Sleeping disturbance
	Triazolam	?		
Case 11	Valproate	?	?	Depression

Table 4 Results of the analysis between the subgroups with patients who received regular medication and those who did not in the Control group.

	Regular medication +	Regular medication −	*p* value
Number	n = 64	n = 84	
Positive rate (%)	21 (32.8)	17 (20.2)	not significant

arrival; 14.3 + 0.6 vs. the second hospital day; 13.2 + 0.6 g/dl).

As all subjects in the Control group that demonstrated positive findings received regular medication, there is a possibility that regular medication (namely, the routinely ingested drugs for the underlying disease) may have been detected by CT in this study. We therefore performed additional analyses. The subjects in the two groups were divided into 2 subgroups, the patients who received regular medication and those who did not. However, the ratio of positive findings on CT in the 2 groups was not statistically significant different (Table 4).

Discussion

This study suggests that the observation on CT of high-density material in the stomach in female patients with a diminished consciousness may suggest the presence of a recently ingested medication or an overdose of drugs. There has thus far been no previous report indicating such a relationship.

Denser materials or higher atomic-numbered elements have an increased radiopacity, which prevents the passage of electromagnetic radiation [10]. Iodine is used as a contrast medium because it has a high atomic number and it has been proven to be safe to use. Any foods high in iodine or higher atomic-numbered elements such as seaweed (a common Japanese food source) have the potential to demonstrate a high-density area on CT scans. The subjects in this study all underwent emergency CT examinations and such subjects might thus have eaten some food before the CT and therefore the positive findings in this study may also potentially represent some partial food remains that are high in iodine or higher atomic-numbered elements. However, the 2 groups underwent the same emergency CT examinations, and the results showed a higher frequency of positive findings in the OD group than in the Control group (70% vs. 0%) based on analyses of high-density deposition, and such findings cannot be explained based on the hypothesis that some food remaining in the stomach may have demonstrated radiopacity.

Common radiopaque medical drugs include iron tablets or heavy metals such as gold. However, the quantity ingested is usually too small to show any effect on plain X-rays [3]. Sleep medications, such as bromvalerylurea includes bromine, which has a relatively high atomic number and an OD with bromvalerylurea could be recognized by plain abdominal roentgen. Major tranquilizers, minor tranquilizers and/or antidepressants generally do not include substances with a high atomic number. However, the tablets or capsules of these drugs are condensed so that an OD of such high-density drugs can thus be easily found by CT using high-contrast resolution.

There is a possibility that regular medication (ingested drugs routinely at the regular dose for the underlined disease) may have been detected by CT in this study because the all subjects in the Control group, who demonstrated positive findings, received regular medication. However, the subgroup analysis in the two groups, including patients who received regular medication and patients that did not, showed no statistically significant difference. Accordingly, this fact minimizes the possibility that regular medication had been detected by CT. In contrast, chemical substances, such as drugs normally have a specific solubility so that the ingestion of large amount of drugs at a time results in a large amount of precipitation so that the CT in this study predicted OD with high specificity (100%) based on analyses of high-density deposition.

This study classified the high-density area in the stomach into 4 categories, based on the CT findings. The results suggest a mechanism for the formation of the 4 categories. The first high-density deposition in the OD group may be the drugs themselves, while, that in the control group may be solid foods which sink to the bottom of stomach due to their weight. The second high-density surface may be floating radio-opaque material with low specific gravity, such as drug powder in the OD or a piece of seaweed in the control group. The third high-density category (diffuse type) may be a mixture of food and drugs in the OD group or radio-opaque material generated by chewing or peristalsis of the stomach in the control group. The fourth high-density area contained 3 high-density spots that may be the drug tablets adhering to the inside of stomach. Radio-opaque foods are generally are broken into pieces and mixed with other foods by chewing or peristalsis of stomach, resulting in reduction of radio-opacity and a chance to sink at bottom of the stomach. However, an overdose occurs due to the ingestion of a large amount of drugs without chewing. In addition, some antipsychotic drugs have an anticholinergic effect, which thus leads to gastroparesis [11]. Accordingly, a large amount of drugs consumed without chewing in association with gastroparesis may sink to the bottom of the stomach, and thereafter appear as the high-density deposits observed in this study.

As the observation on CT of high-density deposition areas in the stomach in a patient presenting with a diminished consciousness may suggest the presence of a recently ingested OD, we propose a diagnostic method to make a differential diagnosis for such unconscious patients using abdominal CT examination. A logical decision tree often used in searching for the cause of unconsciousness divides the categories of diseases that cause unconsciousness into 3 groups: structural lesions (disease of the central nervous system), which may be above or below the tentorium; metabolic and toxic causes including OD; and psychiatric causes [12]. In general, structural lesions have focal features or at least notable asymmetry on neurological examinations. [12] If 1). the history, physical and neuroradiological examination suggest symmetrical and nonstructural unconsciousness after the patient is treated and stabilized, 2). laboratory tests including urinary drug test fail to indicate the presence of any metabolic disease, overdose or infection in the central nervous disease, and 3). a physician fails to obtain information concerning 3a). any kind of proof of an overdose in present illness (some patients may sometimes leave messages by letter, e-mail or telephone to their relatives), 3b). a situation in which a lot of empty drug containers are found near the unconscious patients at the time that they are found unconscious, 3c). psychiatric disease with a history of an overdose, and 3d). self-destructive behaviors such as cut wrists are found in the physical examination, then an abdominal CT examination should thus be performed in order to diagnose OD.

There are some limitations or problems associated with this study. First of all, we did not directly prove that high-density deposition or high-density areas in a subject's stomach did, in fact, represent the presence of drugs. In addition, there were a variety of positive findings in the OD group and false-positive cases in the Control group, and therefore the CT findings themselves may only suggest, rather than definitively prove, a diagnosis of OD. The second point is related to the fact that the CT findings may be useful for making a differential diagnosis of an unconscious patient whose present illness is unknown due to unconsciousness. For example, CT may detect lesions that can cause hypoglycemia, hypotension, hyperammonemia, or paraneoplastic syndrome [13-17]. However, CT is always associated with the disadvantage of radiation exposure to patients presenting with OD, whose prognosis is usually favorable [7, 18]. In addition, CT does not indicate which drugs are ingested. The third point is that a large amount of drugs can move into the intestine and be absorbed, even in the case of an OD, so that the high density may no longer be detected by CT examinations. It is therefore necessary to determine how long the CT can detect such high-density areas of residual drugs in the stomach. The fourth problem is related to the small sample size and the retrospective nature of this study, which may be considered to be somewhat insufficient, and therefore a further prospective study, including a larger number of subjects, is required.

Conclusion. The observation on CT of high-density deposition areas in the stomach in a patient presenting with a diminished consciousness may suggest the presence of a recently ingested overdose of drugs. Accordingly, CT may be useful for diagnosing OD in a comatose patient, one who cannot talk, or one who presents without any other evidence of OD.

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