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Case Report Open Access

The Last Dinner: Fatality of 2-Chloroethanol Intoxication

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Abstract

Objective: 2-Chloroethanol (2-CE) is a solvent with a LD50 of 58 mg/kg orally in rats. In rare condition, grape farmers in Taiwan apply it on grapevines to hasten sprouting and can land themselves in potentially lethal conditions. Severe intoxication presenting with hypotension, respiratory failure, seizure, coma or mortality can occur in 24 hours even only skin or inhalational exposure. It is hard to make the correct diagnosis in cases of unknown contamination history due to lack of specific clinical signs/symptoms or availability of routine laboratory tests.

Cases report: In July 2011, two couples (2 males 2 females, 40-58 years old) in Nantou County of Taiwan suffered from nausea, vomiting, shortness of breath, consciousness change and suspected convulsions 6-12 hours after dining and drinking together. One case was noted to be dead on arrival in the emergency room, and the other three rapidly progressed to coma, hypotension, cardiac arrest in 1-3 hours, and dead eventually after resuscitation. The most important laboratory finding was metabolic acidosis with blood pH value 7.223 to 7.291. This lethal outbreak caused disquiet in the public with respect to food and drink. The grape sprouting agent, 2-CE was proved to be the offender with high concentrations of 2-CE (2 to 15.3 mg/L in heart blood) and its metabolite (chloroacetate 232.6 to 590.5 mg/L in heart blood) detected in patients' samples by Gas chromatography-mass spectrometry two weeks later.

Conclusion: These cases demonstrated that 2-CE might be listed in table of deliberate poisons and should be ruled out in cases of mass poisoning.

Keywords: 2-Chloroethanol; Metabolite; Deliberate poisons

Background

There are several toxins had been used as weapons to kill someone not turn a hair, such as cyanide. 2-chloroethanol (2-CE, Ethylene Chlorohydrin, CAS.NO107-07-3) was once a solvent used for industrial productions in large scale and was noted to be highly toxic in mammalian before [1]. It is a colorless liquid with faint, ether-like odor. In literature, there was few 2-CE intoxication cases reported with unknown mechanisms [2,3].

2-CE has been used in Taiwan for sprouting on grapevines with better harvesting for more than 20 years. Farmers cut old branches of vine every 3cm by knife and stick some colored and diluted 2-CE on it, and vines grow along the grid which is higher than the height of people. Grapevine application carried an accidental risk of inhalation or dermal exposure but also intentional ingestion of 2-CE caused severe intoxication. In report of Deng et al., 17 cases were recorded in 14 years with around 40% of mortality rate [4]. No pathognomonic signs, symptoms or ordinary laboratory tests could be used in clinical differential diagnosis, and delayed diagnosis might impede criminal investigation. Here, we reported an outbreak of deadly 2-CE intoxication in two couples due to drink maliciously adulterated wine in a dinner.

Case Report

In the night of July 6, 2011, two couples of friends had their dinner and drank together after farm work. Someone had complained of bitter tasting of one bottle of rice wine but without any immediate discomforts during meal. Unfortunately, abrupt onset of nausea, vomiting, short of breath and consciousness change developed successively from the midnight to the early morning of next day. The first one is a 37 years old woman. She suffered from nausea, vomiting, shortness of breath and consciousness change after midnight. She was noted to be in shock (blood pressure 67/35 mmHg) and deep comatose states at 4 am while her arriving emergency room of a local hospital. She was referred to a medical center with the impression of acute myocardial infarction due to diffused ST-T wave change of electrocardiogram and found to be cardiac arrest while arrived there. Return of spontaneous circulation was noted after minutes of cardiopulmonary resuscitation. But she was declared to be dead at eight o'clock in the morning even under extracorporeal Membrane Oxygenation (ECMO) treatment. The second one was a 48 years old woman. She suffered from nausea, vomiting, abdominal pain, diarrhoea and shortness of breath at midnight, and was found to be

dead at five o'clock in the morning when she was sent to the hospital. The third patient, the second one's husband, was a 55-year old male. He was noted to be sick and weak at 4 am when he stayed in ambulance with his wife on the way of hospital. His blood pressure was noted to be 90/32 mmHg initially at emergency room, but his condition rapidly got downhill with restless, seizure, shock and deep coma. He died at about 8 o'clock after ineffective resuscitation. The last one was a 40 years old male. He experienced a sudden onset of dizziness, cold extremities, palpitations, vomiting and conscious change near 8 am of the second day morning while his wife was under resuscitation. About one hour later, he suffered from profound shock and deep coma. ECMO therapy and the use of cyanide antidotes did not change the result. He passed away about 23 hours after exposure.

The 4 patients all were subjected to autopsy and collected tissues fluid for chemical assay. Only minimal change with mild tissue swelling, erythematous change over gastrointestinal wall and increased lung weight were found on gross. The pathological report exhibited pulmonary edema, enlargement of nucleus of cardiac myocytes, interstitial edema with cellular necrosis of intestinal mucosa and congestion of intestinal wall. There were no acute reactions on liver, pancreas and brain. Some laboratory findings are summarized in Table 1. This incident had stirred up the issue of food safety due to suspected botulism mistaken by an emergency specialist, and peoples in the island were kept on tenterhooks for more than 2 weeks before it was cleared up to be crime. 2-CE and its metabolite were detected in patients' tissues, blood and urine samples by gas chromatography-mass spectrogram.

	Case 1(F)		Case 2(F)		Case 3(M)		Case 4(M)	
	2-CE	CA	2-CE	CA	2-CE	CA	2-CE	CA
Vomitus (home)	-	-	-	-	442.5	5.5	114	98.6
Stomach contents	2.3	491.2	21.9	229.9	186.2	233.9	9.8	211.9
Bile juice	3.2	1054	41.8	429.6	158.8	841.9	32	929.7
Small bowel fluid	1.8	303.1	14.8	155.2	124.8	466.8	2.5	217.5
Colonic fluid	-	-	21.9	252.9	171	830.4	9.2	286.8
Heart blood	2	290.3	17.6	331.3	15.3	590.5	2.8	232.6
Vitreous fluid	5.2	411.2	58.5	277.7	197.7	467.1	4.5	305.1

Table 1: 2-CE and CA concentration detected in varied samples.

Discussion

These four cases were finally confirmed to be 2-CE intoxication due to drink the maliciously adulterated wine which was found contain 17.6% of 2-CE. Rapid progression and fulminant presentations indicate 2-CE might be one of the highest toxic chemicals and any types of contamination should be concerned. 2-CE is a glycol derivative, commonly used as a solvent in industry with significant vapor pressure, and can be absorbed by inhalation, ingestion, or through the dermal route [2,5]. Its estimated acute oral LD50 to be 71-95 mg/kg for rats and 81-91 mg/kg for mice [6]. Some farmers in Taiwan applied 2-CE on grapevines to hasten sprouting and put themselves on the dangerousness of accident intoxication. There were several cases reported to Poison Center with severe or fatal intoxication after even though only skin or inhalation exposure [4]. Neurological and vascular toxicity were noted as the cardinal presentations in reported cases of severe 2-CE intoxication and would presented varied with unconsciousness, seizure, shock, and metabolic acidosis, also as these four cases. It is frustrated that there is no effectively and specifically antidote instead of the supportive care.

The toxic mechanism on human beings of 2-CE is still blurred and indistinct. In animal study, 2-CE is oxidized to chloroacetaldehyde (CAA) by alcohol dehydrogenase (ADH, EC 1.1.1.1) and subsequently to chloroacetate (CA) by aldehyde dehydrogenase (AL DH, EC 1.2.1.3) [7]. Both CAA and CA were found to be more toxic than the parent compound 2-CE [5,8]. In an isolated rat right atrium model study, CAA was suggested to be the toxic principle of 2-CE-induced cardiovascular toxicity which might be mediated by calcium channel and nifedipine protected against neuronal nitric oxide sybthetase (nNOS)-triggered cardiovascular effects [9,10]. CAA, as a major reactive metabolite of a vinyl chloride or anticancer drug ifosfamide, has also been noted to induce varied cytotoxicity through mitochondria respiratory chain inhibition, cellular glutathione depletion and other oxidative stress pathway [11-14]. These effects can cause damage in energy rich organs, such as brain, heart, and muscle skeletal system, and manifest as renal damage, unconscious, seizure, profound shock, metabolic acidosis, and dead in clinical cases [5]. CA is also demonstrated to induce oxidative stress causing the cellular glutathione depletion and the inhibition of the tricarboxylic acid cycle in mitochondria, which was accompanied by both p38-MAPK signal activation-regulated mitochondria-dependent and endoplasmic reticulum stress-triggered apoptotic pathway leading to neuronal cell death [15,16]. Large dose of monochloroacetate exposure in industrial setting had been found to induce severe hypoglycemia and lactic acidosis, which was suggested through Inhibits liver gluconeogenesis by inactivating glyceraldehyde-3-phosphate dehydrogenase in animal study [8].

Alcohol dehydrogenase inhibitors have been suggested as the potential antidote for 2-CE intoxication. But, alcohol had not proved to be effective in limited cases report [4]. Fomepizole (4-methylpyrazole) is a potently competitive inhibitor of alcohol dehydrogenase that a useful antidote for ethylene glycol or methanol poisoning, but should be initiated immediately to prevent toxic metabolite production that has accumulated [17]. Chen et al. [6] have reported that fomepizole can significant increase median lethal dose (LD50) and reduce the acute toxicity of 2-CE, and decrease the plasma concentration of CAA in rat. But the role of fomepizole in 2-CE intoxication needs more clinical investigations.

Conclusion

In summary, 2-CE is a virulent toxic chemical and causing death in hours if left no treatment. Further studies are needed to identify the mechanism and find the effective antidote for 2-CE intoxication.

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Conflict of Interest

All authors declare that they have no conflicts of interest related to this study.

References

1. Ambrose AM (1950) Toxicological studies of compounds investigated for use as inhibitors of biological processes. II. Toxicology of ethylene chlorohydrin. Arch Ind Hyg Occup Med 21: 591-597.
2. Kvistad PH, Bolle R, Wickstrøm E (1983) Acute poisoning by ethylene chlorohydrin. Intoxication by ingestion of film cement in two children. Hum Toxicol 2: 311-313.
3. Wahlberg JE, Boman A (1978) 2-chloroethanol--percutaneous toxicity of a solvent. Dermatologica 156: 299-302.
4. Deng JF, Yang CC, Tsai WJ, Ger J, Wu ML (2001) Acute ethylene chlorohydrin poisoning: experience of a poison control center. J Toxicol Clin Toxicol 39: 587-593.
5. Lawrence WH, Turner JE, Autian J (1971) Toxicity of ethylene chlorhydrin. I. Acute toxicity studies. J Pharm Sci 60: 568-571.
6. Chen YT, Liao JW, Hung DZ (2010) Protective effects of fomepizole on 2-chloroethanol toxicity. Hum Exp Toxicol 29: 507-512.
7. Johnson MK (1967) Metabolism of chloroethanol in the rat. Biochem Pharmacol 16: 185-99.
8. Sakai A, Shimizu H, Kono K, Furuya E (2005) Monochloroacetic acid inhibits liver gluconeogenesis by inactivating glyceraldehyde-3-phosphate dehydrogenase. Chem Res Toxicol 18: 277-282.
9. Chen YT, Hung DZ, Chou CC, Kang JJ, Cheng YW, et al. (2009) Vasorelaxation effects of 2-chloroethanol and chloroacetaldehyde in the isolated rat aortic rings. Journal of Health Science 55: 525-531.
10. Chen YT, Hsu CI, Hung DZ, Matsuura I, Liao JW (2011) Effects of chloroacetaldehyde in 2-chloroethanol-induced cardiotoxicity. Food Chem Toxicol 49: 1063-1067.
11. Knouzy B, Dubourg L, Baverel G, Michoudet C (2010) Targets of chloroacetaldehyde-induced nephrotoxicity. Toxicol In Vitro 24: 99-107.
12. Nissim I, Horyn O, Daikhin Y, Nissim I, Luhovyy B, et al. (2006) Ifosfamide-induced nephrotoxicity: mechanism and prevention. Cancer Res 66: 7824-7831.
13. Sood C, O'Brien PJ (1996) 2-Chloroacetaldehyde-induced cerebral glutathione depletion and neurotoxicity. Br J Cancer Suppl 27: S287-293.
14. Pourahmad J, Hosseini MJ, Eskandari MR, Rahmani F (2012) Involvement of four different intracellular sites in chloroacetaldehyde-induced oxidative stress cytotoxicity. Iran J Pharm Res 11: 265-276.
15. Chen CH, Chen SJ, Su CC, Yen CC, Tseng TJ, et al. (2013) Chloroacetic acid induced neuronal cells death through oxidative stress-mediated p38-MAPK activation pathway regulated mitochondria-dependent apoptotic signals. Toxicology 303: 72-82.
16. Lu TH, Su CC, Tang FC, Chen CH, Yen CC, et al. (2015) Chloroacetic acid triggers apoptosis in neuronal cells via a reactive oxygen species-induced endoplasmic reticulum stress signaling pathway. Chem Biol Interact 225: 1-12.
17. Brent J (2009) Fomepizole for ethylene glycol and methanol poisoning. N Engl J Med 360: 2216-2223.