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CASE REPORT

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Combined toxicity of methanol and formic acid: two cases of methanol poisoning

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Abstract Two fatalities caused by methanol ingestion are presented. Quantitative analysis of methanol and formic acid using head-space gas chromatography showed concentrations of methanol and formic acid in the femoral blood of each subject of 2.19 mg/ml and 0.41 mg/ml, and 1.96 mg/ml and 0.38 mg/ml, respectively. We concluded that death was due to methanol ingestion and the mechanism causing death involved the combined effects of the anesthetic action of methanol itself and metabolic acidosis by formic acid. Forensic toxicokinetic analysis indicated that both victims had ingested about 100 g of methanol or more.

Key words Methanol · Poisoning · Formic acid · Head-space gas chromatography

Introduction

Methanol is a common industrial solvent used in a variety of commercial products. A relatively low amount of methanol can be detected in human blood as a result of consumption of alcoholic beverages or some endogenous production (Haffner et al. 1998). Methanol, which has an anesthetic action, is metabolized to formic acid via formaldehyde in vivo. In Japan, many fatalities following ingestion of methanol instead of ethanol were observed over several years after World War II during a time of severe food shortages but such reports are quite rare nowadays.

Here we report two cases of death by methanol ingestion. The cause of death in each case was confirmed as the combined toxicity of methanol itself and subsequently formed formic acid, based on the quantitation in blood using head-space gas chromatography (HSGC).

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Case history

Two Caucasian males (the captain, 44 years old and the first officer, 47 years old) were found semicomatose in the cabin of a docked cargo ship. The two men were immediately transported to hospital but the first officer was confirmed dead on arrival. The captain remained unconscious and demonstrated bradycardia, a decrease of spontaneous respiration, severe shock status and severe acidosis. The laboratory results from an arterial blood sample taken while the subject was being ventilated with 100% O_2 gas were as follows; pH: 6.51, pCO_2: 66.3 mmHg, PO_2: 247.7 mmHg, bicarbonate:5.3 mmol/l, base excess: –38.0 mmol/l, sodium: 136 mmol/l, chloride: 95 mmol/l and anion gap: 35.7 mmol/l. The cause of severe acidosis was unconfirmed at that time. The captain was given artificial ventilation, intensive anti-shock therapy including administration of cathecholamine, and sodium bicarbonate to correct acidosis, and survived for a further 10 h but subsequently died.

Autopsy findings of both subjects indicated no external evidence of violence and no particular morphological changes except a slight brain edema and severe lung edema. Congestion of the lungs was also found by histological examination. Postmortem samples from each victim including right and left ventricle blood, femoral blood, cerebrospinal fluid and urine were collected for toxicological investigation and kept at 4 °C until analysis.

A glass filled with a pink coloured liquid and a plastic container filled with a clear liquid were found on the table in the captain's cabin during a subsequent on-the-spot inspection by the police.

Materials and methods

Determination and quantitation of methanol, ethanol, formaldehyde and formic acid were performed using the HSGC method slightly modified according to Anthony et al. (1980), Kuo (1982) and Matsumoto et al. (1989), respectively. Samples of 0.5 ml of biological specimens; the pink coloured liquid and the clear liquid diluted with 20 vols of water were prepared for HSGC.

The apparatus used was a Perkin-Elmer GC-Autosystem with a flame ionization detector and a head-space sampler. The wide-bore capillary column was DPP1-Supelcowax (60-m length × 0.53-mm i.d. and 2 μm film thickness). The temperatures at the injection port, the column oven and detector were 90 °C, 80 °C and 200 °C, respectively.

Table 1 Methanol and formic acid concentrations in biological specimens of the victims (mg/ml)

Specimen	First officer		Captain	
	Methanol	Formic acid	Methanol	Formic acid
Blood: right ventricle	2.11	0.38	1.96	0.42
: left ventricle	2.08	0.42	1.85	0.41
: femoral vein	2.19	0.41	1.96	0.38
Cerebrospinal fluid	2.55	0.46	2.22	0.36
Urine	2.49	0.63	–	–

Results and discussion

Table 1 shows the methanol and formic acid concentrations in each sample. In all samples, we detected methanol and formic acid but did not detect ethanol or formaldehyde. Fatal levels of methanol in blood have been reported over a wide range from 0.2 to 6.3 mg/ml (Pla et al. 1991). Since methanol itself has an anesthetie action, it can cause death in concentrations exceeding 4 mg/ml of blood (The Pharmaceutical Society of Japan 1992). The toxicity of methanol is due to the formation of formic acid which induces metabolic acidosis and leads to death in severe methanol poisoning cases (Ellenhorn and Barceloux 1988) when the blood formic acid concentration exceeds 0.5 mg/ml (Mahieu et al. 1989; Tanaka et al. 1991). Therefore, mortality in methanol poisoning correlates with the severity of acidosis rather than with blood methanol levels (Ellenhorn and Barceloux 1988). Because the blood concentrations of formic acid were slightly lower than 0.5 mg/ml and methanol concentrations were lower than 4 mg/ml, or, in other words, below the fatal levels in both subjects, we concluded that the cause of each death was the toxicity of metabolic acidosis induced by formic acid combined with the anesthetic action of methanol itself.

We detected relatively high levels of methanol in the blood but could not detect formaldehyde in samples from either victim. This is due to the quite rapid biotransformation from formaldehyde to formic acid in vivo (Ellenhorn and Barceloux 1988).

Since we detected methanol only but no ethanol in the pink coloured and clear liquids and did not detect ethanol in blood from the victims we believe that the victims ingested methanol only. The post-ingestion distribution of methanol is quite similar to that of ethanol leading to a higher methanol concentration in the urine than in the blood during the elimination phase (Ellenhorn and Barceloux 1988). Thus, the first officer is believed to have died in the elimination phase. Forensic toxicokinetic analysis indicated that the captain and the first officer ingested 97 g and 107 g of methanol, or more, respectively.

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