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CASE REPORT

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Fatal intoxication with a decalcifying agent containing formic acid

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Abstract A fatality caused by ingestion of a decalcifying agent containing formic acid is reported. Quantitative analysis of formic acid in the form of its methyl ester was performed in different body fluids and organ samples using head-space gas chromatography with flame ionization detection. The blood taken at the time of admission to hospital had a concentration of 370.3 μg/ml, which declined to 13.9 μg/ml after 6.5 h of haemodialysis. Post-mortem concentrations were 855.4 μg/ml (heart blood), 2712 μg/ml (gastric contents), 1128 μg/ml (haemorrhagic fluid from abdominal cavity), 3051 μg/ml (bile), 2664 μg/ml (contents of small intestine), 442.7 μg/g (liver) and 542.3 μg/g (kidney). The most important morphological findings for differentiating between oral and respiratory ingestion were ulceration of the oropharynx and the oesophagus as well as extensive necrotic lesions in the stomach and the duodenum without perforation. Death was caused by massive acidosis, haemolysis, bleeding complications, hepatic and renal failure. Toxicological and morphological findings revealed that a considerable amount of formic acid had been ingested orally with a suicidal intention.

Key words Formic acid · Head-space gas chromatography · Body tissues · Morphology · Body fluids · Poisoning

Introduction

Formic acid is a common industrial compound used in the production of silage, in disinfectants and decalcifying agents and mainly as a precursor in industrial chemical synthesis. Cases of formic acid poisoning are rare; only few have been reported in the literature [1, 2, 3, 4, 5, 6, 7, 8, 9], and the formate concentration was determined in the blood in only one of these cases [7]. The results of quantitative measurements in other body fluids and tissues were not discussed in any of these cases. More details on formic acid concentrations in the blood have been reported in cases of formaldehyde [10, 11, 12] and methanol poisoning [13, 14, 15, 16, 17], in which formic acid is formed as a metabolite. Formic acid induces metabolic acidosis and is responsible for retinal and optic nerve toxicity [15, 18, 19]. Fatal intoxication after oral ingestion of high doses of formic acid are frequently due to acid-induced severe damage to the gastric wall with perforation [9, 20]. In cases without such severe local lesions, death is caused by massive acidosis, excessive haemolysis, bleeding complications and finally hepatic and renal failure [1, 6, 7, 8, 9, 20]. The toxicological basis of this clinical course has not been elucidated in detail. Acidosis is obviously the result of rapid resorption of the acid [7, 20, 21]. Haemolysis is possibly caused by the decrease in pH [7] or by a direct toxic effect of the acid itself [6, 9, 20, 22] by damage to the erythrocyte walls. The extent of haemolysis can serve as a parameter for the severity of the intoxication [20]. Disseminated intravascular coagulation (DIC) and acid-mediated changes in the proteins of the coagulation cascade have been discussed as reasons for the bleeding complications [6, 9]. Hepatic and renal failure in formic acid intoxication may be of secondary origin, but a direct mechanism is also conceivable. Formic acid belongs to the class of chemicals known as protoplasmic poisons and can bind either directly to proteins or indirectly to tissue ions, to interfere with cellular function [1]. Furthermore it is an inhibitor of the mitochondrial cytochrome oxidase of aerobic cells [23].

In this paper a fatal intoxication due to ingestion of a decalcifying agent containing formic acid is reported. For insurance purposes it was necessary to clarify whether it was an occupational accident during a dishwasher cleaning procedure or a case of suicide. In this context the administration route and an estimation of the ingested quantity were of major interest. The questions were answered

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on the basis of morphological findings and by quantitation of formic acid in body fluids and tissues using head-space gas chromatography (HS-GC) with flame ionization detection (FID).

Case history

A 27-year-old male working as a cleaner at a restaurant was found vomiting and complaining of violent abdominal pain after he had cleaned a dishwasher with the decalcifying agent Lami-Kalk (Laminex Labortechnik, Oldenburg, Germany), which contains only formic acid (50–100%) and water, according to the manufacturer's safety data sheet. He was immediately transported to hospital, was artificially ventilated and treated with sodium bicarbonate to correct the clinically diagnosed acidosis. The values of parameters measured in blood on admission to hospital (values in brackets: 0.5 h after admission/normal range) documenting severe metabolic acidosis were pH 7.1 (6.86/normal 7.35–7.42), pCO_2 53 mmHg (70.4/normal 33–45), bicarbonate 14 mmol/l (10.6/normal 21–25) and a base excess of –14 mmol/l (–22/normal –2 to +2). After 3 h haemodialysis was started, but had to be stopped after 6.5 h because of heavy bleeding. The patient died 16.5 h later, 26 h after admission to hospital, with the clinical signs of haemolysis coupled with coagulation defects. The physician assumed an inhalation of formic acid because no ulceration of the mucosa of the pharynx had been seen while intubating the patient. Autopsy was performed 1 day after death.

The police confiscated an empty 1 l bottle of the decalcifying agent and another bottle that was one-quarter full. The bottles were fitted with a screw-type cap with a lift-up lid and only a small opening in the middle. The label bore the inscription "corrosive" and the corresponding hazard symbol as well as the specification that the bottle contained formic acid. The responsible shift supervisor explained that a whole bottle was always used for the cleaning procedure and that the deceased had been instructed to wear safety gloves while doing this. Just before the incident the deceased had gone to the bar to get a glass of water, which was unfortunately not confiscated.

Materials and methods

Samples of femoral blood were collected during hospitalization (at admission, before, during and after dialysis) and stored at 4°C until analysis. Post-mortem samples of heart blood, gastric contents, haemorrhagic fluid from the abdominal cavity, bile, contents of the small intestine, liver and kidney were collected and stored at –18°C until analysis. All blood samples showed some haemolysis. Additionally, the formic acid content of the bottle of Lami-Kalk confiscated by the police was determined.

The concentrations of formic acid in body fluids and tissues were determined by means of head-space gas chromatography (HS-GC) as methyl formate after derivatisation with methanol under acidic conditions with acetonitrile as internal standard according to Kuo [24], with slight modifications. Standard solutions of formic acid in blood and water as well as 0.5 ml samples of blood and body fluids were prepared. The calibration graphs were linear at least over the measured range of 0–2000 µg/ml formic acid. The tissue samples (liver and kidney) were homogenized with an equal amount of water and 0.5 g of the homogenate was used for measurement. As reported in the literature the slope of the standard curve in blood differs from that in urine or water, probably due to a lower solubility of methyl formate in the reaction mixture containing blood [24, 25]. Consequently quantitation of formic acid was performed with two different standard curves for haemorrhagic samples and aqueous specimens (bile, liver and kidney), respectively. Additionally, post-mortem samples (heart blood, gastric contents, haemorrhagic fluid from abdominal cavity and bile) were checked for the presence of methanol and formaldehyde by means of HS-GC. The formic acid content of the confiscated Lami-Kalk bottle was determined by analysing 0.5 ml of a diluted sample (1:1000) of the decalcifying agent.

The samples were measured on a Perkin-Elmer GC-Autosystem fitted with a head-space sampler HS40, a fused-silica capillary column (30 m length, 0.32 mm i.d., 0.5 µm film thickness, open tubular) coated with bonded PE-wax and a flame ionization detector (all Perkin-Elmer, Überlingen, Germany). Injection port, column and detector temperatures were 120°C, 100°C, and 200°C, respectively and the flow rate was 2.8 ml/min (helium). The samples were equilibrated at 80°C for 16 min prior to analysis, the transfer time was 0.02 min.

The histological examination of all relevant organs including the upper respiratory and gastrointestinal tracts was carried out using paraffin-embedded sections stained with haematoxylin and eosin.

Results

Table 1 shows the concentrations of formic acid detected in the different biological specimens but methanol and formaldehyde were not detected in the these samples. The Lami-Kalk bottle was found to contain 60% formic acid (% by weight) and was therefore correctly labelled.

The morphological findings observed were large areas of ulceration in the oropharynx and oesophagus, complete necrosis of the gastric mucosa, oedema and necrotic areas in the deeper tissue layers of the stomach from the submucosa to the subserosal areas but no perforation, 1930 g coagulated blood in the stomach, superficial and focal necrosis of the mucosa of the duodenum (Fig. 1), bilious content of the duodenum with only minor portions of coagulated blood, regular findings in the other parts of the intestine, excessive dilatation and thrombosis of submucosal vessels of the stomach and duodenum (Fig. 1), extreme swelling of the nearly unstained (with haematoxylin and eosin) intravascular erythrocytes, thrombosis of branches of the hepatic portal vein and massive necrosis of hepatocytes (Fig. 2), haemoglobin cylinders in the renal tubuli, tubular necrosis, cutaneous purpura, massive bruising around venipuncture sites; subpleural, subepicardial and subendocardial petechiae, extreme anaemia of internal organs. The face and the upper respiratory tract did not exhibit any pathology findings.

Table 1 Formic acid concentrations in blood, body fluids and tissues

Material	Formic acid concentration
Blood on admission to hospital	370.3 µg/ml
Blood before beginning of dialysis	223.4 µg/ml
Blood during dialysis	8.9 µg/ml
Blood at end of dialysis	13.9 µg/ml
Heart blood	855.4 µg/ml
Haemorrhagic fluid from abdominal cavity	1128 µg/ml
Gastric contents	2712 µg/ml
Contents of small intestine	2664 µg/ml
Bile	3051 µg/ml
Liver	442.7 µg/g
Kidney	542.3 µg/g

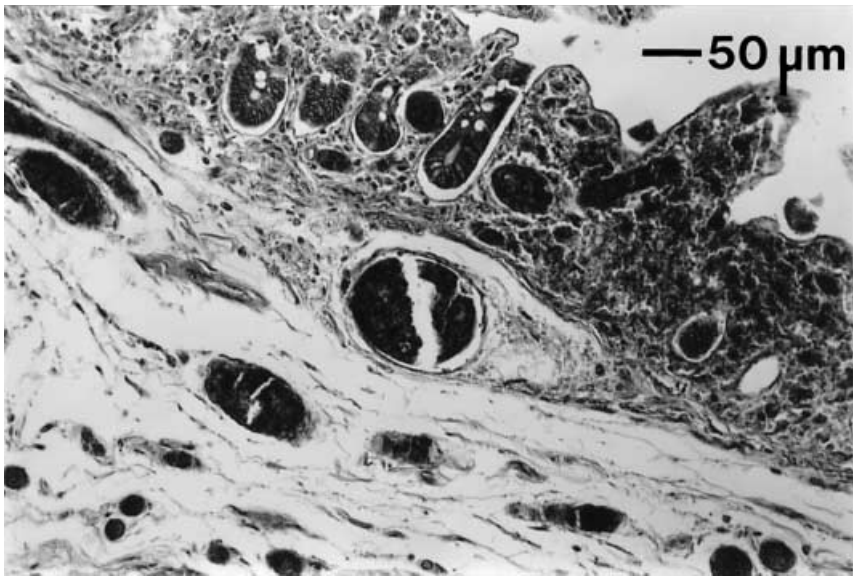

Fig. 1 Duodenum showing mucosal necrosis, excessive dilatation and thrombosis of submucosal vessels (haematoxylin and eosin)

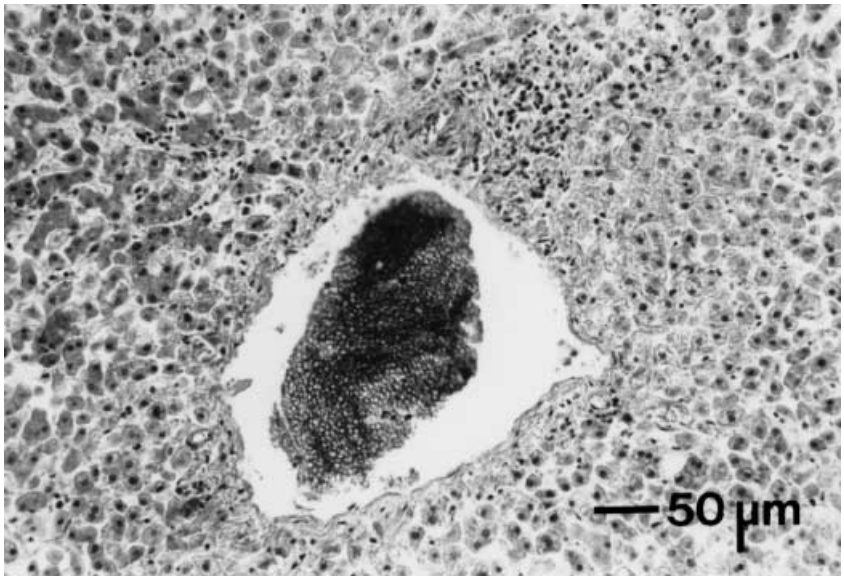

Fig. 2 Liver with massive necrosis of hepatocytes and thrombosis in a branch of the hepatic portal vein (haematoxylin and eosin)

Discussion

As reported in the literature, formic acid concentrations in the blood of healthy humans range from 3.2–56 µg/ml [24, 26, 27, 28, 29, 30]. Hence the formic acid content of the blood at the time of admission to hospital and of the post-mortem heart blood was much greater than normal biological levels. Since methanol and formaldehyde as potential precursors of metabolic formic acid were not detected in the investigated samples, the formic acid concentrations in our case were obviously due to intake of formic acid itself. The high level of formic acid in the post-mortem heart blood in relation to the concentration measured directly after dialysis can be explained by the further absorption of formic acid from the gastrointestinal tract during the 16.5 h after stopping the haemodialysis until death.

All toxicological findings indicated severe poisoning. The values corresponded to formic acid concentrations in cases of fatal formic acid [7], methanol [13, 14, 15, 16, 17] and formaldehyde [10, 11, 12] intoxication (Table 2), all with non-inhalational ingestion. Although the deceased had vomited, the concentrations of formic acid in the contents of the upper intestinal tract (stomach and small intestine) were very high (2712 µg/ml and 2664 µg/ml, respectively), demonstrating that the route of administration had been oral.

The only formic acid blood concentration given in the literature was 348 µg/ml [7] which was measured 2 h after intentional ingestion of approximately 200 ml of a descaling product containing 50% formic acid. In a review of 53 cases of formic acid poisoning with suicidal intention the clinical outcome was described [8] and the authors state that those persons believed to have taken between 15 ml and a mouthful of formic acid were likely to be found

Table 2 Formic acid concentrations in cases of fatal intoxication with formic acid (nos. 1, 2), methanol (nos. 3–9) and formaldehyde (nos. 10–12) (*n.m.* not measured, *ad* on admission to hospital, *pm* postmortem)

No.	Blood (μg/ml)	Kidney (μg/g)	Liver (μg/g)	Bile (μg/ml)	Reference
1	348 (ad)	n.m.	n.m.	n.m.	[7]
2	370 (ad), 855 (pm)	542	443	3051	Reported case
3	230 (pm)	130	510	n.m.	[16]
4	320 (pm)	1190	540	n.m.	[16]
5	380 and 410 (pm, 2 cases)	n.m.	n.m.	n.m.	[17]
6	221–787 (ad, 10 cases)	n.m.	n.m.	n.m.	[14]
7	1040 (ad)	n.m.	n.m.	n.m.	[15]
8	511 and 1197 (ad, 2 cases)	n.m.	n.m.	n.m.	[13]
9	1210 (pm)	n.m.	n.m.	890	[15]
10	100–130 (pm)	n.m.	n.m.	n.m.	[12]
11	300 (ad)	n.m.	n.m.	n.m.	[10]
12	543 (pm)	n.m.	n.m.	n.m.	[11]

dead, whereas oral ingestion of 10 ml could prove fatal regardless of treatment. Because information on the concentration is lacking, the ingested quantity is questionable in these cases. Another study of 45 cases of oral formic acid ingestion showed that 60 g of formic acid (approx. 100 ml of a solution containing 45–60% formic acid) caused death in every case, whereas in smaller quantities there was a good chance of recovery with (intensive) medical treatment. Ingestion of less than 30 g of formic acid was never fatal [9].

We therefore assumed that at least 30–60 g (44–88 ml of a solution containing 60% formic acid) of formic acid was ingested. According to Verstraete et al. [7] accidental ingestion of formic acid usually have a good prognosis, as the pungent odour and the corrosive characteristics prevent the intake of large volumes. Furthermore, our investigations showed that the bottle of decalcifying agent was correctly labelled. No measuring procedure was necessary while cleaning the dishwasher so there was no reason to pour the decalcifying agent into another container, which could lead to confusion. In consideration of all these facts we concluded that the suicidal intent was evident.

The morphological findings also revealed that the formic acid had been ingested orally. There were no lesions in the respiratory tract, especially no erosions, ulceration or necrosis of the respiratory mucosa, which would be expected following inhalation of a highly corrosive agent. The upper gastrointestinal tract exhibited typical findings with extensive ulceration and necrotic areas, especially in the stomach. However, the lethal outcome was not directly related to these local lesions, which did not cause a perforation. Clinically, the patient developed massive acidosis, excessive haemolysis, bleeding complications and finally hepatic and renal failure. A DIC was not confirmed as the cause of the bleeding complications, since laboratory tests could not be performed because of the excessive haemolysis. Histologically thrombosis of submucosal vessels of the stomach and the duodenum as well as thrombosis of branches of the hepatic portal vein were observed, whereas (micro) thrombi were not seen in other organs. Thrombosis of vessels exclusively in areas with the highest intravasal acid concentrations during the resorption phase confirmed the assumption that the acid has a direct effect on the coagulation system [6, 9]. The morphological correlates of the clinically observed hepatic and renal failure (massive necrosis of hepatocytes, tubular necrosis) are unspecific. However, they have also been described in other cases [6, 7, 8, 9, 20]. The documented clinical course and the observed morphological findings were typical for an oral ingestion of high doses of formic acid [6, 7, 9] and did not support the assumption of an inhalation trauma.

In conclusion, on the basis of toxicological and morphological findings a suicide due to oral ingestion of a decalcifying agent containing formic acid could be confirmed and distinguished from accidental respiratory or oral incorporation.

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