

Suicidal ingestion of formalin with fatal complications*

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Abstract. After ingestion of an unknown amount of formalin with suicidal intent, a 55-year-old female and a 34-year-old male were admitted to the hospital with extensive gastrointestinal corrosive damage, circulatory shock, metabolic acidosis, respiratory insufficiency and impairment of renal function, which rapidly progressed to acute renal failure. Metabolic acidosis was in part due to high plasma levels of formic acid, the main metabolite of formaldehyde, and hyperlactatemia. Both patients underwent hemodialysis and hemofiltration treatment. In the male patient, a gastrectomy had to be performed. The further clinical course in the patients was characterized by sepsis and protracted pulmonary complications. Both patients died after developing adult respiratory distress syndrome and global cardiac insufficiency. In vitro experiments on formaldehyde reactivity to proteins yielded evidence for almost complete but reversible binding to plasma and blood. Formaldehyde probably exerts systemic toxicity in the form of its labile Schiff's base with proteins, but not as free formaldehyde.

Key words: Formalin ingestion – Acute renal failure – Hemodialysis – Formic acid concentrations – Gastrointestinal lesions

Formaldehyde is a water-soluble, highly reactive gas which extremely irritates the upper airways. The aqueous solution of formaldehyde – formalin – is used as a conserving agent in pathology departments and as an antiseptic agent in hospitals and households. Formaldehyde is a physiological intermediary metabolite in mammals and plays an important role in the 1-carbon pool as methylene tetrahydrofolate. Due to its chemical reactivity with proteins, the unbound fraction is probably small in relation to the fraction of protein-bound compound. Low or endogenous concentrations of formaldehyde are rapid-

ly metabolized to formic acid or enter the 1-carbon pool via tetrahydrofolate.

Due to the strong irritating effect of formaldehyde and its low threshold of olfactory detection (0.8 ppm) accidental ingestion of formalin occurs rarely [1]. Ingestion of formalin may lead to severe gastrointestinal burning. In acute poisoning, it is not clear whether formaldehyde develops its primary toxic effect only at the site of initial contact or may also reach the circulation and exert systemic toxicity. Shock, which is frequently observed, may be secondary to severe local irritation and/or systemic toxicity. Experience with patients who have suicidally ingested formalin is rather limited [2, 3, 4]. The same is also true for treatment. We report two cases of formalin ingestion with suicidal intent. In vitro experiments were also performed in order to determine the equilibrium between free and protein-bound formaldehyde in plasma and blood.

Patients

Patient 1: A 55-year-old female was found in coma by her husband in the bathroom after she had ingested an unknown amount of formalin with suicidal intent. The patient was a physician who had no history of medical illness. She was admitted with shock (systolic blood pressure 50 mmHg), respiratory insufficiency and metabolic acidosis. The anion gap of 24 mmol/l was probably caused, at least in part, by high plasma levels of formic acid (see Table 1) and hyperlactatemia (1 mmol/l). Gastroscopy revealed multiple peptic plaques on the mucosa of the distal part of the esophagus and the cardia. The gastric and duodenal mucosa showed extensive congestion, diffuse necrosis and hemorrhage. An emergency laparotomy was performed and showed no evidence of gastric perforation. In the subsequent clinical course, renal function rapidly deteriorated to acute renal failure, and the patient underwent daily hemodialysis and hemofiltration. Extensive bilateral pleural effusion were drained by chest tubes. Subsequently respiratory insufficiency developed which progressed to adult respiratory distress syndrome, sepsis and conjugated hyperbilirubinemia. Three weeks after ingestion of the formaldehyde the patient died of global cardiac failure refractory to atecholamine therapy.

Autopsy findings included burns of the gastric mucosa, jejunum and ileum as well as part of the colon (including the sigmoid) with extensive hemorrhagic jejunitis, ileitis and colitis. Further findings includ-

* Dedicated to Prof. Adebahr on the occasion of his 65th birthday

In vitro experiments

Ten ml of pooled plasma was spiked with formaldehyde (10 $\mu\text{g/ml}$) and incubated at 37 °C for 15 min. Levels of free formaldehyde were determined in the blank plasma, spiked blood/plasma, and spiked plasma after ultrafiltration. For quantification, formaldehyde in the plasma samples was transferred into a cooled trap by a stream of nitrogen and then reacted with 3-methyl-benzthiazolon hydrazone, which yielded a tetra azapentamethin cyanine dye [7].

Results

Formic acid concentrations of patient 1 and 2 are summarized in Table 1. Plasma formaldehyde levels in both patients were below the limits of detection. A toxicological screening showed that no compound other than formaldehyde had been ingested by either of the two patients.

Levels of free (unbound) formaldehyde in the spiked plasma and blood samples were also below the limits of detection ($<0.5 \mu\text{g/ml}$). Formaldehyde is almost completely (but reversibly) bound to amino functions of proteins, thereby forming Schiff's bases.

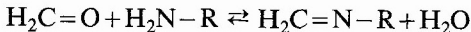


Table 1. Formic acid plasma levels [mmol/l and µg/ml]

Patient 1	Patient 2
6.09 mmol/l (280 µg/ml) on admission	4.57 mmol/l (210 µg/ml) hemofiltration
30 min	4.57 mmol/l (210 µg/ml) art. 1.96 mmol/l (90 µg/ml) ven.
1 h	3.47 mmol/l (160 µg/ml) art. 1.96 mmol/l (90 µg/ml) ven.
2 h	2.82 mmol/l (130 µg/ml) art. 1.96 mmol/l (90 µg/ml) ven.
3 h	2.39 mmol/l (110 µg/ml) art. 0.87 mmol/l (40 µg/ml) ven.
4 h	2.39 mmol/l (110 µg/ml) art. 0.87 mmol/l (40 µg/ml) ven.
5 h	2.82 mmol/l (130 µg/ml) art. 1.52 mmol/l (70 µg/ml) ven.
6 h	2.39 mmol/l (110 µg/ml) art. 1.52 mmol/l (70 µg/ml) ven.

ed hepatosplenomegaly with icterus and moderate congestion of the liver parenchyma.

Patient 2: A 34-year-old male with a history of alcohol abuse ingested an unknown amount of formalin with suicidal intent. He was admitted to the intensive care unit in shock (systolic blood pressure 60 mmHg) with respiratory insufficiency and metabolic acidosis. At least part of the anion gap of 23-mmol/l was due to the plasma levels of formic acid and to hyperlactatemia (0.9 mmol/l). The patient was intubated and ventilated on admission. Gastroscopy revealed extensive necrosis of the distal part of the esophagus as well as of the whole stomach. Additional findings included extensive congestion of the mucosa and diffuse bleeding. An emergency laparotomy was performed and because of penetrating mucosal necrosis, a gastrectomy with blind closure of esophagus and duodenum was performed. The further clinical course was characterized by rapid deterioration of renal function with the development of acute renal failure which necessitated hemodialysis and hemofiltration. Subsequently the patient developed alcohol withdrawal symptoms and a fever. An X-ray of the esophagus with contrast showed a 2-cm leak of the distal esophagus stump and a repeat laparotomy was performed. The patient slowly recovered and was extubated 16 days after admission. An esophagojejunostomy was performed after 5 weeks. A chest X-ray performed after this procedure showed signs of apparent hemothorax and a thoracotomy with drainage was performed. Recurrent atelectasis of the left upper lobe necessitated repeated bronchoscopies with bronchial lavage. Subsequently the clinical course was characterized by persistent pneumonia with fever and recurrent pneumothoraces (Fig. 1). Despite independent ventilation of both lungs with and without high frequency jet ventilation [5], respiratory function deteriorated. The adult respiratory distress syndrome developed and the patient died 8 weeks after the formaldehyde ingestion with signs of global cardiac failure.

At autopsy the findings included hepatomegaly, an intact esophagojejunostomy, 2 pulmonary hematomas (diameter 6 and 8 cm, respectively), and bronchopneumonia of both lungs.

Methods

Analysis of the formaldehyde samples which both patients had ingested gave evidence that these products were not contaminated with methanol. It should be noted that commercially available formalin may contain up to 15% methanol. A chemical-toxicological screening confirmed that no drugs or substances other than formaline had been ingested [6]. Ethanol or methanol could not be detected in plasma samples obtained on admission.

Formic acid levels were determined enzymatically with formiate dehydrogenase (Boehringer Mannheim, FRG).

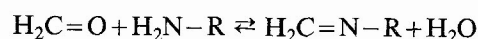
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Discussion

The localization of formaldehyde-induced corrosive damage in the gastrointestinal tract depends on the contact time of the aqueous formaldehyde. As in burns with other substances, severe burns of the esophagus are rather rare because of the comparatively rapid passage. Extensive lesions of the gastric mucosa were found in both patients. The female patient additionally showed corrosive lesions of the jejunum, ileum and in the colon even up to

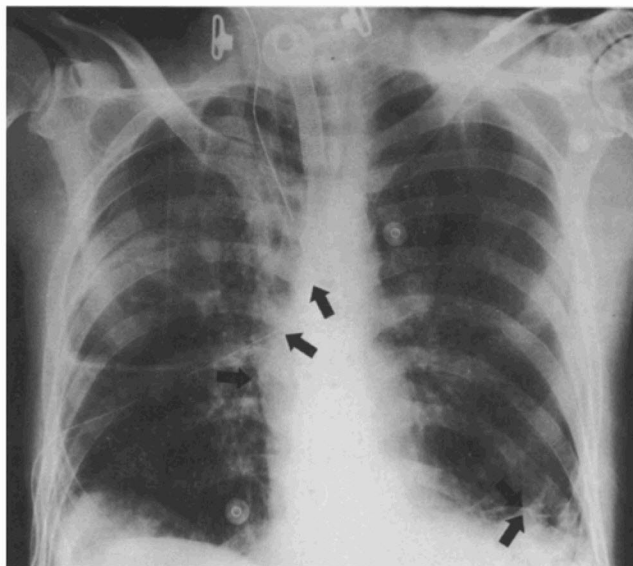


Fig. 1. Chest X-ray of patient 2 three days before death showing intralobular callosity, pneumonia and 5 chest tubes (arrows)

the sigmoid. Formaldehyde plasma concentrations were beyond the limit of detection, probably due to rapid formation of Schiff's bases with plasma proteins. Hepatic metabolism of the labile Schiff's bases leads to formation of formic acid. The high formic acid levels and, to a lesser extent, hyperlactatemia due to circulatory shock probably caused the observed metabolic acidosis. To aid the differential diagnosis of the cause of metabolic acidosis, determination of the anion gap may be useful. It is not clear whether the acute renal failure, which rapidly developed in both patients, was due to toxic effects of plasma constituents altered by reaction with formaldehyde or was due to severe shock. Both patients required catecholamines on admission. Hemolysis was not observed in either.

The clinical efficacy of hemodialysis in removing formic acid was moderate. A clearance of about 60–120 ml/min was calculated for patient 2, which is somewhat lower than values reported by other authors [1]. The fatal outcome in both patients was mainly due to protracted pulmonary complications. There was no evidence for primary pulmonary lesions caused by formalin ingestion. Early bronchoscopy seems to be advisable for diagnosing early pulmonary complications. Progressive conjugated hyperbilirubinemia developed in the female patient. This complication which is frequently associated with polytransfusion and multiple organ failure is of undetermined etiology and is associated with a high mortality [8].

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