Ingestion of formic acid-containing agents—report of three fatal cases

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Summary

Three patients were treated after they had deliberately ingested domestic agents containing formic acid. The major complications included the local effects on the oropharynx, oesophagus and stomach, metabolic acidosis, derangement of clotting mechanisms with haemorrhage and shock, widespread intravascular haemolysis, disseminated intravascular coagulation and the acute onset of respiratory and renal failure. All 3 patients died between 2 and 14 days after admission. It is the authors' belief that intensive therapy from the outset to include exchange transfusion, infusion of clotting factors, high dose steroids, ventilatory support and peritoneal or haemodialysis with parenteral nutrition may perhaps offer a better chance for survival.

Introduction

Formic acid can be found in the home, usually as a constituent of various forms of descaling agent which are sold under a variety of proprietary names (e.g. 'Kleenoff', 'Ataka', 'Furex'). It is therefore one of the few strong acids that are domestically available for accidental or deliberate ingestion. There are 2 brief reports in the English literature (Malizia *et al.*, 1977; Harvey, 1968) describing the clinical course of 3 patients with accidental poisoning and the patients all survived. Two further reports of deliberate ingestion of formic acid appear in the French (Tschantz and Favre, 1975) and Polish (Wiernikowski and Guzik, 1973) literature and one had a fatal outcome. The clinical features are now reported of 3 patients who deliberately ingested agents containing formic acid, all of whom succumbed.

Case 1

A 35-year-old woman was admitted after drinking 3 mouthfuls of a 40% formic acid solution ('Ataka' – a bath stain remover). Within 2 hr she was vomiting fresh blood and passing large quantities of fresh blood per rectum. She complained of abdominal pain and was voiding small amounts of dark red urine. A gross clotting defect was confirmed (prothrombin time, 75 sec, control 12 sec; thrombin time 180 sec, control 15 sec). Serum fibrinogen was not detected and serum fibrinogen degradation product (FDP) concentration was extremely high. Her platelet count was $240 \times 10^9/l$ and remained normal throughout her illness. There was no evidence of disseminated intravascular coagulation on the blood film. Widespread intravascular haemolysis was confirmed by finding large quantities of free Hb in the blood, urine and peritoneal fluid, and a methaemalbumin level of 143 mg % in the blood (normal 6 mg %). She had a profound metabolic acidosis (hydrogen ion activity 72 nmol; pH 7.0), the serum lactate level was normal, and serum ketones were not detected. The blood pH returned to normal within 12 hr after intensive treatment with intravenous sodium bicarbonate.

The haemorrhage was successfully treated with transfusion of fresh blood, fresh frozen plasma and fibrinogen. Infusion of clotting factors was repeated several times depending on coagulation studies, but within 48 hr all clotting tests were normal and remained so. The maximum reticulocyte count was 7%. The massive intravascular haemolysis was treated by exchange transfusion and over the first 24 hr, 20 units of blood were exchanged. The bleeding was assumed to be from upper gastro-

intestinal tract ulceration and she was given oral antacids and i.v. cimetidine. Forty-eight hours after admission all bleeding had stopped and there was no suggestion of continuing haemolysis, but she was anuric. Peritoneal dialysis was started and continued throughout. Pulmonary complications developed on the 3rd day with expectoration of large volumes of foul sputum and signs of consolidation at the left lung base. She required assisted ventilation and antibiotics. Nutrition was maintained intravenously using Vamin glucose and 50% dextrose, and at no time was a nasogastric tube passed. No corticosteroids were given.

On the 10th day, gastroscopy revealed a florid haemorrhagic oesophagitis and there were large areas of sloughing ulceration throughout the stomach. On the 11th day she was weaned off the ventilator and the chest X-ray was now normal. The only outstanding problem at this stage was continuing anuria. On the 13th day she suddenly became shocked and had a massive haematemesis which was uncontrollable and she died on day 14. Coagulation studies at that time were normal.

At post-mortem large areas of ulceration extended throughout the oesophagus and stomach and blood filled the stomach and small bowel. Ulceration extended down to the muscularis mucosa and there was acute tubular necrosis. There was early thrombosis of the hepatic portal veins.

Case 2

A 66-year-old woman who had a past history of ischaemic heart disease and brain stem vascular insufficiency swallowed 50–100 ml of 'Kleenoff' kettle descaler containing 55% formic acid. Shortly before admission she vomited brown fluid. On examination she was in hypovolaemic shock, the pulse was 120/min and the BP unrecordable. She had extensive ulceration of the mouth and pharynx. There were rhonchi in the right lung base and the abdomen was rigid with absent bowel sounds. She was able to respond to oral commands. She was given milk orally, 800 ml of human plasma protein fraction i.v. over 4 hr and a single dose of 300 mg hydrocortisone i.v.

She developed a profound metabolic acidosis (arterial blood hydrogen ion activity 69.2 nmol; pH 7.16); bicarbonate 6.6 and base excess -20 mmol/l which was corrected with i.v. sodium bicarbonate.

She had clinical evidence of aspiration pneumonia and was hypoxic (PO_2 , 8.0 kPa; PCO_2 , 4.19 kPa; one kPa=7.5 mmHg and normal range for PO_2 , 12–15 kPa; and PCO_2 , 4.5–6.8 kPa). Six hours after admission she developed asystole, followed by a respiratory arrest. Sinus rhythm was restored after cardiac massage, and intermittent positive pressure

ventilation was started. She required increasing oxygen concentrations to maintain her PO_2 and a chest X-ray showed bilateral changes suggestive of pulmonary oedema or 'shock' lung. The Hb level was 13.2 g/dl; WCC $11.3 \times 10^9/l$ and platelet count was normal.

She developed intravascular haemolysis and a gross clotting defect: prothrombin time, 35 sec (control 13 sec); kaolin cephalin clotting time, 125 sec (control, 46 sec); resulting in bleeding from venepuncture sites and haematuria. This was corrected with fresh frozen plasma and blood. From 12 hr after admission, she was in acute renal failure and remained anuric until her death.

On the second day she developed recurrent cardiac arrhythmias, which did not require anti-arrhythmic drug therapy, and by the third day she had refractory hypotension despite adequate fluid replacement. She died 5 days after admission. Post-mortem showed extensive erosion of the oesophagus, stomach and duodenum.

Case 3

A 56-year-old male with a past history of asbestosis and duodenal ulceration was admitted one hour after he had ingested a mouthful of 'Kleenoff' kettle descaling agent (containing 55% formic acid). He had severe pain in the mouth and throat and was vomiting 'coffee-ground' material. His oropharynx was inflamed, BP was 130/80 mmHg and pulse 100/min. He had bilateral rhonchi and coarse lung crepitations. There was tenderness in the epigastrium. Initial treatment consisted of morphine, metoclopramide, magnesium trisilicate, milk and i.v. fluids. Prophylactic i.v. cimetidine was given.

The day after admission he was hyperventilating and had developed a tachycardia, hypotension and central cyanosis. He was given oxygen, hydrocortisone 100 mg i.m. 8-hourly and human plasma protein fraction (HPPF). The lung signs remained unchanged and the chest X-ray showed evidence of bilateral patchy consolidation with old fibrotic changes in the right lower lobe. Parenteral antibiotic treatment with ampicillin and flucloxacillin was started. He was oliguric. The blood urea was 16.3, potassium 5.6 and creatinine 0.29 mmol/l; Hb, 15.4 g/dl; WCC, $19.4 \times 10^9/l$ and platelet count, $250 \times 10^9/l$. There was no acidosis.

Two days after admission he was anuric. The blood urea was 27.1 mmol/l and potassium 7.7 mmol/l. There was only a minimal response to i.v. mannitol (200 ml of a 10% solution which was repeated after 2 hr) and peritoneal dialysis was commenced. By the third day sloughing of the mucosa of the soft palate and oropharynx began. Nutrition was now difficult to maintain and parenteral feeding was commenced using Vamin glucose and 50% dextrose (providing

476.2 J, and 9.4 nitrogen g/day) together with water-soluble vitamins and trace element supplements. Owing to deteriorating pulmonary function (PO_2 , 4.98 kPa; Pco_2 , 4.72 kPa) intermittent positive pressure ventilation was commenced on day 5. Chest X-ray at this time showed progressive bilateral consolidation involving both bases and both mid-zones (Fig. 1) compatible with the features of 'shock lung' and he was empirically given 3 pulses of 2 g methylprednisolone daily. The i.m. administration of hydrocortisone 200 mg thrice daily was continued as background steroid cover in view of the short half-life of methylprednisolone. Following ventilation and steroid therapy there was a significant

improvement in his condition, both clinically and radiographically. Other investigations at this time showed: urea, 32 mmol/l; potassium 4.4 mmol/l; Hb, 11.7 g/dl; WCC, $44 \times 10^9/l$; platelets, $113 \times 10^9/l$ and British prothrombin ratio (BPR) was normal.

By the 7th day cutaneous purpura appeared and there was bruising around venepuncture sites. One day later, fresh bleeding appeared from the nose and mouth. The Hb was 9.9 g/dl; WCC $9.6 \times 10^9/l$ and burr cells were present in the peripheral blood. Disseminated intravascular coagulation was supported by the following findings: platelet count, $7 \times 10^9/l$; BPR, 2.8 (patient, 36 sec; control, 13 sec); kaolin cephalin clotting time, abnormal

FIG. 1. Case no. 3. Appearance of chest X-ray on day 5 showing bilateral changes suggestive of 'shock lung'.

FIG. 2. Chest X-ray after treatment with large doses of steroids and ventilation showing clearing of the opacification.

(patient, 51 sec; control, 45 sec) and serum FDP concentration slightly raised at 10–40 $\mu\text{g/ml}$. The fibrinogen titre was normal. He was given vitamin K, fresh frozen plasma and platelet-rich plasma. Tracheostomy was carried out and ventilation continued.

By the 10th day, the urine volume was 100 ml/24 hr and the peritoneal dialysis was satisfactory. The chest X-ray showed improvement with some resolution of the extensive consolidation (Fig. 2). He had oedema of the hands, feet and eyelids with a serum albumin of 22 g/dl. There was no extension of skin bruising or purpura. The BPR was normal and serum FDP concentration was slightly raised at 40 $\mu\text{g/ml}$. Hb was 8.1 g/dl, reticulocyte count was 5%; WCC, $18.9 \times 10^9/\text{l}$ and platelets $< 5.0 \times 10^9/\text{l}$.

On the 11th day, he developed hypotension and tachycardia with no evidence of bleeding and attempts to resuscitate him failed.

At post-mortem the mouth and tongue appeared normal. The oesophagus was normal apart from some superficial ulceration at the upper end. The stomach showed a chronic ulcer and 2 small areas of erosion. The lungs were heavy and severely oedematous with diffuse induration and mild scarring in both lower lobes. Histological examination of the lungs showed scarring with many asbestos bodies, bronchitis and bronchiolitis. The liver was swollen and had a few fine petechiae on the sub-capsular surface. Histology showed tubular necrosis. Examination of the pancreas showed only some small foci of fat necrosis in the peri-pancreatic tissue. The

optic nerves showed no histological abnormality and bone marrow examination was normal. Death was considered to be due to circulatory failure.

Discussion

Although poisoning with formic acid is rare, its presence in the home makes it a potential agent with which to attempt suicide. It is a very pungent acid and this may explain the different prognosis between accidental and deliberate poisoning – larger volumes are more likely to be ingested in the latter instance. Three cases of accidental poisoning are found in the English literature (Malizia *et al.*, 1977; Harvey, 1968) (Table 1). One patient casually ingested an unknown quantity from a bottle which he thought contained cough syrup. A second patient was hit in the face and mouth by a jet of formic acid squirted from a container. The third (a 2-year-old boy) swallowed an unknown quantity of a kettle descaler containing 60% formic acid. All 3 patients survived. In the first 2, symptoms and signs were restricted to the gastrointestinal tract. However, in the young boy there was renal failure which recovered with conservative management, shock, slight derangement of liver function, severe laryngeal stridor requiring tracheostomy and local effects on the oesophagus eventually leading to stricture formation. In 2 further patients reported in the French (Tschantz and Favre, 1975) and Polish (Wiernikowski and Guzik, 1973) literature (Table 1), poisoning was intentional and the resultant complications were more severe. These included renal failure, intravascular haemolysis, bleeding and necrotizing haemorrhagic pancreatitis. One patient died.

Experience of the present 3 cases confirms that deliberate poisoning is associated with grave consequences (Table 1).

The complications were manifest within hours of ingestion. The coagulation defects which gave rise to bleeding were probably associated with a direct proteolytic action of the acid on the clotting factors, although a consumptive coagulopathy was significant in patient No. 3. In none of the patients did the bone marrow appear to have been affected and reticulocytes were produced in normal numbers. Thrombocytopenia was also seen in patient No. 3 and appears to have been associated with diffuse intravascular coagulation although cimetidine which the patient was receiving has been reported to cause a fall in platelet count (James and Prout, 1978). With intensive replacement therapy, the clotting defects were short-lived. There was also clear evidence of massive haemolysis which was probably associated with disruption of the erythrocyte cell membrane by the acid. In the case reported by Wiernikowski and Guzik (1973), the concentration of formic acid in the blood stream of the patient 6–7 hr after ingestion of 50 ml of concentrated formic acid was 3 times greater than that required to induce haemolysis of ox erythrocytes *in vitro*. Exchange transfusion is feasible for acute haemolysis and should be carried out early as this may also be beneficial by removing circulating formic acid.

A further complication occurring early is hypoxaemia and respiratory failure which requires intermittent positive pressure ventilation. It is possible that the extensive opacification seen on chest X-ray in patient No. 3 (Fig. 1) was due to inhalation of formic acid. However, the early appearance of lung changes together with the clinical features of hyperventilation and hypoxia may also suggest the occurrence of 'shock lung'. Although the severe acidosis can cause acute pulmonary oedema by a combination of right and left heart failure together with an increase in pulmonary vascular resistance

TABLE 1. Reported cases of formic acid poisoning with associated complications (+ = present; – = absent)

Case no.	Manner and outcome	Acidosis	Derangement of clotting mechanisms	Diffuse intravascular coagulation	Haemolysis	Renal insufficiency	Respiratory failure	Sloughing of gastrointestinal mucosa	Pancreatitis
1. Malizia <i>et al.</i> case 1	A ✓	–	–	–	–	–	–	–	–
2. case 2	A ✓	–	–	–	–	–	–	–	–
3. (Harvey, 1968)	A ✓	–	–	–	–	+	+	+	–
4. (Tschantz and Favre, 1975)	D†	–	–	–	+	+	–	–	+
5. (Wiernikowski and Guzik, 1973)	D ✓	+	–	–	+	+	–	+	–
Present Series									
Case 1	D†	+	+	–	+	+	+	+	–
Case 2	D†	+	+	–	+	+	+	+	–
Case 3	D†	–	+	+	–	+	+	–	–

A = Accidental; D = Deliberate; ✓ = Survived; † = Died.

(Tintinalli, 1977), patient no. 3 was not acidotic at any time. In addition to antibiotics high doses of steroids together with ventilation were used in this patient. Clinically and radiographically there was improvement in the chest signs (Fig. 2) although at post-mortem there was still evidence of fairly gross lung congestion but no inflammatory cell infiltration.

The metabolic acidosis was profound in patients 1 and 2 and large amounts of bicarbonate were necessary to control the arterial pH. A comparison with methanol poisoning is helpful as this is one of the instances in which a zero plasma bicarbonate may occur (Tintinalli, 1977), the acidosis being due to the accumulation of formic acid and formate. In contrast to the acidosis of methanol poisoning (Bennet, Cary and Mitchell, 1953), the acidosis of formic acid poisoning is immediate and relatively brief when treated.

Acute renal insufficiency appears to supervene in most patients and is due to acute tubular necrosis associated with fluid loss, shock and free haemoglobin in the blood. Peritoneal dialysis may be preferable to haemodialysis since the use of heparin in the latter, may aggravate bleeding from the gastrointestinal tract. However, large losses of protein during peritoneal dialysis (Berlyne *et al.*, 1964) may have contributed to the severe hypoalbuminaemia and circulatory collapse in patient no. 3.

Intravenous nutrition is important and should be commenced as early as possible since naso-gastric feeding may be hazardous in view of the risk of oesophageal perforation. Steroids are reported to reduce the amount of oesophageal scarring and stricture formation in cases of ingestion of strong corrosive alkalis and may have contributed to the little damage of this kind in patient no. 3. Significantly, in the surviving patient with deliberate formic acid poisoning reported by Wiernikowski and Guzik (1973), early treatment with hydrocortisone was instituted. Intravenous cimetidine was given to the present patients, but reports of its value in other instances of gastrointestinal bleeding have been disappointing (Kang *et al.*, 1977). The terminal haemorrhage in case 1 occurred despite cimetidine treatment.

The complications of formic acid intoxication are, therefore, widespread but are all potentially treat-

able. The authors recommend the use of high dose steroids to limit gastrointestinal damage and total parenteral nutrition *ab initio* to avoid the possible danger of oesophageal perforation if nasogastric feeding is attempted. The infusion of clotting factors and exchange transfusion should be resorted to early since both the derangement of clotting mechanisms and intravascular haemolysis appear to be short-lived when treated. Ventilation is necessary for the acute respiratory failure which may perhaps also be improved by the use of high dose steroids. Peritoneal dialysis is usually necessary although this may aggravate circulatory difficulties. The present authors' experience would suggest that the deliberate ingestion of formic acid is a more serious form of poisoning than has hitherto been reported.

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