

A case of methylene chloride poisoning due to ingestion of home-distilled alcohol and potential new treatment with ethanol infusion

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Clinical record

A 51-year-old man presented with sudden onset of confusion and new onset seizures necessitating intubation. He was reported to be alcohol dependent, consuming more than 25 standard drinks per day, and was a heavy smoker. There was no other medical history of note and the patient was not taking regular medications.

On the day of presentation, the patient was well and followed his typical pattern of alcohol consumption. In the evening, he visited a friend and returned home. Later that evening, his son noted him to be confused and profusely diaphoretic. Shortly after, his son witnessed activity consistent with a tonic-clonic seizure. The seizure was self-limiting and the duration unclear.

The ambulance service was summoned and upon their arrival another brief seizure was witnessed, after which the patient was intubated due to profound coma. Midazolam, fentanyl and suxamethonium were administered to facilitate intubation. Morphine and midazolam infusions were commenced after intubation. Paramedics at the scene recorded a blood glucose concentration of 7.1 mmol/L (reference interval [RI], 3.9–5.8).

Upon arrival at our hospital emergency department, the patient's blood pressure was 135/100 mmHg, his heart rate was 112 beats/min, oxygen saturation was 96%, FiO_2 was 50%, and he had a temperature of 34.3°C. Arterial blood gas analyses revealed a pH of 7.14, PO_2 of 290 mmHg, PCO_2 of 50 mmHg, bicarbonate concentration of 16 mmol/L and base excess of -14 mmol/L. The lactate level was 6.6 mmol/L (RI, 0.5–1.6 mmol/L), sodium concentration was 138 mmol/L (RI, 136–146 mmol/L) and chloride concentration was 110 mmol/L (RI, 96–106 mmol/L).

A lumbar puncture and computed tomography (CT) scan of the brain were performed, and both were unrevealing. After transfer to the intensive care unit, an unexplained rising carboxyhaemoglobin (COHb) concentration was noted on blood gas analysis. The initial concentration was 12.2%; by 7 hours into his admission, the concentration had increased to 20.3% despite ventilation with an FiO_2 of 50%. The COHb concentration continued to rise and peaked at 29% 11 hours after admission, despite 100% oxygen. Concurrent with this, carbon dioxide concentrations were difficult to control. Despite a minute volume of

ABSTRACT

We describe a case of a 51-year-old man who ingested methylene chloride and presented with the classical clinical features. He developed an acute abdomen that required repeated laparotomy. The effect of an ethanol infusion on carboxyhaemoglobin concentrations in this case was also of interest and could potentially be a new treatment modality.

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15 L, carbon dioxide concentrations remained at around 45 mmHg, limiting compensatory attempts to counter the metabolic acidosis.

During the first few hours of intensive care, the patient developed a distributive shock, confirmed with pulse contour analysis of the femoral arterial line. Renal replacement therapy was commenced because of worsening acidosis and oliguria.

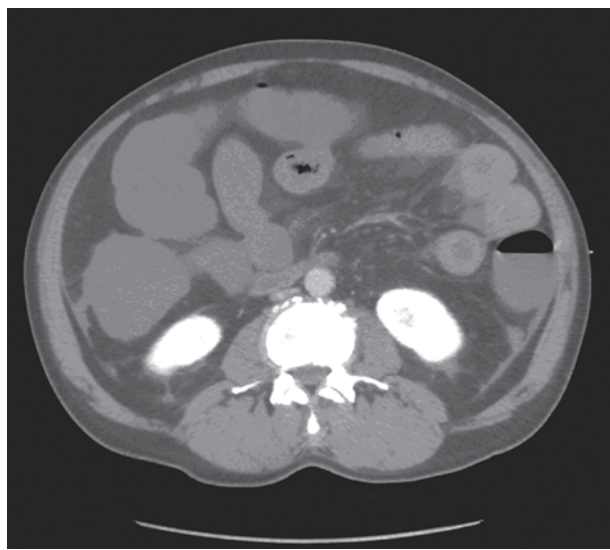
An osmolar gap was calculated from a serum sample taken 10 hours after admission. Measured serum osmolarity was 315 mmol/L and the osmolar gap was 20 mmol/L (RI, <12 mmol/L). A toxicologist's opinion was sought immediately, given the unexplained metabolic derangements and lack of a clear diagnosis.

The events of the previous evening then became more apparent. While at his friend's house, the patient had consumed an unknown volume of home-distilled alcohol ("grappa"). The friend had obtained this from a third party who did not consume any of the grappa and remained well. The patient was also known to have his own supply of grappa. It is unclear whether he drank any of this on the day of presentation.

Given the history of home-made distilled alcohol use, widened osmolar gap and a rising COHb concentration despite ventilation with a high FiO_2 , the possibility of methylene chloride and a toxic alcohol (most likely methanol) ingestion were raised. Unfortunately, no laboratory was available to perform measurements of methanol or methylene chloride concentration on patient samples.

The potential methylene chloride-induced COHb was treated with 100% oxygen. The potential toxic alcohol

Figure 1. Computed tomography scan showing non-enhancement of small bowel wall and loops of thickened bowel consistent with ischaemia

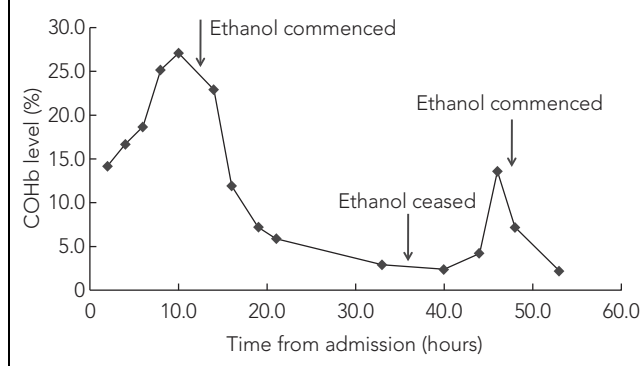


component was treated with alcohol dehydrogenase (ADH) inhibition. Thus, an ethanol infusion was commenced with target concentration range of 22–44 mmol/L. High flux renal replacement therapy was instituted and calcium folinate was commenced as cofactor therapy. Fomepizole was not available for administration.

Concurrent with the toxicology referral, urgent CT scan of the abdomen and an urgent surgical referral were arranged because of progressive abdominal distension and large-volume reddish-brown nasogastric aspirates (700 mL). The CT scan revealed signs of ischaemic bowel (Figure 1). At the initial laparotomy, which took place 14 hours after admission, ischaemic, but not infarcted, small bowel was noted. A thrombus in the superior mesenteric artery was also removed. The abdomen was left open, given the high likelihood of raised intra-abdominal pressures. A re-look laparotomy was planned for the next day. A faecal containment device was inserted and this drained 2800 mL of reddish-brown fluid in the first 48 hours. The reddish-brown appearance of the fluid was thought to be possibly related to a corrosive mucosal injury, but equally could have resulted from the ischaemic insult. An emergency laparotomy was undertaken early on Day 2 because of progressive abdominal swelling. About 25 cm of infarcted small bowel was removed.

The ethanol infusion was ceased on Day 2, for reasons that are not clear from reviewing the case file. Of note, the ethanol infusion was recommenced 12 hours later (48 hours after admission) because the COHb concentration, which had been less than 5%, rose to 15% despite an FiO_2

Figure 2. Plot of carboxyhaemoglobin (COHb) concentration over time



of 50% (Figure 2). A fall in the COHb level was seen after ethanol was reintroduced.

At a repeat laparotomy on Day 3, a small section of non-viable small bowel was removed and the abdomen was closed. Over the next few days, the distributive shock resolved. The ethanol infusion was ceased on Day 5 and there was no rebound rise in the carbon dioxide level. The patient was extubated on Day 9, taking some time to wake from the opioid and benzodiazepine coma. At the time of extubation, there was a mild delirium but no visual symptoms were apparent.

Nutrition was supplied parenterally until Day 9, when nasogastric feeds were introduced. At ICU discharge, the patient remained anuric and on renal replacement therapy. High-output diarrhoea persisted for the entirety of the ICU admission but eventually settled.

After ICU discharge, the patient remained on haemodialysis for a 4 weeks. His renal function eventually recovered completely, with estimated glomerular filtration rate above 90 mL/min. The patient had a brief return to ICU 19 days after admission for a transient unexplained reduction in conscious state, which required intubation. Magnetic resonance imaging and electroencephalogram were unremarkable, and there were no obvious neurological sequelae.

In addition to the complex medical issues, this case raised public health concerns. Given the likelihood of a toxic ingestion, and the possibility of others being exposed, the Victorian Department of Health was notified. The patient's family was asked to contact the individual who provided the distilled alcohol. Two samples were obtained for analysis — one from the friend's grappa and another from the patient's supply. The patient's family had stated that he never made his own grappa but always bought it from local home distillers. The friend was advised to discard the remainder of the substance, because of its likely toxicity. Both samples were forwarded to a Department of Health laboratory. The

sample from the friend was positive for methylene chloride (12 mg/L) and methanol (140 mg/L). The patient's grappa supply was positive only for methanol (1900 mg/L).

Based on case reports that demonstrated acute human toxicity following oral ingestion of methylene chloride in amounts of 384–4794 mg/kg body weight, the Department's report concluded that although methylene chloride was detected in the sample consumed by the patient, the concentration was insufficient to explain his grave clinical state. It suggested that the patient could have consumed methylene chloride from another source.

As the product was made for personal use with no commercial transactions involved, and no other individuals had been reported to become unwell in a similar fashion, there was no further Department investigation into this matter. The origin and distributor of the specific grappa consumed by the patient was unknown. This made it difficult to issue anything other than generic advice about the risks of home-distilled alcohol.

Discussion

Methylene chloride (also known as dichloromethane) is a clear, colourless, volatile liquid used as an industrial chemical and commonly found in paint stripping products, but has many uses including degreasers, aerosol propellant (eg, for paint sprays), blowing agent for polyurethane foams, photographic film and electronics production and plastics manufacture.

Poisoning occurs when this substance is either inhaled, ingested or absorbed dermally.¹⁻⁴ Occupation exposure via inhalation is the most significant as it can cause pneumonitis. Ingestion may cause gastrointestinal corrosion, haemorrhage, and necrosis.⁵ Skin contact produces burning sensation, numbness and pain, and burns have been reported. All routes can cause systemic effects, including altered state of consciousness, seizures and production of carboxyhaemoglobin (COHb).⁶

Methylene chloride is rapidly absorbed via the inhalational and oral routes.⁴ It is metabolised slowly to carbon monoxide (CO) via the cytochrome P450 mixed function oxidase system (including CYP 2E1). Carbon dioxide, formaldehyde and inorganic chloride are also products of liver metabolism. Non-metabolised methylene chloride is excreted unchanged via the lungs, as are its metabolites CO and carbon dioxide.⁶⁻⁸

Unlike inhalational CO poisoning, the elevated COHb following methylene chloride exposure is usually less marked but has an apparent longer half-life and can persist for hours to days.^{3,7}

The carbon dioxide production explains the difficulty in managing the respiratory acidosis despite large minute volume ventilation in this patient.

Methylene chloride has direct solvent toxicity (causing central nervous system depression) and toxicity due to its CO metabolite. Among solvents commonly used in household or industrial settings, methylene chloride is the only agent to cause an elevated COHb concentration — prolonged, high COHb concentration after ingestion of an unknown solvent is pathognomonic of methylene chloride poisoning. Interestingly, the most widely available paint stripper in the local chain of hardware stores contains 87% methylene chloride and 13% methanol.

Toxicity usually manifests within 1–2 hours of significant exposure. In severe cases, as seen with this patient, hypotension, respiratory depression, coma, convulsions, pulmonary and cerebral oedema, cardiac arrhythmias and cardiac arrest can occur.⁶ Hepatic injury and renal toxicity, including anuria, haematuria and renal tubular necrosis, have been reported previously.³ A reduced oxygen carrying capacity secondary to COHb also contributes to organ ischaemia.

Management is supportive, with meticulous fluid balance, inotropes as required, dialysis for renal failure and acidosis, and 100% oxygen for hypoxia and elevated COHb.⁹

There are a few case reports of the use of hyperbaric oxygen (HBO) therapy in methylene chloride-induced COHb,^{10,11} but there is no high-quality evidence supporting its routine use.⁶ In fact, the hospital with the only hyperbaric chamber in our city is not supportive of the use of HBO for CO poisoning, even from the more common inhalational exposures. Thus, HBO is not a therapeutic option for methylene chloride poisoning in our region.

Interestingly, the ethanol infusion used to treat the presumed concomitant methanol poisoning in our patient also decreased the production of COHb. This was an inadvertent discovery that seemed to attenuate both the toxic alcohol toxicity and methylene chloride-induced COHb. It is thought that as ethanol inhibits cytochrome P450 2E1, it competitively inhibited the metabolism of methylene chloride and thus, production of its metabolites.¹²

Fomepizole is not readily available in Australia and ADH inhibition was achieved using ethanol. ADH inhibition is required to prevent metabolism of the toxic alcohol to its acidosis-producing toxic metabolites while dialysis clears the parent compound. The effect of an ethanol infusion of inhibiting methylene chloride-induced COHb has not previously been reported.

CASE REPORTS

Conclusion

This case demonstrates the severe toxicity of methylene chloride ingestion with multiorgan system failure and corrosive injury to the gastrointestinal tract. It also highlights the need to be suspicious of a rising COHb when an unknown solvent is ingested, as it is pathognomonic of methylene chloride poisoning.

Home-distilled alcohol is known to be fraught with problems and is well documented to be associated with methanol toxicity but occasionally can also be the source of inadvertent ingestion of other solvents, such as methylene chloride.

Although the Department of Health report concluded the grappa ingested by the patient had insufficient concentrations of methylene chloride, the temporal relation between the consumption of the grappa and his rapidly deteriorating clinical state would suggest that the home-distilled grappa may have been at least contributory. However, it is noted that the patient was drinking in his garage at the time of his collapse and may have inadvertently consumed another product containing methylene chloride.

Interestingly, the use of an ethanol infusion, initially used to treat the suspected toxic alcohol ingestion, also contributed in preventing the production of COHb by inhibiting the metabolism of methylene chloride and should be considered in all methylene chloride ingestions.

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Competing interests

None declared.

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