

A case of methanol poisoning

甲醇中毒個案

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A 29-year-old male took about 300 ml industrial alcohol in a suicidal attempt. The industrial alcohol was later confirmed to be methanol. He presented to the emergency department 10 hours post-ingestion with an anion gap metabolic acidosis and an osmol gap of 76.7 mOsm/kg. Ethanol infusion was started in the emergency department at 11 hours post-ingestion before the availability of serum methanol level. The clinical diagnosis of toxic alcohol ingestion was based on the history, arterial blood gases results and the presence of a significant osmol gap. The patient was then admitted to the intensive care unit for ethanol therapy and haemodialysis. Prompt initiation of ethanol therapy and the subsequent intensive care prevented the development of life-threatening complications of methanol poisoning in this case. (*Hong Kong j.emerg.med.* 2007;14:94-98)

一名 29 歲的男子服下 300 毫升工業酒精企圖自殺。而工業酒精其後被證實為甲醇。服毒後 10 小時他到急症室求診，呈現陰離子差代謝性酸中毒及滲透差 76.7 毫滲克分子／公斤。在獲得血清甲醇水平之前，急症室已於服毒 11 小時後開始輸注乙醇。基於病歷，動脈血液氣體化驗結果及存在相當大的滲透差，臨床診斷為服下有毒酒精。病人其後被收進深切治療部作乙醇治療及血液透析。迅速展開乙醇治療及其後的深切治療防止了這甲醇中毒個案發展威脅生命的併發症。

Keywords: Acidosis, alcohols, ethanol

關鍵詞：酸中毒、酒精、乙醇

Case report

A 29-year-old male took about 300 ml industrial alcohol and a small amount of red wine in a suicidal attempt in August 2005. He was brought to the emergency department 10 hours later. On arrival, he

was asymptomatic. The initial vital signs were: GCS 15/15, BP 126/82 mmHg, pulse rate 67/min, temperature 36.6°C, respiratory rate 16/min, and oxygen saturation of 100% on room air. The physical examination was normal and there was no visual impairment.

Blood was drawn at 10 hours post-ingestion for arterial blood gases on room air. The initial results were: pH 7.28, pCO₂ 27 mmHg (3.6 kPa), pO₂ 114 mmHg (15.2 kPa), HCO₃⁻ 12.4 mmol/L, base excess -12.6 mmol/L, Na⁺ 146.6 mmol/L, K⁺ 4.3 mmol/L, Cl⁻ 102 mmol/L, anion gap 36.5 mmol/L. Further laboratory tests for the anion gap metabolic acidosis were performed: urea 4.5 mmol/L, spot glucose 6.6 mmol/L, lactate 1.26 mmol/L, ethanol

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undetectable, measured serum osmolality 381 mOsm/kg. The calculated serum osmolality was 304.3 mmol/L, with an osmol gap of 76.7 mOsm/kg. Based on the history and laboratory findings, toxic alcohol ingestion was diagnosed and treated accordingly. The methanol level at 10 hours post-ingestion was 61.2 mmol/L (Table 1) although the result was only available at about 12 hours after admission (22 hours post-exposure).

The patient was treated by a loading dose of 400 ml 10% ethanol (7.2 ml/kg) infusion over 30 minutes in the emergency department. It was prepared by 40 ml 100% ethanol made up to 400 ml with 5% dextrose solution. He was admitted to the intensive care unit (ICU).

In the ICU, 10% ethanol infusion was continued at a rate of 50 ml/hr (0.9 ml/kg/hr). The metabolic acidosis was slightly improved at 14 hours post-ingestion, with an anion gap of 33.8 mmol/L. Because of the presence of significant metabolic acidosis and high osmol gap, haemodialysis with an ultrafiltration rate of 50 ml/hr was started. The ethanol infusion rate was gradually increased to 150 ml/hr (2.7 ml/kg/hr) during haemodialysis due to persistent suboptimal blood ethanol level. During ethanol infusion, the patient remained fully conscious (with arousable sleeps) and there was no hypoglycaemic episode. Intubation was not needed in this case. Folic acid 50 mg intravenously (IV), thiamine 50 mg IV, and pyridoxine 250 mg IV were also given in the early phase of treatment.

The metabolic acidosis and osmol gap were rapidly corrected after the initiation of haemodialysis. At 28 hours post-ingestion, the osmol gap was normalized

and the metabolic acidosis was nearly completely corrected. Haemodialysis was therefore stopped, with ethanol infusion continued at a slower rate of 100 ml/hr (1.8 ml/kg/hr). Ethanol infusion was eventually stopped at 49 hours post-ingestion after confirming a low methanol level. Figure 1 shows the changes of the anion and osmol gaps, methanol and ethanol levels during the clinical course.

The total ICU stay for this patient was 55 hours. The patient was all along asymptomatic. There was a slightly elevated amylase level of 102 IU/L (normal <100) at 19 hours post-ingestion. Ophthalmologist examination showed no abnormal findings. Psychiatrist consultation was arranged and a diagnosis of parasuicide episode was made. The patient was discharged home after a hospital stay of four days.

Discussion

Methanol poisonings have been reported in both western and Chinese literatures. As methanol is cheaper than ethanol, it is sometimes used to fortify illicit spirits in developing countries. Mass poisoning outbreaks with significant mortality and morbidity can occur.¹ In Hong Kong, sporadic cases of methanol poisoning usually resulted from suicidal attempt after the consumption of methanol containing products. Classically, methanol is used as antifreeze in windshield washing fluids and fuel deicing agents.² However, antifreeze is not commonly used in Hong Kong. Instead, methanol is used as an industrial or laboratory solvent, and also as a fuel source for picnic stove or alcohol lamp. Although industrial alcohol usually refers to highly concentrated ethanol, there are reports in

Table 1. Blood test results

Time post-ingestion (hour)	10	24	28	40	52
pH	7.28	7.44	7.45	7.38	7.43
Base excess (mmol/L)	-12.6	-1.3	-0.6	-2.0	-0.5
Anion gap (mmol/L)	36.5	20.6	19.5	19.6	16.9
Osmol gap (mOsm/kg)	76.7	-3.6	-15.3	-2	-6.8
Serum methanol (mmol/L)	61.2	8.7	3.6	3.6	—
Serum ethanol (mmol/L)	0	13.7	15.3	30.1	2.1

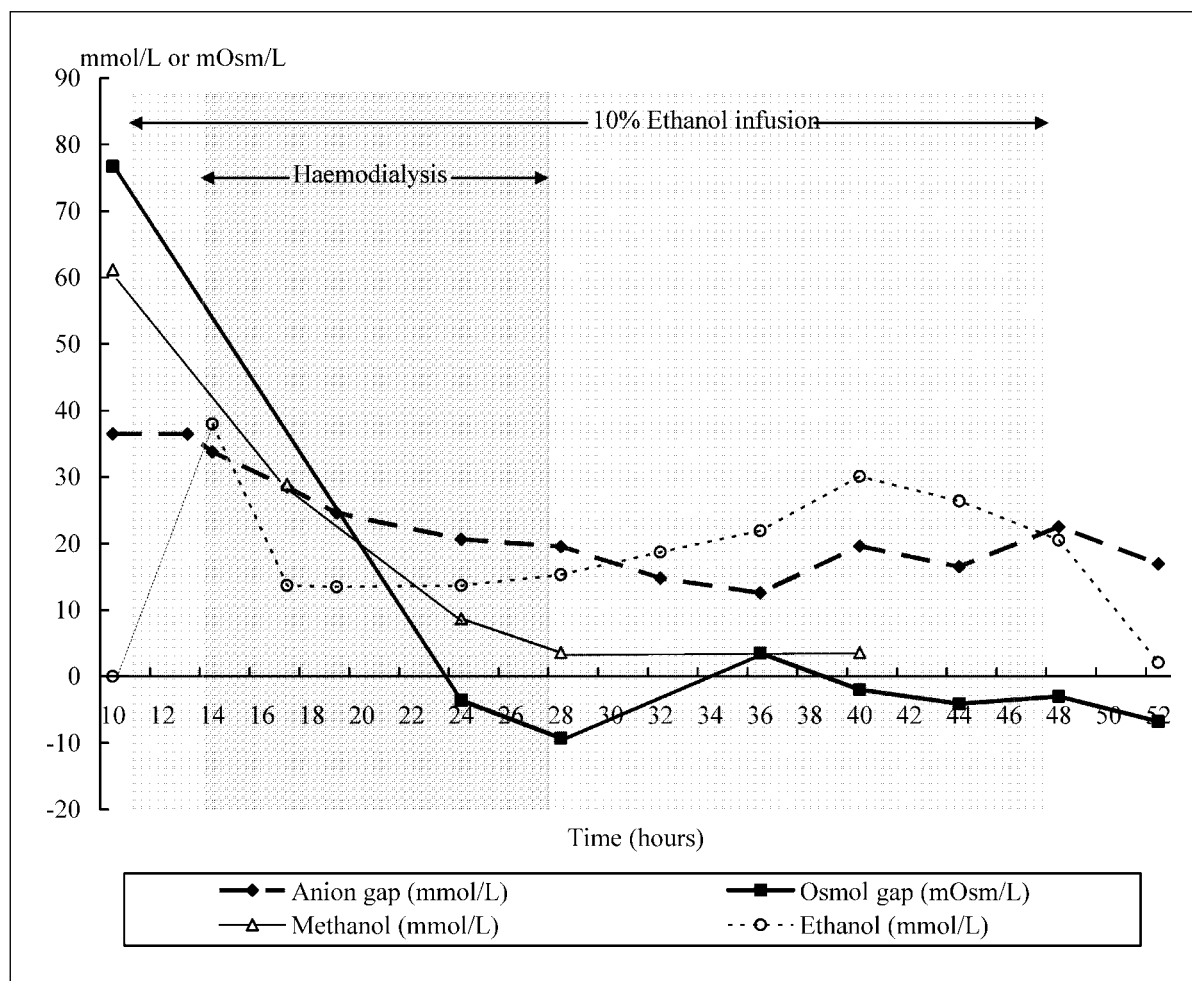


Figure 1. Anion gap, osmol gap, methanol and ethanol levels during the clinical course.

the Chinese literature that methanol is also marketed as industrial alcohol. Being in close geographic proximity to China, we may encounter imported cases of methanol poisoning, and possibly local outbreaks secondary to imported illicit spirits.

The diagnosis of methanol poisoning is made by a combination of a history of suspected toxic alcohol intake, clinical features, and laboratory tests. Diagnostic and treatment guidelines are available in major literatures.^{3,4} A documented plasma methanol level greater than 6.25 mmol/L (20 mg/dL) is diagnostic of methanol poisoning.⁴ However plasma methanol level may not be readily available. One should not wait for a methanol level before initiating treatment in cases of clinically suspected methanol poisoning as

illustrated by our case. In emergency situation, the osmol gap and arterial blood gases are more useful in making the diagnosis and assessing the severity of methanol poisoning.

The osmol gap is a rapid approximation of the unmeasured, osmotically active substances in the serum based on the difference between the measured osmolality and the calculated osmolarity. In methanol poisoning, the osmol gap estimated the methanol concentration in blood:

$$\begin{aligned} \text{Osmol gap } (O_G) &= \text{Measured osmolality } (O_M) - \\ &\text{Calculated osmolarity } (O_C) \\ \text{Calculated osmolarity } (O_C) &= 2 (\text{sodium}) + \text{glucose} \\ &+ \text{urea} + \text{ethanol} \end{aligned}$$

*All units expressed as serum concentration in mmol/L. Note that American textbooks have a different calculation method as they are not using SI units.

The range of normal osmol gap is -2 ± 6 mOsm/L. Toxic alcohol ingestion should be suspected if an osmol gap is greater than 10 mOsm/L. When the osmol gap is greater than 50 mOsm/L, it should be considered nearly diagnostic of toxic alcohol ingestion.⁵ However, a normal or negative osmol gap does not rule out toxic alcohol poisoning. For example, a person with a baseline osmol gap of -8 mOsm/L will still have a negative osmol gap (about -2 mOsm/L) when the plasma methanol level reaches the potential toxic level of 6.25 mmol/L (20 mg/dL). Moreover, late in the course of methanol poisoning, the blood methanol level falls as methanol is metabolized into formic acid. Formic acid is charged and electrically balanced by sodium, and therefore, does not contribute to the osmol gap.³ Consequently, the osmol gap can be normal despite of clinical methanol poisoning with delayed presentation.⁶

Arterial blood gas analysis is a rapid way of determining serum pH, bicarbonate and anion gap. Clinical symptoms and mortality in methanol poisoning correlate closely with the degree of metabolic acidosis.^{1,3,7} The generation of formic acid and, to a lesser extent, lactic acid contributes to the anion gap metabolic acidosis during methanol poisoning. However a significant anion gap may not be present early in the course of methanol poisoning, as the rate of formic acid production is limited by the alcohol dehydrogenase (ADH) pathway. Moreover in patients with methanol ingestion and concomitant ethanol ingestion, methanol metabolism is inhibited and metabolic acidosis may not be evident. So the absence of anion gap metabolic acidosis cannot exclude the possibility of methanol poisoning.⁶

The management of a patient with methanol poisoning includes inhibition of the metabolism of methanol into formic acid with either fomepizole or ethanol, correction of metabolic acidosis with sodium bicarbonate, increasing the metabolism of formic acid

to carbon dioxide by the administration of folic acid or folic acid, and arrangement of haemodialysis if necessary.³ Both fomepizole and ethanol are potent inhibitors of ADH, and are considered as effective antidotes in methanol poisoning. Fomepizole has been available in Hospital Authority's hospitals since July 2006. Because of the high acquisition cost, fomepizole should be reserved for patients who have contraindications to ethanol infusion. These include: (1) children, which are prone to ethanol-induced hypoglycaemia; (2) patients on disulfiram, or developing disulfiram-like reactions upon ethanol infusion; and (3) patients with history of alcohol-induced pancreatitis.

Ethanol is a competitive antagonist of ADH. Its affinity for ADH is estimated to be 10 times greater than that of methanol.³ If administered soon after methanol ingestion, ethanol prevents the formation of formic acid. This inhibition of hepatic methanol metabolism results in a significant increase in the elimination half-life of methanol. It was reported that the median elimination half-life of methanol during ethanol therapy was 43.1 hours (ranged 30.3-52 hours).⁸ The recommended blood ethanol concentration during ethanol therapy is 21.7 mmol/L (100 mg/dL).⁷

In order to attain this blood level rapidly, a loading dose of ethanol of 0.8 g/kg (0.8 ml/kg 100% ethanol) is recommended. Preferably the loading dose is to be given intravenously although oral loading is also acceptable with adjustment of the dosage to account for the oral bioavailability of ethanol. It should be diluted by intravenous fluid (e.g. 5% dextrose) to a 10% ethanol solution, and given intravenously over 20-60 minutes as tolerated by the patient.⁵

To maintain an ethanol concentration of 21.7 mmol/L (100 mg/dL), ethanol has to be administered at rate of 66-130 mg/kg/hr. A higher dose is required in chronic alcoholics (100-154 mg/kg/hr), and in those undergoing haemodialysis (250-350 mg/kg/hr).⁵ The patient should be monitored in an intensive care unit to observe for signs of central nervous system and respiratory

depression, and to monitor the serum ethanol and glucose concentration. Ethanol therapy should be continued until the serum methanol concentration is <6.25 mmol/L (20 mg/dL) and the patient is asymptomatic with a normal arterial pH.³

Once ADH is adequately blocked, the decision to use haemodialysis to enhance the elimination of formic acid and methanol depends on the actual clinical scenario. Indications for haemodialysis in methanol poisoning include significant metabolic acidosis (pH <7.25-7.30), renal impairment, clinically significant poisoning with visual impairment or deteriorating vital signs, or a high methanol concentration >15.6 mmol/L (50 mg/dL).³ In our case, haemodialysis was started early in ICU due to a significant metabolic acidosis. This was later supported by the high methanol level (61.2 mmol/L) before haemodialysis. Without haemodialysis, it will take several days to eliminate such a high methanol level.

During the early phase of ICU treatment, intravenous folinic acid, thiamine and pyridoxine were given. In animal models and in vitro human cell experiments, folinic acid and folic acid enhance the metabolism of formic acid, forming carbon dioxide and water.³ Since the toxic effects associated with methanol poisoning are attributed largely to formic acid accumulation, it is thereby postulated that the administration of folinic acid or folic acid can reduce methanol toxicity. Folinic acid is the metabolically reduced form of folic acid and is the primary bioactive form in enhancing formic acid metabolism. It is therefore the drug of choice in methanol poisoning. If folinic acid is not immediately available, folic acid is a reasonable alternative. The administration of thiamine and pyridoxine in our case was an empirical treatment for possible ethylene glycol poisoning. During the early phase of treatment, it is difficult in distinguishing methanol poisoning from ethylene glycol poisoning. With the confirmation of an undetectable blood ethylene glycol level, thiamine

and pyridoxine were no longer needed in the treatment of the methanol poisoning.

In conclusion, this case illustrates how methanol poisoning can be diagnosed in the emergency setting without the immediate availability of blood methanol level. Early initiation of ethanol therapy, enhanced elimination with haemodialysis and ICU supportive care in this case prevented the development of life-threatening complications, despite a relatively high initial methanol level.

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