

## METHANOL POISONING, CASE REPORTS AND LITERATURE REVIEW

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### Abstract

Acute methanol poisoning produces severe metabolic acidosis, increased anion and osmol gaps. These metabolic disturbances are chiefly due to accumulation of formic acid which can lead to serious neurological sequelae. If renal dysfunction develops then rapid deterioration and increased mortality can occur. Early diagnosis and treatment can reduce the morbidity and mortality. Treatment includes infusion of sodium bicarbonate and administration of ethanol parenterally or orally to inhibit the production of formic acid from methanol. Haemodialysis helps the removal of methanol and formic acid from circulation and also corrects the acidosis. Two cases of methanol poisoning are described. Both patients took a mixture of methanol and ethanol in different amount with different outcomes.

### Introduction

Methanol (methyl alcohol) is a colorless, volatile liquid used as a solvent in various industrial products like paints, varnishes and antifreeze solutions<sup>1,2</sup>. It is added to ethanol to make denatured spirits which are unsuitable for consumption. In most cases, the minimum lethal dose varies over a wide range from 30-240 ml of 40% methanol.

Acute methanol poisoning is rare in Kuwait, it poses a diagnostic challenge to a physician especially if the patient does not volunteer history of methanol ingestion. In most cases, denatured spirits are ingested because ethanol is prohibited by law and is not easily available. Moreover, spirits are cheaper and when mixed with ethanol gives better "kicks" (euphoria).

Incidence of methanol poisoning among expatriates and some ethnic groups in Kuwait increases during religious feasts and New Year's celebration.

### Case 1

A 30 year old Asian male laborer was admitted in the Medical Department in a tertiary referral centre with a history of severe abdominal pain of one-week duration. Pain was mainly in the epigastrium and right hypochondrium. There was no radiation to the back or shoulders. He had repeated attacks of vomiting of small quantity of watery fluid. Three days prior to admission, he developed decreased urine output and breathing difficulty. On the day of admission, he complained attacks of blurring of vision.

Poisoning was suspected but he vehemently denied the intake of alcohol or any other toxic substances.

At the time of admission, the pulse rate was 100/min which was regular; BP 110/80 mmHg; temperature 36.6 C; respiration 28/min; and peripheral cyanosis was present. He was mildly jaundiced and had a deep sighing type of respiration (Kussmaul's respiration).

Liver was enlarged 3 cm below right costal margin, soft, tender with smooth surface. Spleen was not felt and there was not ascites. Fundus exam. was normal. Initially, pupils were reacting normally.

Initial laboratory investigations showed: blood urea 18 mmol/L; serum creatinine 220  $\mu$ mol/L; serum bilirubin 80  $\mu$ mol/L and ALT 543 u/L. Blood gas analysis showed pH 7.286; PCO<sub>2</sub> 1.62 kPa; PO<sub>2</sub> 10.32 kPa; HCO<sub>3</sub> 5.5 mmol/L; saturation 93.2%, suggesting presence of metabolic acidosis. His renal and liver function progressively deteriorated. Anion gap (Na + K) – (Cl + HCO<sub>3</sub>) was 34.5 mmol/L (N: 8-16 mmol/L). Measured osmolality was 312 mos/kg of water and estimated osmolality 291 mos/kg of water. Hence, osmol gap was 21 m osmol/kg of water (N:10 m osmol/kg of water). Serum amylase was mildly raised. Urine showed no oxalate crystal. He was treated symptomatically with intravenous fluids and antispasmodics. On November 8, 1994 his condition deteriorated further and he told that his symptoms started after he took bottles of a mixture of ethanol and methanol in different proportions. He took it one week prior to admission during religious festival celebrations. He also admitted that he used to drink alcohol.

On day two, he was then shifted to Intensive Care Unit (ICU) at another hospital where he received intravenous sodium bicarbonate and was subjected to haemodialysis. He was also put on dopamine infusion to maintain blood pressure. On day 2 in ICU, he became unconscious, breathing became labored and his pH decreased to 7.1 and PCO<sub>2</sub> to 2.8 kPa.

On day 3 in ICU, his blood gas analysis apparently showed that he was mechanically ventilated. But he continued to deteriorate and his pupils became dilated and fixed. He died the next day. Ethanol was not given as it

was thought that there would be no methanol in the blood. Toxicology report which came later showed long chain fatty acids and a number of industrial stabilizers but no methanol, free formats or ethylene glycol.

## Case 2

A 35-year-old Asian patient was admitted to the Medical Department in our tertiary referral centre with a history of repeated vomiting and epigastric pain of one-week duration. Initially he denied any precipitating factors, however after three days; he admitted taking a mixture of small quantity of methanol and ethanol during New Year's celebration. He continued to take small quantities of this mixture until his admission to the hospital. He denied any visual problems. At the time of admission, he was conscious and oriented; pulse was 80/min; BP 110/80 mmHg, temperature 36.6 C; respiration 20/min. There was epigastric tenderness. Liver was just palpable and there was no splenomegaly or ascites.

Blood investigations showed blood sugar 5 mmol/L, serum bilirubin 27  $\mu$ mol/L; and GGT 102 U/L (N: 15-85 U/L). Hepatitis virology was negative. Serum methanol could not be estimated, as he did not give any history initially. He responded well to symptomatic treatment and was discharged without any complication.

## Discussion

Methanol (wood alcohol) is readily absorbed from gut. Between 5-20% is eliminated from the kidneys and lungs as such. It is metabolized slowly in the body to its toxic products such as formaldehyde and formic acid<sup>1-5</sup>, the former being toxic to retinal cells<sup>5,6</sup>. Both methanol and ethanol are initially oxidized to aldehydes in the presence of alcohol dehydrogenase (ADH). Ethanol has ten times greater affinity for ADH than methanol thus, plasma ethanol

concentration of 30-60 mmol/L can prevent metabolism of methanol, which then eliminated unchanged through kidneys and lungs. This fact plays an important role in the onset of the symptoms and outcome of methanol poisoning. Following methanol ingestion, symptoms appear after 12-24 hours. During this lag, toxic metabolites accumulate before the onset of symptoms of metabolic acidosis. Serum formate level has been shown to correlate better with the clinical findings compared to methanol levels. Clinical manifestations of early stages include: lethargy, headache, nausea and vomiting<sup>1,6</sup>. Patient may present with severe epigastric pain as a result of cases presented, mimicking acute pancreatitis. As severe acidosis develops, Kussmaul's respiration is seen. Visual disturbances in the form of blurred vision and dilated pupils which do not react to light are commonly observed<sup>3,6,7</sup>. Central nervous system may be involved and thus, patient can present with confusion, agitation, stupor, fits, faints or coma<sup>2,7</sup>. Computed tomography may reveal cerebral infarction, especially involving the putamen<sup>1,2</sup>.

Treatment consists of gastric lavage, if the patient is conscious and presents in early stage, Sodium bicarbonate is administered intravenously to combat severe acidosis<sup>5,8</sup>. Various reports suggest that administration of sodium bicarbonate reduces morbidity and mortality. Ethanol administration either parenterally or orally plays the main role in the treatment of methanol poisoning<sup>1,5,7</sup>. It inhibits conversion of methanol to its toxic metabolites. Ethanol, 10% solution in water is given as a continuous infusion. In conscious

patients, ethanol 0.6 gm/kg may be given orally. Haemodialysis is another important technique to remove methanol and formate from circulation and should be used in all cases with ocular manifestation, renal impairment and/or peak methanol >50 mg/dl. Folate (folic acid) is an important cofactor in the oxidation of formate to carbon dioxide and water. Thus, it may play a role as a therapeutic adjunct in the treatment of methanol poisoning<sup>9</sup>.

The two patients mentioned above had ingested mixture of methanol and ethanol in variable proportions. These were the reasons for the late onset of symptoms. Both patients denied initially intake of alcohol, hence, blood levels for ethanol and methanol were not carried out. The first patient presented in the late stages of poisoning with increased anion and osmol gaps, severe metabolic acidosis, renal failure and nervous system involvement<sup>10</sup>. In spite of potent treatment the patient died.

In case 2, the patient mixed a small quantity of methanol with ethanol and thus, escaped from serious complications. In the first case, we assume that the patient consumed a mixture containing methanol more than ethanol, and in amounts sufficient to produce high levels of formate and acidosis. In one report, mortality rate was 44% in those cases who had high CO<sub>2</sub> content.

In conclusion, methanol poisoning should be suspected in any patient presenting with epigastric pain, blurred vision; and laboratory results indicating metabolic acidosis with increased anion and osmol gaps. Early diagnosis and treatment with infusion of ethanol, sodium bicarbonate and haemodialysis can reduce the morbidity and mortality.

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