Methanol poisoning: two cases with similar plasma methanol concentrations but different outcomes

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Methanol poisoning continues to be a serious problem in industrial nations, where numerous commercial products contain potentially toxic amounts of methanol. Methanol is a common component of paints, varnishes, antifreeze solutions, gasoline mixtures and various solvents. Industrial uses are expanding, and the incidence rate of methanol poisoning is likely to increase. Methanol is ingested accidentally or deliberately as a substitute for ethanol and as an agent in suicide attempts. Numerous "epidemics" of methanol poisoning have been reported.[1] The number of cases reported annually in Canada between 1980 and 1987 ranged from 21 to 59.[2] Rapid diagnosis and treatment are necessary to prevent death and to minimize the neurologic sequelae.

Two young women recently presented to our hospital with methanol poisoning. They had similar plasma methanol concentrations at approximately the same time after ingestion, but their different outcomes highlight the factors that affect outcome in methanol poisoning.

Case reports

Case 1

A 17-year-old-woman (patient 1) mistakenly ingested photocopying diluent (methanol) at a party between 2000 and 2400 of day 0. She also consumed ethanol, but the volumes of the alcohols could not be determined. The next day she complained of headache and was lethargic. She was taken to a local hospital on day 2 at 0200, approximately 26 hours after the alcohol had been ingested. Her skin was cold and clammy; she was breathing rapidly, was confused and was in moderate distress. There were no other symptoms and no ocular abnormalities. Her temperature was 35.6°C, pulse rate 102 beats/min, with a regular rhythm, and blood pressure 136/84 mm Hg.

Laboratory tests (Table 1) revealed severe metabolic acidosis, with a serum anion gap (calculated as [sodium (Na) + potassium (K)] − [chloride (Cl) + bicarbonate (HCO_3^-)], where the levels of Na, K, Cl and HCO_3^- are in millimoles per litre) of 45.4 (normally 8 to 16) mmol/L. The plasma methanol concentration was 26 mmol/L, as determined by the method of Solon, Watkins and Mikkelsen.[3] No other toxic substances, including ethanol, ethylene glycol, acetaminophen and salicylates, were detected in the blood.

Over the next 8 hours the patient was given oxygen by mask, saline (1500 mL) and 8.4% sodium bicarbonate (600 mL) intravenously, and 95% ethanol (120 mL) by nasogastric tube. Urine output in the same period was 1220 mL.

The patient was transferred to the General Hospital, St. John's, Nfld., on day 2 at 1145. She was slipping in and out of consciousness but responding to pain; gag and pupillary reflexes were normal. Her temperature was 36°C, pulse rate 122 beats/min, with a regular rhythm, respiration 20 beats/min and regular, and blood pressure 120/80 mm Hg. Edema of the optic discs was noted.

Laboratory tests (Table 1) showed metabolic

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acidosis, with a serum anion gap of 23.3 mmol/L, measured osmolality of 352 (normally 280 to 300) mmol/kg of water and calculated osmolality (calculated as 2Na + glucose [Glu] + urea nitrogen, where the levels of Na, Glu and urea nitrogen are in millimoles per litre) of 294.4 mmol/kg; thus, the osmolar gap was 57.6 mmol/L. The plasma levels of methanol and ethanol were 18 and 35 mmol/L respectively; no other toxic substances were detected in the blood.

The patient underwent hemodialysis for 4 hours; 78 g of ethanol was given during the first hour and 40 g each hour thereafter. After dialysis the patient continued to be given ethanol (10 g/h by nasogastric tube), saline (150 mL/h intravenously) and oxygen (by mask).

By day 3 at 1000 the blood values listed in Table 1 had returned to normal, the plasma ethanol concentration was 39 mmol/L, and there were no traces of methanol in the blood. All treatment was stopped. A blood sample taken early on day 3 showed a peak plasma ethanol level of 53 mmol/L. The patient was discharged on day 6, with no apparent sequelae, and was well 1 year later.

Case 2

An 18-year-old woman (patient 2) who was at the same party as patient 1 also mistakenly ingested photocopying diluent between 2000 and 2400 of day 0. The amount of diluent consumed was not known. Apparently no ethanol was ingested.

The patient was unwell all day 1, with malaise and drowsiness, and was taken to a local hospital on day 2 at 0030, approximately 1½ hours before patient 1 and 24 hours after having ingested the alcohol. She was moribund and not alert and had a major generalized seizure. Two doses of diazepam, 10 and 5 mg, were given intravenously. Her pulse rate was 100 beats/min, with a regular rhythm, and blood pressure 130/66 mm Hg. She had fixed mid-range pupils that did not respond to light. The patient was neurologically depressed, totally flaccid and unresponsive to stimuli, including attempts to elicit reflexes.

Laboratory tests (Table 1) revealed severe metabolic acidosis, with an anion gap of 42.5 mmol/L. The blood sample showed a plasma methanol concentration of 26 mmol/L but no other toxic substances, including ethanol, ethylene glycol, acetaminophen and salicylates.

Over the next 4 hours 3000 mL of normal saline and 100 mL of 8.4% sodium bicarbonate were given intravenously, and 45 mL of 95% ethanol was given by nasogastric tube. Respiratory arrest occurred at 0500. An endotracheal tube was inserted and spontaneous respiration maintained. Therapy with dopamine was started at 7.5 μg/min; the dose was increased to 15 μg/min while the patient was transported to the General Hospital by air ambulance.

At the hospital the patient had no spontaneous movements or respiration and was given oxygen, 16 breaths/min. Her pupils were dilated and fixed, and there were no brain-stem reflexes (gag, cough or blink). Her pulse rate was 160 beats/min and blood pressure 80/60 mm Hg.

Laboratory tests (Table 1) showed severe metabolic acidosis, with a serum anion gap of 40.2 mmol/L, and a measured osmolality of 367 mmol/kg, with an osmolar gap of 43.7 mmol/L. The plasma levels of methanol and ethanol were 19 and 24 mmol/L respectively; no other toxic substances were detected in the blood.

The patient received 20 g of ethanol per hour for 4 hours during hemodialysis. The blood pressure was labile and maintained with dopamine, norepinephrine bitartrate and epinephrine hydrochloride. Saline, 500 mL/h, was given intravenously.

After dialysis the patient continued to be given dopamine (20 μg/min), norepinephrine bitartrate (2 μg/min) and epinephrine hydrochloride (0.02 μg/kg of body weight per minute initially, with increases to

Table 1: Blood values of two patients on day 2 after methanol ingestion

	Patient 1		Patient 2	
Value (and normal range)	0230	1345	0045	1030
pH (7.35–7.45)	7.08	7.23	6.59	7.08
Carbon dioxide				
Partial pressure, mm Hg (35–45)	10.6	20.8	17.7	17.1
Total content, mmol/L (22–32)	3.5	9.6	2.2	5.7
Bicarbonate level, mmol/L (21–26)	3.2	8.9	1.6	5.2
Serum levels, mmol/L				
Sodium (135–145)	145	143	151	154
Potassium (3.5–5.0)	4.6	3.2	5.1	3.4
Chloride (95–110)	101	114	112	112
Glucose (3.6–6.1)	7.0	4.7	15.2	10.4
Urea nitrogen (3.5–7.0)	5.2	3.7	4.3	4.9

0.04 and then 0.12 μg/kg per minute), as well as ethanol (7 and then 40 g/h). An early-morning blood sample on day 3 showed a peak plasma ethanol concentration of 117 mmol/L. The patient's condition continued to deteriorate, and at 0500 on day 3 there were episodes of atrial fibrillation; blood pressure and brain-stem activity were not detectable. Therapy was stopped, and the patient died at 0800.

Discussion

Methanol is absorbed readily from the gut, exhibits zero-order elimination kinetics, has a half-life of 2 to 24 hours and is metabolized slowly to the toxic products formaldehyde and formic acid. Between 10% and 20% is eliminated unchanged through the lungs and 3% through the kidneys.[4] Formaldehyde, which is toxic for retinal cells, does not accumulate, because it is rapidly oxidized to formic acid. The enzyme primarily responsible for methanol oxidation is alcohol dehydrogenase (ADH) in the liver. When ethanol is present it is preferentially metabolized, because it has a greater affinity for ADH than does methanol; the latter is then eliminated by nonmetabolic routes,[1,5] and there is less metabolic acidosis. Plasma ethanol concentrations of 30 to 60 mmol/L are clinically regarded as optimal for saturating ADH and preventing methanol metabolism.

People with methanol poisoning usually present clinically about 24 hours after ingesting the alcohol.[6] The initial narcotic effects of methanol are much milder than those of ethanol. At first the person feels ill, with weakness, headache and nausea. There may be severe epigastric pain similar to that with acute pancreatitis. As acidosis develops, visual disturbances begin. Methanol depresses the central nervous system and may cause confusion, agitation, stupor or coma. An ophthalmic examination may reveal dilated, sluggish pupils, and hyperemia and edema of the optic discs, which may progress to optic atrophy.[7]

Laboratory tests show severe metabolic acidosis, with high anion and osmolar gaps.[8,9] Methanol and formic acid are present in the plasma. The combination of metabolic acidosis, visual problems and abdominal pain should always suggest methanol poisoning.[7] Treatment consists of gastric lavage (in early presentation of a conscious patient), administration of sodium bicarbonate (to rapidly reverse the metabolic acidosis) and ethanol (to inhibit methanol metabolism) and hemodialysis, especially when the plasma methanol concentration exceeds 16 mmol/L.[10,11]

The circumstances surrounding the two patients' ingestion of methanol were similar: the two had been at the same party, they had ingested the methanol at about the same time (although only patient 1 ingested ethanol in addition), the volume of alcohol ingested could not be determined, and apparently no other toxic substances were ingested. As well, approximately 24 to 26 hours after the alcohol ingestion, blood samples from both women showed no ethanol, but the plasma methanol levels were 26 mmol/L. In patient 1 ethanol was absent from the blood sample, probably because the amount ingested was readily metabolized in preference to the methanol. In patient 2, who had not consumed ethanol, methanol would have been more readily oxidized to toxic metabolic products, resulting in more marked metabolic acidosis and a worse clinical presentation. The plasma methanol concentration of 26 mmol/L in the two patients therefore represents different points in the methanol concentration curve; patient 2 was likely to have had an earlier and a larger methanol peak than patient 1. In most reported fatal cases the plasma methanol level was greater than 31 mmol/L, although the toxic dose varied markedly. In addition, there was little relation between the ingested amount, the latent period and the severity of symptoms. The correlation between death and the degree of acidosis was stronger than that between death and the plasma methanol level. Patients who ingested both methanol and ethanol were more likely to survive than those who ingested only methanol.[9]

Patient 2 likely consumed more methanol than patient 1, and in the apparent absence of ethanol the methanol was metabolized more efficiently to formaldehyde and formic acid. This would account for her different outcome despite earlier presentation to the local hospital.

Conclusion

Methanol poisoning should be suspected when metabolic acidosis, epigastric pain, headache and visual disturbances occur in the absence of an odour of alcohol on the breath and significant ethanol levels in the blood. In any case of methanol ingestion (especially when the plasma methanol concentration is more than 16 mmol/L) aggressive treatment with sodium bicarbonate to rapidly correct the acidosis, ethanol to delay the metabolism of methanol to its toxic products and hemodialysis will greatly increase the chances of survival and may prevent ocular damage. The prognosis should not be made on the basis of the plasma methanol level alone: the severity of acidosis and the clinical presentation are better indicators of outcome.

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Conferences

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Oct. 15, 1993: Nursing Clinic Day
North York, Ont.
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Oct. 20-22, 1993: Hygiene and Health Management in the Working Environment — 3rd International Symposium
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Oct. 20-22, 1993: Tobacco-Free Canada — 1st National Conference on Tobacco or Health; organized around the goals and the seven strategic directions of the National Strategy to Reduce Tobacco Use in Canada. Member organizations on the planning committee are: Alberta Health, Canadian Cancer Society, Canadian Council on Smoking and Health, Health and Welfare Canada, Heart and Stroke Foundation of Canada, Nova Scotia Department of Health and Ontario Ministry of Health
Ottawa
Tobacco-Free Canada: 1st National Conference on Tobacco or Health, conference organizer, Taylor & Associates, PO Box 46066, 2339 Ogilvie Rd., Gloucester, ON K1J 9M7; tel (613) 747-0262, fax (613) 745-1846

Oct. 27-29, 1993: 1st North American Regional Conference of Rehabilitation International — Partners for Independence: Models that Work (cohosted by the Canadian Rehabilitation Council for the Disabled and the United States Council for International Rehabilitation)
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Nov. 4-7, 1993: Philosophic Foundations of Bioethics — International Perspectives
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Deadline for abstracts: Apr. 15, 1993
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Nov. 5, 1993: Social Work Clinic Day
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Sept. 18-23, 1994: XIIth International Congress of Neuropathology (in conjunction with the annual meetings of the Canadian Association of Neuropathologists and the American Association of Neuropathologists)
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