MASS METHANOL POISONING: A CLINICO-BIOCHEMICAL ANALYSIS OF 10 CASES

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ABSTRACT

Methanol is a common ingredient in many household products and intoxication can arise easily from inadvertent exposure through ingestion, inhalation or percutaneous absorption. We analysed ten cases of methanol poisoning who presented with visual, neurological and gastrointestinal symptoms, of whom one died and nine were successfully detoxified with ethanol and bicarbonate infusions. Clinical symptoms were not found to correlate with the severity of poisoning. Serum methanol level was found to correlate significantly with arterial pH (correlation coefficient -0.74, p=0.014) and serum standard bicarbonate levels (correlation coefficient -0.87, p=0.001). We found that an arterial pH of <7.33 or a serum standard bicarbonate of <20 mmol/L correlated well with a serum methanol level of >45 mg/dL ie severe poisoning (χ^2 test with Yate's correction factor, p<0.02). We conclude that arterial pH or serum standard bicarbonate levels can be used as surrogate indicators of the severity of methanol poisoning. They can be used to guide physicians in the method of detoxification (ie whether intravenous or oral ethanol or dialysis should be used) whilst awaiting serum methanol levels in cases where the index of suspicion for methanol poisoning is high. Some cases of severe poisoning can be successfully treated with oral ethanol if the intravenous form is not available.

Keywords: *methanol, pH, bicarbonate, detoxification, ethanol*

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INTRODUCTION

Methanol or wood alcohol is a clear, colourless and odourless liquid that is found commonly in household products like antifreeze, varnish, paint thinner, paint remover and windshield wiper fluid. Hence it can easily be consumed by mistake. Methanol itself is harmless but when metabolised by hepatic alcohol dehydrogenase into formaldehyde and formic acid, it causes a severe high anionic gap metabolic acidosis which is directly toxic to body tissues, especially the brain and the eye. The exact lethal dose is not known but it is estimated to be 1 to 2 mL/kg body weight. Methanol can be absorbed through the gastrointestinal tract, through the skin or by inhalation and peak serum levels are attained in 30 to 90 minutes[1,2]. It takes about 24 hours (range 1 to 72 hours) before signs and symptoms of intoxication are manifested. Detoxification is by administering ethanol since the affinity of alcohol dehydrogenase for ethanol is ten to twenty times more than for methanol. Ethanol can be administered orally in less than 40% concentration, or intravenously in less than 20% concentration via a central line. The latter route is preferred if the enteral absorption is suspected or if rapid detoxification is needed. The aim is to maintain a serum ethanol level of 100 to 150 mg/dL. Haemodialysis should be commenced if the methanol levels exceed 50 mg% or if there are visual, mental involvement, severe acidosis or renal impairment. Intravenous sodium bicarbonate should also be given if the pH is less than 7.2 as this will reduce the amount of diffusible formic acid from permeating the blood brain barrier. Folic acid has been shown to increase the rate of formate metabolism in primates and has been recommended for humans with methanol poisoning as the vitamin is quite innocuous. 4-methyl-pyrazole is a potent inhibitor of alcohol dehydrogenase and can be administered orally; however it is still an investigational drug.

An episode of mass methanol poisoning at the Sembawang Drug Rehabilitation Centre gave us the opportunity to study retrospectively the clinico-biochemical markers that could predict severity of poisoning. These can be used to guide the physician in choosing the appropriate mode of detoxification whilst awaiting methanol assays which may not be available in every hospital.

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METHOD

Fifteen detainees from the drug rehabilitation centre were admitted to Changi Hospital; one was comatose whilst the rest had complaints of dizziness, blurring of vision, nausea or epigastric discomfort. History from the warden revealed that they had ingested a cocktail of orange juice and paint thinner. Arterial blood gas, serum urea, electrolytes, creatinine, calcium, magnesium, phosphate, full blood count, liver function tests and blood toxicology were done. Out of the 15 detainees, only 10 were confirmed to have raised methanol levels in the serum. As toxicology assays are not available in our hospital, all the suspected cases were started on oral ethanol whilst awaiting the methanol level. Those confirmed to have raised methanol in the blood had a follow-up sample sent 6 to 24 hours later. The clinical and biochemical data of the patients were traced and analysed retrospectively.

RESULTS

Severe methanol poisoning is present when the serum methanol level exceeds 45 to 50 mg/dL[3-7]. We took 45 mg/dL as the lower limit of severe methanol poisoning. Three out of the 10 patients had mild methanol poisoning with serum methanol levels ranging from 9 to 17 mg/dL. The other 7 patients had serum methanol ranging from 48 to 127 mg/dL ie severe poisoning.

The commonest symptoms reported were blurring of vision (5/10) and nausea/vomiting/epigastric discomfort (5/10). Four had neurological symptoms or signs, namely dizziness or

drowsiness. There was no significant correlation between symptom complex and severity of poisoning ($p>0.05$, χ^2 test with Yate's correction). This may be due to different symptom thresholds in patients. However, it is noteworthy that the only mortality in our series was comatose with papilloedema, fixed, dilated pupils, hypotensive and had a serum methanol of 127 mg/dL.

The results of the blood tests are shown in Table I. We studied the correlation of these laboratory tests with the serum methanol levels. Only serum standard bicarbonate and arterial pH had a significant correlation with the serum methanol level (correlation coefficient -0.87, p=0.001 and correlation coefficient -0.74, p=0.014 respectively). Serum calcium, magnesium, phosphate, alanine amino-transferase (ALT), aspartate amino-transferase (AST), alkaline phosphatase (SAP), creatinine and total white cell count did not have any significant correlation with the methanol level (correlation coefficient, $p>0.05$) (Table I).

We noted that all 7 patients with serum methanol levels above 45 mg/dL had a pH<7.33 and a serum standard bicarbonate <20 mmol/L (Table II). This was statistically significant using the χ^2 test with Yate's correction ($p<0.02$).

Only one patient received intravenous ethanol in spite of which the serum methanol level rose; this was probably due to continued intestinal absorption of methanol which may take up to 9 hours to peak. Haemodialysis was contraindicated in this patient as he was profoundly hypotensive. Nine out of 10 patients were treated with oral ethanol, although in 6 patients, their methanol levels were in the severe range where intravenous ethanol might have been preferred. This was because the first batch of methanol assays took up to one day to be ready, by which time, the follow-up blood samples showed methanol levels which had declined to the undetectable or mild range (Table II). All patients with pH <7.2 received intravenous sodium bicarbonate therapy (3/10).

In the final outcome, one patient died and eight survived without any visual or neurological sequelae (Table II). One patient had a visual acuity of 6/36 at discharge which on follow-up two years later, developed into total blindness in the right eye and counting fingers in the left eye due to optic atrophy.

Table I – Correlation of laboratory tests with serum methanol levels

	Mean	Range	Correlation coefficient	p value
Serum methanol level (mg/dL)	63.7	9 - 127	NA	NA
Standard bicarbonate (mmol/L)	15.64	3.1 - 26.1	-0.87	0.001
pH	7.213	6.636 - 7.404	-0.74	0.014
Total white cell count ($x10^6$/L)	13.27	8.2 - 19.6	0.443	0.25
Serum creatinine (μmol/L)	116	80 - 245	0.585	0.413
Serum calcium (mmol/L)	2.2	1.87 - 2.47	-0.339	0.651
Serum magnesium (mmol/L)	1.02	0.87 - 1.11	0.261	0.572
Serum phosphate (mmol/L)	0.74	0.39 - 1.22	-0.206	0.570
ALT (IU/L)	24	4 - 57	0.661	0.094
AST (IU/L)	55	16 - 249	0.615	0.215
SAP (IU/L)	134	84 - 214	0.318	0.818

DISCUSSION

Although the small number in our series of methanol poisoning does not carry the statistical weight of larger Western series[3,4], it has several important clinical implications.

Of all the clinical symptoms and blood tests analysed, only serum standard bicarbonate and arterial pH correlated significantly with the serum methanol level. Our series shows that a cut-off value of <20 mmol/L for serum standard bicarbonate level or <7.33 for arterial pH correlates very significantly with a serum methanol level >45 mg/dL (ie severe methanol poisoning). Serum bicarbonate and arterial pH can thus be used as surrogate indicators of the severity of methanol poisoning before the actual methanol levels are known. The physician can then quickly decide whether to use oral or intravenous ethanol or dialysis to detoxify the patient. Early detoxification is crucial as methanol has a latent period of up to 72 hours before being metabolised into toxic formaldehyde and formic acid. It is during this window period that ethanol should be administered to mop up the binding sites of alcohol dehydrogenase.

Schwartz et al in 1981, recommended that haemodialysis be started when serum methanol levels exceed 100 mg/dL; they found that conservative treatment with bicarbonate and ethanol was adequate in some moderately poisoned patients[5]. However, other authors later recommended a more cautious level of 50 mg/dL or when there is irreversible acidosis, mental or visual symptoms or when the ingested methanol is more than 30 mL[6,7]. Some even recommend dialysis when the serum methanol exceeds 25 mg/dL[1]. Others recommend the use of intravenous ethanol when the serum methanol levels are from 20 to 50 mg/

Table II – Severity of poisoning vs pH, standard bicarbonate, treatment modality and outcome

Severity of poisoning	mild			severe						
Patient No.	1	2	3	4	5	6	7	8	9	10
Serum methanol (mg/dL)	9	11	17	48	65	83	87	89	101	127
Standard bicarbonate (mmol/L)	25.3	26.1	26.1	13.6	10.6	10	9.1	17.8	14.7	3.1
pH	7.344	7.404	7.397	7.245	7.21	7.184	7.126	7.314	7.273	6.636
Ethanol treatment	oral	oral	oral	oral	oral	oral	oral	oral	oral	i/v
PostRx serum methanol (mg/dL)	6	7	not available	2.5	7	20	11	16	6	130
Outcome at discharge	well	well	well	well	well	impaired vision	well	well	well	dead

dL[6]. It is interesting to note that in our series, 6/7 of the patients with serum methanol more than 45 mg/dL were treated successfully with oral ethanol. It may be that their successful detoxification with oral therapy was possible because they were identified early (within 24 hours) and their gastrointestinal absorption of ethanol was normal. Hence oral ethanol should be commenced if intravenous ethanol is not readily available from the pharmacy. It is recommended that oral ethanol be administered at a loading dose of 800 mg ethanol/kg body weight and a maintenance dose of 80 to 130 mg/kg/hour to maintain a serum ethanol level of 100 to 150 mg/dL. The maintenance dose may have to be increased to 150 mg/kg/hour in the chronic alcoholic or those receiving activated charcoal and up to 250 to 350 mg/kg/hour in those on haemodialysis[1].

CONCLUSIONS

Our study shows that serum standard bicarbonate and arterial pH are reliable indicators of the severity of methanol poisoning; a serum bicarbonate <20 mmol/L or a pH <7.33 would indicate a serum methanol >45 mg/dL. In the event that intravenous ethanol is not available, oral ethanol should be started first. Acidosis should be corrected with intravenous bicarbonate. Some cases of severe methanol poisoning can be treated very successfully with oral ethanol if they are identified early.

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