



METHANOL POISONING; CHALLENGING DIAGNOSIS AND MANAGEMENT WITHOUT FOMEPIZOLE AND ETHANOL.

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ABSTRACT: Acute methanol poisoning produces severe metabolic acidosis, increased anion and osmolal gaps. These metabolic disturbances are due to accumulation of formic acid with has serious neurological sequelae. If renal functions starts deteriorating that is associated with increased mortality. Early diagnosis and treatment can reduce morbidity and mortality. Treatment include infusion of sodium bicarbonate and administration of ethanol orally or parentally to inhibit the production of formic acid from methanol. Hemodialysis is helpful in removal of methanol and its breakdown products from circulation and also in correcting acidosis. We report the case of a boy admitted to the emergency room with a history of acute illness, characterized by nausea, vomiting, blurred vision, and shortness of breath. Arterial blood gases showed severe metabolic acidosis with high anion gap. He had ingested large quantity of alcohol containing methanol. The patient was managed with hemodialysis and strong intravenous hydration. He improved well and made a full recovery.

Key words: Methanol poisoning, Metabolic acidosis,

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BACKGROUND

Methanol poisoning is rarely described in the literature; some cases are reported as accidental ingestion and few cases are reported as deliberate use. For this reason, we report here a case of methanol poisoning which was unusual in its presentation, discussing clinical and laboratory manifestations, management, and evolution. Methanol poisoning should be suspected in any patient presenting with epigastric pain, blurred vision and laboratory results indicating metabolic acidosis with increased anion and osmolal gaps irrespective of renal function tests. Early diagnosis and treatment can reduce the morbidity and mortality.

CASE PRESENTATION

A 20 year old unmarried gentleman, shopkeeper by profession presented with complains of recurrent vomiting and Progressive drowsiness for 36 hours and Blurring of vision, shortness of breath for 12 hours.

He ingested 1 Litre of non-branded locally manufactured alcohol 36 hours ago after which he

had 2 episodes of vomiting, vomiting free period of 24 hours, followed by 9 episodes. At the same time he complained of progressive drowsiness but no h/o irritability, aggressive behavior, headache, fits, blurring of vision at that time. After further 24 hours he developed complain of worsening shortness of but no h/o productive cough, haemoptysis, sweating, palpitations and chest pain. Progressively worsening blurring of vision with no h/o orbital pain, watering, itching or trauma.

EXAMINATION

Patient was lying in bed not fully oriented in time place and person with following vitals: Pulse 112/min (regular), blood pressure 130/80 mm of Hg, temperature 98.6 F, and respiratory rate 30/minute. General physical examination was unremarkable.

Systemic examination revealed Glasgow coma scale=12/15, pupils mid dilated and sluggishly reactive to light, later on patient developed bilateral afferent pupillary defect (APD). Figure-1.



Figure-1. Dilated pupils with b/l afferent pupillary defect

In motor system, he moving all limbs, reflexes normal, plantars down going. Signs of meningeal irritation were negative. Fundoscopy showed disc edema with erythema, hemorrhage at 11 o'clock position on right side. He just appreciated hand movements. Rest systemic examination was unremarkable.

INVESTIGATIONS

CBC normal, RFT's normal, LFT'S normal, BSL normal, Serum amylase and lipase normal.

URINE ROUTINE: PH 5.0, proteins ++, glucose nil, blood ++, WBC 2, oxalates absent (post Urinary bladder catheterization), urinary ketones negative.

ABGs: PH 7.13, PCO₂ = 6.7, PO₂ = 82.2, Sat O₂ = 93%, HCO₃ = 2.2, sodium = 133, chloride = 75, Anion gap = 55.8, Serum osmolality: calculated = 284, measured 304 = osmolal gap 20.

Electrocardiography (ECG), Ultrasound abdomen, Chest x-ray (PA view) normal. Alcohol screen was done only by a private sector lab with special request serum methanol level was 9 mg/dl, ethanol and ethylene glycol levels were negative.

We therefore assumed the possibility of Methanol intoxication, Ethylene glycol intoxication, Lactic acidosis and started managing patient with I/V fluids, I/V NaHCO₃ (total 450 ml was given), Tab

folic acid 5mg through N/G QID, Inj. Thiamine 10mg I/V stat then I/V OD, Tab pyridoxine 50mg through N/G BD, Inj. Omeprazole 40mg I/V OD, Inj. Metoclopramide I/V TID, Inj. Ceftriaxone 1g I/V BID, Inj. Metronidazole 500 mg I/V TID.

Patient underwent a session of haemodialysis for 4 hours through a double lumen catheter placed in right internal jugular vein.

The patient improved progressively after hemodialysis with correction of his metabolic acidosis. Biochemical profile of patient remained stable throughout the hospital stay. (Table-I and II)

	At presentation	After HCO ₃ replacement	After dialysis
PH	7.13	7.2	7.39
PCO ₂	6.7	18.2	41
PO ₂	82.2	88	88
HCO ₃	2.2	11.7	23
ANION GAP	55.8	46.3	12

Table-I. Evolution of acid base balance

	Day 1	Day 3	Day 5
UREA mg/dl	25	28	30
CREATININE mg/dl	0.6	0.5	0.8
ALBUMIN g/l	4.4	4.0	3.9
GLUCOSE mg/dl	123	108	117
AST	35	40	38
ALT	30	38	28
LDH	288	250	221

Table-II. Trend of laboratory findings

Ophthalmology department prescribed lutein 10 mg/day as even after dialysis patient was having limited colour vision. He was given lutein therapy for 6 months during which patients colour vision gradually turned to normal.

MRI brain with contrast was done on next day of dialysis and showed subcortical white matter and basal ganglia hyper-intensity and low-signal-intensity bilateral putaminal foci.

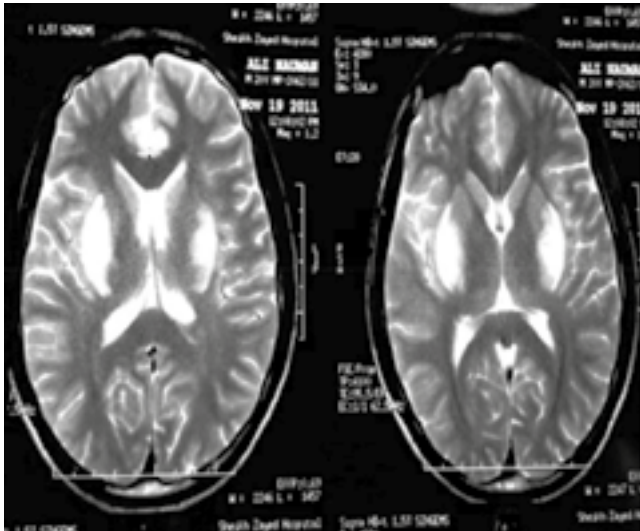


Figure-2. MRI Brain with contrast

Patient was followed for 18 months during which his examination and investigations were unremarkable.

DISCUSSION

Methanol is a chemical with the formula CH_3OH (often abbreviated MeOH) and is very toxic to the humans. Methanol acquired the name “wood alcohol” because it was once produced chiefly as a byproduct of the destructive distillation of wood. Today, industrial methanol is produced in a catalytic process directly from carbon monoxide, carbon dioxide, and hydrogen. The pathways for poisoning are inhalation, cutaneous, and digestive tract, in most cases by swallowing. Methanol poisoning in children is rare and there are only isolated reports of homicidal poisoning and seizures.^{1,2}

Methanol is the simplest alcohol being only a methyl group linked to a hydroxyl group. It is a light, volatile, colorless, flammable liquid with a distinctive odor very similar to that of ethanol (drinking alcohol).³ However, unlike ethanol, methanol is highly toxic and unfit for consumption. At room temperature, it is a polar liquid, and is used as an antifreeze, solvent, fuel, and as a denaturant for ethanol. It is also used for producing biodiesel via trans esterification reaction. Clinical features are inebriation progressing to coma, seizures and

extra-pyramidal features, confusion, agitation, stupor, fits, faints, coma,^{4,5} blurring of vision, disc edema, retinal sheen, Optic neuritis, Ischemia or hemorrhage in basal ganglia especially putamen⁵, nausea, vomiting, abdominal pain, pancreatitis, hypotension progressing to shock, tachypnea. The clinical manifestations of methanol poisoning are well summarized by the stages of intoxication which are described as follows.

In the first phase, there is minimal decrease in central nervous system activity, weakness, dizziness, and nausea.

The second phase is marked by the development of metabolic acidosis characterized by vomiting, abdominal pain, confusion, visual disturbances, photophobia, blurred vision, bilateral mydriasis, unresponsiveness to light, and occasional blindness.

In the third phase, in direct relation to the degree of metabolic acidosis, neuronal injury occurs with retinal necrosis and hemorrhage in the basal ganglia of the brain. At this stage there is hypotension, coma, and Kussmaul breathing. Our patient was considered to be in the third phase of methanol toxicity.

Diagnosis of methanol poisoning is based on the suspicion of ingestion, the presence of visual disturbances, the onset of metabolic acidosis with elevated anion and osmolal gaps, and markedly increased liver enzymes.

Confirmation is by determining the plasma levels of methanol. The toxic methanol dose is 10–30 mL (100 mg/kg), although lower intakes have caused blindness. It is lethal above 60–240 mL (340 mg/kg). A dose of 30 mL of 100% methanol can be considered fatal.

Concentrations above 0.2g/L are toxic, values higher than 0.5g/L indicate severe poisoning, and concentrations above 0.9g/L are potentially deadly. Serum formate levels have been shown to correlate better with the clinical findings compared to methanol levels. If ingested, as little

as 10 ml of pure methanol can cause permanent blindness by destruction of optic nerve; 30 ml is potentially fatal, although the median lethal dose is typically 100 ml (1-2 ml/kg of pure methanol).⁶

Methanol is rapidly absorbed from the gastrointestinal tract, giving peak plasma levels after 30–90 minutes. The serum half-life ranges from 14 to 30 hours and is distributed freely. Metabolism is hepatic. Excretion is Pulmonary/renal. The kidney, in untreated patients, removes less than 5%.

Treatment consists of gastric lavage, if the patient is conscious and presents in early stage, sodium bicarbonate is administered intravenously to combat severe acidosis.⁷ Various reports suggest that administration of sodium bicarbonate reduces morbidity and mortality. Ethanol administration either parentally or orally plays the main role in the treatment of methanol poisoning.⁵ It inhibits conversion of methanol to its toxic metabolites. 10% solution is given as a continuous infusion. In conscious patients, ethanol 0.6gm/kg may be given orally. In developed countries fomepizole is used in methanol toxic ingestion and acts to inhibit the breakdown of this toxin into their active toxic metabolites. Fomepizole is a competitive inhibitor of the enzyme alcohol dehydrogenase⁸, found in the liver. By competitively inhibiting the first enzyme in the metabolism of methanol, fomepizole slows the production of the toxic metabolites. The slower rate of metabolite production allows the liver to process and excrete the metabolites as they are produced, limiting the accumulation in tissues such as the kidney and eye. As a result, much of the organ damage is avoided. Fomepizole is most effective when given soon after ingestion of ethylene glycol or methanol. Delaying its administration allows for the generation of harmful metabolites.⁹ In developing countries like Pakistan fomepizole is not used due to unavailability but our case has shown that even without using fomepizole and i.v

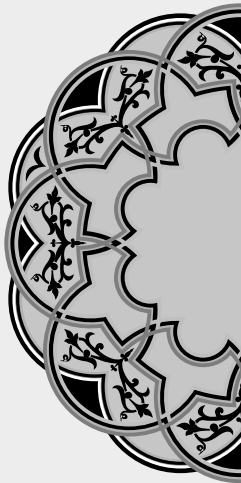
ethanol, methanol intoxication can be treated.

Hemodialysis 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 greater than 50mg/dl. Folate 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.¹⁰

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*“By learning you will teach;
by teaching you will learn.”*

Latin Proverb

AUTHORSHIP AND CONTRIBUTION DECLARATION

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