Case Report

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Rare Case Report on Methanol Toxicity and Early Diagnosis and Successful Management

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Abstract

Mortality associated with methanol has been of great concern. Methanol is also known as methyl alcohol, wood alcohol, spirit and carbinol. The occurrence of cases has been prevalent in developing nations especially in low socioeconomic status people mainly in countries like India, Cambodia, Kenya, Libya, Indonesia, Equador, Estonia, Nicaragua, Pakistan, Turkey, Uganda; etc. Knowledge of the pathophysiological changes that occur in the body after methanol consumption is essential for all practising doctors. This case report mainly highlights the metabolism of methanol and its physiological effect on the body and management of methanol poisoning. Conversion of methanol to formaldehyde and formic acid by hepatic enzyme alcohol dehydrogenase triggers the onset of clinical symptoms. The appearance of clinical symptoms start as early as 30 min to 12 hour. If left untreated patient may develop uncompensated metabolic acidosis, blindness, seizures, hypoglycemia, and dyselectrolemia. Funduscopic examination and ABG should be carried out. The main stay of treatment is ethanol, folinic acid, aldehyde dehydrogenase inhibitor and hemodialysis. The basic steps in approach must be carried out in the emergency department and followed-up with meticulous monitoring in the intensive care unit for salvage as well as prevention of long-term sequelae. In Tripoli, Libya over 1000 patients were poisoned with a fatality rate of 10%. In Kenya 2 outbreaks resulted in approx. 341 and 126 patients with case fatality rate of 29% and 21% respectively. Ethanol poisoning in Malwani near Malad, Mumbai claimed large number of deaths due to delay in suspecting and diagnosis and delay in management principles of management are designed to tackle this type of disaster in future. There are several guidelines for the management of methanol poisoning, but in India at primary health care resources of investigation and treatment are limited. In India there are also unauthorized production of alcohol, who mixes methanol with alcohol for early kick and secondly it is cheaper than alcohol. Methanol is generally used for solvent in printing and copy solutions, polishes, paints and stabilizers. They are also used as antifreeze and as additive in gasoline. Methanol is known as an industrial alcohol and is mixed up with alcohol and used for medical purpose. Methanol is well absorbed following inhalation, ingestion or cutaneous expression.

Keywords: Methanol; Mortality; Funduscopic examination; Metabolism.

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Introduction

Methanol (CH_3OH) is a toxic alcohol which is found in various household and industrial agents. The term "toxic alcohols" is a collective term that includes methanol, ethylene glycol, and isopropyl alcohol. Methanol exposure can be extremely dangerous, if left untreated can lead to significant mortality and morbidity. Methanol poisoning is most often due to accidental or intentional ingestions, and accidental epidemic poisonings due to distilling and fermenting errors and beverage contamination. Products that contain methanol include windshield washer fluid, gas line antifreeze, carburetor cleaner, copy machine fluid, perfumes, food warming fuel and other types of fuels. Exposures can cause varying degrees of toxicity and can require a range of treatments from close laboratory monitoring to antidotal therapy and dialysis.

The primary treatments are either ethanol or fomepizole, and unlike ethylene glycol toxicity, dialysis is often recommended.

Case History

A 36-year-old male came to ER with C/O blurring of vision and diplopia since yesterday night after consumption of alcohol (brand unknown) in moderate amount, patient is chronic alcoholic since 7–8 years, H/O back pain, lower back since morning. H/O vomiting one episode yesterday night after consumption of alcohol. Nausea present today. H/O fever with generalized weakness since 2–3 days. No H/O loss of consciousness, seizures, syncope, trauma, loose stools, cough, rashes. No other comorbidities.

Vitals were BP- 170/110 mm Hg, pulse-124/ min, SpO_2-98%, afebrile, RBS-207 mg%, patient conscious and oriented ABG done in ER s/o pH-7.091, PCO_2-20.8, PO_2-116, Na-140, K-5.6, Ca-1.35, Cl-97, Lac-3.3, Hb-17.8, HCO_3-6.0.

- High anion gap metabolic acidosis with uncompensated resp alkalosis, anion gap-36
- NG tube inserted to start ethanol as competitive inhibitor of methanol metabolism
- LEFT radial arterial line secured under complete aseptic precaution.
- Hemodialysis as soon as possible.
- Sodium bicarbonate infusion started.
- Urine dipstick done s/o Ketone +VE

Investigation Sent

Urine drug assay, CBC, KFT, LFT, urine osmolality, urine R/M, C/S, paired blood C/S, HBA1c, viral markers, s. amylaze and lipase, USG abdomen, CXR, CT Head.

Treatment Started

Inj Leucovorin Folinic acid 50 mg/ml stat in 100 ml NS and 6th hourly.inj Optineuron, inj pantop, inj Emeset, inj Sodabicarb 50 ml IV stat and infusion started @20 ml/hr, IV Fluid 0.9% NS 1 liter stat, IV 0.9% NS 500 ml @100 ml/hr, NJ Thiamine 300 mg daily (In order to prevent wernicke's encephalopathy), ethanol given by NG tube 10 ml in 100 ml of water every hourly, Tab Chlordiazepoxide 10 mg PO 6th hourly (to prevent alcohol withdrawal).

Results

Table 1: Investigations results of USG abdomen s/o hepatomegaly with Gr II fatty liver

Investigations	
Blood	
Hb-18.1	Platelet-337
Hb-18.1	Platelet-337
TLC- 16.8 (N-62.8%, L-27.2%)	HBA1c- 5.1
Sodium-133, Potassium-5.41	Screat-1.42
Urea-17.1	
LFT	
GGTP-521	Total Protien -9.83
Albumin-5.21	ALK-PHOS-225
Amylaze-63	LIPASE-24.48
SGOT-364	SGPT-211
S Osmolality-352,	INR-1
Paired blood C/S-Sterile	Viral markers-neg
S. Alcohol-34	Urine R/M- protein-++, Sp gravity-1.03, pH-6
Urine C/S- Sterile	
	Urine Drug Assay: Negative for amphetamines, cannabinoids, opiates, cocaine, barbiturates, benzodiazepines

Hospital Stay

After initiating the treatment patient was shifted to medical ICU. Soon after patient sensorium was altered. Patient was taken on NIV 50% FiO_2 maintained SpO_2-98%. Patient was maintained on IV infusion of propofol as patient was agitated. On same night patient was taken on hemodialysis

during and after dialysis patient general condition improved and sensorium gradually improved. patient had an episode of hypoglycemia which was corrected with 25% dextrose.

- On 2nd day had hypokalemia for which IV KCl given and syp potklor was started.
- Urine showed 4–6 pus cells hence inj tazact 4.5 gm stat and 4.5 gm tds started
- Inj $MgSO_4$ 2 gm IV stat and 1 gm IV bd was started.
- Patient was shifted to ward on 3rd day
- Patient was discharged on 4th day, on discharge patient general condition was normal,vision improved, acidosis improved.

Discussion

Methanol as alcohol is rapidly absorbed through gastro-intestinal tract, so the average absorption half-life is 5 minutes and reaches to maximum in 30–60 minutes. Methanol is rapidly distributed in body fluids. Methanol is not toxic by itself, but its metabolites are toxic. The absorption of methanol can be delayed in the presence of ethanol or food. Methanol is metabolized in different phases mainly in the liver. In first step of degradation methanol is transformed in formaldehyde via enzyme alcohol dehydrogenase. This reaction is slower than the next step, the transformation of formaldehyde into formic acid by aldehyde dehydrogenase. The half-life of formaldehyde is 1–2 minutes.

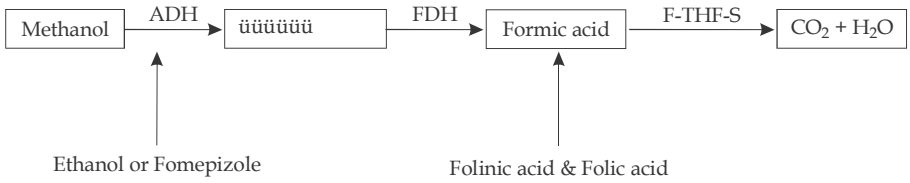


Fig. 1: Metabolism of methanol. ADH: Alcohol Dehydrogenase; FDH: F-THF-S: 10-Formyl tetrahydrofolate Synthetase; All the toxieffect of methanol are due to formaldehyde and formic acid.[11]

Formic acid is further oxidized to carbon dioxide and water in the presence of tetrahydrofolate. The metabolism of formic acid is very slow; thus, formic acid often accumulates in the body, which results in metabolic acidosis. Figure 1 explain the pathway of metabolism.

Clinical Manifestations

Clinical manifestations of poisoning with methanol depend on the amount of methanol and consumption of ethanol and food along with methanol. Consumption of methanol alone initiate within 0.5–4 hours of ingestion and reaches to its peak in 30–60 minutes.

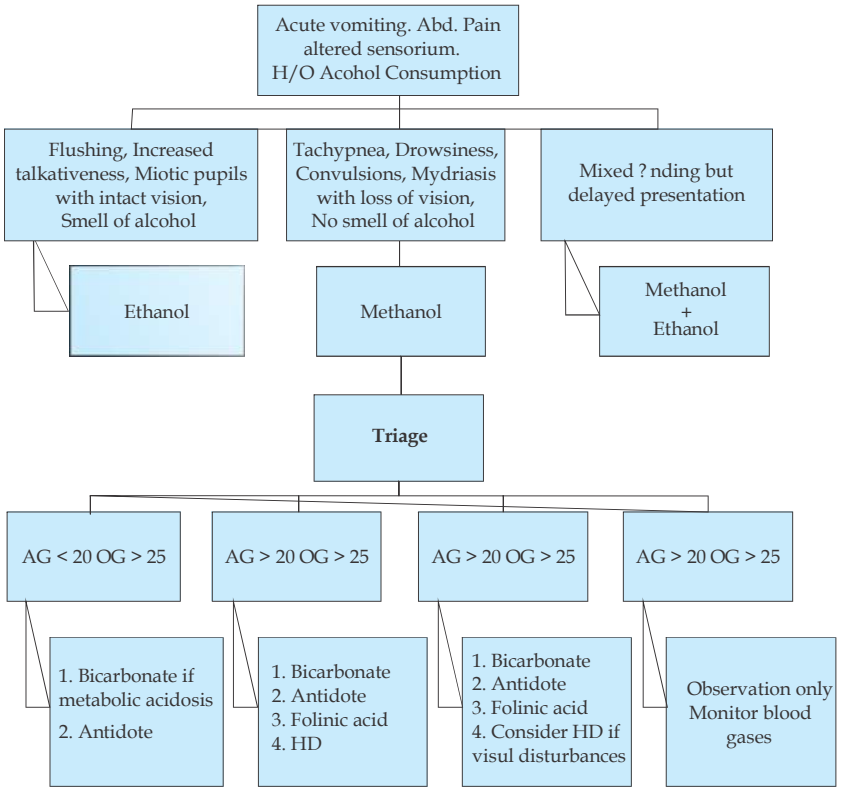
Initially patient presents with drowsiness and ataxia in later stages drowsiness may progress to obtundation and deep coma. Early symptoms also include nausea, vomiting, abdominal pain, confusion, vision disturbance, lethargy and vertigo. Associated ethanol consumption will delay manifestations of methanol poisoning.

When adulterated alcohol is the cause, manifestations are seen after 12–24 hours. Left untreated methanol poisoning can lead to significant mortality and morbidity. After a latent period of 12– 24 hours, decompensated metabolic acidosis occurs; which presents as acute dyspnea and dizziness. The period of latency depends on the dose absorbed and ethanol consumed.

Interference with neural axoplasmatic transport by formaldehyde and/or formate probably accounts for the ocular manifestations. This formate is toxic to mitochondria as it inhibits cytochrome C oxidase resulting in anaerobic metabolism.

Formaldehyde is toxic to visual fibers leads to blurred vision, photophobia, changes in visual field, accommodation disorder, diplopia, blindness and less commonly nystagmus. Optic nerve demyelination has been reported to be due to formic acid destruction of myelin. The major damage occurs at retrolaminar optic nerve with intra-axonal swelling and organelle destruction. Little or no change in retina noted.

Methanol also causes hemorrhagic and nonhemorrhagic damage to putamen in severe poisoning. As a result patient may develop



AG (Anion Gap) = ([Na^+] – [Cl^-] + [HCO_3^-])
OG (Osmoting Gap) = Measured Osmolality (MO) – Calculated Osmolality (CO)
CO = 2 × NA + GLU/1.8 + BUN/2.8
GLU = Blood Glucose level; BUN = Blood Urea Nitrogen

Fig. 2: Plan of triage at tertiary care center emergency room[11]

parkinsonism or other dystonic/hypokinetic picture. Severe metabolic acidosis with anion gap and increased osmolality are highly suggestive of methanol and/or ethylene glycol poisoning. Fig. 2 describes the triage in emergency room at tertiary health care center.

Differential diagnosis: A key point in management of methanol poisoning is early suspicion and treatment. Since emergency estimation of serum methanol concentration is not available in most parts of the country, clinical differential diagnosis is very important.

Patient presents with drowsiness, convulsions, h/o intake of alcohol early suspicion of methanol consumption should be thought.

Patient may present with tachypnea, acidotic breathing (shallow and rapid kussmaul's breathing). However, ethanol poisoning leads to alcoholic ketoacidosis resulting in mild acidemia. Ethylene glycol may also be suspected. In ethylene glycol poisoning calcium oxalate crystals may form and accumulate in blood and other soft tissues.

The other differential diagnosis that can be suspected are arsenic poisoning, cocaine poisoning, pseudoseizure, CO poisoning.

Investigations

Investigations required to support the diagnosis. Serum methanol, serum formaldehyde and urine formic acid should be sent, but availability of these tests is itself questionable. Treatment should be started immediately on clinical suspicion alone (Fig. 3). Fundoscopy, ABG, s electrolytes should also be done.

For Detection of Methanol and its Products

Serum methanol level: Estimation of serum alcohol level is probably important in early hours of intoxication. Serum methanol level >20 mg/dl indicates severe poisoning. But this test is unavailable at most centers. Serum formaldehyde and formic acid presence confirms the diagnosis of methanol consumption. Urinary formic acid level is estimated by gas chromatography.

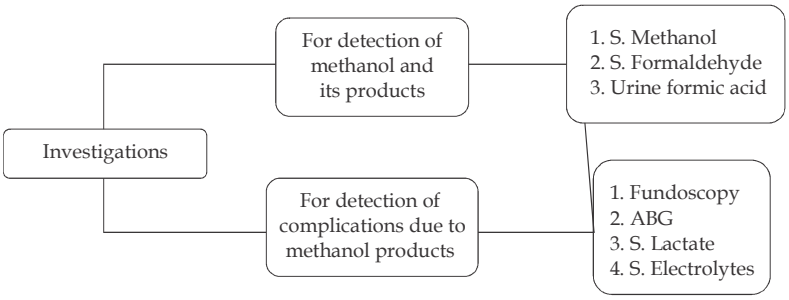


Fig. 3: Investigations in methanol poisoning[11]

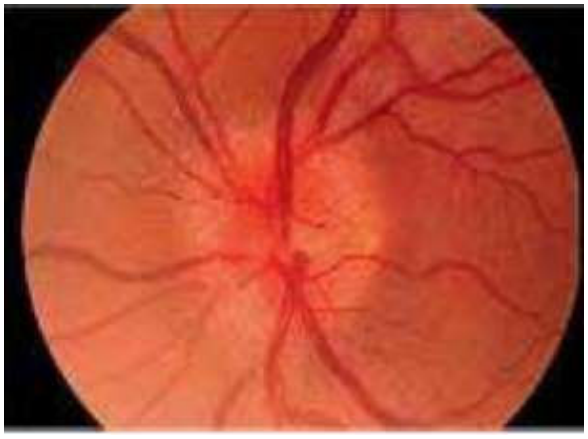


Fig. 4: Fundus picture showing hyperemic disk[11]

For Detection of Complications Due to Methanol Products

Fundoscopy: Manifestation of papillitis and hyperemic optic disc indicates formaldehyde toxicity when ophthalmic symptoms are also present (Fig. 4).

Arterial blood gases—ABG in severe toxicity shows pH < 7.3, HCO_3 < 20 mEq/L. $PaCO_2$ is decreased as a compensatory mechanism. High anion gap >20 with high osmolol gap indicates methanol toxicity (Table 2).

Serum lactic acid-serum lactic acid level is increased due to formaldehyde. Tissue hypoxia leads to Circulus Hypoxicus (Fig. 5).

Other investigations to done—Blood sugar level, Liver function tests, Electrolytes, ECG. X-ray chest is required in critical patients. Electrolytes should be done in all cases to calculate the anion gap.

Anion gap is calculated as (Na) – (Cl + HCO_3)

It is normally 8–12.

In methanol poisoning, it is increased to more than 20.

Serum osmolality – this is calculated as

$$2 \times Na^{+} \left\{ \begin{matrix} \text{Blood} \\ \text{Glucose} + \\ 1.8 \end{matrix} \right\} \text{Blood Urea Nitrogen } 2.8$$

Table 2: Criterial of diagnosing methanol toxicity

S. No	
1.	Documented plasma methanol concentration >20 mg/dL (>200 mg/L).
2.	Documented recent histroy of ingesting toxic amounts of methanol and osmolal gap >10 mOsm/kg.
3.	History or strong clinical suspicion of methanol poisoning wit at least two of the following criteria:
	a. Severe metabolic acidosis i.e. Arterial pH <7.3
	b. Serum bicarbonate <20 mEq/L (mmol/L)
	c. Osmolal gap >10 mOsm/kg
Any one of the three	

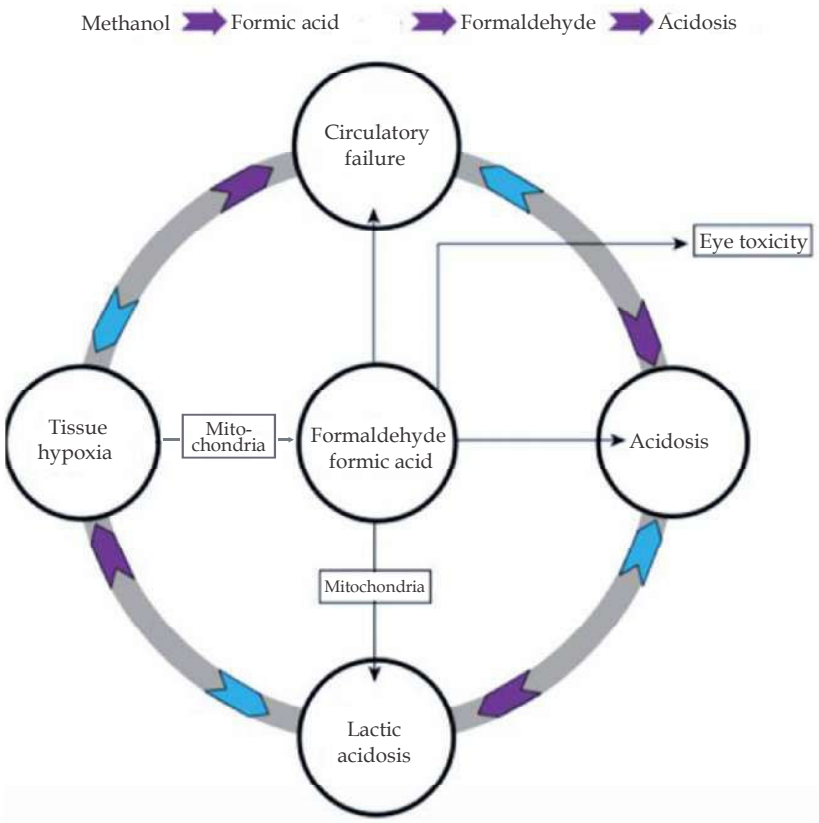


Fig. 5: Diagrammatic representation of circulus hypoxicus.[11]

Table 3: Ethanol dosageregimens

A.	**Loading Dose of Ethanol**			
	1. Intravenous: 7.6–10 mL/kg of a 10% solution Dextrose 5%. Ethanol is available as 5% of 10% solutions in Dextrose 5%; the latter is preferred.			
	2. Oral: 0.8–1 mL/kg of 95% Ethanol, administered PO in orage juice.			
B.	**Maintenance Dose of Ethanol**			
	10% ethanol IV mL/kg/hr)	40% ethanol PO (mL/kg/hr)	95% ethanol PO (mL/kg/hr)	Hemodialysis with 10% ethanol IV (mL/kg/hr)
Moderate drinker	1.4	0.3	0.15	2.7
Chronic drinker	2	0.4	0.2	3.9
Non-drinker	0.8	0.2	0.1	2.7

Management

- Ethanol is believed to compete with methanol for alcohol dehydrogenase thus preventing metabolism of methanol. ADH has 10–20 fold greater affinity for ethanol than methanol. Ethanol is administered via iv or orally to maintain the blood level of ethanol 100 mg/dl.
- Fomipizole/ 4 methylpyrazole are also competitive inhibitor of alcohol dehydrogenase. Fomipizole is given as 15 mg/kg as loading followed by 10 mg/kg every 12 hourly for 24 hr. They are relative easier to administer and does not cause hypoglycemia and sedation. But it is not available in India.
- Folinic/folic acid 50 mg 6th hourly to accelerate the elimination of formic acid.
- Prompt medical care is necessary. Supportive therapy is directed to airway management,

correcting electrolyte disturbances and providing adequate hydration.

- Metabolic acidosis may prompt for early administration of iv bicarbonate. Bicarbonate administration may reverse the vision disturbances. In addition bicarbonate may help in decreasing the amount of formic acid.
- Hemodialysis is indicated: 1—when > 30 ml of methanol has been consumed, 2—serum methanol level >20 mg/dl, 3— observation of visiual complication, 4—no improvement in acidosis despite bicarbonate administration.
- Intravenous methylprednisolone followed by oral prednisolone or topical steroids may salvage vision.

Conclusion

In view of the above-mentioned case it was learned that early suspicion and early intervention was the key element in favorable outcome.

WHO in 2010 has endorsed a global strategy to reduce the harmful effects of alcohol. Following policy options and interventions are suggested:

- developing good quality control with regard to production and distribution of alcoholic beverages;
- regulating sales of informally produced alcohol and bringing it into the taxation system;
- creating an efficient control and enforcement system, including tax stamps;
- developing or strengthening tracking and tracing systems for illicit alcohol;
- ensuring necessary cooperation and exchange of relevant information on combating illicit alcohol among authorities at national and international levels;
- issuing relevant public warnings about contaminants and other health threats from informal or illicit alcohol.

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