REVIEW ARTICLE

Methanol Poisoning

DB Kadam[1], Sonali Salvi[2], Ajay Chandanwale[3]

Abstract

Mortality associated with methanol has been of great concern time and again. The concurrence of cases from a particular area raises doubts about methanol as the culprit. Knowledge of the patho-physiological changes that occur in the body after methanol consumption is essential for all practicing doctors. This article elucidates the clinical presentation and emergency management of these cases under the framework of basic physiological and biochemical phenomena after methanol exposure.

Conversion of methanol to formaldehyde by hepatic enzyme alcohol dehydrogenase triggers the cascade of metabolic events. The manifestations begin as early as 30 minutes and progress to decompensated metabolic acidosis in about 12 hours, if left untreated. Seizures, hypoglycemia and blindness frequently complicate the picture. Acute kidney injury warrants urgent haemodialysis. Fundoscopic examination and arterial blood gas analysis are the key diagnostic elements. The management comprises of intravenous sodium bicarbonate, correction of dyselectrolytemia, ethanol, folic acid and haemodialysis, if necessary. 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.

Methanol poisoning in Malwani near Malad, Mumbai claimed large number of deaths due to delay suspecting and diagnosis led to delay in management.[1] Hence following principles of management are designed to tackle this type of disaster in future.

There are in several guidelines for the management of methanol intoxication in literature. However, in resource limited settings and primary health care level, all the investigative and treatment modalities are not readily available. This article aims at diagnosis and optimum management of methanol poisoning at incipient level so that large scale morbidity and mortality is prevented.

The most common cause of methanol poisoning in India is adulteration of alcoholic drinks. These alcoholic drinks are illicit liquor produced by unauthorized persons. Methanol claims to give early kick when mixed with alcohol. Hence, adulteration is done. Secondly, it is cheaper than ethanol, which makes it suitable for mixing.

The other subset of patients with methanol poisoning presents as suicidal or accidental ingestion. Methanol is used as a solvent in printing and copy solutions, adhesives, paints, polishers and stabilizers. It is also used for window cleaners, antifreeze, as a fuel in alcohol lamp and as an additive in gasoline. Methanol is known as an industrial alcohol and is mixed up with ethanol that is used for medical purposes to prevent ingestion of the same. This is colored, usually blue, to identify medical alcohol called as denatured spirit. Consumption of this for the purpose of suicidal attempt is another way of presentation.

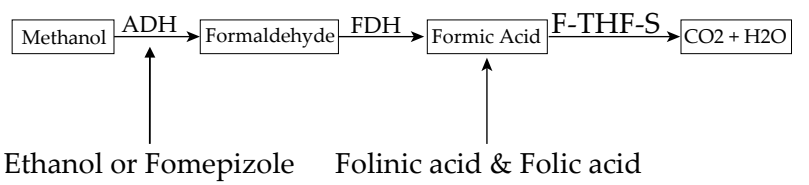

Fig. 1: Metabolism of methanol. ADH: Alcohol Dehydrogenase; FDH: Formaldehyde dehydrogenase; F-THF-S: 10-Formyl Tetrahydrofolate Synthetase; All the toxic effects of methanol are due to formaldehyde and formic acid

Absorption, Distribution and Metabolism

Methanol as an alcohol is rapidly absorbed through gastro-intestinal tract, so the average absorption half - life is 5 minutes and reaches maximum serum concentration within 30 – 60 minutes and well dissolves in body water. 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. The initial enzyme in its metabolism is alcohol dehydrogenase (Figure 1)

Clinical Manifestations

Clinical manifestations of poisoning with methanol alone initiate within 0.5 – 4 hours of ingestion and include nausea, vomiting, abdominal pain, confusion, drowsiness and central nervous system suppression. Patients usually do not seek help at this stage. Associated ethanol consumption will delay manifestations of methanol poisoning. When adulterated alcohol is the cause, manifestations are seen after 12 – 24 hours. In this group, many patients will arrive together with the same symptoms and from same residential area. Left untreated, methanol poisoning can lead to significant mortality and morbidity.[2]

After a latent period of 12– 24 hours, decompensated metabolic acidosis occurs; which presents as acute

[1]Professor & Head, [2]Associate Professor, Department of Medicine, [3]Dean, B.J. Govt. Medical College, Pune, Maharashtra

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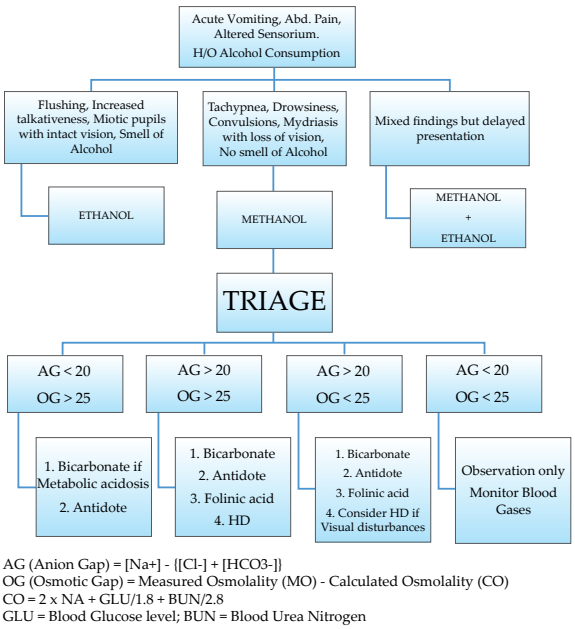

AG (Anion Gap) = [Na+] - {[Cl-] + [HCO3-]}
OG (Osmotic Gap) = Measured Osmolality (MO) - Calculated Osmolality (CO)
CO = 2 x NA + GLU/1.8 + BUN/2.8
GLU = Blood Glucose level; BUN = Blood Urea Nitrogen

Fig. 2: Plan of triage at tertiary care centre emergency room

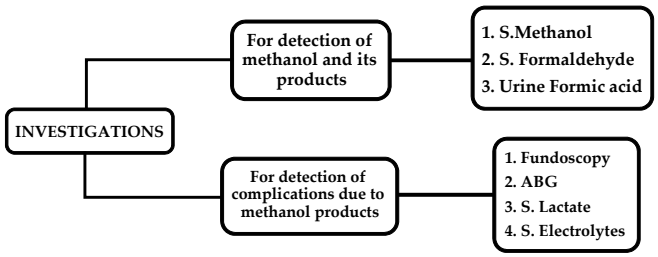

Fig. 3: Investigations in methanol poisoning

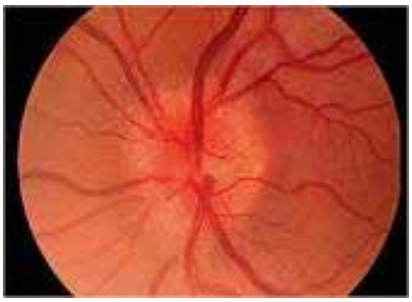

Fig. 4: Fundus picture showing hyperemic disc

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. Formaldehyde is toxic to visual fibres leads to blurred vision, photophobia, changes in visual field, accommodation disorder, diplopia, blindness and less commonly nystagmus. Blurred vision with unaltered consciousness is a strong suspicion for methanol poisoning.

Severe metabolic acidosis with anion gap and increased osmolality are highly suggestive of methanol and/ or ethylene glycol poisoning. Figure 2 describes the triage in casualty.

Important Differential Diagnoses

An important point in management of toxic alcohols, particularly methanol poisoning, is proper and early diagnosis. Since emergency estimation of serum methanol concentration is not available in most parts of the country, clinical differential diagnosis is very important.

Convulsions and central nervous symptoms: Central nervous symptoms, particularly convulsions are the signs of severity of toxic alcohol intoxication and hypoglycemia.

Tachypnea and acidemia: Acidemia is a noteworthy laboratory finding in the differential diagnosis of toxic alcohol and the non-toxic alcohol. The body response to acidemia is tachypnea and hyperventilation (Kussmaul's breathing). This is diagnosed by the normal cardiovascular and respiratory findings in presence of acute dyspnea. However, ethanol poisoning leads to alcoholic ketoacidosis resulting in mild acidemia.

Ethylene glycol is metabolized by the enzyme alcohol dehydrogenase to glycolic acid (GA), which is then transformed into glyoxylic acid. Glyoxylic acid is further converted to highly toxic oxalate. Calcium oxalate crystals may form and accumulate in blood and other tissues. The precipitation of calcium oxalate in the renal cortex results in decreased glomerular filtration and renal insufficiency.

Investigations

Investigations are done to support the clinical diagnosis. They are not a must for starting treatment. Treatment should be started immediately on clinical suspicion alone (Figure 3).

For Detection of Methanol and its Products

Serum methanol level: Estimation of serum alcohol level is probably important in early hours of intoxication. This is unavailable in most of the centres. Serum methanol level > 20 mg/dl indicates severe poisoning.

Serum formaldehyde or formic acid level: Presence of these indicates definite methanol poisoning. These tests are not available in most centres.

Urinary formic acid level: Formic acid in urine is estimated by a gas chromatographic method. Evidence of formic acid in urine is confirmative of methanol poisoning. However, this facility may not be available at all the centres.

Detection of toxic alcohols in blood and/ or body fluid: WHO has recommended the following methods for detection of toxic alcohols in blood or body fluid like saliva. These are qualitative and based on colorimetry. Two of these are enzyme-based methods (alcohol oxidase and alcohol dehydrogenase) and other two utilize oxidizing agents (sodium periodate and potassium permanganate). A combination of these methods allows us to detect all three important alcohol intoxications: methanol, ethylene glycol, and diethylene glycol. These methods utilize easily obtainable and relatively inexpensive reagents and no sophisticated equipment. All the studies can be completed within 40 minutes and thus can be performed either in a clinical facility or even outside the facility as the patient is being transported.[3]

For detection of complications due to methanol products:

Fundoscopy: Presence of papillitis

indicated by hyperemic red optic disc indicates formaldehyde toxicity when ophthalmic symptoms are present (Figure 4).

Arterial blood gases: Blood gas analysis in severe toxicity reveals severe metabolic acidosis with pH < 7.3 and HCO3 < 20 mEq/L. PaCO2 is reduced and PaO2 is raised. Most patients with severe poisoning will present with pH < 7.0 and HCO3 < 5, which is a life threatening situation.

Serum lactic acid: Lactic acid level is raised secondary to formaldehyde induced mitochondrial toxicity. Tissue hypoxia leads to CIRCULUS HYPOXICUS as shown in figure 5.

Other investigations for end organ toxicity: 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 + HCO3)

It is normally 8 – 12.

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

Serum osmolality – this is calculated as

$$2 \times Na + \left\{ \frac{\text{Blood Glucose}}{1.8} \right\} + \left\{ \frac{\text{Blood Urea Nitrogen}}{2.8} \right\}$$

It is measured directly by freezing point technique. A Gap of more than 25 between calculated and measured one indicates presence of abnormal alcohol. Vapor pressure method should not be utilized. Vapor pressure depression osmometers cannot detect the presence of volatiles (alcohols) in solution, whereas freezing point instruments can, because volatile solute increases the total vapor pressure of solutions.

Treatment

Sodium Bicarbonate: Life threatening complication of methanol intoxication is severe metabolic acidosis. Hence correction of acidosis is of prime importance. Sodium bicarbonate deficit is calculated as 0.5 x body weight in kg x (18 – observed bicarbonate). This calculated deficit is injected to patient in ml as half dose bolus and half dose over next 30 minutes. Repeat arterial blood gas analysis is done every two hourly and correction as above is given till pH normalizes. If pH is less than 7 and/or S. Bicarbonate is less than 5, full correction is warranted.

Correction of electrolyte imbalance: especially hyperkalemia and hypokalemia should be detected promptly and corrected.

Serum Sodium level can be low due to the presence of methanol and should be monitored and corrected.

Ethanol administration – oral administration of ethanol as 1 ml/kg of absolute alcohol diluted in 4 volumes of water is given as loading dose and followed by 0.5 ml/kg alcohol every 2 hourly. In practice one can use foreign liquors on sale like whisky, rum, brandy, gin as 60 ml stat and 30 ml every 2 hourly till acidosis persists or for 12-24 hours. If the patient is unconscious then same can be given through Ryle's tube. Intravenous alcohol drip can be given if absolute alcohol is available as 30 ml in one pint of 5% dextrose every 4 – 6 hourly depending on patients condition. Close watch should be kept on hypoglycemia and electrolyte imbalance, especially hypokalemia, in patients on ethanol therapy. Oral alcohol group should receive additional histamine H2 receptor blocker and proton pump inhibitor to prevent vomiting and aspiration pneumonia.[4]

Fomepizole – 15 mg/kg as bolus followed by 10 mg/kg every 12 hourly for 24 hours. However availability is an issue for this drug.[5]

Hemodialysis: Patients with severe metabolic acidosis (pH < 7.1 and HCO3 < 10) will require hemodialysis for rapid correction of acidosis and elimination of methanol. Hemodialysis should be done with femoral vein as vascular access with 250 -300 ml/min as blood pump speed, - 50 as transmembrane pressure and for 4 – 6 hours duration. Hemodialysis leads to rapid clearance

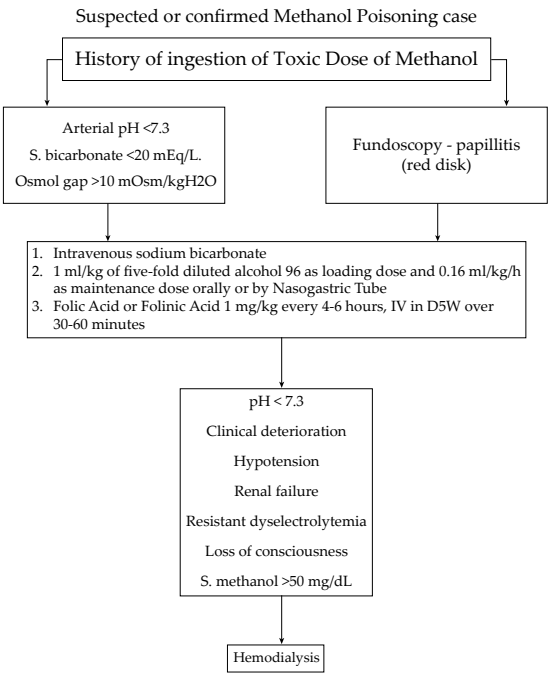

Fig. 5: Following is the algorithm suggested for management of methanol poisoning

Methanol → Formaldehyde → Formic acid → Acidosis

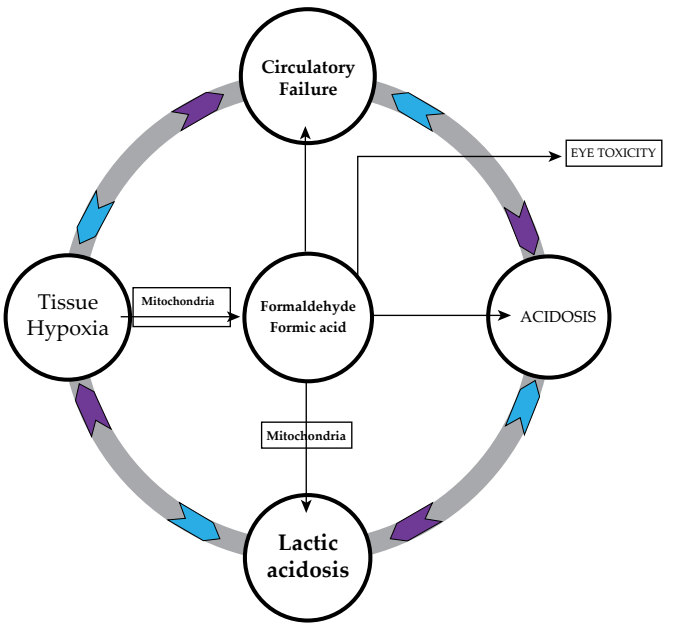

Fig. 6: Diagrammatic representation of circulus hypoxicus

of methanol and its toxic products. Patient should be hemodynamically stable with resuscitation methods prior to hemodialysis.[6]

Folinic acid/folic acid: this degrades formic acid into carbon dioxide and ($CO_2 + H_2O$). Hence folinic acid or folic acid should be administered. Folic Acid or Folinic Acid 1 mg/kg (usually 50 mg) every 4-6 hours, IV in 5% Dextrose over 30-60 minutes.[7]

Approach to Methanol Poisoning Epidemics

By definition, occurrence of more than three cases of methanol poisoning in one area within 24 hours is suggestive of methanol poisoning epidemic. When this is noted, should be communicated to public health authorities and police administration. Public announcement system should be put to use in this locality and persons drinking alcohol from the same source should be advised to report at medical centre even if they are asymptomatic. This plays an important role in prevention of methanol poisoning morbidities and mortalities. Immediately on suspicion of methanol poisoning epidemic, all neighboring medical institutes should be alerted for having sufficient stock of sodium bicarbonate and hemodialysis facilities should be kept ready. In Maharashtra such epidemics are seen predominantly around the following festivals/days – 2nd day of Holi, Gatar Amavasya (the day prior to Shravan month), Bhau beej (4th day of diwali)

When to Suspect?

Any person coming with vague generalized symptoms and

Severe acute dyspnea

Visual symptoms

History of alcoholic drink in past 24 – 48 hours

Urine examination shows severe acidic pH

Papillitis on fundoscopic examination

ABG showing severe metabolic acidosis (pH < 7.3) with no overt cause on history and clinical examination.

In centres where there are no facilities available for ABG

As soon as methanol poisoning is suspected and patient has acidotic breathing with urine pH strong acidic, sodium bicarbonate 100 ml should be given stat and 100 ml in drip of normal saline should be started and the patient should be referred at higher centre after giving loading dose of 60 ml ethanol.

In centres where ABG is available but dialysis facility is not available, patients can be managed with acidosis correction by sodium bicarbonate, competitive inhibition by ethanol and addition of folic/folinic acid. Fomepizole if available can be given. Most of the patients can successfully be managed without mortality and morbidity at such centers. Only patients with pH < 7.1 and bicarbonate < 10 meq/L, despite correction done by intravenous sodium bicarbonate, should be considered for hemodialysis due to constraints of available facility.

In centers where hemodialysis facility is available:

In addition to sodium bicarbonate, ethanol, folic acid therapy, hemodialysis should be considered early in all patients with severe acidosis and symptoms of decreased visual acuity or 'fogging of vision' (also called as the "snowstorm effect").

In methanol epidemic, one doctor/paramedic should be assigned for each patient for close follow up and monitoring. Repeated ABGs, electrolytes, blood sugar levels and vital parameters measurements are required for these patients.

Long Term Sequelae

Visual deficits and neurological impairment are the residual defects seen. These have been described as long as after six years in a study.

Optic nerve atrophy, temporal pallor of the optic nerve head, visual field defects, and loss of visual acuity (severe to deep blindness) are the vision related abnormalities. Polyneuropathy and encephalopathy manifesting as ataxic gait and sensory impairment on the distal part of the legs are the usual neurological incapacities that can be observed in surviving cases.[8]

Our Experience of Methanol poisoning

In the year 2005, we had 21 patients of methyl alcohol consumption. Patients were triaged on the basis of arterial blood gas analysis report (pH< 7.2, serum bicarbonate less than 10 Meq/L) and fundoscopic findings of acute papillitis. On fundoscopy, retinal changes were observed in eight patients. Out of these, three patients had severe papillitis. Acidosis was present in six patients. All the cases were treated with oral alcohol by nasogastric tube. Injection sodium bicarbonate was administered to all six patients with acidosis. In four patients, we had to resort to hemodialysis. Mechanical ventilator support was required in three hypoxic patients and these were those who had severe changes on fundoscopy. Mortality occurred in two cases and one patient on ventilator recovered. Of the three patients with papillitis, two expired. Hence, severe fundoscopic features can be used to predict poor outcome in methanol poisoning if there is no access to blood methanol levels.

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