Methanol Poisoning

By

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- Methanol is a highly toxic alcohol obtained from distillation of wood
- Methanol itself produces mainly inebriation, its metabolic products may cause metabolic acidosis, blindness, and death after a characteristic latent period of 6–30 hours

Synonyms

- Methyl alcohol;
- Methyl hydroxide;
- Monohydroxymethane;
- Colonial spirit;
- Columbian spirit;
- Pyroxylic spirit;
- Wood alcohol;
- Wood naphtha;
- Wood spirit

Physical Appearance

- Colourless, highly polar, flammable liquid
- Pure methanol-faintly sweet odour at ambient temperatures
- Crude methanol-repulsive, pungent odour
- Methanol has bitter taste.

Uses and Sources

- Antifreeze (10 to 50%)
- Carburetor cleaner (20%)
- Denatured spirit (5 to 10%):
- Embalming fluid (20%)
- Leather dyes (30%)
- Paint remover
- Varnish and shellac (5%)
- Windshield washing fluid (35 to 95%).

Usual Fatal Dose

- About 70 to 100 ml .

- Serious toxicity may occur from ingestion of 0.25 ml/kg of 100% methanol, and fatalities might occur from ingestion of 0.5 ml/kg of 100% methanol.

- The ACGIH recommended workplace exposure limit (TLV-TWA) for inhalation is 200 ppm as an 8-hour time-weighted average, and the level considered immediately dangerous to life or health (IDLH) is 6000 ppm

Toxicokinetics

- Rapidly absorbed through the skin, respiratory tract and gastrointestinal tract
- Peak plasma levels are usually reached within 30 to 60 minutes following ingestion.
- A long latent period (roughly 18 to 24 hours) usually is seen before toxic symptoms develop
- Methanol is readily absorbed and quickly distributed to the body water (Vd = 0.6 L/kg).

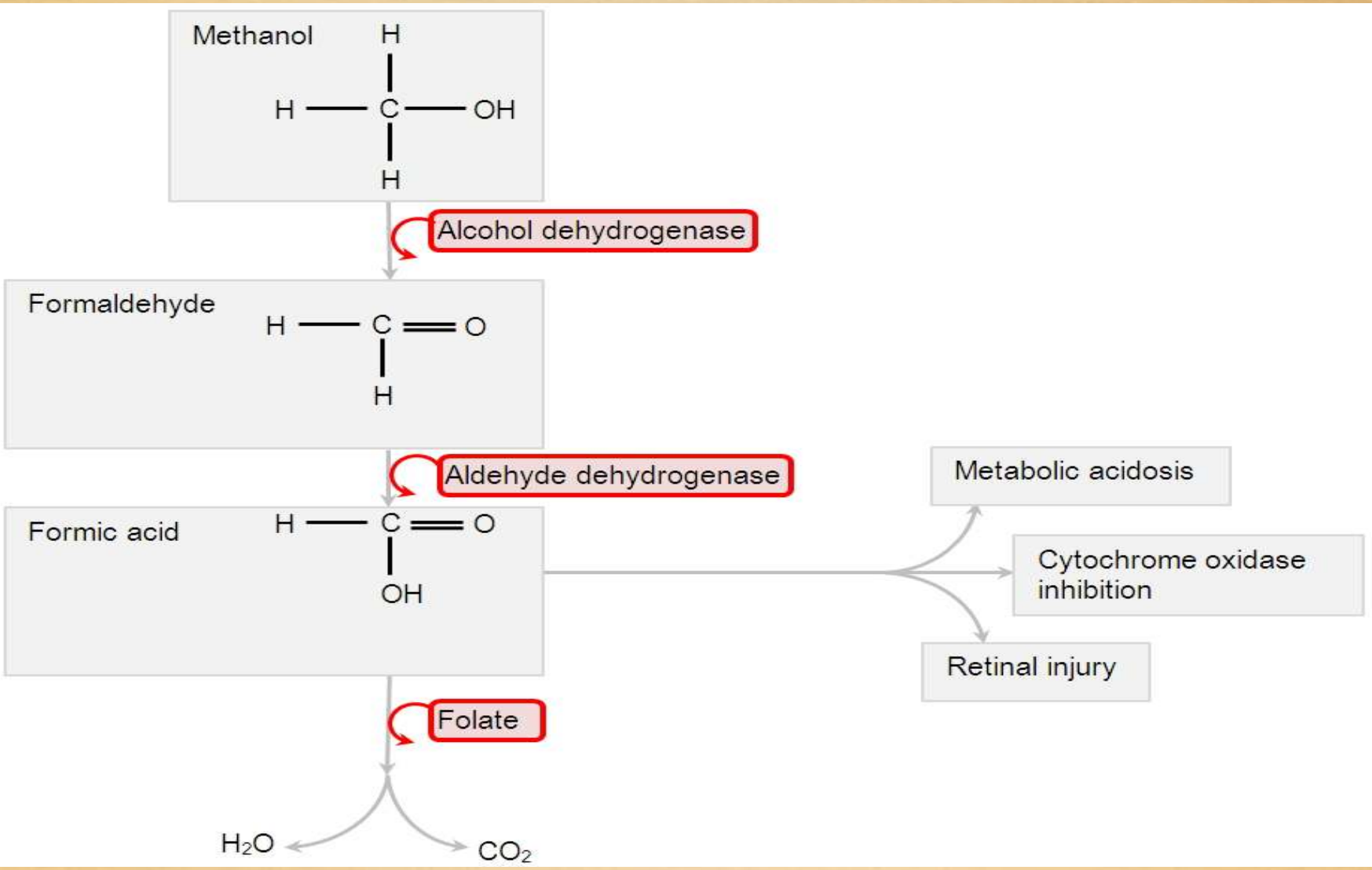
- It is not protein bound.
- It is metabolized slowly by alcohol dehydrogenase via zero-order kinetics, at a rate about one-tenth that of ethanol.
- There are two pathways for metabolism of formic acid, oxidation via the catalase-peroxidase system, or metabolism by the tetrahydrofolic acid-dependant one-carbon pool which is catalysed by 10-formyl-tetrahydrofolate synthetase.

- Since metabolism is slow, significant levels of methanol can be found in the body for up to seven days after ingestion.
- The reported “half-life” ranges from 2 to 24 hours.
- Only about 3% is excreted unchanged by the kidneys and less than 10–20% through the breath.

Mode of Action

- In the liver, methanol is metabolised to formaldehyde (by alcohol dehydrogenase) and then to formic acid (by aldehyde dehydrogenase) which is responsible for retinal toxicity as well as metabolic acidosis.

- Systemic acidosis is caused by both formate and lactate, while blindness is caused primarily by formate.

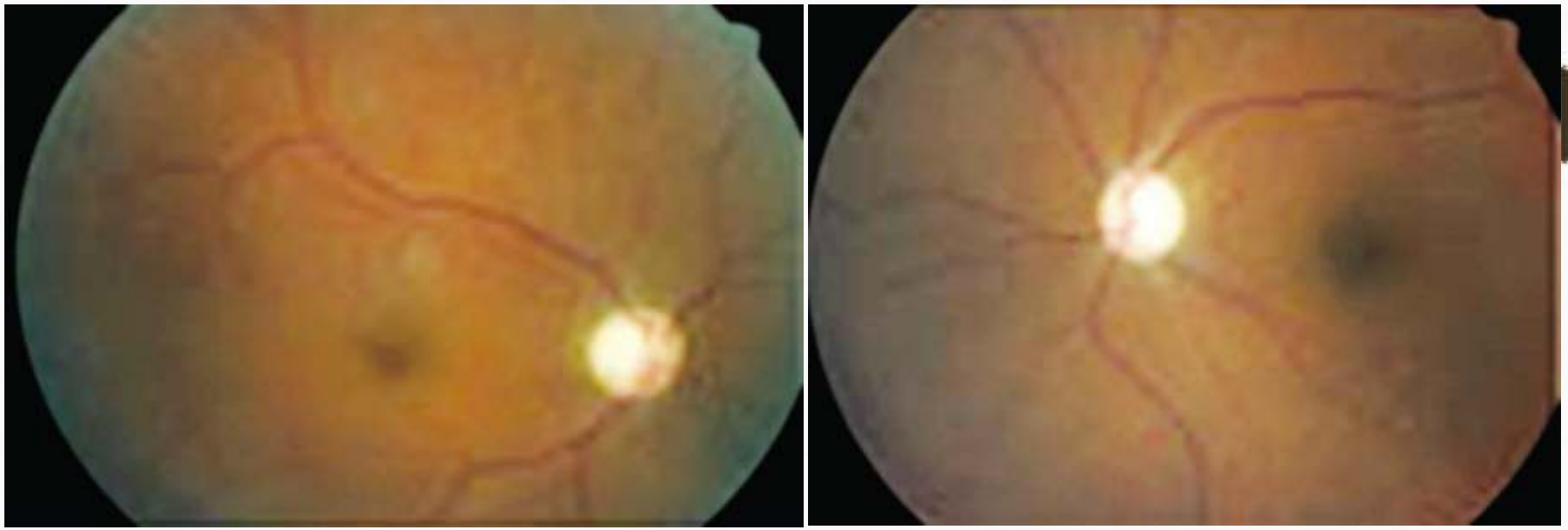

Methanol
H
H
C
OH
H
Alcohol dehydrogenase
Formaldehyde
H
C
O
H
Aldehyde dehydrogenase
Formic acid
H
C
O
OH
Metabolic acidosis
Cytochrome oxidase inhibition
Retinal injury
Folate
H_2O
CO_2

Clinical Features

- Symptoms may be delayed for 12 to 24 hours (Range: 1 to 72 hours). The earliest manifestations include vertigo, headache with stiff neck (meningismus), nausea, vomiting, and abdominal pain.

- Later there is ocular toxicity characterised by blurred or dimmed vision (“flashes” or “snowstorm”), and photophobia.
- Constricted visual fields, spots before the eyes, sharply reduced visual acuity, optic atrophy, blindness, and nystagmus have all been described.
- Ophthalmologic examination usually reveals dilated pupils with sluggish light reaction. Fixed dilated pupils suggest severe poisoning.
- Fundoscopy reveals hyperaemia of optic disc followed by retinal oedema. Irreversible sequelae include optic atrophy and visual field impairment

Fundoscopic picture—methanol poisoning



- Metabolic acidosis (high anion gap) is usually severe. A pH of less than 7.0 and bicarbonate less than 10 mEq/L are not uncommon following significant intoxication.

- The onset of acidosis may be delayed up to 18 to 48 hours, especially if ethanol has also been ingested. Therefore, the absence of acidosis does not rule out a significant methanol ingestion

- Other features include tachycardia, hypotension, and hypothermia.
- Convulsions are a late feature and may be followed by coma.
- Hypomagnesaemia, hypokalaemia, and hypophosphataemia have been reported.
- Occasionally a patient develops transient Fanconi syndrome (hypouricaemia, hypophosphataemia, glycosuria, and hyperchloraemic metabolic acidosis).

- Acute necrotising pancreatitis may result from severe methanol poisoning
- Cause of death is usually respiratory failure, which may precede the cessation of heart beat by several minutes
- Fatal methanol poisoning cases, marked sinus bradycardia may develop with widening of the pulse pressure.
- Severe hypotension

- Most common permanent sequelae following recovery from severe poisoning are optic neuropathy, blindness, Parkinsonism, toxic encephalopathy, and polyneuropathy.

- Permanent ocular abnormalities may include pallor of the optic disc, attenuation and sheathing of retinal arterioles, a diminished pupillary light reaction, reduced visual acuity, central scotomata, and defects of optic nerve fibre bundles.

Diagnosis

- CBC, electrolytes, urinalysis, and arterial blood gases in symptomatic patients or those with a history of significant exposure
- Measure serum pH and electrolytes
- High anion gap acidosis.
- Elevated osmolal gap.
- Hypophosphataemia.
- Elevated creatine phosphokinase.
- Elevated amylase.

- Blood methanol level: more than 50 mg/100 ml indicates serious poisoning. A detectable formic acid level may be consistent with methanol poisoning, as methanol is metabolized to formic acid.
- CT Scan/MRI—Symmetrical areas of necrosis in the putamen of the brain are a classic finding in cases of acute lethal methanol toxicity.

Treatment

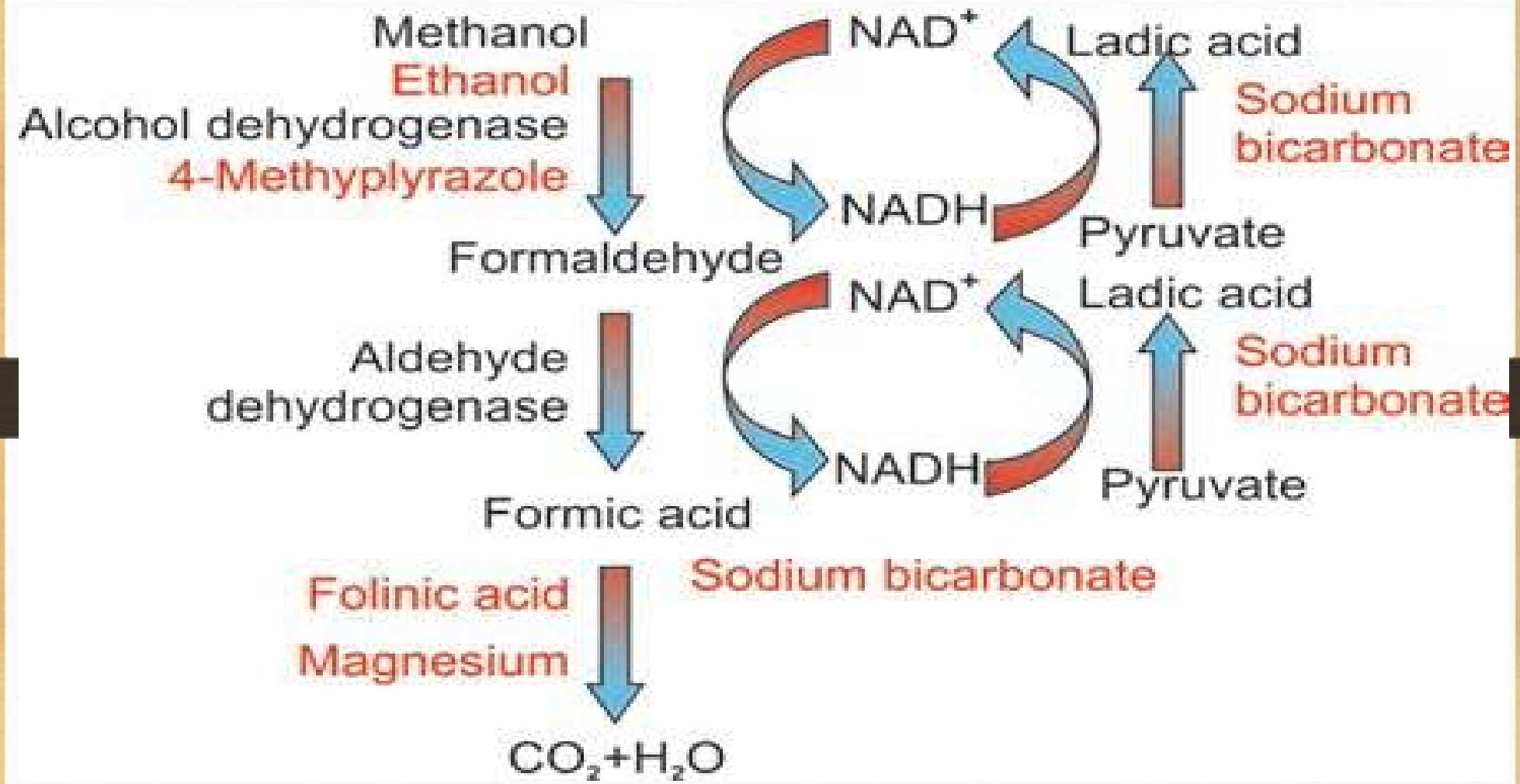
- Patients with abnormal vital signs, visual disturbances, pulmonary oedema, evidence of renal dysfunction, high methanol levels, significant acidosis, or coma should be admitted to an intensive care unit.

- Stomach wash with sodium bicarbonate.
- Ipecac-induced emesis is not recommended because of the potential for CNS depression.
- Activated charcoal does not adsorb significant amounts of methanol.
- Its use in the face of ingestion may be indicated to prevent absorption of co-ingested substances.
- Maintain an open airway and assist ventilation if necessary
- Treat coma and seizures if they occur

Antidotes

- Ethanol is the specific antidote since it preferentially competes for the same enzyme (alcohol dehydrogenase) and prevents the metabolism of methanol which is then excreted unchanged in the urine.

- Ethanol has about 20 times the affinity for alcohol dehydrogenase compared to methanol.



Methanol antidotes–mechanism of action

- This competitive effect of ethanol gains 195 more time for excretion of unchanged methanol from the body, and it also inhibits the formation of methanol metabolites that produce severe acidosis.

- Formic acid is metabolised to carbon dioxide and water via a folate dependant system.

- 10% ethanol at a dose of 10 ml/kg administered IV over 30 minutes, followed by 1.5 ml/kg/hr, so as to produce and maintain a blood ethanol level of 100 mg/100 ml.

- Blood ethanol levels should be maintained at 100 to 130 mg/100 ml (21.7 to 28.2 mmol/L). It is safer to maintain a blood ethanol concentration greater than 130 mg/100 ml than to have it fall below 100 mg/100 ml.

- Alternatively, 1 ml/kg of 95% ethanol in fruit juice (180 ml) can be given orally over30 minutes. For maintenance, administer 0.17 to 0.28 ml/kg/hr as 50% ethanol in fruit juice.

- If neither of these is practicable, give 125 ml of a distilled alcoholic beverage (gin, vodka, whisky, or rum) orally, diluted in glucose solution or juice, and repeat as required cautiously.

Ethanol therapy should be continued until the following criteria are met

- Methanol blood concentration, measured by a reliable technique, is less than 10 mg/100 ml
- Formate blood concentration is less than 1.2 mg/100 ml.
- Methanol-induced acidosis (pH, blood gases), clinical findings (CNS), electrolyte abnormalities (bicarbonate), serum amylase, and osmolal gap have resolved.

- Patients who concurrently ingested ethanol and methanol may have a normal acid-base profile despite a dangerously elevated blood methanol level.
- Consider implementing the ethanol treatment regimen in these patients until a methanol level can be determined.
- Determine blood ethanol level before beginning ethanol therapy and modify the loading dose accordingly

- In Western countries, a new antidote has been introduced viz., 4 methyl pyrazole (4MP), or fomepizole which does not cause CNS depression (unlike ethanol).
- Upto 20 mg/kg of 4MP in divided doses have been given for 5 days without any demonstrable toxicity

- The usual dose is 15 mg/kg, followed 12 hours later by 10 mg/kg 12th hourly for 4 doses, and then increased to 15 mg/kg 12th hourly for as long as necessary.

- Fomepizole is easier to use clinically, requires less monitoring, does not cause CNS depression or hypoglycaemia, and may obviate the need for dialysis in some patients.

- Sodium bicarbonate IV : 500 to 800 ml of 7.5% solution, slowly.

- Folinic acid IV: 1 to 2 mg/kg, 6th hourly. It hastens the elimination of formic acid. Folinic acid (5-formyltetrahydrofolic acid, i.e. 5-FTHF), or leucovorin or citrovorum factor is a biologically active form of folic acid (pteroylglutamic acid) which is an essential water soluble vitamin.

- For convulsions: Attempt initial control with a benzodiazepine (diazepam or lorazepam). If seizures persist or recur administer phenobarbitone.

- Haemodialysis is very effective in removing methanol, formaldehyde, and formic acid. While ethanol treatment is also quite effective, it is extremely difficult to maintain therapeutic ethanol levels for long periods of time.

- Haemodialysis is strongly recommended in patients with acidosis or serum methanol levels of greater than 25 to 50 mg/100 ml. Haemoperfusion is not effective.

- Peritoneal dialysis and continuous venovenous haemofiltration are less effective.

Thank You