

# TOXIC ALCOHOL

## Introduction

The term toxic alcohols traditionally refer to alcohols other than ethanol, not intended for ingestion. Toxic alcohols consist of methanol, ethylene glycol, isopropanol (isopropyl alcohol), benzyl alcohol and diethylene glycol.

Alcohols are rapidly absorbed after ingestion but not completely bioavailable because of metabolism by gastric alcohol dehydrogenase as well as by first pass metabolism. Significant toxic alcohol toxicity usually occurs by oral route but infants may have toxicity after dermal absorption.

Without intervention toxic alcohols are metabolized through successive oxidation by alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) into their toxic metabolites. Treatment is aimed at blocking conversion of the toxic alcohol into the toxic metabolite as well as removal of the toxic alcohol by dialysis.

## Toxic alcohols:

| Toxic alcohol     | Commercial application  | Metabolite   | Effect  |
|-------------------|---|--|---|
| Methanol          | Windshield washer fluid, denaturants in paint and varnish removers. Denatured alcohol for lab use.  | Formaldehyde, formic acid  | Metabolic acidosis, retinal toxicity                                  |
| Ethylene glycol   | Automobile coolant and antifreeze   | Glycoaldehyde, glycolic acid, oxalic acid                                  | Metabolic acidosis, hypocalcemia and nephrotoxicity                   |
| Isopropanol       | Rubbing alcohol (70% isopropanol), solvent in household products including Dettol®  | Acetone  | Causes the most CNS depression. Ketosis without acidosis. Hypotension |
| Diethylene glycol | Wallpaper remover, automotive power steering, antifreeze, gas conditioning formulations and brake fluid. Has been used illegally as a sweet tasting cheap glycerin substitute and as a diluent in medication preparations | 2-hydroxyacetic acid (HEAA). No evidence of conversion to ethylene glycol. | Renal cortical necrosis, neurotoxicity                                |

| Toxic alcohol  | Commercial application   | Metabolite   | Effect   |
|----------------|--|--------------|--|
| Benzyl alcohol | Preservative in bacteriostatic normal saline, some IV medications and some ophthalmic preparations | Benzoic acid | Causes “gasping baby syndrome” in infants at large doses. May cause eye irritation & necrosis if concentration of more than 1% applied into the eye. |

## Methanol/ethylene glycol poisoning:

### Diagnosis:

- History of methanol or ethylene glycol ingestion with a wide anion gap metabolic acidosis.
  - Patients may also present with visual disturbances, neurologic deficit, abdominal pain and vomiting.
  - A **wide anion gap** can be used to diagnose poisoning in lieu of osmol gap if serum ethanol levels cannot be measured.
  - Anion gap measurement:  $[Na - (HCO_3 + Cl)]$ , all units in mmol/l
  - In early presentation a wide osmol gap will be detected but this gap normalizes later.
- Measured osmolality-calculated osmolality= Osmol gap
- Calculated osmolality:  $2(Na + K) + Urea + Glucose + Ethanol$  (all units in mmol/l).
- Normal osmol gap ranges from  $-2 \pm 6$  mOsm/L. A gap of more than 10 is clinically significant but is not diagnostic of toxic alcohol ingestion. A markedly elevated osmol gap is strongly suggestive of toxic alcohol ingestion.

## Baseline Investigations

- ABG
- RP, RBS, blood alcohol level and serum osmolality level to calculate osmol gap.
- Coagulation profile, LFT, CE, ECG as indicated
- CT Brain & CXR as indicated
- Blood and urine methanol levels can be measured in selected laboratories, the following must be sent:
  - Blood: 3ml in grey cover bottle
  - Urine: 20ml in universal container with sodium fluoride or 3 ml in grey cover bottle
  - Specimen of alleged toxin
- A serum formate level has been shown to accurately diagnose methanol poisoning but is currently unavailable in Malaysia.

## Prehospital Care

- Assess airway, breathing and circulation.
- Provide ventilation and insert LMA if necessary.
- Verify history of toxic alcohol ingestion and bring the bottle to ED if possible.
- Insert an IV line and administer fluid bolus if patient noted to be hypotensive.
- Check DXT and administer Dextrose if DXT less than 4 mmol.
- Triage to red or yellow zone after consultation with managing emergency physician.

## In-hospital Management

- Assess airway, breathing and circulation, stabilize as necessary. Fluid boluses followed by vasopressors should be given for hypotension.
- Nasogastric aspiration can be performed in patients who present within 1 hour of consumption.
- Activated charcoal is generally not recommended except in cases of significant, recent ingestion or in cases of co-ingestion of toxins that can be bound by activated charcoal.
- Sodium bicarbonate as infusion should be given to correct severe acidosis.
- The following vitamins must be administered:
  - a) IV Folinic acid/Leucovorin calcium- 1mg/kg up to 50mg every 4-6 hours (Methanol)
  - b) IV Thiamine 100mg OD (Ethylene glycol)
  - c) IV/PO Pyridoxine 50mg every 4-6 hours (Ethylene glycol)
- Fomepizole or ethanol should be administered as soon as possible to block conversion of toxic alcohols. Fomepizole is the preferred antidote as it is easily administered with fewer side effects and monitoring requirements as compared to ethanol. For ethanol to be an effective antidote serum levels must be carefully titrated and maintained.
- Dialysis should be commenced as indicated

### Fomepizole:

A loading dose of 15mg/kg IV followed by 10mg/kg IV every 12 hours for the subsequent 2<sup>nd</sup> to 5<sup>th</sup> doses. Each dose should be diluted in 100ml NS or 5% Dextrose and infused over 30 minutes.

Subsequent doses if required: 15mg/kg IV every 12 hours.

In patients undergoing dialysis same dosages are administered except that the drug is given 6 hours after the first dose and 4 hours thereafter.

Vital sign monitoring is required during infusion as the drug may cause bradycardia and hypotension.

Due to its high cost, administration of fomepizole should be decided after consensus during breakouts. Fomepizole may be administered for the first day of treatment followed by ethanol infusion subsequently. Fomepizole may obviate the need for hemodialysis in selected patients.

**Ethanol:**

The chart below can be used as a guide for dosing:

| <b>LOADING DOSE</b>   |   |   |
|---|---|---|
| <b>20% Oral Ethanol (40 proof)</b>  |   | <b>10% IV Ethanol</b>   |
| 0.8 gm/kg (4ml/kg) diluted in juice administered orally or via a nasogastric tube   |   | 0.8gm/kg (8ml/kg) administered over 20 to 60 minutes as tolerated |
| If the patient concurrently has ingested ethanol, then the ethanol loading dose must be modified so that the blood ethanol level does not exceed 100 to 150 mg/dL |   |   |
| <b>MAINTENANCE DOSE</b>   |   |   |
| <b>Patient</b>  | <b>20% Oral Ethanol (40 proof)</b>                              | <b>10% IV Ethanol</b>   |
| Non -drinker  | 80 to 130mg/kg/hr (0.4-0.7ml/kg/hr) PO or via nasogastric tube  | 80 to 130mg mg/kg/hr (0.8-1.3ml/kg/hr)                            |
| Chronic alcoholic   | 150mg/kg/hr (0.8ml/kg/hr) PO or via nasogastric tube            | 150mg/kg/hr (1.5ml/kg/hr)   |
| During dialysis   | 250 to 350mg/kg/hr (1.3-1.8ml/kg/hr) PO or via nasogastric tube | 250 to 350mg/kg/hr (2.5-3.5ml/kg/hr)                              |

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Treatment should be titrated to a blood ethanol level of 100mg/dL. If your hospital does not have blood ethanol measurement, titrate ethanol infusion to patient's clinical condition i.e. patient starts to show improvement without adverse effects.

Patient must be monitored in ICU if IV ethanol infusion is given- potential adverse effects of hypotension, tachycardia, CNS/respiratory depression, hypoglycemia, electrolyte derangement, and gastritis.

Ethanol infusion is preferably avoided in pediatric and pregnant patients.

**Dialysis:**

Treatment with just ethanol/fomepizole infusion without hemodialysis has been successful in patients who are minimally toxic, without renal impairment and in ethylene glycol poisoning. Dialysis is indicated if any of the following is present:

- Significant metabolic acidosis
- Signs of end organ toxicity including coma, seizures and renal failure
- Methanol level of more than 50mg/dL

Treatment should be continued until serum methanol level is less than 20mg/dL or patient shows clinical improvement with correction of metabolic acidosis, osmol gap, serum electrolytes and renal function.

## Treatment Summary

| Toxic alcohol     | Vitamins  | Treatment                                      |
|-------------------|---|--|
| Methanol          | Folate or folinic acid- 1mg/kg up to 50mg every 4-6 hours | Block and wash                                 |
| Ethylene glycol   | Thiamine 100mg & Pyridoxine 50mg every 4-6 hours          | Block and wash                                 |
| Isopropanol       | -   | Wash- if refractory to fluids and vasopressors |
| Diethylene glycol | -   | Wash, block in severe cases                    |
| Benzyl alcohol    | -   | Supportive & symptomatic.                      |

## Disposition

- Patients requiring intravenous ethanol infusion should preferably be admitted to ICU.
- All patients presenting with suspicion of toxic alcohol ingestion must be admitted. Symptoms may take up to 24 hour to manifest.
- Report all cases suspected of toxic alcohol poisoning to public health.

## References:

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