Our Vision
To provide every patient with the care we want for those we love the most

NHS
Norfolk and Norwich University Hospitals
NHS Foundation Trust

Trust Guideline for the Management of Toxic Alcohols (Ethylene glycol and methanol) with Fomepizole

A clinical guideline recommended

For use in:	A+E, AMU, Medical and Surgical wards
By:	Clinicians
For:	Adults with poisoning from toxic alcohols
Division responsible for document:	Divisions 1 and 2 – Medical and Surgical
Key words:	Poisoning, Ethylene glycol, Methanol, Fomepizole
Name of document author:	Dr Duduzile Musa
Job title of document author:	Consultant in Acute Medicine
Name of document author's Line Manager:	Dr Timothy Gilbert
Job title of author's Line Manager:	Consultant Cardiologist and Chief of Medicine
Assessed and approved by the:	Clinical Guidelines Assessment Panel (CGAP) If approved by committee or Governance Lead Chair's Action; tick here ✓
Date of approval:	18/03/2021
Supported by:	Renal Medicine, Clinical Biochemistry and Pharmacy
Ratified by or reported as approved to (if applicable)**:**	Clinical Safety and Effectiveness Sub-Board
To be reviewed before: This document remains current after this date but will be under review	18/03/2024
To be reviewed by:	Author
Reference and / or Trust Docs ID No:	ID No: 10510
Version No:	3
Description of changes:	Changes in the collection times.
Compliance links: *(is there any NICE related to guidance)*	None
If Yes - does the strategy/policy deviate from the recommendations of NICE? If so why?	N/A

This guideline has been approved by the Trust's Clinical Guidelines Assessment Panel as an aid to the diagnosis and management of relevant patients and clinical circumstances. Not every patient or situation fits neatly into a standard guideline scenario and the guideline must be interpreted and applied in practice in the light of prevailing clinical circumstances, the diagnostic and treatment options available and the professional judgement, knowledge and expertise of relevant clinicians. It is advised that the rationale for any departure from relevant guidance should be documented in the patient's case notes.

The Trust's guidelines are made publicly available as part of the collective endeavour to continuously improve the quality of healthcare through sharing medical experience and knowledge. The Trust accepts no responsibility for any misunderstanding or misapplication of this document.

Trust Guideline for the Management of Toxic Alcohols (Ethylene glycol and methanol) with Fomepizole

Version and Document Control:

Version Number	Date of Update	Change Description	Author

This is a Controlled Document

Printed copies of this document may not be up to date. Please check the hospital intranet for the latest version and destroy all previous versions.

Trust Guideline for the Management of Toxic Alcohols (Ethylene glycol and methanol) with Fomepizole

Quick reference guidance

ETHYLENE GLYCOL POISONING

Ethylene Glycol poisoning known or suspected:

Weigh the patient
Arterial or venous blood gas (check the severity of acidosis)
Basic chemistry (calculate anion gap and renal function)
Serum bone profile and glucose
Serum paracetamol and salicylate level
Finger prick plasma ketones
Serum ethanol concentration (calculate osmolal gap)
Serum osmolality (confirm diagnosis)
Serum methanol, ethylene glycol, and isopropanol concentrations to establish diagnosis (grey top) ***(discuss with Duty Biochemist – however do not delay treatment whilst waiting for this result)***
Electrocardiogram
Urinalysis (for oxalate crystals) (white bottle)

Ethylene glycol poisoning

Documented or suspected recent history of more than 10g (approx. 10ml of100%) methanol/ethylene glycol ingestion and an osmolar gap > 10 mOsm/L

OR

Suspected methanol/ethylene glycol ingestion and an osmolar gap > 10 mOsm/L or a high anion gap metabolic acidosis without there being another likely cause (check for urinary oxalate crystals or lactate gap)

Fomepizole

Early presentation, mild acidosis

or

Haemodialysis

Late presentation, renal failure, severe acidosis

Fomepizole

Block alcohol dehydrogenase with Fomepizole (all doses should be given over 30 minutes)

Loading dose: 15 mg/kg IV diluted to a final volume of 250 mL sodium chloride intravenous infusion 0.9% or dextrose

Maintenance: 10 mg/kg IV diluted to a final volume of 250 mL sodium chloride intravenous infusion 0.9% or dextrose every 12 hours (starting 12 hours after the loading dose given). Maximum 4 doses.

After 4 doses: 15 mg/kg IV diluted to a final volume of 250 mL sodium chloride intravenous infusion 0.9% or dextrose every 12 hours.

Trust Guideline for the Management of Toxic Alcohols (Ethylene glycol and methanol) with Fomepizole

Quick reference guidance

METHANOL POISONING

Methanol poisoning known or suspected:

Weigh the patient
Arterial or venous blood gas (check the severity of acidosis)
Basic chemistry (calculate anion gap and renal function)
Serum bone profile and glucose
Serum paracetamol and salicylate level
Finger prick plasma ketones
Serum ethanol concentration (calculate osmolal gap)
Serum osmolality (confirm diagnosis)
Serum methanol, ethylene glycol, and isopropanol concentrations to establish diagnosis (grey top) ***(discuss with Duty Biochemist – however do not delay treatment whilst waiting for this result)***
Electrocardiogram
Urinalysis (for oxalate crystals) (white bottle)

Methanol poisoning

Documented or suspected recent history of more than 10g (approx. 10ml of100%) methanol/ethylene glycol ingestion and an osmolar gap > 10 mOsm/L

OR

Suspected methanol/ethylene glycol ingestion and an osmolar gap > 10 mOsm/L or a high anion gap metabolic acidosis without there being another likely cause (check for urinary oxalate crystals or lactate gap)

Fomepizole

Early presentation, no visual disturbance

or

Haemodialysis

Late presentation, Visual disturbance, acidosis

Fomepizole

Block alcohol dehydrogenase with **Fomepizole** (all doses should be given over 30 minutes)

Load: 15 mg/kg IV diluted to a final volume of 250 mL sodium chloride intravenous infusion 0.9% or dextrose

Maintenance: 10 mg/kg IV diluted to a final volume of 250 mL sodium chloride intravenous infusion 0.9% or dextrose every 12 hours (starting 12 hours after the loading dose given). Maximum 4 doses.

After 4 doses: 15 mg/kg IV diluted to a final volume of 250 mL sodium chloride intravenous infusion 0.9% or dextrose every 12 hours.

Stop: continue until ethylene glycol or methanol concentration is undetectable OR ethylene glycol concentration is less than 50 mg/L ***AND*** acidosis and signs of systemic

Trust Guideline for the Management of Toxic Alcohols (Ethylene glycol and methanol) with Fomepizole

Objective/s

To safely manage the evaluation and treatment of methanol and ethylene glycol poisoning.

Background

Poisoning with ethylene glycol or methanol can occur through attempted inebriation, unintentional ingestion or intentional self-harm.

Clues to diagnosis of Ethylene glycol poisoning

Ethylene glycol is an ingredient of antifreeze and ingestion of antifreeze is the major cause of poisoning. The principal clinical features are some degree of inebriation or alteration in consciousness, nausea, vomiting, hyperventilation, hypocalcaemia and sometimes tetany. Biochemical features include high anion gap metabolic acidosis, oxalate crystalluria and acute renal failure. Often the calcium is low or low normal at presentation and there is a high osmolar gap. Untreated ethylene glycol poisoning can lead to multiorgan failure and death.

Clues to the diagnosis of Methanol poisoning

Methanol poisoning can occur from the ingestion of windscreen washer fluid or as a consequence of drinking “moonshine” alcohol. Ingestion of even small quantities results in a profound metabolic acidosis and visual changes which progress to blindness and can lead to multi-organ failure and death.

Visual symptoms include blurred vision, appearance of a snow field, decreased visual acuity and colour vision, central scotoma or blindness.

Pathophysiology

Ethylene glycol is metabolised in the liver initially by an enzyme called alcohol dehydrogenase and then eventually to glycolic acid and oxalic acid metabolites which cause profound metabolic acidosis. Oxalic acid binds with calcium to form calcium oxalate crystals which precipitate in the urine. Ethylene glycol can be excreted by the urine unchanged.

Adults and children ingesting more than 0.1g/kg (0.09mL/kg) of **pure** ethylene glycol should be referred to hospital for assessment and those ingesting more than 0.15g/kg (0.13mL/kg) of **pure** ethylene glycol may require an antidote.

Methanol is metabolised in the liver initially by an enzyme called alcohol dehydrogenase and then eventually to formic acid which causes profound metabolic acidosis. Formic acid causes retinal toxicity and blindness.

Ingestion of just 10mL of pure methanol has resulted in blindness.

Trust Guideline for the Management of Toxic Alcohols (Ethylene glycol and methanol) with Fomepizole

Diagnosis of Ethylene glycol or methanol poisoning [1,2]

To diagnose ethylene glycol or methanol poisoning you will need to do the following:

- Weigh the patient (treatment is weight based)
- Arterial or venous blood gas (check the severity of acidosis)
- Basic chemistry (calculate anion gap and renal function)
- Serum bone profile and glucose
- Serum paracetamol and salicylate level
- Finger prick plasma ketones
- Serum ethanol concentration (calculate osmolal gap)
- Serum osmolality (confirm diagnosis)
- Serum methanol, ethylene glycol, and isopropanol concentrations to establish diagnosis (grey top) ***(discuss with Duty Biochemist – however do not delay treatment whilst waiting for this result)***
- Electrocardiogram
- Urinalysis (for oxalate crystals) (white bottle)

Ethylene glycol and methanol levels

After discussion with the Duty Biochemist or Consultant on call, ethylene glycol and methanol samples are sent to an external laboratory to be analysed. Samples must be delivered to the NNUH Laboratory by **13.00h** to ensure preparation of the sample and paperwork required for transport the same day in the courier that leaves the NNUH laboratory from Monday to Thursday.

This courier guarantees delivery before midday the following day, which allows analysis of the sample and reporting the result on that day. If required, transport outside this collections (13:00 Mon-Thu) can be organised with a special courier if this is agreed with the Duty Biochemist or Consultant - but it is much more expensive!

An ethylene glycol level by the external lab is provided 7/7. Methanol testing is available 09.00-17.00 Monday to Friday. A minimum of 2mL of blood volume in a Fluoride oxalate tube (grey top) are required for each test, with the result reported as mg/L.

Biochemical features of toxic alcohol ingestion

Patients with toxic alcohol ingestion should have a high anion gap metabolic acidosis and will have a high osmolar gap.

High anion gap metabolic acidosis

Anion Gap = $Na^+ – (Cl^- + HCO_3^-)$ should be normally <11mmol/L

Consider the differential diagnosis of a high anion gap acidosis:

CATMUDPILES

Cyanide; **C**arbon Monoxide

Alcoholic ketosis (high serum alcohol, high ketones, high osmolar gap)

Toluene

Methanol; **M**etformin

Uraemia (elevated urea and creatinine. NB may be a consequence of toxic alcohol poisoning but normal osmolar gap)

Diabetic ketoacidosis (high glucose, high finger prick ketones)

Paracetamol; **P**araldehyde; **P**ropylene glycol

Iron; **I**soniazid

Lactic acidosis (high serum lactate, normal osmolar gap). NB ***lactate may be elevated in ethylene poisoning due to the inability of laboratory instruments to differentiate between lactate and glycolate, a metabolite of ethylene glycol***

Ethanol

Salicylates

(Tricyclic antidepressant poisoning (widened QRS on ECG, divergent squint, urinary retention)

Determine the osmolar gap

Osmolar gap = Serum osmolality – calculated osmolality

Calculated osmolality = (2x plasma Na^+ + glucose + urea)

Normally < 10mOsm/L

Fomepizole [3,4]

Fomepizole is a competitive antagonist of alcohol dehydrogenase and can be used to treat both methanol and ethylene glycol poisoning. Fomepizole is the preferred antidote since, unlike ethanol, it does not require regular monitoring of blood concentrations or cause inebriation. It is particularly useful in patients who are at risk of coma, those who have liver dysfunction or have recently been exposed to disulfiram or metronidazole, and pregnant women.

Fomepizole – currently only kept in ITU and the emergency drug cupboard

Indications for Fomepizole treatment

Ethylene glycol poisoning

Documented suspicion that more than 10 g (9.12 mL of 100%) of ethylene glycol has been ingested by an adult particularly within the last 12 hours

OR

Any amount of ethylene glycol has been ingested and there is objective evidence of toxic alcohol exposure, e.g. high anion gap metabolic acidosis **OR** osmolar

gap greater than 10 mOsm/kg without there being another likely cause (e.g. ethanol intoxication OR urinary oxalate crystals present

Methanol poisoning

Documented suspicion that more than 10 g (12.7 mL of 100%) of methanol has been ingested by an adult within the last 12 hours

OR

Any amount of methanol has been ingested and there is objective evidence of toxic alcohol exposure, e.g. high anion gap metabolic acidosis **OR** osmolar gap greater than 10 mosmols/kg without there being another likely cause (e.g. ethanol intoxication).

Doses of Fomepizole for toxic alcohol poisoning

The loading dose is 15mg/kg IV diluted to a final volume of 250mL in 0.9% sodium chloride or glucose 5% over 30 minutes.

Followed by maintenance doses of 10mg/kg IV diluted to a final volume of 250mL in 0.9% sodium chloride or glucose 5% over 30 minutes every 12 hours (starting at 12 hours after the loading dose is given) for a maximum of 4 doses; followed by 15 mg/kg IV diluted to a final volume of 250mL in 0.9% sodium chloride or 5 % glucose over 30 minutes every 12 hours thereafter.

Stop: continue until ethylene glycol or methanol concentration is undetectable OR ethylene glycol or methanol concentration is less than 50 mg/L **AND** acidosis and signs of systemic toxicity has resolved.

Note: for patients weighing >110kg, fomepizole dose should be calculated using a maximum of 110kg rather than the patients actual weight.

Other Treatments

Ethanol [5]

Ethanol is an effective block to alcohol dehydrogenase but is associated with more complications. **If there is any delay in obtaining fomepizole, administer ethanol urgently initially, followed by fomepizole when available.**

Load: 10 mL/kg of a 10 % ethanol solution IV over 30 minutes OR oral loading dose equivalent to 800 mg/kg absolute (100%) ethanol. This can be given in the form of whisky, gin or vodka (40% ethanol) in a dose of 2.5 mL/kg body weight (about 175 mL spirits for a 70 kg adult).

Maintenance: please refer to ToxBase for maintenance dosing.

Stop: continue until ethylene glycol or methanol concentration is undetectable OR ethylene glycol or methanol concentration is less than 50 mg/L **AND** acidosis and signs of systemic toxicity has resolved.

The Norfolk and Norwich Hospital currently stocks no options that would enable intravenous ethanol treatment; please use the oral dosing should both Fomipezole and intravenous ethanol be unavailable.

Gastritis and vomiting are occasionally encountered when using the enteral route for antidotal ethanol therapy, in addition to the other adverse effects of ethanol.

Cofactor Therapy

All patients who have ingested methanol should receive folinic acid/folinate 30 mg intravenously 6 hourly for 48 hours or until acidosis resolves

All patients who have ingested ethylene glycol should receive Pabrinex Intravenous High Potency 2 ampoules three times a day for 48 hours

Metabolic Acidosis

If metabolic acidosis persists despite correction of hypoxia and adequate fluid resuscitation consider correction with intravenous sodium bicarbonate. Consider central venous access; 8.4% and 4.2% sodium bicarbonate can cause localised necrosis in the event of extravasation.

Haemodialysis

Severe poisoning should be treated by haemodialysis and is effective
effective in removing methanol, ethylene glycol and their metabolites and can shorten the duration of poisoning in addition to correcting metabolic abnormalities.

Indications for haemodialysis are any one of the following:

- Concentrations greater than 500 mg/L (0.5 g/L; 16 mmol/L)
- Visual disturbance
- Features of CNS toxicity
- Severe metabolic acidosis
- Renal failure
- Deteriorating condition despite supportive measures
- Severe electrolyte imbalance
- A desire to shorten the duration of the poisoning.

If in any doubt about whether haemodialysis or fomepizole is more appropriate please discuss with the Consultant Renal Physician on call.

In general fomepizole should be used in those with early presentation and without renal failure and haemodialysis in those with renal failure or severe acidosis.

Clinical audit standards

All patients with toxic alcohol ingestion have the correct dose of fomepizole or haemodialysis

Distribution list / dissemination method

Intranet

Summary of development and consultation process undertaken before registration and dissemination

Discussed within the Acute Medicine Governance, Pharmacy, Clinical Biochemistry and Renal Medicine

References

1. Miller H, Barceloux D, Krenzelok E, Olson K, Watson W. American Academy of Clinical Toxicology Practice Guidelines on the Treatment of Ethylene Glycol Poisoning. Journal of Toxicology: Clinical Toxicology. 1999;37(5):537-560.

2. The American Academy of Clinical To, Barceloux D, Randall Bond G, Krenzelok E, Cooper H, Allister Vale J. American Academy of Clinical Toxicology Practice Guidelines on the Treatment of Methanol Poisoning. Journal of Toxicology: Clinical Toxicology. 2002;40(4):415-446.

3. Brent J, McMartin K, Phillips S, Burkhart K, Donovan J, Wells M et al. Fomepizole for the Treatment of Ethylene Glycol Poisoning. New England Journal of Medicine. 1999;340(11):832-838.

4. Brent J, McMartin K, Phillips S, Aaron C, Kulig K. Fomepizole for the Treatment of Methanol Poisoning. New England Journal of Medicine. 2001;344(6):424-429.

5. Zakharov S, Pelclova D, Navratil T, Belacek J, Komarc M, Eddleston M et al. Fomepizoleversusethanol in the treatment of acute methanol poisoning: Comparison of clinical effectiveness in a mass poisoning outbreak. Clinical Toxicology. 2015;53(8):797-806.

6. Sivilotti M. Methanol and ethylene glycol poisoning: Management [Internet]. Uptodate.com. 2021 [cited 17 March 2021]. Available from: https://www.uptodate.com/contents/methanol-and-ethylene-glycol-poisoning-management?search=ethylene%20glycol%20poisoning&source=search_result&selectedTitle=2~39&usage_type=default&display_rank=2#H255409132

7. TOXBASE - poisons information database for clinical toxicology advice [Internet]. Toxbase.org. 2021 [cited 17 March 2021]. Available from: https://www.toxbase.org/General-Info/Antidotes---doses-and-sources/Ethanol---antidote/