TOXBASE .org

Users Update

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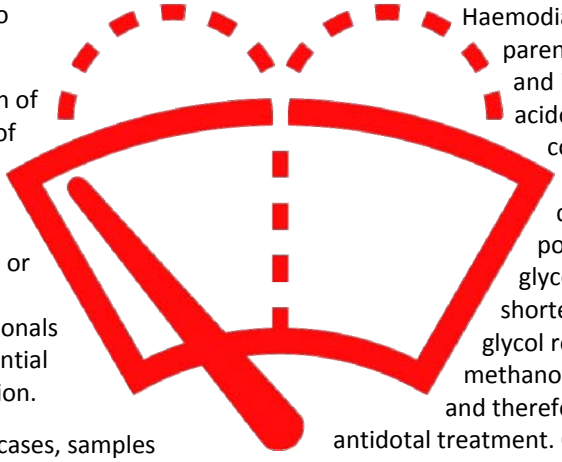
UK National Poisons Information Service 0344 892 0111

UK Teratology Information Service 0344 892 0909

THE BLIND DRUNK

In these colder months many of us stock up on antifreeze to aid our journey to work in the morning. This serves as a timely reminder of the dangers of toxic alcohol poisoning, a relatively rare but serious cause of self-poisoning.

Ethylene glycol and methanol, present in many preparations of antifreeze and screen wash, are alcohols which if ingested may cause significant toxicity including metabolic acidosis, renal failure and, in the case of methanol, irreversible blindness. Following ingestion, an initial period of intoxication will be apparent until metabolism of the relatively non-toxic parent compound to the toxic metabolites occurs. Ethylene glycol is metabolised to glycoaldehyde and then glycolic, glyoxylic and oxalic acids; methanol is metabolised to formaldehyde and formic acid.



The goal of treatment is early instigation of antidote therapy to prevent formation of the toxic metabolites. Unfortunately, many patients who present with toxic alcohol poisoning may be unable to provide an accurate history of ingestion or may even be unaware that they have ingested a toxic alcohol. Health professionals therefore need to be aware of this potential poison and the need for early intervention.

To complicate the assessment of these cases, samples usually need to be sent to specialist toxicology laboratories to obtain ethylene glycol and methanol concentrations (NPIS can advise laboratory details). Therefore surrogate markers of ingestion (osmolar gap and anion gap) may be used to determine the need for antidote therapy. The interpretation of the osmolar and anion gaps require some knowledge of the pharmacology and metabolism of toxic alcohols. Patients will initially show a high osmolar gap following ingestion while the anion gap may be normal. As the parent compound is broken down to its toxic metabolites the osmolar gap will start to fall and the anion gap will rise. Therefore the result of the osmolar and anion gaps will depend on the time at which the patient presents to hospital following ingestion. It is important to remember that other potential causes of a raised osmolar gap (eg ethanol intoxication) should be excluded.

The first-line antidote for toxic alcohol poisoning is fomepizole. This is a competitive inhibitor of alcohol dehydrogenase and acts to prevent breakdown to the toxic metabolites allowing the parent compound to be eliminated unchanged. Fomepizole has now largely superseded the traditional antidote ethanol due to significantly fewer associated adverse effects and greater ease of administration. Fomepizole should be administered where there is either suspicion that toxic alcohol ingestion has occurred or where there is objective evidence of toxic alcohol exposure (eg high anion gap, metabolic acidosis or raised osmolar gap greater than 10 mosmols/kg) without an alternative cause (eg ethanol intoxication). Treatment should continue until the plasma ethylene glycol or methanol concentration can be confirmed as less than 50 mg/L, the limit of detection in many laboratories.

Haemodialysis is an additional treatment modality which may be considered in patients following toxic alcohol ingestion. Haemodialysis is effective in removing both the parent compound and the toxic metabolites and indications for use include severe acidosis, renal failure, deteriorating clinical condition despite best supportive care, severe electrolyte imbalance and a desire to shorten the duration of poisoning. The half-lives of both ethylene glycol and methanol are significantly shortened through haemodialysis (ethylene glycol reduced from 12 hours to 3 hours; methanol reduced from 55 hours to 3 hours) and therefore this may be preferred to prolonged antidotal treatment. Often patients receive both fomepizole and haemodialysis and, like fomepizole, haemodialysis should be continued until the plasma toxic alcohol concentration is undetectable and the acidosis has resolved.

The assessment, treatment and management of toxic alcohol poisoning is complex and requires interpretation of blood results not commonly used in everyday medicine. The NPIS are here to help and the newly updated toxic alcohol poisoning management pages on TOXBASE provide step by step guidelines for healthcare professionals at the frontline. We would also encourage contact with the NPIS via the 24-hour telephone line to discuss all cases where toxic alcohol ingestion is being considered.

Further information from *TOXBASE*®:

~ *consult the product monographs by searching for* ***'ethylene glycol'*** *or* ***'methanol'***

~ *find information on how to calculate anion or osmolar gap within the* ***General info menu*** > ***Treatment FAQs***

Recently published

Brandenburg R, et al. The need for ICU admission in intoxicated patients: a prediction model. Clin Toxicol 2017; 55: 4-11. http://dx.doi.org/10.1080/15563650.2016.1222616

Day R, et al. Exposures to traditional automatic dishwashing tablets and a comparison with exposures to soluble film tablets reported to the United Kingdom National Poisons Information Service 2008–2015. Clin Toxicol 2017; 55: 206-12. http://dx.doi.org/10.1080/15563650.2016.1264588

Day R, et al. The impact of an international initiative on exposures to liquid laundry detergent capsules reported to the United Kingdom National Poisons Information Service between 2008 and 2015. Clin Toxicol 2017; 55: 213-16. http://dx.doi.org/10.1080/15563650.2016.1267359

Day R, et al. Toxicity from automotive screenwashes reported to the United Kingdom National Poisons Information Service (NPIS) from 2012 to 2015. Clin Toxicol 2017; 55: 221-26. http://dx.doi.org/10.1080/15563650.2016.1271130

van Eijkeren JCH, et al. Modeling the effect of succimer (DMSA; dimercaptosuccinic acid) chelation therapy in patients poisoned by lead. Clin Toxicol 2017; 55: 133-41. http://dx.doi.org/10.1080/15563650.2016.1263855

van Eijkeren JCH, et al. Modelling dimercaptosuccinic acid (DMSA) plasma kinetics in humans. Clin Toxicol 2016; 54: 833-9. http://dx.doi.org/10.1080/15563650.2016.1221508

Kamour A, et al. Central nervous system toxicity of mefenamic acid overdose compared to other NSAIDs: an analysis of cases reported to the United Kingdom National Poisons Information Service. Br J Clin Pharmacol 2016; online early: https://dx.doi.org/10.1111/bcp.13169

Vliegenthart ADB, et al. Circulating acetaminophen metabolites are toxicokinetic bio-markers of acute liver injury. Clin Pharmacol Ther 2016; online early: https://dx.doi.org/10.1002/cpt.541

Recent new and updated pages

New TOXBASE® monographs:

3-methyl-2-(3-methylphenyl)morpholine
5,5-dimethyl-2-phenyl-morpholine
5-(2-fluorophenyl)-1,3-dihydro-7-nitro-2H-1,4-benzodiazepin-2-one
Acer pseudoplatanus (sycamore)
Agnus castus
Anakinra
Brancico XL
Cerbera manghas/Cerbera odollam
Cif anti-bacterial multipurpose spray & Cif easylift kitchen spray
Corsodyl mouthwash (alcohol free)
Cucurbitaceae
Daclizumab
Eculizumab
Fosfomycin trometamol
Harpic 100% limescale remover – original
Imiquimod
N-(1-phenethylpiperidin-4-yl)-N-phenylacrylamide
N-(2-fluorophenyl)-N-[1-(2-phenylethyl)-4-piperidinyl]-propanamide
Opicapone
Pipexus
Ramucirumab

Updated TOXBASE® monographs:

ABC Powder Fire Extinguisher
Acebutolol
Acetic anhydride
Acetyl bromide
Acrolein
Ammonium chloride
Atenolol
Axsain
Antifouling Paint
Benzocaine
Betaxolol
Bisoprolol
Bupivacaine
Capsaicin
Capsicum
Care Allergy Defence
Carteolol
Carvedilol
Celiprolol
Chubb Fire Extinguisher - Powder
Cinchocaine
Cleaning Liquid - Household
Esmolol
Ethylenediamine
Flecainide
Labetalol
Levobunolol
Lidocaine
Mexiletine
Nadolol
Nebivolol
Nitromethane
Oxprenolol
Pepper spray
Propafenone
Qutenza
Sotalol
Timolol
Umeclidinium bromide
Ursodeoxycholic acid

Unknown drugs of abuse

Patients often present having taken an unknown drug of abuse. In addition, the chemical content and the doses at which they are present in street drugs and in products previously referred to as “legal highs” may vary greatly and labels may not accurately reflect the contents. Multiple chemical ingredients are common.

When faced with such a presentation management should be guided by recognition of the clinical picture, or ‘toxidrome’. Note that some chemicals have mixed toxic features and you may need to consider more than one toxidrome, especially when more than one chemical is involved in a product.

General information on types of drugs of abuse and typical features/toxidromes is available on TOXBASE. Search for the term ‘**drugs of abuse**’ to review this information and use the links provided to reach management advice.

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