Ethanol, Methanol and Ethylene Glycol – Laboratory Investigation

Ethylene glycol is rapidly metabolised with peak concentrations occurring 1 to 4 hours after ingestion. In the first few hours after ingestion a high osmolar gap develops, but then falls as the ethylene glycol is metabolised and the anion gap increases. Therefore, if a patient presents early they may have a normal anion gap, a normal pH but their osmolar gap may be raised. It is important to remember that a metabolic acidosis only develops after some ethylene glycol has been metabolised. A high anion gap metabolic acidosis suggests a late presentation, but it is important to remember that there are other causes such as methanol ingestion, diabetic or alcoholic ketoacidosis, renal failure, multi-organ failure. If several hours has elapsed since ingestion then urine glycolic acid levels may be informative. Do not wait for results of ethylene glycol and/or methanol analyses before starting treatment, since these can take up to twenty four hours.

Initial investigations:

Requests for methanol and/or ethylene glycol analysis will only be referred to external laboratories if there is a strong clinical suspicion and the following tests have been performed:

(Serum tube – gold topped
Urea and electrolytes (including chloride and bicarbonate)
Serum osmolality
Calcium profile
Paracetamol and salicylate

Fluoride oxalate – grey topped tube
Glucose
Ethanol
Lactate (N.B. presence of ethylene glycol metabolites cause positive interference with lactate measurements on blood gas analysers and to a lesser extent with the laboratory biochemistry analyser)

Gas analyser heparinised syringe
Venous (pH) blood gases (do not use derived bicarbonate to calculate anion gap – see below)

Total blood tubes required:

Serum – gold topped x1
Fluoride Oxalate – grey topped x3 (1 for all of the above assays +1 for ethylene glycol and +1 for methanol)
Gas analyser heparinised syringe x 1

Urine (x1 white topped containers)
orGANIC acid (glycolic acid) estimation.
Dipstick for urine ketones
Referral indicated if there is:

1) non-ketotic, non-lactic high anion gap metabolic acidosis
   Anion gap (see equation 4)
2) non-ethanolic high osmolar gap
   Osmolar gap (see equations 1-3)
3) unexplained clinically significant hypocalcaemia

Osmolarity can be calculated using a number of different formulae, all of which are variations upon:

\[2[Na^+] + [\text{Urea}] + [\text{Glucose}] = \text{calculated osmolarity}\]  
(Equation 1)
where all concentrations are in mmol/L

Where ethanol is present then the above formula can be adjusted to take this into account. In LTHT plasma ethanol is reported in mg/dl and so must first be converted to mmol/L by dividing by 4.6:

\[2[Na^+] + [\text{Urea}] + [\text{Glucose}] + [\text{Ethanol}] = \text{calculated osmolarity}\]  
(Equation 2)
where all concentrations are in mmol/L

Osmolar Gap = measured osmolality – calculated osmolarity  
(Equation 3)

An osmolar gap >10 mOsm/kg suggests the presence of an osmotically active substance other than those used to calculate the osmolarity i.e. ethylene glycol and or methanol may be present.

It is important to stress that since the ‘normal’ osmolar gap is ±10 mOsm/kg this technique cannot be used to rule out significant ingestion of methanol, or ethylene glycol, especially if presentation has been delayed.

\[([Na^+] + [K^+] - ([Cl^-] + [HCO_3^-])) = \text{Anion gap mmol/L}\]  
(Equation 4)

A normal anion gap is up to 18 mmol/L and must be calculated using a measured HCO3- (i.e. laboratory HCO3-), not a derived HCO3- from the blood gas analyser.

Dr Mike Bosomworth
Consultant Clinical Biochemist
Clinical Service Lead for Blood Sciences and Specialist Laboratory Medicine.

Mr Stephen Bush
Consultant in Emergency Medicine
Clinical Director, Urgent Care

20th June 2014