Cofactors for Ethylene Glycol and Methanol Poisoning

In their 2009 annual report, the American Association of Poison Control Centers reported 91,973 exposures to toxic alcohols, resulting in over 30 deaths. Nearly half of these deaths were due to ethylene glycol or methanol. Ethylene glycol and methanol themselves are not toxic, but their metabolites cause inebriation, nausea and vomiting, metabolic acidosis, hemodynamic instability and seizures. Oxalic acid, a metabolite of ethylene glycol, chelates with serum calcium and precipitates as crystals in renal tubules, while formic acid, a methanol metabolite, damages the optic nerves and retina. Due to rapid absorption and inability to bind to activated charcoal, gastrointestinal decontamination is limited in effectiveness. Current treatment modalities incorporate alcohol dehydrogenase antagonists (fomepizole or ethanol) and hemodialysis. Although their efficacy has not been studied in clinical trials, Vitamin-B cofactors may be administered to promote alternative metabolism of toxic alcohols to non-toxic metabolites. The products of these metabolic pathways are then really eliminated. (See supplemental page for metabolic pathway figures for ethylene glycol and methanol).

In patients exposed to ethylene glycol, 100mg thiamine and 100mg pyridoxine can be administered IV daily to stimulate the conversion of glycolic acid and glyoxylic acid to non-toxic alpha-hydroxy-beta-keto adipate and glycine, respectively. Theoretically, these pathways can limit accumulation of oxalic acid, preventing renal toxicity as well as metabolic acidosis. In the methanol poisoned patient, administration of folic acid 1mg/kg IV every four hours (max 50mg/dose) may enhance the metabolism of toxic formic acid to carbon dioxide and water. Leucovorin (folinic acid) is the active form of folic acid and may be given as the initial dose followed by folic acid.

While the effectiveness of vitamin-B cofactors has not been proven in clinical studies, the potential benefits of administration outweigh any risk of adverse reaction. Poisoned patients should be cared for and triaged based on current poison center guidelines for supportive care and established indications for fomepizole and hemodialysis.

Kevin M. Nork  
PharmD Candidate, Class of 2012  
University of Maryland School of Pharmacy

DID YOU KNOW THAT… “bath salts” will soon be illegal in the U.S.?

From January 1, 2011 through August 31, 2011, U.S. poison centers received 4,720 calls about synthetic stimulants labeled as “bath salts” or “plant food”. Users of these drugs have developed toxic effects including tachycardia, hypertension, agitation, paranoia and psychosis. Many states have banned the stimulants, and Maryland is moving to impose a ban soon. The U.S. Drug Enforcement Administration announced that it is using emergency scheduling authority to control three synthetic stimulants for at least one year while determining whether a permanent ban is warranted. Read more about “bath salts” at www.aapcc.org and in the February 2011 ToxTidbits at www.mdpoison.com/publications/toxtidbit_archive.html.

Subscribe to ToxTidbits and read past issues at www.mdpoison.com.
Metabolism of Methanol and Ethylene Glycol

Methanol

↓

Alcohol dehydrogenase

Formaldehyde

↓

Aldehyde dehydrogenase

Formic acid

↓

Folic acid

CO₂ + H₂O

Ethylene glycol

↓

Alcohol dehydrogenase

Glycoaldehyde

↓

Aldehyde dehydrogenase

Glycolic acid

↓

Lactate dehydrogenase, Glycolic acid oxidase

Thiamine

Glyoxyllic acid

↓

α-hydroxy-β-ketoadipic acid

Pyridoxine

Glycolic acid oxidase

Oxalic acid

Glycine

Supplement to September 2011 ToxTidbits