Newsletter for the TDM and Toxicology Division of AACC

Winter 2012

Therapeutics & Toxins News

Inside this issue:

"Toxic effects of ethylene glycol cause CNS depression, nausea, and renal failure"

Ethylene Glycol Toxicity

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Ethylene glycol ($C_2H_6O_2$) is a compound that can be found in most automobiles. When mixed with water, ethylene glycol acts as both an anti-freeze and a heat transfer agent for internal combustion engines and some electronic devices. Because ethylene glycol is found in many items used on a daily basis it is also a fairly common oral toxin, both accidently and maliciously. Ethylene glycol has a sweet taste, making it a particularly hazardous toxin for children and pets if containers of this product are left unsecured. The effects of intoxication with ethylene glycol often include respiratory and central nervous system depression, nausea, metabolic acidosis, and renal failure [1]. If not treated promptly, organic acids produced from the metabolism of ingested ethylene glycol can have serious and sometimes lethal consequences. According to a 2009 report from the American Association of Poison Control Centers, there were 4,852 single-substance exposures to ethylene glycol, with 11% of these cases resulting in serious injury or death [2].

Logo for Therapeutic and Toxin Newsletter

In humans, the LD50 of ethylene glycol is thought to be approximately 1,400-1,600 mg/kg [3]. Once in the body, ethylene glycol itself is eliminated rather quickly ($t_{1/2}$: 2-5 hrs) [4]. Toxicity from ingestion of ethylene glycol is not from the compound itself, but primarily a product of its metabolism which results in the accumulation of various organic acids. The rate-limiting step in this metabolic process is mediated by alcohol dehydrogenase to form glycoaldehyde. Further metabolism of glycoaldehyde is provided by aldehyde dehydrogenase and other enzymes, leading to the toxic

Ethylene Glycol Toxicity (continued from page 1)

accumulation of organic acids such as glycolic acid, glyoxylic acid, and oxalic acid (Fig.1). Glycolic acid is the predominate metabolite and it is the greatest contributor in causing severe metabolic acidosis. Oxalic acid production is a particular problem because this metabolite can precipitate calcium to cause renal damage in affected individuals.

Determination of ethylene glycol intoxication is often challenging due to the rapid elimination of the compound, the time lapse between ingestion and investigation, and if subjects are found unconscious. Manufacturers of antifreeze products often include fluorescein in their formulations. This additive can sometimes allow emergency room personnel to quickly detect its fluorescence around the mouth and in urine using ultraviolet light (i.e.Woods' lamp). Laboratory diagnosis of ethylene glycol ingestion can be determined by various methods. The presence of hexagonal oxalate crystals in the patient's urine by microscopy is a sign of possible ethylene glycol intoxication, yet this test may lack in sensitivity. A red flag, for intoxication with ethylene glycol or other toxic alcohols, is an elevated osmolal and anion gap. If the patient has ingested the compound many hours prior to being tested, then there may be a false negative result due to its short half-life. The most sensitive method for detecting and quantifying ethylene glycol is gas chromatography; however, this is a labor-intensive method and may not be available to all emergency room facilities. The recent development of a rapid detection method for ethylene glycol by enzymatic assays on automated analyzers is another choice for diagnosis of intoxication [5]. Enzymatic assay methods can be adapted to previously existing automated chemistry instrumentation in most hospital laboratories. This methodology will enable ethylene glycol testing to become more assessable to hospital laboratories and decrease turnaround time to improve patient care.

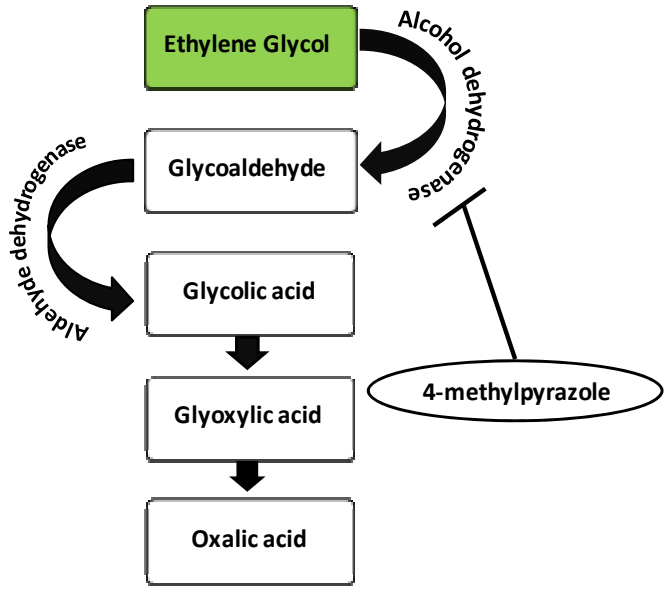
"Toxic metabolites of ethylene glycol cause metabolic acidosis."

Treatment of ethylene glycol intoxication is dependent on the duration of intoxication, physiological symptoms, and concentration of toxic metabolites. Acidosis may be treated with the administration of bicarbonate to buffer the reduction in pH. When ethylene glycol concentrations are > 20 mg/dL, treatment with competitive inhibitors of alcohol dehydrogenase (ethanol or 4-methylpyrazole) are recommended to decrease the production of organic acids [6]. Treatment with 4-methylpyrazole is preferred over ethanol because of the lack of additional CNS depression, but is too costly for some emergency services to keep in stock (~$1,000/dose). When ethylene glycol concentrations are ≥ 50 mg/dL, hemodialysis is indicated to remove this toxic metabolite from circulation which helps correct the pH imbalance [6].

Laboratory testing for ethylene glycol is important for diagnosis and managing therapy for patients with toxicity. Analytical methods that have high sensitivity, specificity, and rapid turnaround will benefit patient care.

Ethylene Glycol Toxicity (continued from page 2)

Figure 1—Ethylene Glycol Metabolism



"Ethylene glycol poisoning elevates both the anion and osmolal gap."

References

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2. Bronstein, A.C., et al., *2009 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 27th Annual Report.* Clin Toxicol (Phila), 2010. **48**(10): p. 979-1178.
3. Agency for Toxic Substances and Disease Registry, *Toxicological profile for Ethylene Glycol*, US Dept of Health and Human Services, Editor. 2010: Atlanta, GA.
4. Baselt, R.C., *Disposition of toxic drugs and chemicals in man*. 7th ed. 2004, Foster City, Calif.: Biomedical Publications. xvii, 1254 p.
5. Juenke, J.M., et al., *Rapid and specific quantification of ethylene glycol levels: adaptation of a commercial enzymatic assay to automated chemistry analyzers.* Am J Clin Pathol, 2011. **136**(2): p. 318-24.
6. Barceloux, D.G., et al., *American Academy of Clinical Toxicology Practice Guidelines on the Treatment of Ethylene Glycol Poisoning. Ad Hoc Committee.* J Toxicol Clin Toxicol, 1999. **37**(5): p. 537-60.
7. http://www.cdc.gov/niosh/ershdb/EmergencyResponseCard_29750031.html
8. http://emedicine.medscape.com/article/814701-workup

Newsletter Survey

The Editorial Board would like to survey the membership on the value of the TDM /Toxicology Division Newsletter. Based on information from the 2011 Business meeting and luncheon, there was a suggestion to eliminate the newsletter and update the current TDM/Toxicology Division website to create a forum that is more engaging. We value your opinion. Please take the time to fill out the survey and email it to kamisha.johnson-davis@aruplab.com. Thank you!

Please fill out the survey and email it to kamisha.johnson-davis@aruplab.com

1) What is your level of interest in the association's newsletter?

- ○ High Interest (Read regularly, cover to cover)
- ○ Medium Interest (Skim for articles of interest)
- ○ Low Interest (Read occasionally)
- ○ No Interest
- ○ Undecided

2) How important to you is the regular newsletter sent by the association?

- ○ Very Important
- ○ Somewhat Important
- ○ Not Very Important
- ○ Not at all Important
- ○ Undecided

3) How satisfied are you with the layout of the newsletter?

- ○ Very Satisfied
- ○ Somewhat Satisfied
- ○ Satisfied
- ○ Somewhat Dissatisfied
- ○ Dissatisfied
- ○ Undecided

4) How satisfied are you with the quality of the writing?

- ○ Very Satisfied
- ○ Somewhat Satisfied
- ○ Satisfied
- ○ Somewhat Dissatisfied
- ○ Dissatisfied
- ○ Undecided

Newsletter Survey (Continued from page 4)

5) How satisfied are you with the overall content?

- Very Satisfied
- Somewhat Satisfied
- Satisfied
- Somewhat Dissatisfied
- Dissatisfied
- Undecided

6) How satisfied are you with the timeliness of the information presented in the newsletter?

- Very Satisfied
- Somewhat Satisfied
- Satisfied
- Somewhat Dissatisfied
- Dissatisfied
- Undecided

7) How satisfied are you with the practicality and helpfulness of the information presented in the newsletter?

- Very Satisfied
- Somewhat Satisfied
- Satisfied
- Somewhat Dissatisfied
- Dissatisfied
- Undecided

8) How satisfied are you with your ability to submit information or articles for inclusion in the newsletter?

- Very Satisfied
- Somewhat Satisfied
- Satisfied
- Somewhat Dissatisfied
- Dissatisfied
- Undecided

9) How much do you agree or disagree that the issues covered are important to association members?

- Strongly Disagree
- Disagree
- Undecided
- Agree
- Strongly Agree

Newsletter Survey (continued from page 5)

10) Do you feel the newsletter effectively provides information important to the overall needs of the members?

- ○ Yes
- ○ No
- ○ Don't Know

11) What, if any, information or sections would you like to see included in the newsletter in the future?

12) What, if any, sections do you think should be removed from the newsletter?

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13) Overall, how satisfied are you with the regular newsletter?

- ○ Very Satisfied
- ○ Somewhat Satisfied
- ○ Satisfied
- ○ Somewhat Dissatisfied
- ○ Dissatisfied
- ○ Undecide

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UPCOMING MEETINGS OF INTEREST

SOCIETY OF TOXICOLOGY (SOT)
Annual Meeting
March 11-15, 2012, Moscone Convention Center, San Francisco, CA.
www.toxicology.com

MIDWEST ASSOCIATION FOR TOXICOLOGY AND THERAPEUTIC DRUG MONITORING (MATT)
Annual Meeting
May 2-4, 2012, Hyatt Lodge, Oakbrook, IL
www.midwesttox.org

SOUTHWESTERN ASSOCIATION OF TOXICOLOGISTS
Annual Meeting
May 3-5,2012, Marriot Courtyard—Wichita at Old Town, San Antonio, TX
www.sat-tox.org

CALIFORNIA ASSOCIATION OF TOXICOLOGISTS
May 2012
www.cal-tox.org

THE INTERNATIONAL ASSOCIATION OF FORENSIC TOXICOLOGISTS (TIAFT)
Annual Meeting
June 3-8, 2012, Hamamatsu, Japan
www.tiaft.org

SOCIETY OF FORENSIC TOXICOLOGISTS (SOFT)
Annual Meeting
July 1-6, 2012, Boston, MA
www.soft-tox.org

AMERICAN ASSOCIATION FOR CLINICAL CHEMISTRY (AACC)
Annual Meeting
July 15-19, 2012, Los Angeles, CA.
www.aacc.org

THE AMERICAN ACADEMY OF CLINICAL TOXICOLOGY
North American Congress of Clinical Toxicology
October 1-6, 2012, Las Vegas, NV

"Please attend the TDM/Tox Division Lunchtime meeting at the 2012 AACC Annual Conference in Los Angeles."

Please contact Dr. Kamisha Johnson-Davis at kamisha.johnson-davis@aruplab.com if you are interested in joining the editorial board or if you have ideas or article contributions for this newsletter.

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DRUGS IN THE NEWS

Drug Shortages:

Atropine sulfate injection
Bleomycin injection
Bupivacaine hydrochloride injection
Diltiazem injection
Furosemide injection
Levofloxacin injection
Lidocaine Hydrochloride injection
Lorazepam injection
Methotrexate
Metoclopramide injection
Midazolam injection
Morphine Sulfate injection
Naloxone
Naltrexone oral tablet
Tobramycin solution for injection
Zinc injection

http://www.fda.gov/Drugs/DrugSafety/DrugShortages/ucm050792.htm