Ethylene Glycol and Methanol Poisoning Treatment

UKHealthCare

For many years, the only pharmacologic treatment for ethylene glycol or methanol toxicity was ethanol, given either orally or by continuous intravenous infusion.[1] Although effective for these indications, concern exists regarding ethanol's harmful side effect profile. The formulary at UK Hospital includes another antidote for ethylene glycol toxicity, fomepizole (Antizol®), which is also FDA-approved for methanol poisonings. Fomepizole is a competitive inhibitor of alcohol dehydrogenase, with an affinity for the enzyme 8,000 times that of ethanol.[2] Alcohol dehydrogenase catalyzes the metabolism of ethylene glycol to glycoaldehyde, which is then oxidized to produce glycolic acid, glycoxylic acid, and oxalic acid. The metabolic acidosis and renal tubular damage associated with ethylene glycol ingestion are caused primarily by glycolic and oxalic acids respectively.[3, 4] Alcohol dehydrogenase also catalyzes the conversion of methanol to formaldehyde with subsequent oxidation to formic acid, resulting in the ocular damage and blindness associated with this metabolite.[1, 5]

Fomepizole is effective in preventing the formation of toxic metabolites that are responsible for the complications of ethylene glycol and methanol poisoning. It appears to be most useful in patients who present soon after intoxication and who have not yet developed complications of ingestion. Largely due to the low incidence of methanol and ethylene glycol toxicities, comparison studies between ethanol and fomepizole are currently not available. The main disadvantage of fomepizole over ethanol is the acquisition cost. This difference in cost is magnified in patients with severe toxicity requiring hemodialysis, during which fomepizole needs to be dosed every four rather than every 12 hours. Unlike ethanol, fomepizole is not commonly associated with adverse effects such as CNS depression, hypoglycemia, hypothermia and agitation. Treatment with fomepizole *may* reduce costs if patients can be admitted to acute care areas rather than the intensive care unit while receiving the antidote. The dosing regimen of fomepizole does not require the frequent monitoring and subsequent adjustment of therapy that are necessary with ethanol treatment. Other laboratory monitoring, such as ethylene glycol and methanol serum concentrations, are still necessary.[1, 3]

For these reasons, fomepizole's indication for use at UKH has been expanded to include both ethylene glycol and methanol toxicity. In addition, there are no longer UKH formulary restrictions for use according to the following guidelines.

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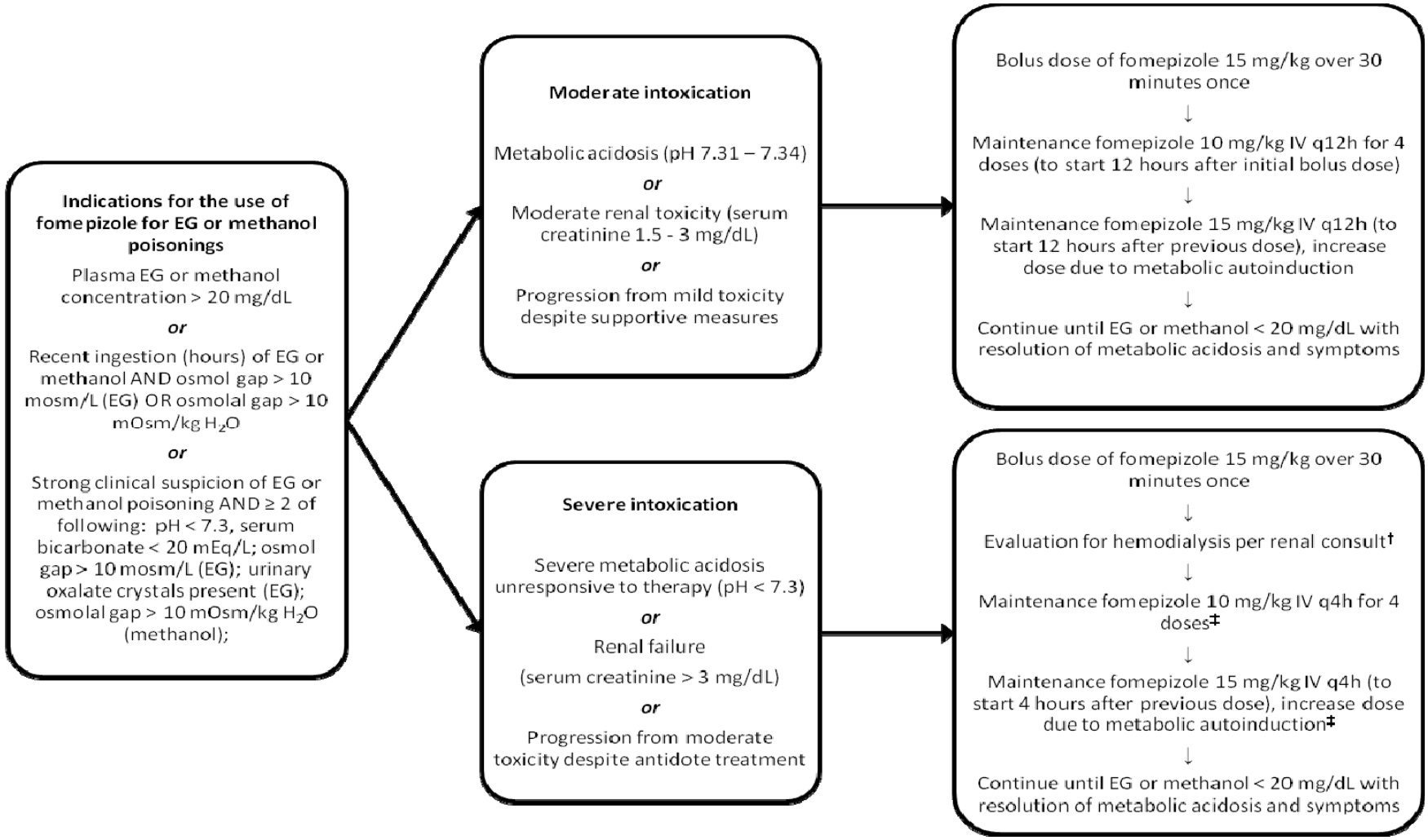
Guidelines for the Management of Ethylene Glycol (EG) and Methanol Poisoning



† If hemodialysis NOT indicated per renal consult, follow moderate intoxication treatment algorithm

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‡ Fomepizole dosing in hemodialysis

DOSE AT THE BEGINNING OF HEMODIALYSIS	
If < 6 hours since last fomepizole dose	Do not administer next scheduled dose.
If ≥ 6 hours since last fomepizole dose	Administer next scheduled dose.
DOSE DURING HEMODIALYSIS	
Administer dose every 4 hours.	
DOSE AT THE COMPLETION OF HEMODIALYSIS	
Time between last dose and end of hemodialysis	***Dose administered at end of hemodialysis session***
< 1 hour	Do not administer dose at end of hemodialysis.
1-3 hours	Administer 50% of next scheduled dose.
> 3 hours	Administer next scheduled dose.
MAINTENANCE DOSE AFTER HEMODIALYSIS	
Give next scheduled dose 12 hours from last fomepizole dose if indicated.	

If fomepizole is indicated BUT there is history of hypersensitivity to fomepizole, ethanol should be used per the following guidelines (table 2). Ethanol should be titrated to a level of 100 mg/dL until ethylene glycol or methanol levels are below 20 mg/dL (see table 3 for ethanol contraindications).

Table 2. Therapeutic Doses of Ethanol Based on Patient's Drinking History		
	Absolute Ethanol Dose	Volume of 10% IV Ethanol Solution
Loading dose	600-700 mg/kg	7.6 - 10 mL/kg in D5W over 30 minutes
Nondrinker		
Maintenance dose	66 mg/kg/hr	0.83 mL/kg/hr
Maintenance dose during hemodialysis	169 mg/kg/hr	2.13 mL/kg/hr
Chronic drinker		
Maintenance dose	154 mg/kg/hr	1.96 mL/kg/hr
Maintenance dose during hemodialysis	257 mg/kg/hr	3.26 mL/kg/hr

Table 3. Ethanol Contraindications
Recovering alcoholic
History of seizures
Requiring close monitoring of CNS function
Concurrent use of **disulfiram** (Antabuse®) or **metronidazole** (Flagyl®)
Patient who is abstinent for religious reasons

References:

1. Barceloux DG, Bond GR, Krenzelok EP, Cooper H, Vale JA. American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. J Toxicol Clin Toxicol 2002;40:415-46.
2. Antizol [package insert]. In. Palo Alto, CA: Jazz Pharmaceuticals, Inc; 2006.
3. Barceloux DG, Krenzelok EP, Olson K, Watson W. American Academy of Clinical Toxicology Practice Guidelines on the Treatment of Ethylene Glycol Poisoning. Ad Hoc Committee. J Toxicol Clin Toxicol 1999;37:537-60.
4. Brent J, McMartin K, Phillips S, et al. Fomepizole for the treatment of ethylene glycol poisoning. Methylpyrazole for Toxic Alcohols Study Group. N Engl J Med 1999;340:832-8.
5. Brent J, McMartin K, Phillips S, Aaron C, Kulig K. Fomepizole for the treatment of methanol poisoning. N Engl J Med 2001;344:424-9.