Update in Poison Management

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- No financial disclosures

Update in Poison Management

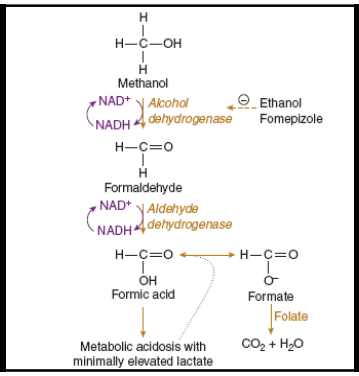
- Fomepizole
- Octreotide
- Lipid emulsion therapy (Intralipid®)
- Insulin/glucose

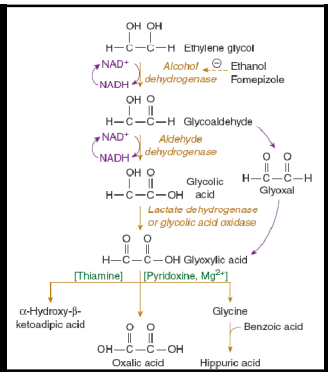
Antidote Use

- 95% of poisonings require no antidote use
- Occasionally it is critical

"There are some instances where nothing other than the timely use of a specific antidote or antagonist will save a patient"

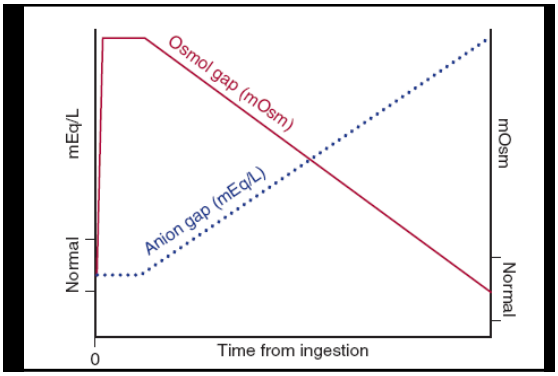
Fomepizole

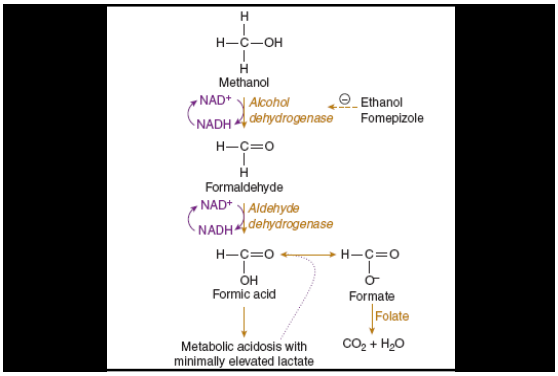




Fomepizole

- Blocks alcohol dehydrogenase
- Used in animals since 1970's
- Approved for use in US in 1997
- Used for methanol, ethylene glycol
  - Also for butoxyethanol, monobutlyl ethers



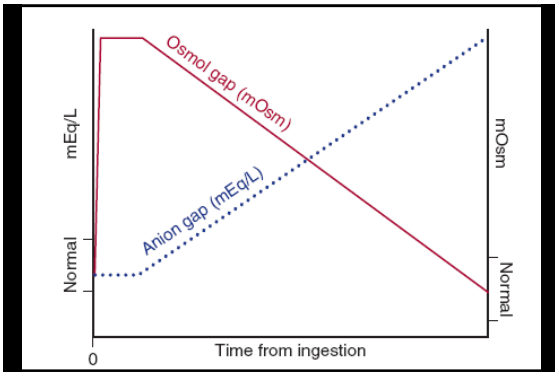


Why is Ethanol a Bad Antidote?

- CNS depression
- Respiratory depression
- Hypotension
- Gastritis and pancreatitis
- Metabolic problems
  - Hypoglycemia
  - Hyponatremia/Free water intoxication
- Serum ethanol level must be closely monitored
- Dosing errors and adverse reactions common
- Low cost is only advantage
  - Overall cost of ethanol is HIGHER

Fomepizole Limitations

- Does not completely eliminate need for dialysis



Fomepizole Limitations

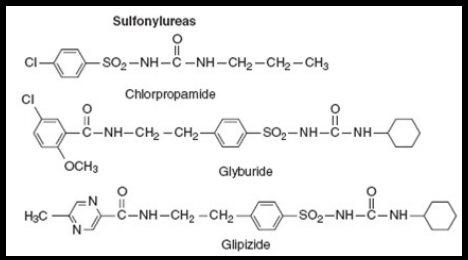
- Does not completely eliminate need for dialysis
- Medication cost is higher
- Adverse effects
  - Local irritation at infusion site (most common)
  - Headache
  - Rash
  - Slight elevation of AST/ALT
  - Nausea (high doses)
  - Vomiting (high doses)
  - Bradycardia (very rare)
  - Hypotension (very rare)

Fomepizole vs Ethanol

- *Goldfrank's Toxicologic Emergencies 9th Edition*
  - Fomepizole is preferred to ethanol.
  - Ethanol should only be used if fomepizole is not readily available.
  - Hospitals should be encouraged to stock fomepizole.
- Dosing
  - 15 mg/kg IV loading
  - 10 mg/kg IV q 12 H x 4 doses
  - If >48 hours needed, increase dose to 15 mg/kg IV q 12 H

Octreotide

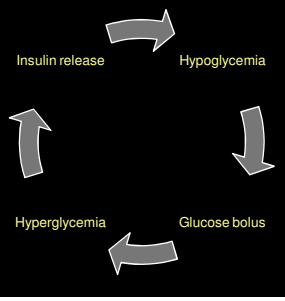
Sulfonylurea Hypoglycemics



Sulfonylurea Toxicity

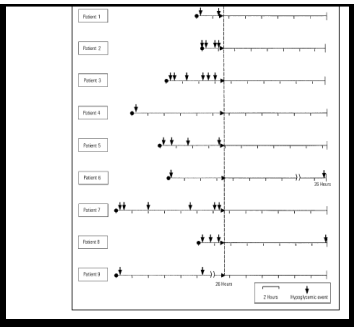
- Overdose or renal failure results in supratherapeutic level
- Onset of hypoglycemia is HIGHLY variable
  - As late as 21 hours with glyburide
  - As late as 48 hours with chlorpropamide
- Review of 98 pediatric exposures, 25 (27%) had hypoglycemia
  - Average onset 4.3 hours, range 0.5-16 hours
  - *Quadrani DA, Spiller HA, Widder P. Five-year retrospective evaluation of sulfonylurea ingestion in children. J Toxicol Clin Toxicol . 1996;34:267-270.*
- Prospective study of 185 pediatric exposures, 56 (30%) had hypoglycemia
  - Average onset 5.3 hours, range 1-21 hours
  - *Spiller HA, Villalobos D, Krenzelok EP, et al. Prospective multicenter study of sulfonylurea ingestion in children. J Pediatr. 1997;131:141-146.*

Sulfonylurea Hypoglycemia Treatment



Octreotide

- Long-acting somatostatin analog
  - Stops pancreatic insulin release
- Essential for treatment of refractory hypoglycemia induced by sulfonylureas and quinine
- Used to treat endocrine and neoplastic diseases
  - Acromegaly
  - Carcinoid tumor
  - Vasoactive intestinal peptide tumors
  - Pituitary tumors
  - Pancreatic islet cell tumors
  - Esophageal varices
  - Secretory diarrhea



McLaughlin SA, Crandall CS, McKinney PE: Octreotide: An antidote for sulfonylurea-induced hypoglycemia. Ann Emerg Med 2000;36:133-138.

Octreotide

- Indications:
  - Refractory sulfonylurea-induced hypoglycemia in adults
  - Any sulfonylurea-induced hypoglycemia in children
- OCTREOTIDE IS NOT FOR ACUTE HYPOGLYCEMIA!
- Dosing 1 mcg/kg or 50 mcg subcutaneously q 8-12 H
- Hospital admission, glucose checks based half-life of sulfonylurea
- Octreotide adverse effects
  - Pain at injection site
- Diazoxide?
  - Before the development of octreotide, diazoxide was commonly used
  - Diazoxide no longer used in US to treat hypoglycemia
  - Octreotide is far preferable to diazoxide

Lipid Emulsion Therapy

Lipid Emulsion Therapy (Intralipid®)

- Lipid emulsion used parenteral nutrition and in medications.
- Used for bupivacaine toxicity for >10 years
  - Calcium channel blockers
  - Beta blockers
  - Cyclic antidepressants

Weinberg GL, VadeBoncouer T, Ramaraju GA, et al. Pretreatment or resuscitation with a lipid infusion shifts the dose–response to bupivacaine induced asystole in rats. Anesthesiology . 1998;88:1071-1075.

Lipid Sink

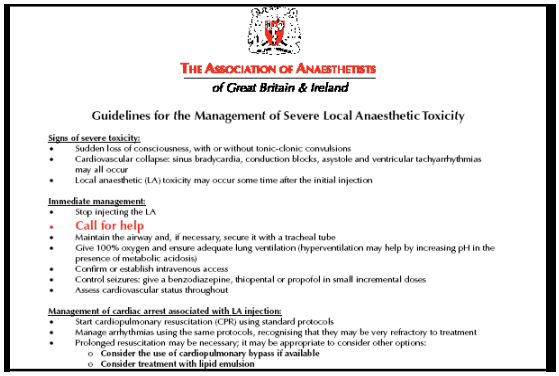
- Most widely accepted and plausible theory
- Lipid emulsion draws lipophilic drug out of tissues
- Most evidence supports this theory
- Consistent with rapid effect
- Other mechanisms
  - Metabolic energy source- no direct evidence supports this
  - Activation of Ca^{+} channels- no direct evidence supports this
- LipidRescue.Org™

Lipid Emulsion Therapy

- Use for bupivacaine and possibly other local anesthetic toxicity
  - Ventricular dysrhythmia or asystole
  - Keep lipid emulsion where bupivacaine is used
- A bolus dose of 1.5 mL/kg of 20% IFE followed by infusion for 30 to 60 minutes of 0.25 mL/kg/min or 15 mL/kg/h
- Consider for cardiotoxic doses of
  - Verapamil
  - Propranolol
  - Antidepressants (tricyclic, bupropion)

Lipid Emulsion Therapy

- DO NOT USE PROPOFOL
  - To get necessary lipid require 12 x normal dose of propofol!
- Adverse effects
  - None reported with antidotal use
  - Overdose of lipid emulsion may cause ARDS
- Avoid
  - Allergy to egg or soybean
  - Myocardial infarction



THE ASSOCIATION OF ANAESTHETISTS
of Great Britain & Ireland

Guidelines for the Management of Severe Local Anaesthetic Toxicity

Signs of severe toxicity:
- Sudden loss of consciousness, with or without tonic-clonic convulsions
- Cardiovascular collapse: sinus bradycardia, conduction blocks, asystole and ventricular tachyarrhythmias may all occur
- Local anaesthetic (LA) toxicity may occur some time after the initial injection

Immediate management:
- Stop injecting the LA
- **Call for help**
- Maintain the airway and, if necessary, secure it with a tracheal tube
- Give 100% oxygen and ensure adequate lung ventilation (hyperventilation may help by increasing pH in the presence of metabolic acidosis)
- Confirm or establish intravenous access
- Control seizures: give a benzodiazepine, thiopental or propofol in small incremental doses
- Assess cardiovascular status throughout

Management of cardiac arrest associated with LA injection:
- Start cardiopulmonary resuscitation (CPR) using standard protocols
- Manage arrhythmias using the same protocols, recognising that they may be very refractory to treatment
- Prolonged resuscitation may be necessary; it may be appropriate to consider other options:
  - **Consider the use of cardiopulmonary bypass if available**
  - **Consider treatment with lipid emulsion**

Lipid Rescue Limitations

- Is recommendation for lipid rescue for all severe local anesthetic toxicity wrong?
  - ***Yes***
- Should lipid rescue be used specifically for bupivacaine and lipophilic local anesthetics or all local anesthetic toxicity?
  - ***Are there local anesthetics for which lipid rescue will not be useful?***

Insulin/Glucose Therapy

- Initially described for calcium channel blocker toxicity in 1999
- *Yuan TH, Kerns WP, Tomaszewski CA, Ford MD, Kline JA. Insulin glucose as adjunctive therapy for severe calcium channel antagonist poisoning. J Toxicol Clin Toxicol. 1999;37:463-467.*
- Also used for beta blocker toxicity, though evidence is not as strong

Insulin/Glucose Pathophysiology

- Healthy myocardium uses free fatty acids for energy
- Stressed myocardium uses carbohydrates
- In calcium channel blocker (CCB) and beta blocker (BAA) toxicity myocardium uses carbohydrates for metabolism
  - More severe shock requires more carbohydrate
  - Insulin/glucose provides metabolic support
- CCB toxicity induces hyperglycemia by inhibiting pancreatic insulin release

Insulin/Glucose Cases

- 78 reported cases
  - 72 CCB
  - 5 combined CCB-BAA
  - 1 BAA
  - Overall survival 88% when insulin therapy is used

Goldfrank's Toxicologic Emergencies 9th Ed

Insulin/Glucose Dosing

- Myocardial function estimated via emergency department ultrasonography
- If decreased myocardial function is present:
- 1 Unit/kg bolus of regular human insulin with 0.5 g/kg of dextrose
  - If blood glucose is greater than 400 mg/dL (22.2 mmol/L) dextrose bolus is not necessary.
- An infusion of regular insulin 0.5 to 1 Unit/kg/h.
- Start continuous dextrose infusion beginning at 0.5 g/kg/h.
- Dextrose is best delivered as D 25 W or D 50 W via central venous access to lessen large fluid volumes.

Insulin/Glucose Dosing

- Reassess myocardial function every 20-30 minutes starting insulin
- Improvement typically takes 30 minutes or more to begin
- If cardiac function remains depressed or there is persistent hypotension, the insulin dose can be increased
  - Doses up to 2.5 Units/kg/h have been used
  - The blood glucose should be monitored every 30 minutes until stable and then every 1 to 2 hours.
  - The dextrose infusion should be titrated to keep blood glucose between 100 and 250 mg/dL (5.5 to 14 mmol/L).
- The serum potassium concentration should be measured, maintain > 2.5 mEq/L

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