Intravenous Fat Emulsion

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Objectives

• List indications for the use of IVFE
• Identify the risks and benefits of IVFE preparations

What is IV Fat Emulsion

• Mixture of long chain fatty acids
  – Omega 6, 3, and 9 fatty acids
  – Alpha Linoleic Acid makes up small percentage
  – Small amount of Vitamin E to reduce oxidative stress
• Designed to prevent fatty acid deficiency in patients on long term parenteral nutrition
• Source of energy/calories for patients on parenteral nutrition
• Huge breakthrough for parenteral nutrition

Formulations - US

• First product came to market in 1961
  – Original product was Safflower Oil
    • ~77% Omega 6 fatty acids, lacked alpha linoleic acid
• Soybean Oil Based Products
  – Intralipid
  – Liposyn III
• In the US it is mostly derived from soybean oil
  – Mostly Omega 6 Fatty Acids (50% of fatty acid profile)
  – Omega 3 and Omega 9 Fatty acids make up additional profile
    (25% each)
  • 7:1 ratio Omega 6 to Omega 3 Fatty Acids
• Soybean Oil and Olive Oil
  – Clinolipid
    • FDA approved in October 2013

Formulations - International

• Soybean Oil
• Soybean Oil/MCT Oil (50:50)
• Soybean Oil/Olive Oil (20:80)
• Soybean Oil/MCT Oil/Fish Oil (40:50:10)
• Soybean Oil/MCT Oil/Olive Oil/Fish Oil (30:30:25:15)
• Fish Oil

Omega 3 and Omega 6 Fatty Acids
Inflammatory Cascade

**USP (United States Pharmacopeia) Standards**

- Mean droplet diameter for lipid injectable emulsions must be <500 nm or 0.5 µm, irrespective of the concentration.
- Large globule content:
  - The volume-weighted, large-diameter fat globule limits of the dispersed phase, for a given lipid injectable emulsion must not exceed 0.05%.
- 0.05% is max limit in order to prevent embolic events.

**IV stability**

- Increased risk of loss of emulsion with 3-in-1 parenteral nutrition mixtures
  - i.e. Cracking emulsion
- Current Soybean oils are mostly long chain fatty acids (Omega 6 Fatty Acids)
- Mixtures of Medium Chain and Long Chain fatty acids offer great stability and less likely to “crack” the emulsion.
**Uses**

- **Parenteral Nutrition**
  - Can be administered separately (2 in 1)
  - Can be combined with dextrose and amino acid (3-in-1 or TNA)
  - Usual dose 20-30% of non-protein calories
  - Limit of 1-1.5 g/kg/day on day 1 of therapy
  - Provide needed fatty acids to prevent deficiency
  - Provide dense source of energy to limit amount of dextrose and volume that must be given

**Parenteral Nutrition – Pediatric/Neonates**

- Initial Dose – 1-2 g/kg/day
  - Increase by 0.5-1 g/kg/day to max of 3 g/kg/day
- Caution regarding excessive rates of infusion in Neonates
  - Low rates of clearance
  - Can have intravascular accumulation in lungs

**Uses - LAST**

- **Local Anesthetic Systemic Toxicity (LAST)**
  - Background
    - Occurs when local anesthetic is introduced systemically
      - Either via accidental vascular administration OR via delayed tissue depot absorption
      - Peripheral nerve blocks carry highest risk → 0.075 to 0.1% of procedures
WHAT IS LIPID RESCUE?

- Proposed antidote for severe LAST
- Administration of IV lipid emulsion in the event of cardiovascular collapse
- Mechanism of action
  - Not completely understood
  - Most widely accepted:
    - The “Lipid Sink”; its emulsion creates an expanded lipid phase which draws toxic drug from tissue into the lipid phase
  - Other theory:
    - Counteracts local anesthetic inhibition of myocardial fatty acid oxidation
  - Current recommendations based on a handful of case reports and animal studies

When To Use Lipid Rescue?

- Still an area of debate
- Not recommended at the first signs of LAST
  - ASA Newsletter: can prevent progression in many cases with supportive care
    - i.e. 100% O2, treatment of convulsions, etc.
- Not recommended to wait for complete cardiovascular collapse
- Base use on clinical severity and rate of progression of LAST

Use In Non-Anesthetic Overdoses

- Case reports of successful resuscitations:
  - Beta blockers (propranolol)
  - Calcium channel blockers (verapamil)
  - Parasiticides
  - Herbicides
  - Psychotropic agents
    - Tricyclic antidepressants, bupropion, lamotrigine, haloperidol
- Primary MOA: “lipid sink”
- These are lipophilic agents that have similar sodium channel blocking properties to local anesthetics
- No guidelines for use in non-anesthetic overdose exist

Journal of Medical Toxicology 2009. 4(3): 184-91
Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine 2010. 18: 51-8
www.lipidrescue.org
**Administration - Nutrition**

- **Hang Time**
  - 3in1 infusions can be hung for 24 hours once mixed
  - 2in1 or when the fat emulsion is infused separately, the fat emulsion should only hang for 12 hours
  - Risk of Malassezia furfur
- **Set Changes**
  - Replace tubing used to administer fat emulsions (those combined with amino acids and glucose in a 3-in-1 admixture or infused separately) within 24 hours of initiating the infusion
  - If admin via separate infusion
    - Hang higher than other infusions due to low specific gravity

**Administration - Nutrition**

- **Filter**
  - Clinolipid and Intralipid
    - Use filter 1.2 or larger
  - Liposyn
    - No filter needed
  - Nutrilipid
    - Use 1.2 micron filter
    - Avoid admin in DHEP containing IV sets
- **3-in-1 solutions can obscure signs of precipitation**
  - Care must be taken to ensure Ca and Phos concentrations are within acceptable ranges

**Administration – Lipid Rescue**

- **Bolus dose:**
  - 1.5mL/kg over 1 minute followed by continuous infusion
  - Repeat bolus dose every 5 minutes up to 3mL/kg total dose until adequate circulation is restore
  - Maximum of 2 repeat boluses is permitted
- **Continuous Infusion**
  - 0.25mL/kg/min for 30-60 minutes
  - May increase rate to 0.5mL/kg/min if blood pressure declines
  - Maximum total dose: 10mL/kg is recommended

www.lipidrescue.org
Monitoring

• Initial infusion
  – Allergic reaction (dyspnea, cyanosis, fever)
  – Derived from egg phospholipids so some contraindicated with egg allergy
• Serum Triglycerides
  – High doses are associated with elevated triglycerides, possibly due to saturation of elimination mechanism
  – S/Sx’s pancreatitis
• LFTs, Bilirubin
  – hepatobiliary disorders are associated with PN therapy: steatosis, cholestasis, and gallbladder sludge/stones

Questions/Discussion

• How many of you have used lipid emulsion for anesthetic toxicity?
• How many of you have used lipid emulsion for drug overdoses?
• How many of our institutions limit use of fat emulsions due to potential for inflammatory and oxidative stress?