Lipid Emulsions In Parenteral Nutrition

The Abc Of Parenteral Lipid Emulsions

P. Austin (UK)
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The ABC of parenteral lipid emulsions

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No conflict of interest related to this presentation
Learning objectives

a) Understand the history of lipid emulsions in parenteral nutrition

b) Know the biochemical nature and types of lipid emulsions, including phytosterols and peroxides

c) Understand the main characteristics (compatibility, stability, clearance,...) and compounding issues
History

Animals

1678: IV lipid (animals; C. Wren)
1869: SC fat (dogs)
1915: IV fat emulsion into animals

Humans

1869: SC fat (adult)
1920: IV fat emulsions (children in US)
1945: Commercial lipid preparations based on cotton seed oils
1961: Intralipid developed by Wretlind in Sweden
1964: FDA banned fat emulsions derived from cotton seed oils
1980-: New types of lipid emulsion
Typical lipid emulsion formulation

- Glycerol
- Egg phosphatides
- Sodium hydroxide q.s.
- Triglycerides
  - = 20g/100mL in 20% w/v
  - lipid emulsion

Water for Injection q.s.
Triglycerides (TAG)

- Glycerol
  - Fatty acid
  - Fatty acid
  - Fatty acid
Fatty acids

Saturated
- coconut oil
- caprylic
- capric

Unsaturated
- n3 (PUFA)
  - soybean oil
  - linolenic*
  - EPA
  - DHA
- n6 (PUFA)
  - Linoleic*
  - soybean oil
- n9 (MUFA)
  - oleic
  - soybean & olive oils

* = essential fatty acid
# Fatty acid composition (% of total*)

## Examples of commercial lipid emulsions

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>Soybean oil</th>
<th>Intralipid 20% w/v</th>
<th>Clinoleic 20% w/v</th>
<th>Lipofundin 20% w/v</th>
<th>SMOF 20% w/v</th>
<th>Omegaven 10% w/v</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long chain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linolenic</td>
<td>8.5</td>
<td>7.5</td>
<td>2.0</td>
<td>3.5</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>Linoleic</td>
<td>51.0</td>
<td>53.0</td>
<td>18.5</td>
<td>27.0</td>
<td>19.5</td>
<td></td>
</tr>
<tr>
<td>Oleic</td>
<td>23.0</td>
<td>24.5</td>
<td>64.0</td>
<td>12.7</td>
<td>30.0</td>
<td></td>
</tr>
<tr>
<td>Medium chain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caprylic</td>
<td></td>
<td>26.0</td>
<td>18.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capric</td>
<td></td>
<td>19.6</td>
<td>10.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very long chain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EPA</td>
<td></td>
<td>0.0</td>
<td>2.3</td>
<td>20.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DHA</td>
<td></td>
<td>0.1</td>
<td>2.3</td>
<td>22.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% accounted for</td>
<td>82.5</td>
<td>99.0</td>
<td>84.5</td>
<td>98.3</td>
<td>97.4</td>
<td>43.1</td>
</tr>
</tbody>
</table>

* = average (composition is subject to natural variability)
Phytosterols

% w/w of lipid

- Intralipid 20% w/v
- Clinoleic 20% w/v
- Lipofundin 20% w/v
- SMOF 20% w/v
- Omegaven 10% w/v

Natural product (soybean oil)

Peroxidation

• Peroxidation is a chain reaction of lipid degradation:
  - affects PUFAs (e.g. from soybean and fish oils)
  - begins with an interaction between oxygen and hydrogen, and leads to the formation of free radicals
  - the extent is indicated by measuring lipid peroxides

• Relevant factors include:
  - availability of oxygen
  - presence of antioxidants (e.g. vitamins C and E)
  - presence of transition elements (e.g. copper or iron)
Vitamin K

- a natural component of lipid emulsions
- could block effect of warfarin or may need to supplement

<table>
<thead>
<tr>
<th>Vitamin K provision from examples of lipid emulsions</th>
<th>Clinoleic</th>
<th>SMOF</th>
<th>Intralipid</th>
</tr>
</thead>
<tbody>
<tr>
<td>500mL lipid emulsion µg</td>
<td>7.5 – 25</td>
<td>75 – 125</td>
<td>300</td>
</tr>
<tr>
<td>Multivitamin* µg</td>
<td>0</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>Total µg</td>
<td>7.5 - 25</td>
<td>225 - 275</td>
<td>450</td>
</tr>
</tbody>
</table>

* One vial of Cernevitt with Clinoleic, or 10mL Vitlipid N Adult with SMOF and Intralipid
General considerations

• **Benefits** include:
  - energy dense and low osmolarity compared to glucose
  - IV route bypasses the lymphatic system (chyle leak role)
  - prevents essential fatty acid deficiency

• **Risks to manage** include:
  - potential allergies to lipid emulsions
  - lipid particle size and filtration
  - lipid can accumulate inside IV catheter
  - other medicines e.g. propofol or heparin
Controversial considerations

- **Selection of flush**
  - compatibility of flush choice with lipid (and TPN formulation)

- **Ratio of lipid to glucose**

<table>
<thead>
<tr>
<th>Risk factor (adult patients)</th>
<th>For a 30 to 60 year old male of 70kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid ≥1g/kg</td>
<td>≥70g</td>
</tr>
<tr>
<td>Glucose ≥4g/kg</td>
<td>≥280g</td>
</tr>
<tr>
<td>Parenteral energy ≥80% BEE</td>
<td>≥1270kcal</td>
</tr>
</tbody>
</table>

Compounding considerations

- Infection risk
  - lipid emulsion putatively supports strong microbial growth

- Formulation
  - assessment of stability (examples to follow)
Alert
28 March 2007

Immediate action
Action
Update
Information request

Ref: NPSA/2007/20
Infection risk: microbial growth

Figure 3. Growth of different microbial species in lipid emulsion (red) and in parenteral nutrition with (green) and without (blue) lipid over a 48-h period (unmatched data analysis).

Stability: lipid emulsion dilution

If stable:
- Water
- Emulsifier
- Lipid emulsion

Increase volume:
- 1.5a
- 1.5b
- 1.5c

Likely stable:
- Water
- Emulsifier
- Lipid emulsion

Could be unstable:
- Water
- Emulsifier
- Lipid emulsion

Subject to other components or other differences
Stability: cation additions

- Normal emulsion
- Aggregation
- Coalescence
- Free oil

Water, Lipid globule
Recommended reading

- **Stability assessment of lipid** in parenteral nutrition

In summary

a) Available lipid emulsions vary in composition, which can result in different characteristics.

b) Prescription of lipid emulsions should account for each patient and also safety considerations.

c) Appropriate pharmaceutical assessment and compounding practices are required for lipid emulsions (and all parenteral nutrition).