INTRAVENOUS LIPID EMULSION (ILE) IN PARENTERAL NUTRITION: ASSESSING NEW OPTIONS

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Disclosures

Fresenius Kabi, Inc:
• Consultant & Speaker’s Bureau

Baxter Healthcare:
• Consultant
Learning Objectives

Upon completion of this session, the learner will be able to

1. Describe the similarities and differences between ILE formulations.
2. Identify patient populations that would benefit from a non-soybean centered ILE.
# FDA Approved ILE

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Intralipid&lt;sup&gt;1,2&lt;/sup&gt;</th>
<th>Nutrilipid&lt;sup&gt;3&lt;/sup&gt;</th>
<th>Clinolipid&lt;sup&gt;2,4&lt;/sup&gt;</th>
<th>Smoflipid&lt;sup&gt;5&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oil Source</td>
<td>Soybean Oil</td>
<td>Soybean Oil</td>
<td>Olive Oil 80% Soybean Oil 20%</td>
<td>Soybean Oil 30% MCT 30% Olive Oil 25% Fish Oil 15%</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Fresenius Kabi/Baxter*</td>
<td>B.Braun Medical</td>
<td>Baxter</td>
<td>Fresenius Kabi</td>
</tr>
</tbody>
</table>

## Fat Composition (%, mean values)<sup>1-6</sup>

<table>
<thead>
<tr>
<th>Fat Composition</th>
<th>Intralipid&lt;sup&gt;1,2&lt;/sup&gt;</th>
<th>Nutrilipid&lt;sup&gt;3&lt;/sup&gt;</th>
<th>Clinolipid&lt;sup&gt;2,4&lt;/sup&gt;</th>
<th>Smoflipid&lt;sup&gt;5&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>Linoleic</td>
<td>53</td>
<td>53</td>
<td>17.9</td>
<td>19.5</td>
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<tr>
<td>α-Linolenic</td>
<td>7.5</td>
<td>7.5</td>
<td>2.4</td>
<td>2.5</td>
</tr>
<tr>
<td>Eicosapentaenoic</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2.3</td>
</tr>
<tr>
<td>Docosahexaenoic</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2.3</td>
</tr>
<tr>
<td>α-Tocopherol (mg/L)</td>
<td>38</td>
<td>N/A</td>
<td>32</td>
<td>163-225</td>
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<tr>
<td>Phytosterols (mg/L)&lt;sup&gt;6&lt;/sup&gt;</td>
<td>439</td>
<td>311</td>
<td>274</td>
<td>178</td>
</tr>
<tr>
<td>ω3 : ω6 ratio</td>
<td>1 : 7</td>
<td>1 : 7</td>
<td>1 : 9</td>
<td>1 : 2.5</td>
</tr>
</tbody>
</table>

MCT, medium chain triglycerides; N/A, not available

*Distributed

1. Intralipid Prescribing Information, 2015
3. Nutrilipid Prescribing Information 2014
5. Smoflipid Prescribing Information 2016
Omega-3 polyunsaturated fatty acids produce which of the following?

A. Arachidonic acid  
B. Thromboxane A2  
C. Resolvins E1/D1  
D. Leukotriene B4
Metabolic Pathways of \( \omega 3, \omega 6, \omega 9 \)

**Omega-3 Fatty Acids**
- **Alpha-Linolenic Acid**
  - 18:3 \( \omega 3 \)
- **Octadecatetraenoic Acid**
  - 18:4 \( \omega 3 \)
- **Eicosatetraenoic Acid**
  - 20:4 \( \omega 3 \)
- **Eicosapentaenoic Acid (EPA)**
  - 20:5 \( \omega 3 \)
- **Docosapentaenoic Acid**
  - 22:5 \( \omega 3 \)
- **24:5 \( \omega 3 \)**
- **24:6 \( \omega 3 \)**
- **Docosahexaenoic Acid (DHA)**
  - 22:6 \( \omega 3 \)

**Omega-6 Fatty Acids**
- **Linoleic Acid**
  - 18:2 \( \omega 6 \)
- **Gamma-Linolenic Acid**
  - 18:3 \( \omega 6 \)
- **Dihomo-Gamma-Linolenic Acid**
  - 20:3 \( \omega 6 \)
- **Arachidonic Acid**
  - 20:4 \( \omega 6 \)
- **Docosatetraenoic Acid**
  - 22:4 \( \omega 6 \)
- **Docosapentaenoic Acid**
  - 22:5 \( \omega 6 \)
- **24:4 \( \omega 6 \)**
- **24:5 \( \omega 6 \)**
- **Docosapentaenoic Acid**
  - 22:5 \( \omega 6 \)

**Omega-9 Fatty Acids**
- **Oleic Acid**
  - 18:1 \( \omega 9 \)
- **Octadecadienoic Acid**
  - 18:2 \( \omega 9 \)
- **Eicosadienoic Acid**
  - 20:2 \( \omega 9 \)
- **Eicosatrienoic Acid**
  - 20:3 \( \omega 9 \)
- **Eicosatrienoic Acid (Mead Acid)**
  - 20:3 \( \omega 9 \)

**Metabolic Pathways**
- Delta-6-desaturase
- Delta-5-desaturase
- Elongase
- Beta-oxidation

Metabolic Pathways of ω3, ω6, ω9

Omega-3 Fatty Acids

Alpha-Linolenic Acid (18:3 ω3)

- Octadecatetraenoic Acid (18:4 ω3)
- Eicosatetraenoic Acid (20:4 ω3)
- Eicosapentaenoic Acid (EPA) (20:5 ω3)
- Docosapentaenoic Acid (22:5 ω3)
- 24:5 ω3
- 24:6 ω3
- Docosahexaenoic Acid (DHA) (22:6 ω3)

Specialized Pro-resolving Mediators

E-series Resolvins

Omega-6 Fatty Acids

Linoleic Acid (18:2 ω6)

- Gamma-Linolenic Acid (18:3 ω6)
- Dihomo-Gamma-Linolenic Acid (DHGLA) (20:3 ω6)
- Arachidonic Acid (20:4 ω6)
- Docosatetraenoic Acid (22:4 ω6)
- 24:4 ω6
- 24:5 ω6
- Docosapentaenoic Acid (DPA) (22:5 ω6)

Docosahexaenoic Acid (DHA) (22:6 ω3)

Weak Inflammatory Eicosanoids

3-series Prostaglandins
3-series Thromboxanes
5-series Leukotrienes

Potent Pro-inflammatory Eicosanoids

2-series Prostaglandins
2-series Thromboxanes
4-series Leukotrienes

Anti-inflammatory Epoxyeicosatrienoic Acids

ω3 vs. ω6 Fatty Acids

Dietary intake of EPA + DHA is 0.1 g/day

Inhibit Production of Interleukin (IL)-1 beta, Tumor Necrosis Factor-alpha, IL-6 and IL-2

COX, cyclooxygenase; LOX, lipoxygenase; PG, prostaglandin; LT, leukotriene

Calder PC. Nutrients 2010;2(3):355-74
**SPM Anti-Inflammatory and Pro-Resolving Defining Functions**

- Accelerate the resolution of acute inflammation
- Limit neutrophil infiltration
- Promote efferocytosis of apoptotic cells
- Enhance microbial killing and clearance
- Counter regulation and sequestration of cytokines
- Down regulation of prostanoids

**Mediator** | **SPM Selective Actions**
--- | ---
RvD1 | Enhances cognitive function
RvD2 | Regulates vascular endothelium
RvD5 | Macrophage phagocytosis
PD1 | Neuro-protective
RvE1 | Reduces platelet aggregation
Omega-3 polyunsaturated fatty acids produce which of the following?

A. Arachidonic acid
B. Thromboxane A2
C. Resolvins E1/D1
D. Leukotriene B4
ILE & ? Fat Embolism Syndrome

- 20% Lipofundin (50% MCT/50% Soybean) 0.21 g/kg/hr for 1 hr
- Heterogeneous ICU ARDS group (n=8)
- PaO$_2$/FiO$_2$ decreased from 129 → 95

ILE in Acute Respiratory Distress Syndrome

- ILE administration may have clinical consequences in severe lung injury or ARDS
  - ↓ diffusion capacity with changes in alveolar capillary membrane
  - Deposition of fat particles in the reticuloendothelial system
- Dosages > 0.1 g/kg/hr will impair oxygenation for the duration of the infusion
  - ↓ PaO₂/FiO₂
- Assess benefits vs. risks
  - Essential fatty acid deficiency

Reticuloendothelial System

- Pulmonary alveolar macrophages produced in lungs
- Kupffer’s cells produced in liver
Which of the following is recommended from the published available guidelines for intravenous lipid emulsions?

A. For malnourished critically ill patients the weekly dose should not exceed 50 grams throughout hospitalization
B. Use of lower content of ω6 fatty acids/soybean oil for critically ill patients in the first week
C. Medium chain triglycerides are the preferential fuel for critically ill patients and may be administered alone
D. Use of 100% fish oil has been shown to reduce mortality, ventilator days, and hospital length of stay
Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Stephen A. McClave, MD1; Beth E. Taylor, RD, DCN2; Robert G. Martindale, MD, PhD3; Malissa M. Warren, RD4; Debbie R. Johnson, RN, MS5; Carol Braunschweig, RD, PhD6; Mary S. McCarthy, RN, PhD7; Evangelia Davanos, PharmD8; Todd W. Rice, MD, MSc9; Gail A. Cresci, RD, PhD10; Jane M. Gervasio, PharmD11; Gordon S. Sacks, PharmD12; Pamela R. Roberts, MD13; Charlene Compher, RD, PhD14; and the Society of Critical Care Medicine† and the American Society for Parenteral and Enteral Nutrition†
When to Use PN in ICU?

- For low nutrition risk patients, exclusive PN should be withheld over the first 7 days after ICU admission even if volitional intake & early EN not feasible (Very Low)

- For high nutrition risk or severely malnourished patients when EN is not feasible, initiate exclusive PN as soon as possible after ICU admission

- Supplemental PN be considered after 7–10 days if unable to meet > 60% of energy/protein EN needs

McClave SA, et al. JPEN J Parenter Enteral Nutr 2016;40:159-211
Feeding Recommendations

• If utilizing PN:
  
  • Hypocaloric dosing ($\leq 20 \text{ kcal/kg/day}$ or 80% of estimated energy needs) with adequate protein ($\geq 1.2 \text{ g/kg/day}$) initially over the 1\textsuperscript{st} week of ICU admission (Low)
  
  • Withholding or limiting soybean oil-based fat emulsion (ILE) during the 1\textsuperscript{st} week following initiation of PN to 100 g/week (often divided into 2 doses/week) if concern for essential fatty acid deficiency (Very Low)
  
  • Consider use of alternative ILE over soybean oil-based ILE if available
  
  • Terminate PN when $\geq 60\%$ of target energy requirements are being delivered by EN

McClave SA, et al. JPEN J Parenter Enteral Nutr 2016;40:159-211
Fat-free PN in ICU (No Soybean-Based ILE)

57 trauma patients
Study Duration: 10 days

Control PN (w/ILE)
(n=30, Mean Age 33 ± 10 yrs)
28 kcal/kg/day non-protein kcal
(~24% from IVFE)
1.6 g/kg/day protein

Hypocaloric PN (w/o ILE)
(n=27, Mean Age 32 ± 9 yrs)
21 kcal/kg/day non-protein kcal
1.6 g/kg/day protein

IVFE: Intralipid 10% or 20% infused over 10-12 hours daily

Fat-free PN in ICU (No Soybean-Based ILE)

- 28 (n=30) vs. 21 (n=27) kcal/kg/day for 10 days
- 1.6 g protein/kg/day
- Mean age 33 yrs
- 82% Male
- APACHE II 22

Graph showing:
- Infections: Soybean oil-based PN (39) vs. No ILE PN (15) with p=0.01
- Ventilation (days): Soybean oil-based PN (27) vs. No ILE PN (18) with p=0.02
- ICU (days): Soybean oil-based PN (29) vs. No ILE PN (18) with p=0.03
- LOS (days): Soybean oil-based PN (39) vs. No ILE PN (27)
Reduced ω-6:ω-3 ratio (Approximately 2:1) has no immunosuppressive effects

Mean days of rat heart graft survival

- Saline (Control): 7.8
- Soybean oil: 10.4 \( p < 0.01 \)
- Safflower oil: 13.3 \( p < 0.01 \)
- Fish oil: 12.3 \( p < 0.01 \)
- Safflower/Fish oil: 6.7

Which of the following is recommended from the published available guidelines for intravenous lipid emulsions?

A. For malnourished critically ill patients the weekly dose should not exceed 50 grams throughout hospitalization

B. **Use of lower content of ω6 fatty acids/soybean oil for critically ill patients in the first week**

C. Medium chain triglycerides are the preferential fuel for critically ill patients and may be administered alone

D. Use of 100% fish oil has been shown to reduce mortality, ventilator days, and hospital length of stay

Andrew Rhodes, MB BS, MD(Res) (Co-chair); Laura E. Evans, MD, MSc, FCCM (Co-chair); Waleed Alhazzani, MD, MSc, FRCPC (methodology chair); Mitchell M. Levy, MD, MCCM; Massimo Antonelli, MD; Ricard Ferrer, MD, PhD; Anand Kumar, MD, FCCM;


• Recommend against the administration of early PN alone or PN in combination with EN (but rather initiate early EN) in critically ill patients with sepsis or septic shock who can be fed enterally (strong recommendation, moderate quality of evidence)

• Recommend against the administration of PN alone or in combination with EN (but rather to initiate IV glucose and advance EN as tolerated) over the first 7 days in critically ill patients with sepsis or septic shock for whom early enteral feeding is not feasible (strong recommendation, moderate quality of evidence)


• Recommend against the use of ω3 fatty acids as an immune supplement in critically ill patients with sepsis or septic shock (strong recommendation, low quality of evidence)

• Recommend against the use of the following to treat sepsis and septic shock:
  – IV selenium (strong recommendation, moderate quality of evidence)
  – Arginine (weak recommendation, low quality of evidence)
  – Glutamine (strong recommendation, moderate quality of evidence)

• No recommendation about the use of carnitine for sepsis and septic shock

What Do Clinical Guidelines Say?

American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) position paper¹:
“Alternative oil-based ILEs are safe and effective alternatives to soybean oil ILEs for a source of energy and essential FAs and may have potential biochemical and/or clinical benefits”

Canadian Critical Care Nutrition guidelines²:
“When PN with IV lipids is indicated, IV lipids that reduce the load of ω-6 fatty acids/soybean oil emulsions should be considered”

ESPEN guidelines for critically ill patients³:
• “Lipids should be an integral part of PN for energy to ensure essential fatty acid provision in long-term intensive care unit patients”
• “This may include fish oil-enriched and olive oil-based lipid emulsions”

ESPEN guidelines for surgical patients⁴:
• “Postoperative PN including omega-3-fatty acids should be considered only in patients who cannot be adequately fed enterally”

Soybean oil-based ILE vs. Alternative ILE

  - ICU for minimum of 72 hours & mechanical ventilation within 48 hours of admission
  - Requiring PN for minimum of 5 days
    - Provided ~1409 kcal/day
  - Mean age ~64 yrs
  - 62% male
  - 68% surgical
  - APACHE II ~22
    - 16% no lipid emulsion
    - 49% soybean oil-based
    - 14% medium-chain triglyceride-based
    - 16% olive oil-based
    - 4% fish oil-based

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>Soybean Oil (n = 223)</th>
<th>Lipid Free (n = 70)</th>
<th>MCT Oil (n = 65)</th>
<th>Olive Oil (n = 74)</th>
<th>Fish Oil (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical Ventilation Duration (d)*</td>
<td>4.9 (2.6-16)</td>
<td>8.7 (4.4-16.8)</td>
<td>5.3 (2.9-10.6)</td>
<td>5 (2.4-10.5)</td>
<td>5 (2.9-10.9)</td>
</tr>
<tr>
<td>ICU Length of Stay (LOS, d)*</td>
<td>10.9 (7.1-22.2)</td>
<td>11 (6.7-21.8)</td>
<td>9.6 (6.8-21.4)</td>
<td>7.9 (5.9-15.8)</td>
<td>7 (4.7-13.1)</td>
</tr>
<tr>
<td>Hospital LOS*</td>
<td>28.1 (17.1-54.6)</td>
<td>27.7 (12.9-60.1)</td>
<td>31.9</td>
<td>22.1 (15.8-48.5)</td>
<td>14.1</td>
</tr>
<tr>
<td>Mortality within 60 days</td>
<td>63 (28.3%)</td>
<td>13 (18.6%)</td>
<td>20 (30.8%)</td>
<td>11 (14.9%)</td>
<td>2 (10.5%)</td>
</tr>
</tbody>
</table>

* Median (interquartile range)

Soybean oil-based ILE vs. Alternative ILE

Cumulative Likelihood of Being Discharged from ICU Alive vs. Days from Admission to ICU

Fish oil
Olive oil
Lipid-free
MCT
Soybean oil

## Study Design

- Meta-analysis
- Sample: elective surgical and ICU patients
- 13 ICU studies (n=762)
- 10 surgery studies (n=740)

## Purpose

- Clinical efficacy and safety of ω3 PUFA-enriched ILE compared to standard (non-enriched) ILE

## Summary of Findings

- Mortality rate: no difference
- Infection rate: significant reduction in ω3 ILE surgical pts, not ICU patients
- LOS: significant reduction in ω3 ILE group for both ICU and surgical patients
- Lung gas exchange: significant increase in ω3 ILE groups

## Study Design
- Meta-analysis
- Sample: Major surgical patients receiving for 5-7 days post-op
  - 21 studies (n=1487)

## Purpose
- Clinical efficacy and safety of $\omega_3$ PUFA-enriched ILE compared to standard (non-enriched) ILE

## Summary of Findings
- Mortality rate: no difference
  - Odds Ratio (OR) = 1.5 (95% Confidence Interval (CI) 0.54-4.19, $p = 0.44$)
- Infection rate: significant reduction in $\omega_3$ ILE group
  - OR = 0.53 (95% CI 0.35-0.81, $p = 0.003$)
- LOS: significant reduction in $\omega_3$ ILE group by mean of -2.14 days
  - 95% CI -3.02 to -1.27 days, $p < 0.001$
Fish Oil-containing ILE

- Meta-analysis of 10 randomized clinical trials (n=733)
  - Effects of fish oil-containing ILE in EN and PN for critically ill adults

<table>
<thead>
<tr>
<th>Clinical Outcome</th>
<th>Effect</th>
<th>95% Confidence Intervals</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>RR 0.90</td>
<td>0.67 – 1.20</td>
<td>0.46</td>
</tr>
<tr>
<td>Duration of Ventilation</td>
<td>WMD -1.14</td>
<td>-2.67 – 0.38</td>
<td>0.14</td>
</tr>
<tr>
<td>Hospital Length of Stay</td>
<td>WMD -3.71</td>
<td>-9.31 – 1.88</td>
<td>0.19</td>
</tr>
<tr>
<td>ICU Length of Stay</td>
<td>WMD -1.42</td>
<td>-4.53 – 1.69</td>
<td>0.37</td>
</tr>
<tr>
<td>Infections</td>
<td>RR 0.64</td>
<td>0.44 – 0.92</td>
<td><strong>0.02</strong></td>
</tr>
</tbody>
</table>

Risk ratio = RR; weighted mean difference = WMD.

**Fish Oil-containing ILE**

![Graph showing the effects of infections of parenteral fish oil containing emulsions](image)

### Table 1: Effects of fish oils on infections of parenteral fish oil containing emulsions

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Fish Oils</th>
<th>LCT or LCT+MCT</th>
<th>Risk Ratio</th>
<th>Year</th>
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<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
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<tr>
<td>5.15.1 PN based trials</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grecu</td>
<td>0</td>
<td>8</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Friesecke</td>
<td>10</td>
<td>83</td>
<td>11</td>
<td>82</td>
</tr>
<tr>
<td>Wang 2009</td>
<td>6</td>
<td>28</td>
<td>9</td>
<td>28</td>
</tr>
<tr>
<td>Grau-Carmona</td>
<td>17</td>
<td>81</td>
<td>29</td>
<td>78</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>200</td>
<td>195</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>33</td>
<td>50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00; Chi² = 1.17, df = 3 (P = 0.76); I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 2.26 (P = 0.02)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

### Figure 3

Figure 3 Effects on infections of parenteral fish oil containing emulsions (n = 5). CI, Confidence interval; EN, Enteral nutrition; LCT, Long-chain triglycerides; MCT, Medium-chain triglycerides; M-H, Mantel-Haenszel test; PN, Parenteral nutrition.

ICU Lipids Study: MCT/Soybean/Fish vs. MCT/Soybean Oil-based PN

• Prospective, double-blind, randomized, multicenter controlled trial in 17 Spanish surgical/medical ICUs (4.4% of pts screened)
  • Requiring 3-in-1 PN for at least 5 days & APACHE II ≥ 13
    • Study ILE (n=81): 50% MCT / 40% Soybean / 10% Fish Oil
    • Control ILE (n=78): 50% MCT / 50% Soybean Oil
• Mean age 61 yrs, 73% male, APACHE II 21
• 52% surgical & 48% medical
  • 46% sepsis, 29% septic shock, 12% pancreatitis*, 17% trauma, 9% cancer
• PN provided for 9 days:
  • 1.4 g Protein/kg/day with 1737 (Study) vs. 1782 (Control) kcal/day
    – 1 g/kg/day as lipid emulsion
• Prevalence of nosocomial infection: 21% vs. 37.2% (p=0.038)
• ICU mortality: 32.5% vs. 20.5% (p=0.106)

* p=0.049

Phytosterol Intake & Plasma Phytosterol

* - Significantly different from others on same day, \( p < 0.05 \)

Preterm infants receiving PN

<table>
<thead>
<tr>
<th>Phytosterol Intake &amp; Plasma Phytosterol (mg/L)</th>
<th>Day 0</th>
<th>Day 7</th>
<th>Day 14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soybean 100%</td>
<td>*</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>MCT/soybean 50%</td>
<td>*</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>MCT/soybean 40%/fish</td>
<td>*</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Olive/soybean 20%</td>
<td>*</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>SMOF (30% soybean)</td>
<td>*</td>
<td>*</td>
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</tbody>
</table>


Single-center, parallel-group trial in preterm infants with birth weight 500-1249 g who received PN from the first hour of life (50% of energy intake from PN & 50% from enteral route). Neonates were randomized to one of five ILE: soybean oil (n=30), soybean oil/MCT (n=30), soybean oil/MCT/fish oil (n=27), olive oil/soybean oil (n=29) and soybean/MCT/olive oil/fish oil (n=28)
Stigmasterol is one of the three major phytosterols present in soybean oil ILE

- Promotes cholestasis by inhibiting nuclear receptor FXR, thereby reducing hepatocyte expression of genes including bile salt export pump, a determinant of bile secretion

- Fish oil-based ILE has no phytosterols
  - Similar effects to a no lipid PN on preventing cholestasis or liver injury

- Adding Stigmasterol to Fish oil-based ILE
  - Produced cholestasis and liver injury
  - Serum Stigmasterol concentration correlated with severity of cholestasis
Mouse Liver Architecture and ILE Content

HCD = high carbohydrate diet for 19 days (QOD ILE)

Summary

• Lipids are essential in the human diet and can be particularly influential in critically ill patients with evidence of malnutrition

• ω6 fatty acids have pro-inflammatory effects

• ω3 fatty acids have anti-inflammatory effects

• Biological effects of fatty acids are dose dependent

• Guidelines and systematic reviews currently recommend limiting ω6 saturated and polyunsaturated fatty acids

• Composition of commercially-available IVLE varies and provides differing combinations of fatty acid types

• High phytosterol content may be a factor in the development of PN-associated liver disease