Mixed Oil Intravenous Lipid Emulsion
The Journey From Soybean to Fish Oil

Manpreet S. Mundi, MD
Oley Foundation
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Disclosures

• Industry support: Research Grant from Fresenius Kabi

• Off-labeled use: None
Objectives
The Journey From Soybean to Fish Oil

- Describe history and development of intravenous lipid emulsion (ILE)
- Describe complications associated with ILE
- Describe data regarding mixed oil ILE
Intravenous Lipid Emulsions (ILE) History

• 17th century: William Courten described intravenous olive oil in dog
  • Severe respiratory distress \(\rightarrow\) fat embolism
Intravenous Lipid Emulsions (ILE)

History

• 19th century: Cholera epidemic
  • Thomas Latta: described IV infusion of saline in 3 cholera patients
    • One survived
  • Edward Hodder (1873): described IV milk infusion in 3 patients
    • 2 of them survived
    • Adverse effects – due to fat being given intravenously

Intravenous Lipid Emulsions (ILE)

History - Cotton Seed Oil

- 20th century (1920 - 1950's): great deal of work into development of safe IVLE
  - Lipomul®

**Letters to the Editor**

**LIPOMUL-I.V. (FAT EMULSION FOR INTRAVENOUS INFUSION)**

Parenteral nutrition by the intravenous infusion of fat emulsions has been investigated for many years. A recently developed preparation, Lipomul-I.V. (Upjohn), containing cottonseed oil, glucose and soybean phosphatide, and providing 900 calories per 600 cc. of fluid volume, has been administered by us to critically ill patients to determine their tolerance for this material.

Fifteen patients with a variety of debilitating diseases received a total of 100 infusions of 600 cc. each. The number of infusions per patient ranged from 1 to 26. There were no severe reactions in any of the patients, and no changes in blood pressure, pulse or temperature were observed. Three patients had transient flushing of the skin, and 1 complained of an unpleasant taste at the base of the tongue.

From these observations it would appear that the intravenous administration of this fat emulsion is a safe and practical procedure for providing a high concentration of calories when oral nutrition is inadequate.

J. H. Epstein, M.D.
V. E. Shocken, M.D.
L. K. Alpert, M.D.

George Washington University Hospital and the Department of Medicine, George Washington University School of Medicine, Washington, D.C.
Intravenous Lipid Emulsions (ILE)
History—Cotton Seed Oil

• 20th century (1920’s - 1950’s): great deal of work into development of safe IVLE
  • Lipomul®
    • Pulled off of the market due to adverse effects
      • Fever and chills
      • Nausea and vomiting
      • Hypoxia
Intravenous Lipid Emulsions (ILE) History-Soybean Oil

- 20th century (1960’s): Schubert and Wretlind
  - Intralipid®
    - Soybean oil
    - Egg yolk phospholipids
    - Glycerin
Intravenous Lipid Emulsions (ILE) Benefits

- 20th century (1960’s): Schubert and Wretlind
  - Soybean Oil ILE
Fatty Acids Physiology

• How many Carbons
  • Short Chain: 1-5 carbon chains
  • Medium Chain: 6-12 carbon chains
  • Long Chain: 13-21 carbon chains
  • Very long Chain: 22 or more

• Double bonds:
  • Saturated
  • Unsaturated

SO ILE Benefits

- 20th century (1960’s): Schubert and Wretlind
- Meguid et al: Replaced 1/3 of dextrose calories with SO ILE

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 14</td>
<td>Day 1</td>
<td>Day 14</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>62.9 ± 3.2</td>
<td>62.8 ± 1.5</td>
<td>65.9 ± 3.1</td>
<td>69.2 ± 3.9</td>
</tr>
<tr>
<td>Albumin (3.5–5.0 g/dl)</td>
<td>3.1 ± 0.16</td>
<td>3.1 ± 1.4</td>
<td>3.3 ± 0.25</td>
<td>3.1 ± 0.18</td>
</tr>
<tr>
<td>Glucose (60–135 mg/dl)</td>
<td>114.2 ± 10.0</td>
<td>107.1 ± 5.8</td>
<td>158.0 ± 21.5</td>
<td>158.0 ± 20.3</td>
</tr>
<tr>
<td>Triglycerides (20–200 mg/dl)</td>
<td>120.0 ± 21.7</td>
<td>134.0 ± 2.3</td>
<td>174.0 ± 23.2</td>
<td>155.2 ± 25.4</td>
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<tr>
<td>Serum osmolality (280–300 mOsm/L)</td>
<td>277.0 ± 12.4</td>
<td>281.0 ± 2.0</td>
<td>283.6 ± 4.8</td>
<td>283.0 ± 3.5</td>
</tr>
<tr>
<td>T. bilirubin (0.1–1.2 mg/dl)</td>
<td>0.6 ± 0.1</td>
<td>0.7 ± 0.2</td>
<td>0.7 ± 0.2</td>
<td>0.4 ± 0.05</td>
</tr>
<tr>
<td>SGOT (1–41 mU/ml)</td>
<td>26.1 ± 6.0</td>
<td>46.9 ± 9.4</td>
<td>26.2 ± 11.0</td>
<td>23.0 ± 6.0</td>
</tr>
<tr>
<td>LDH (100–220 mU·ml)</td>
<td>237.9 ± 25.7</td>
<td>263.9 ± 35.6</td>
<td>248.0 ± 43.2</td>
<td>224.8 ± 40.6</td>
</tr>
<tr>
<td>Alkaline phosphatase (30–110 mU/ml)</td>
<td>113.8 ± 15.3</td>
<td>223.9 ± 37.3</td>
<td>128.8 ± 33.0</td>
<td>161.4 ± 38.2</td>
</tr>
</tbody>
</table>

* p ≤ 0.05
* Normal range.
SO ILE

Benefits

• 20th century (1960’s): Schubert and Wretlind
  • Soybean Oil ILE
    • Good source of non-protein calories
    • Good source of essential fatty acids
    • Improved glycemic control
      • 15% of patients had glucose intolerance
        (>250 mg/dl or >13.9 mmol/L)
      • 2 patients were noted to have chronic pancreatitis

Case Presentation
SO ILE

• A. L. is a 32 year-old with history of myopathic intestinal dysmotility and pseudo-obstruction who has been dependent on HPN since age 15.

• August 2011: diagnosed with AML after presenting with blurred vision, dizziness, and chest pain.
  • WBC 63K with 18% blasts and 13% promyelocytes
  • Allogenic stem cell transplant after chemotherapy

Case Presentation

SO ILE

- Noted to have abdominal pain and elevated LFTs
  - Total bilirubin increased 1.3 mg/dl to 3.3 mg/dL from August 2011 to January 2012
  - Alk phos 670 U/L
  - ALT 218 U/L
  - AST 163 U/L
  - Liver biopsy: findings consistent with IFALD
Case Presentation
Complications: IFALD

• Noted to have abdominal pain and elevated LFTs
  • Total bilirubin increased 1.3 mg/dl to 3.3 mg/dL from August 2011 to January 2012
  • Alk phos 670 U/L
  • ALT 218 U/L
  • AST 163 U/L
  • Liver biopsy: findings consistent with IFALD

**DIAGNOSIS:**
Liver, needle biopsy: Features consistent with TPN effect, characterized by mildly active steatohepatitis (grade 1 of 3) with foci of cholate injury and cytoplasmic clearing within the hepatocytes. The trichrome stain shows periportal fibrosis (stage 2 of 4) (see comment).
SO ILE
Complications

- High $\omega$-6 to $\omega$-3 ratio

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Manufacturer/Distributor</th>
<th>Lipid Source</th>
<th>Linoleic</th>
<th>$\alpha$-Linolenic</th>
<th>EPA</th>
<th>DHA</th>
<th>$\omega$-6:$\omega$-3 Ratio</th>
<th>$\alpha$-Tocopherol, mg/L</th>
<th>Phytosterols, mcg/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intralipid</td>
<td>Fresenius Kabi/Baxter</td>
<td>100% soybean oil</td>
<td>44–62</td>
<td>4–11</td>
<td>0</td>
<td>0</td>
<td>7:1</td>
<td>38</td>
<td>342.89 ± 5.87</td>
</tr>
<tr>
<td>Liposyn III</td>
<td>Hospira</td>
<td>100% soybean oil</td>
<td>54.5</td>
<td>8.3</td>
<td>0</td>
<td>0</td>
<td>7:1</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Nutrilipid</td>
<td>B. Braun</td>
<td>100% soybean oil</td>
<td>48–58</td>
<td>4–11</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Clinolipid</td>
<td>Baxter</td>
<td>20% soybean oil 80% olive oil</td>
<td>13.8–22</td>
<td>0.5–4.2</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>SMOFlipid</td>
<td>Fresenius Kabi</td>
<td>30% soybean oil 30% MCTs 25% olive oil 15% fish oil</td>
<td>21.4</td>
<td>2.5</td>
<td>3</td>
<td>2</td>
<td>2.5:1</td>
<td>200</td>
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Fatty Acids Physiology

• How many Carbons
  • Short Chain: 1-5 carbon chains
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• Double bonds:
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Intravenous Lipid Emulsions (ILE)
Pro-inflammatory

Intravenous Lipid Emulsions (ILE)

Pro-inflammatory

Omega-6 Fatty Acids

Arachidonic Acid (AA)
20:4n-6

Cyclooxygenase (COX)

Prostaglandin E2 (PGE2)
Prostaglandin I2 (PGI2)
Thromboxane A2 (TXA2)

Lipoxygenase

Leukotrienes
Leukotriene B4 (LTB4)
Leukotriene C4 (LTC4)
Leukotriene E4 (LTE4)

More Pro-Inflammatory

Omega-3 Fatty Acids

Eicosapentaenoic Acid (EPA)
20:5n-3

Cyclooxygenase (COX)

Prostaglandin E3 (PGE3)
Prostaglandin I3 (PGI3)
Thromboxane A3 (TXA3)

Lipoxygenase

Leukotrienes
Leukotriene B5 (LTB5)
Leukotriene C5 (LTC5)
Leukotriene E5 (LTE5)

Less Pro-Inflammatory
Intravenous Lipid Emulsions (ILE) Pro-inflammatory

- **High $\omega$-6 to $\omega$-3 ratio**
  - EPA and DHA $\rightarrow$ E-series and D-series resolvins
  - Dampen acute leukocyte responses
  - Facilitate resolution of inflammation
- **$\omega$-3 PUFAs directly control transcription factors such as PPARs and sterol-regulatory element binding proteins**
  - Bind to DNA and regulate inflammatory processes.

Intravenous Lipid Emulsions (ILE)  
Pro-inflammatory

- High $\omega$-6 to $\omega$-3 ratio
- Suppression of reticuloendothelial system (RES)
  - SO ILE provided at a rate of 0.13 g/kg/h over 10 hours daily for 3 days

Intravenous Lipid Emulsions (ILE) Phytosterols

- High $\omega$-6 to $\omega$-3 ratio
- Suppression of reticuloendothelial system (RES)
- High phytosterol content

### Concentrations of Selected FAs, % by Weight

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<th>$\alpha$-Linolenic</th>
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<th>$\alpha$-Tocopherol, mg/L</th>
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<tr>
<td>IVFEs available in United States</td>
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<td>2.5</td>
<td>3</td>
<td>2</td>
<td>2.5:1</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30% MCTs</td>
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<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>25% olive oil</td>
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<tr>
<td></td>
<td></td>
<td>15% fish oil</td>
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<td>80% olive oil</td>
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### Phytosterols, mcg/mL

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>342.89 ± 5.87</td>
<td>439.07 ± 5.72</td>
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<tr>
<td>NA</td>
<td>NA</td>
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<tr>
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</tr>
<tr>
<td>207</td>
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</table>
Intravenous Lipid Emulsions (ILE) Phytosterols

- High $\omega$-6 to $\omega$-3 ratio
- Suppression of reticuloendothelial system (RES)
- High phytosterol content

<table>
<thead>
<tr>
<th>Oil</th>
<th>Phytosterol Content, mg/100 g$^a$</th>
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<tbody>
<tr>
<td>Corn</td>
<td>952</td>
</tr>
<tr>
<td>Safflower</td>
<td>444</td>
</tr>
<tr>
<td>Soybean</td>
<td>221</td>
</tr>
<tr>
<td>Olive</td>
<td>176</td>
</tr>
<tr>
<td>Palm (source of MCT)</td>
<td>49</td>
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</table>

Intravenous Lipid Emulsions (ILE)
Pro-inflammatory – Major Guidelines

- **SCCM/ASPEN 2009**: In first week of ICU, PN should be given without soy-based lipids

- **SCCM/ASPEN 2016**: Recommend withholding soy-based lipids (or limiting to max 100 gm/week if EFAD likely) during first week in ICU

- **Canadian**: When PN indicated, use IV lipids that reduce load of omega-6 FAs/soybean oil lipids

- **ESPEN**: Lipid emulsions should be an integral part of PN for energy and to ensure essential fatty acid provision in long-term ICU patients

1. SA McClave (JPEN 2009;33:277)
2. SA McClave (JPEN 2016;40:159)
3. R Dhaliwal (NCP 2013;29:29)
Case Presentation
Complications: IFALD

- Decreased ILE (Intralipid) from 50g 3 times per week to 50g once every 2 weeks.
  - Dextrose was increased due to weight loss to >500 g per day
  - December 2012: Total bilirubin was 0.4 mg/dL.
Case Presentation
Pancreatitis

• July 5\textsuperscript{th}, 2014: presented with severe acute epigastric pain

• Pancreatitis
  • Lipase >3,000 U/L
  • CT: peri-pancreatic fluid and edema
  • TAG increased from 71 mg/dL in July of 2011 to 520 mg/dL in July of 2014
  • Workup for other causes was negative
Case Presentation
Pancreatitis

• July 2014 to May 2015: presented with recurrent episodes of pancreatitis
  • Attempts were made to reduce his dextrose
  • During one episode:
    • Insulin level 96.7 mcIU/mL (reference range, 2.6–24.9 mcIU/mL)
    • C-peptide level was 20.7 ng/mL (reference range, 1.1–4.4 ng/mL)
    • Glucose level of 163 mg/dL
Evolution of parenteral lipid emulsions

---|---|---|---|---|---|---
1956
Cottonseed

PN lipid emulsion (olive oil and lecithin) administered to a 5-month-old boy with severe malnutrition

100% soy emulsion became the first industrially available PN lipid

MCT/LCT emulsions made of soy and coconut oil

80% olive, 20% soy

Fish oil supplement

Structured mixture of MCT and LCT

Fish oil–containing mixed formulas

Case Presentation
Range of Inflammatory Effects from IVLE

- Safflower oil
- Soybean oil
- Olive oil
- Fish oil

More Pro-inflammatory

- Medium chain triglyceride oil
- PN without lipid emulsion

Less Pro-inflammatory
Intravenous Lipid Emulsions (ILE) Alternative options: MCT

• Medium Chain Triglycerides (MCT)
  • ILE with MCT available outside the U.S. since the mid-1980s
    • Added to some ILEs to decrease $\omega$-6 fatty acid$^2$
    • Are always mixed with soybean oil for EFAs$^2$
  • MCT is found in coconut oil palm kernel oil$^2$
  • Provides rapidly available kcal/g$^{1,3}$
  • Efficient triglyceride bloodstream$^3$

Intravenous Lipid Emulsions (ILE)
Alternative options: Olive Oil

**Olive Oil (OO)**
- ILE with OO available outside the U.S. since 1990s approved by FDA
  - Provides small amounts of linoleic and α-linolenic acid for EFA
- Provides MUFA, primarily oleic acid
- Less prone to lipid peroxidation than PUFA
- Not converted into active mediators of inflammatory processes

Intravenous Lipid Emulsions (ILE)
Alternative options: Fish Oil

• Fish Oil (FO)
  • ILE with FO available outside the U.S. since mid-1990s
  • Very rich in omega-3 fatty acids
    • Less inflammatory
  • EPA and DHA can give rise to\(^1-^3\):
    • SPM – dampen acute leukocyte response and facilitate resolution of the inflammatory response.
    • D- and E-series resolvins
  • Conditional essential fatty acids\(^4\)
    • Arachidonic Acid, EPA and DHA

3. Mundi, JPEN, November 21, 2017,
Case Presentation
Pancreatitis

• July 2014 to May 2015: presented with recurrent episodes of pancreatitis

• Attempts were made to reduce his dextrose
  • Gradually reduced to 200g/day
  • Weight begins to decrease → 52kg (BMI <19 kg/m²)

• Request FDA to allow compassionate use of FO ILE

• Begin enteral feeds at night
Case Presentation
Fish Oil ILE

• BMI was now <19 kg/m²
  • Diagnosed with chronic fatigue as he was not able to sleep at night with 3 pumps (FO ILE, HPN, and EN)
Smoflipid
Mixed oil lipid emulsion (MO ILE)

- 4-oil: 30% SO, 30% MCT, 25% OO, and 15% FO
- Improved $\omega$-6:$\omega$-3 ratio\(^1\)

<table>
<thead>
<tr>
<th>Lipid Emulsion</th>
<th>$\omega$-6:$\omega$-3 Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>SO</td>
<td>7:1</td>
</tr>
<tr>
<td>MCT/LCT</td>
<td>7:1</td>
</tr>
<tr>
<td>SO/OO</td>
<td>9:1</td>
</tr>
<tr>
<td>FO</td>
<td>1:8</td>
</tr>
<tr>
<td>Smoflipid</td>
<td>2.5:1</td>
</tr>
</tbody>
</table>

Smoflipid
Mixed oil lipid emulsion (MO ILE)

- 4-oil: 30% SO, 30% MCT, 25% OO, and 15% FO
- Improved $\omega$-6:$\omega$-3 ratio$^1$
- Improved phytosterol content

Smoflipid
Mixed oil lipid emulsion (MO ILE)

- 4-oil: 30% SO, 30% MCT, 25% OO, and 15% FO
- Improved $\omega$-6:$\omega$-3 ratio
- Improved phytosterol content
- Clinical outcomes:
  - Adults and pediatric patients.
  - Safe and well tolerated.
  - Noted improved liver studies
  - Noted improved $\alpha$-tocopherol levels
  - Duration of follow-up 5-28 days

Smoflipid
Mixed oil lipid emulsion (MO ILE)

• SCCM/ASPEN: Alternative IVFEs may provide outcome benefit over soy-based IVFE, (no rec’s due to not available in USA at time of publishing)¹

Smoflipid
Mixed oil lipid emulsion (MO ILE)

- **SCCM/ASPEN**: Alternative IVFES may provide outcome benefit over soy-based IVFE, (no rec’s due to not available in USA at time of publishing)¹
- **Canadian**: Insufficient data to recommend type of lipid to reduce use of soy-based IVFE²
- **ESPEN (Surgery)**: Post-op PN including Ω-3 FAs in pts on inadequate EN requiring PN³
- **ESPEN (ICU)⁴,⁵:
  - Olive oil-based PN is well tolerated in ICU pts
  - Mixed LCT/MCT lipids show specific clinical advantages over soybean LCT alone
  - Adding EPA, DHA to IVLEs have + effects on cell membranes and immune responses
  - Fish oil-enriched lipid emulsions probably decrease LOS in critically ill pts
  - IVLEs (LCT, MCT, or mixed emulsions) can be given safely at rate of 0.7-1.5 gm/kg/d

---

Mixed Oil ILE 1\textsuperscript{st} case

- December 2016: MO ILE was approved
  - Started MO ILE at 50 g/d and then gradually titrated up to 70g/day 7 days per week
  - Dextrose was titrated up to 320g/day
  - Weight increases to 61 kg (BMI >20kg/m\textsuperscript{2})
Mixed Oil ILE  
15 cases

- 15 patients utilizing MO ILE for 12 months

<table>
<thead>
<tr>
<th>Baseline Demographics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>48±13</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>8/7</td>
</tr>
<tr>
<td>Duration of MO-IVLE at analysis (days)</td>
<td>380±57</td>
</tr>
<tr>
<td>Indication for MO-IVLE (n)</td>
<td></td>
</tr>
<tr>
<td>Short Bowel Syndrome</td>
<td>6</td>
</tr>
<tr>
<td>Bowel obstruction/Motility Disorder</td>
<td>5</td>
</tr>
<tr>
<td>Enterocutaneous fistula</td>
<td>1</td>
</tr>
<tr>
<td>Radiation Enteritis</td>
<td>1</td>
</tr>
<tr>
<td>Lymphangiomatosis</td>
<td>1</td>
</tr>
<tr>
<td>Necrotizing pancreatitis with duodenal fistula</td>
<td>1</td>
</tr>
</tbody>
</table>
## Mixed Oil ILE

15 cases

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-MO ILE</th>
<th>Post-MO ILE</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>21.4 ± 4.4</td>
<td>22 ± 3</td>
<td>0.21</td>
</tr>
<tr>
<td><strong>Total calorie per day (kcal)</strong></td>
<td>1744 ± 472</td>
<td>1669 ± 478</td>
<td>0.40</td>
</tr>
<tr>
<td><strong>% Calorie from Amino acid (%)</strong></td>
<td>24 ± 5.1</td>
<td>23.2 ± 5.8</td>
<td>0.26</td>
</tr>
<tr>
<td><strong>% Calorie from Dextrose (%)</strong></td>
<td>65 ± 8.4</td>
<td>54.4 ± 5.8</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>% Calorie from Lipid (%)</strong></td>
<td>9.9 ± 8.9</td>
<td>22.4 ± 8.2</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>ILE (g/kg/day)</strong></td>
<td>0.29 ± 0.28</td>
<td>0.59 ± 0.34</td>
<td>0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-MO ILE</th>
<th>Post-MO ILE</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alkaline Phosphatase (U/L)</strong></td>
<td>139 (47-2064)</td>
<td>147 (49-818)</td>
<td>0.80</td>
</tr>
<tr>
<td><strong>Aspartate Transaminase (U/L)</strong></td>
<td>56 (20-289)</td>
<td>39 (12-86)</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>Alanine Transaminase (U/L)</strong></td>
<td>70 (20-401)</td>
<td>53 (14-141)</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>Total Bilirubin (mg/dL)</strong></td>
<td>1.1 (0.2-4.2)</td>
<td>0.6 (0.3-3)</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>Triglyceride (mg/dL)</strong></td>
<td>113 (28-225)</td>
<td>123 (30-271)</td>
<td>0.99</td>
</tr>
</tbody>
</table>
Mixed Oil ILE: Summary

- **Intolerant to SO ILE**
  - Safe in prolonged use (n=15 close to 12 months)
  - Good source of non-dextrose calories

- **Critically Ill**
  - Option in the first week over SO ILE
  - Trials in adults and pediatric patients
  - Improved LFTs$^{1,2,3}$ Lower IL-6$^{4}$

- **Home Parenteral Nutrition**
  - Option over SO ILE
  - Trials in adults and pediatric
  - Lower LFTs$^{5,6}$, Lower TG$^{7}$

- Current data from trials of 5-28 day follow-up
- Long-term data pending

References:

1. Diamond JPEN 2017
2. Rayyan JPEN 2012
3. Tomsits J Pediatr Gastroenterol Nutr. 2010
6. Goulet JPEN 2010
7. Wu JPEN 2014
Mayo Clinic
Locations

Questions & Discussion

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