The Association between a Four-Oil Lipid Emulsion and Parenteral Nutrition Associated Liver Disease–Related Laboratory Values in Adults Receiving Home Parenteral Nutrition

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Statement of Disclosures

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## Agenda

- **Background**
- **Objective**
- **Methods**
- **Results**
- **Conclusions**
- **Strengths, Limitations, Take Aways**
Background

Home parenteral nutrition (HPN) is recommended for patients unable to meet their nutrition needs through an oral or enteral route

- Includes lipid injectable emulsions (ILE) as a macronutrient component, traditionally composed of soybean oil (SO); good source of essential fatty acids
- Pro-inflammatory nature of SO ILE is a potential factor in parenteral nutrition associated liver disease (PNALD) development
- Four-oil ILE is now FDA-approved for use as calorie source in adults
  - 30% SO, 30% medium-chain triglycerides (coconut oil), 25% olive oil, 15% fish oil
  - Fatty acids in fish oil contain anti-inflammatory properties
  - Potential benefit in treatment of PNALD with use of four-oil ILE; little data exists in HPN population
Objective

This study evaluated the association between a four-oil lipid emulsion and PNALD-related lab values in adult HPN patients with baseline abnormal liver function tests (LFTs).
Methods

Study sites:
• 12 branches of a large home infusion company in 9 states

Inclusion criteria:
• Adult HPN patients with baseline abnormal:
  • Alkaline phosphatase (ALP)
  • Alanine aminotransferase (ALT)
  • Aspartate aminotransferase (AST) or
  • Total bilirubin (T bili)
    x1.5 times the upper limit of normal
• Receiving four-oil ILE (Smoflipid®)

77 patients included in the study
Methods

Data collected retrospectively at 6 different time points over 12 months (Baseline [four-oil ILE initiation], 1, 2, 3, 6 and 12 Months)

Primary Outcome Measures:

• Changes in ALP, ALT, AST and T bili between time points
  
  High levels are indicative of liver disease

Secondary Outcome Measures:

• Changes in TG
  
  High levels are indicative of lipid intolerance

• Reports of essential fatty acid deficiency (EFAD)
  
  Physical symptoms: dry, scaly skin rash
  
  Elevated triene:tetraene ratio
## Results: Participant Characteristics

### TABLE 1. BASELINE CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF SAMPLE (N=77)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD</th>
<th>Range</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>54.2 ± 13.3</td>
<td>21–77</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>58.0 ± 15.0</td>
<td>34.0–127.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>20.6 ± 5.0</td>
<td>12.1–48.3</td>
</tr>
<tr>
<td>Four-oil ILE intake (g/kg)</td>
<td>0.7 ± 0.3</td>
<td>0.04–1.74</td>
</tr>
<tr>
<td><strong>n</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>45</td>
<td>58.4</td>
</tr>
<tr>
<td>Male</td>
<td>32</td>
<td>41.6</td>
</tr>
</tbody>
</table>

Mean 17.3 ± 29.9 months receiving HPN prior to Four-Oil ILE initiation

Key: SD, standard deviation; yr, year; kg, kilograms; BMI, body mass index; kg/m², kilograms per meters, squared; ILE, lipid injectable emulsion
Results: Participant Characteristics

FIGURE 1. PRIMARY HPN INDICATION OF SAMPLE (N=77)
Results: ALT

FIGURE 2. COMPARISON OF ALT LEVELS BETWEEN TIME POINTS WHILE RECEIVING FOUR-OIL LIPID EMULSION

ALT values reported in units per liter
Median values reported with interquartile range (IQR)

* p≤0.05: Baseline to 1 Month, 2 Month, 3 Month, 6 Month & 12 Month; 1 Month to 6 Month & 12 Month; 2 Month and 3 Month to 6 Month
Kruskal-Wallis tests and post hoc Mann-Whitney U tests were used to detect changes between time points
Results: AST

FIGURE 3. COMPARISON OF AST LEVELS BETWEEN TIME POINTS WHILE RECEIVING FOUR-OIL LIPID EMULSION

- AST values reported in units per liter
- Median values reported with interquartile range (IQR)
- *p<0.05: Baseline to 1 Month, 2 Month, 3 Month, 6 Month & 12 Month
- Kruskal-Wallis tests and post hoc Mann-Whitney U tests were used to detect changes between time points
Results: ALP

**FIGURE 4. COMPARISON OF ALP LEVELS BETWEEN TIME POINTS WHILE RECEIVING FOUR-OIL LIPID EMULSION**

ALP values reported in international units per liter
Median values reported with interquartile range (IQR)

* p≤0.05: Baseline to 2 Month, 3 Month, 6 Month & 12 Month; 1 Month to 12 Month
Kruskal-Wallis tests and post hoc Mann-Whitney U tests were used to detect changes between time points
Results: T Bili

FIGURE 5. COMPARISON OF T BILI LEVELS BETWEEN TIME POINTS WHILE RECEIVING FOUR-OIL LIPID EMULSION

T bili values reported in milligrams per deciliter
Median values reported with interquartile range (IQR)
Results were not statistically significant
Kruskal-Wallis tests and post hoc Mann-Whitney U tests were used to detect changes between time points
Results: TG

FIGURE 6. COMPARISON OF TG LEVELS BETWEEN TIME POINTS WHILE RECEIVING FOUR-OIL LIPID EMULSION

TG values reported in milligrams per deciliter
Median values reported with interquartile range (IQR)
Results were not statistically significant
Kruskal-Wallis tests and post hoc Mann-Whitney U tests were used to detect changes between time points
Results: Essential Fatty Acid Deficiency

EFAD manifestation

- There were two reports of physical manifestations of EFAD (dry, flaky skin) at the Baseline (n=1) and Month 1 (n=1) time point in the same patient
- No triene: tetraene ratio results were reported for any subject at any time point
## Conclusions

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<thead>
<tr>
<th>ALT</th>
<th>AST</th>
<th>ALP</th>
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<tbody>
<tr>
<td>• Statistically significant decrease from Baseline to Month 12</td>
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<tr>
<td>• Initial return from abnormal values at Baseline to normal at Month 2</td>
<td></td>
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<tr>
<td>• Month 12 values near normal</td>
<td></td>
<td></td>
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<tr>
<td>• Statistically significant decrease from Baseline to Month 12</td>
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<tr>
<td>• Sustained return from abnormal values at Baseline to normal at Month 1</td>
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<tr>
<td>• Statistically significant decrease from Baseline to Month 12</td>
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<tr>
<td>• Trend toward normal values from Baseline to Month 12</td>
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## Limitations & Strengths

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<thead>
<tr>
<th>LIMITATIONS</th>
<th>STRENGTHS</th>
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<tr>
<td>Retrospective design only allows for association, not causation</td>
<td>Data was collected over 12-month period - longer than most comparable studies</td>
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<td>Volume &amp; frequency of soy-based ILE was not always known prior to change to four-oil ILE</td>
<td>Four-oil ILE dosing was comparable - slightly higher than most related studies</td>
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<td>Unable to make definitive conclusions about EFAD</td>
<td>Intake of four-oil ILE was relatively stable over 12 months, slightly increased over time</td>
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<td>Relatively large sample size compared to related studies</td>
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Take Away Points

• Further studies are necessary to confirm benefit of four-oil ILE over SO ILE in adult HPN patients with PNALD-related lab values

• Continue using strategies to reduce risk of PNALD development
  • Avoid overfeeding of nutrients, ensure appropriate dextrose & ILE provision, cycle infusion over fewer hours

• Consideration of four-oil ILE use in adult HPN patients with abnormal LFTs after appropriate formula adjustments have been implemented and elevated LFTs persist
References

Thank You

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