Deciphering the Pros and Cons of Available Lipid Emulsions for Use in the Preterm Infant

Camilia R. Martin, MD MS
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Disclosure Information

Camilia R. Martin, MD

I have the following financial relationships to disclose:

<table>
<thead>
<tr>
<th>Affiliation / Financial Interest</th>
<th>Organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultant</td>
<td>Fresenius Kabi</td>
</tr>
<tr>
<td>Scientific Board</td>
<td>Alcresta, Sancilio, Laurent, Prolacta</td>
</tr>
<tr>
<td>Research Grant</td>
<td>Abbott Nutrition, Sancilio, Alcresta</td>
</tr>
</tbody>
</table>

I will be discussing the scientific literature of non-FDA approved lipid emulsions.
Objectives

1. Review the importance of fatty acids and early lipid provision in preterm health
2. Discuss the practice evolution in using lipid emulsions and gaps that remain for adequacy in the preterm infant
3. Discuss the current scientific literature in fourth generation lipid emulsions for preterm infants
4. Offer a potential clinical approach in selecting lipid emulsion types

Lipid: Definition

- Organic compound that is readily soluble in nonpolar solvents but not in polar solvents (e.g. water)
- Examples of lipids: sterols, cholesterol, monoglycerides, diglycerides, triglycerides, phospholipids, and sphingolipids
- Major functions
  - Nutritional: energy, gluconeogenesis, essential fatty acids
  - Biologic: structural component of cell membrane, cell signaling, regulation of inflammation, organogenesis, immune reactivity
Biologic Importance of Fatty Acids

DHA and polyunsaturated fatty acids (PUFAs) are important in:

1. Maintaining the structure of the cell — fluidity (enhanced by double bonds) & function

2. Molecular interaction facilitated by fluidity initiating signaling to the nucleus

3. Regulating the production of proteins

DHA Signaling

NPD1 = Neuroprotectin D1
Protection against oxidative stress triggered apoptosis

BDNF = Brain Derived Neurotrophic Factor

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Plasma Levels Approximate Brain Levels

BDNF Serum Levels Lower in Preterm vs. Term Newborns

Omega 3 PUFA Deprivation Decreases Frontal Cortex BDNF Protein
Omega-3 and Retinopathy of Prematurity

Mouse pups exposed to 75% O2 from P7 – P12

Mean DHA levels for all infants

Low DHA Levels are Linked to the Development of Chronic Lung Disease (CLD)

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DHA & AA Metabolites Attenuate Lung Injury

Room Air  
Increased Oxygen  
Hyperoxia

Resolvin D1 (RvD1)  
Lipoxin A4 (LXA4)  
RvD1 & LXA4

Histology (H&E): 200x

Martin et al, Plos one 2014
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PUFAs, Necrotizing Enterocolitis & Intestinal Inflammation

Decrease P2YR1 and TL1A gene expression

IL-1β & NFKB mRNA expression in human fetal HIEC after fatty acid supplementation and IL-1β stimulation.
### Alterations in Select Fatty Acids & Ratios Associated with Increased Risk of CLD & Late-Onset Sepsis

<table>
<thead>
<tr>
<th>CLD</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA</td>
<td>0.9 (0.7, 1.1)</td>
<td>0.4</td>
</tr>
<tr>
<td>AA</td>
<td>0.9 (0.6, 1.3)</td>
<td>0.6</td>
</tr>
<tr>
<td>DHA</td>
<td>2.5 (1.3, 5.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>LA: DHA</td>
<td>8.6 (1.4, 53.1)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Late-onset sepsis</th>
<th>Hazard ratio (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA</td>
<td>0.8 (0.7, 0.96) (1.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>AA</td>
<td>1.4 (1.1, 1.7)</td>
<td>0.02</td>
</tr>
<tr>
<td>DHA</td>
<td>1.4 (1.0, 2.0)</td>
<td>0.08</td>
</tr>
<tr>
<td>LA: DHA</td>
<td>4.6 (1.5, 14.1)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Models adjusted for gestational age, gender, growth restriction, severity of illness, total Intralipid intake

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### Accruing Evidence for Fatty Acids & Neonatal Health

1. Inflammation
2. Organogenesis
3. Immune function
4. Angiogenesis
5. Neurodevelopment

Challenge remains in harnessing the biologic potential of fatty acids with bedside translation.
Lipid Emulsions

- PN including lipid delivery life saving
- Advanced critical care medicine
- Prevented essential fatty acid deficiency
- High source of calories, energy delivery
- Provided a balance of nutrients – gluconeogenesis
- All benefits we still enjoy today
Intralipid® for the Preterm Infant

These concerns led to slow initiations and advancement
Limitations in final dose
Largely losing the benefit of intravenous lipid delivery in acutely ill preterm infants
**Postnatal Changes of Fatty Acids in Preterm Infants (1992)**

Change in percentage fatty acid (arachidonic and docosahexaenoic) composition of plasma choline phosphoglycerides after preterm birth in 10 infants.

<table>
<thead>
<tr>
<th>n</th>
<th>G.A. wks mean (SD)</th>
<th>B. wt g mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>30.5 (3.29)</td>
<td>1,367 (386)</td>
</tr>
</tbody>
</table>

**Fish Oil in the Treatment of Severe PN-Associated Liver Disease (PNALD) (2006)**

- Supported n3 benefits to human health, specifically pediatric, infants
- Highlighted the inadequacies of intralipid in providing a direct source of DHA
Postnatal Changes in Fatty Acids (2011)

Lipid Emulsions - FDA Approvals in US

• IL developed in 1962, FDA approved in 1972; though life saving, fails to meet the unique fatty acid requirements in the preterm infants
• 12 years from first Omegaven study; 26 from Leaf’s first study
• Access to a lipid emulsions with a range of n-6 to n-3 fatty acids; but none (except for intralipid) approved for preterm infants
2016 – SMOFlipid approval for adults

Does this offer a better alternative for maintenance parenteral lipid delivery?

Let’s review composition in context of the needs of the preterm infant
TABLE 1. Characteristics of commercially available intravenous lipid emulsions used in reported randomized controlled trials (27,36–39)

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Intralipid 20%</th>
<th>ClinOleic 20%</th>
<th>Lipofundin 20%</th>
<th>SMOFlipid 20%</th>
<th>Omegaven 10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year of introduction</td>
<td>1960s</td>
<td>1990s</td>
<td>1980s</td>
<td>2000s</td>
<td>1990s</td>
</tr>
<tr>
<td>Soya bean</td>
<td>100</td>
<td>20</td>
<td>50</td>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>MCT</td>
<td>0</td>
<td>0</td>
<td>50</td>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>Olive</td>
<td>0</td>
<td>80</td>
<td>0</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>Fish</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>15</td>
<td>100</td>
</tr>
</tbody>
</table>

Fatty acids (% of total fatty acid)

| Linoleic acid | 53 | 18.7 | 29.1 | 37.2 | 4.4 |
| Arachidonic acid | 0.2 | 0.5 | 0.2 | 0.1 | 0.1 |
| α-Linolenic acid | 5 | 2.3 | 4.5 | 4.2 | 1.8 |
| Eicosapentaenoic acid | 0 | 0 | 0 | 0.7 | 0.4 |
| Docosahexaenoic acid | 0 | 0 | 0 | 0.4 | 0.2 |
| n-6n-3 ratio | 7:1 | 9:1 | 7:1 | 2.5:1 | 1.8 |

Phytosterols (mg/L) based on Angsten et al (39)

| Phytosterols (mg/L) based on Xu et al (27) | 430.07 ± 5.27 | 274.38 ± 2.60 | 278.14 ± 5.09 | 507 |
| Phytosterols (mg/L) based on Xu et al (27) | 500 |
| α-Tocopherol (mg/L) | 38 | 32 | 85 ± 20 | 500 |

FO, fish oil; MCT, medium-chain triglycerides; OO, olive oil; SO, soya bean oil.

* Data in the table are the mean value when an interval is given from the manufacturer (39).

1 Independently evaluated concentration of 9 different phytosterols and squalene (27).
### Total Bilirubin Levels

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean difference IV, fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deshpande (2009)</td>
<td>100.7</td>
<td>26.3</td>
<td>21</td>
<td>101.8</td>
<td>32.8</td>
<td>21</td>
<td>11.5%</td>
<td>-1.10 (-18.47, 16.27)</td>
</tr>
<tr>
<td>Gobel (2003)</td>
<td>128.7</td>
<td>58.1</td>
<td>22</td>
<td>120.3</td>
<td>58.0</td>
<td>22</td>
<td>2.7%</td>
<td>7.90 (-28.32, 44.12)</td>
</tr>
<tr>
<td>Kooiker (2011)</td>
<td>61.8</td>
<td>45.1</td>
<td>22</td>
<td>58.1</td>
<td>58.4</td>
<td>22</td>
<td>5.1%</td>
<td>3.50 (-22.66, 29.66)</td>
</tr>
<tr>
<td>Wang (2015)</td>
<td>70.02</td>
<td>45.1</td>
<td>22</td>
<td>63.49</td>
<td>51.8</td>
<td>22</td>
<td>9.6%</td>
<td>5.13 (-13.92, 24.18)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>128</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 0.33$, df = 3 ($P = 0.89$), $I^2 = 0$

Test for overall effect: $Z = 0.47$ ($P = 0.64$)

### Conjugated Bilirubin Levels

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean difference IV, fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deshpande (2009)</td>
<td>90.6</td>
<td>39.3</td>
<td>40</td>
<td>80.37</td>
<td>37.6</td>
<td>40</td>
<td>12.3%</td>
<td>-10.23 (-6.63, 27.09)</td>
</tr>
<tr>
<td>D’Asenzo 2.5 (2014)</td>
<td>107.7</td>
<td>27.4</td>
<td>26</td>
<td>116</td>
<td>28.1</td>
<td>26</td>
<td>9.9%</td>
<td>-13.30 (-27.39, 6.79)</td>
</tr>
<tr>
<td>D’Asenzo 3.5 (2014)</td>
<td>100.9</td>
<td>25.7</td>
<td>20</td>
<td>111.7</td>
<td>20.1</td>
<td>20</td>
<td>10.3%</td>
<td>-10.32 (-28.67, 8.07)</td>
</tr>
<tr>
<td>Rayyan (2012)</td>
<td>94.9</td>
<td>68.1</td>
<td>24</td>
<td>98.2</td>
<td>74.7</td>
<td>24</td>
<td>1.9%</td>
<td>-3.40 (-46.21, 39.41)</td>
</tr>
<tr>
<td>Skountsiou (2010)</td>
<td>104.66</td>
<td>44.6</td>
<td>14</td>
<td>104.8</td>
<td>46.5</td>
<td>14</td>
<td>3.5%</td>
<td>-4.80 (-36.54, 26.94)</td>
</tr>
<tr>
<td>Tomits (2010)</td>
<td>80.89</td>
<td>62.14</td>
<td>26</td>
<td>80.31</td>
<td>61.73</td>
<td>25</td>
<td>3.0%</td>
<td>-0.56 (-33.42, 32.36)</td>
</tr>
<tr>
<td>Vlaardingenbroek (2014)</td>
<td>81.07</td>
<td>28.4</td>
<td>28</td>
<td>89</td>
<td>28.3</td>
<td>28</td>
<td>28.3%</td>
<td>-8.00 (-19.69, 3.69)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>184</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 4.21$, df = 6 ($P = 0.62$), $I^2 = 0$

Test for overall effect: $Z = 1.38$ ($P = 0.17$)

Total (95% CI): 312

Heterogeneity: $\chi^2 = 5.82$, df = 10 ($P = 0.63$), $I^2 = 0$

Test for overall effect: $Z = 0.91$ ($P = 0.36$)

Test for subgroup differences: $\chi^2 = 1.29$, df = 1 ($P = 0.26$), $I^2 = 22.3$

### 4.1.1 OQ/ISO vs. SO

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean difference IV, fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deshpande (2009)</td>
<td>2.7</td>
<td>1.5</td>
<td>24</td>
<td>3.4</td>
<td>1.6</td>
<td>21</td>
<td>52.9%</td>
<td>-0.70 (-1.61, 0.21)</td>
</tr>
<tr>
<td>Gobel (2003)</td>
<td>2.11</td>
<td>4.78</td>
<td>22</td>
<td>1.05</td>
<td>2.24</td>
<td>20</td>
<td>8.8%</td>
<td>-0.16 (-1.17, 0.85)</td>
</tr>
<tr>
<td>Wang (2015)</td>
<td>12.5</td>
<td>6.15</td>
<td>50</td>
<td>11.5</td>
<td>6.13</td>
<td>51</td>
<td>8.9%</td>
<td>1.00 (-1.92, 3.93)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>96</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 0.49$, df = 2 ($P = 0.17$), $I^2 = 43$

Test for overall effect: $Z = 0.66$ ($P = 0.51$)

### 4.1.2 SIMOF vs. SO

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean difference IV, fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rayyan (2012)</td>
<td>10.26</td>
<td>5.8</td>
<td>19</td>
<td>12.83</td>
<td>7.2</td>
<td>22</td>
<td>2.8%</td>
<td>-2.67 (-5.65, 1.14)</td>
</tr>
<tr>
<td>Vlaardingenbroek (2014)</td>
<td>2.4</td>
<td>3</td>
<td>48</td>
<td>2.9</td>
<td>3.4</td>
<td>48</td>
<td>26.6%</td>
<td>-0.50 (-1.78, 0.78)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>67</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 0.49$, df = 1 ($P = 0.33$), $I^2 = 0$

Test for overall effect: $Z = 1.12$ ($P = 0.26$)

Total (95% CI): 163

Heterogeneity: $\chi^2 = 4.76$, df = 4 ($P = 0.31$), $I^2 = 16$

Test for overall effect: $Z = 1.18$ ($P = 0.25$)

Test for subgroup differences: $\chi^2 = 0.34$, df = 1 ($P = 0.56$), $I^2 = 0$
Fourth Generation Lipid Emulsions & Neonatal Outcomes Compared to Soybean Oil

This review **did not find any significant differences** in the clinically important outcomes of death, growth, lung disease or severe eye disease (retinopathy of prematurity ≥ stage 3) with the use of newer alternative LE compared with the conventional pure soy oil based LE.

Fourth Generation Lipid Emulsions & Postnatal Fatty Acids

- No clear benefit or outcome differences in a population of all neonates including prevention of liver injury (though suggestive in small studies)
- 100% Fish Oil effective in treatment of severe PNALD; but not appropriate for maintenance therapy

- **Does it help with the postnatal fatty acid levels?**
FA & metabolic changes bring our question in focus.

We should not only be interested in the potential health benefits of LCPUFAs, but also what is the potential harm?
Essentiality of Arachidonic Acid

1) Growth
2) Primary fatty acid in preterm brains till early term (Martinez, 1992)
3) Reduction associated with 40% increase in nosocomial sepsis (Martin, 2011)
4) Provision of its distal metabolite (Lipoxin A4) improves alveologenesis in murine hyperoxia induced lung injury (Martin, 2015)

Martinez Jped 1992

AA

DHA

Essentiality of Arachidonic Acid

1) Growth
2) Primary fatty acid in preterm brains till early term (Martinez, 1992)
3) Reduction associated with 40% increase in nosocomial sepsis (Martin, 2011)
4) Provision of its distal metabolite (Lipoxin A4) improves alveologenesis in murine hyperoxia induced lung injury (Martin, 2015)
Clinical Decision Making in Parenteral Lipid Emulsion Use in the Preterm Infant

n-6 vs n-3 Dominant Lipid Emulsions

<table>
<thead>
<tr>
<th></th>
<th>Intralipid</th>
<th>Fish-Oil Based Lipid Emulsions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total energy (Kcal/k/d)</td>
<td>--</td>
<td>-</td>
</tr>
<tr>
<td>Fatty Acid Profiles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linoleic Acid</td>
<td>↑↑</td>
<td>↑</td>
</tr>
<tr>
<td>Arachidonic Acid</td>
<td>↓↓</td>
<td>↓</td>
</tr>
<tr>
<td>DHA</td>
<td>↓↓</td>
<td>↓</td>
</tr>
<tr>
<td>EPA</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>n-6:n-3</td>
<td>↑, --</td>
<td>↓↓</td>
</tr>
<tr>
<td>Phytosterols</td>
<td>↑</td>
<td>SMOF (1/2) to none</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>min</td>
<td>↑↑</td>
</tr>
</tbody>
</table>

(decrease TG – lipogenesis; inhibit platelet function; ? inc. bleeding time)
Which Lipid Emulsion to Choose?

My Logic

1. What is the indication? Maintenance different from therapeutic (established liver failure; traumatic brain injury)
2. What is the goal? (Assuming for now total energy delivery and utilization is the same)
   a. Prevent cholestasis, PNALD in non-surgical infant

   Important to recognize that most preterm infants with short courses of IL, do NOT get Cholestasis/PNALD

Epidemiology of SBS

Table 2. Percent of patients receiving PN for >14 days who developed a direct bilirubin >2.0 mg/dl

<table>
<thead>
<tr>
<th></th>
<th>PN for 14–28 days (%)</th>
<th>PN for 29–56 days (%)</th>
<th>PN for 57–100 days (%)</th>
<th>PN for &gt;100 days (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates having no surgery</td>
<td>15 6 46 71 100</td>
<td>40 40 60 50</td>
<td>35 67 100</td>
<td>55 100</td>
</tr>
<tr>
<td>&gt;1000 g</td>
<td>15 6 46 71 100</td>
<td>40 40 60 50</td>
<td>35 67 100</td>
<td>55 100</td>
</tr>
<tr>
<td>1000–1499 g</td>
<td>15 6 46 71 100</td>
<td>40 40 60 50</td>
<td>35 67 100</td>
<td>55 100</td>
</tr>
<tr>
<td>750–999 g</td>
<td>12 4 35 34 50</td>
<td>35 64 100</td>
<td>34 50 100</td>
<td>34 50 100</td>
</tr>
<tr>
<td>500–749 g</td>
<td>21 4 35 34 50</td>
<td>35 64 100</td>
<td>34 50 100</td>
<td>34 50 100</td>
</tr>
<tr>
<td>&lt;500 g</td>
<td>21 4 35 34 50</td>
<td>35 64 100</td>
<td>34 50 100</td>
<td>34 50 100</td>
</tr>
</tbody>
</table>

| Neonates having surgery or ECMO | 33 33 100 | 33 33 100 | 33 33 100 | 33 33 100 |
| NEC with laparotomy               | 33 33 100 | 33 33 100 | 33 33 100 | 33 33 100 |
| NEC with surgical drain<sup>2</sup> | 33 33 100 | 33 33 100 | 33 33 100 | 33 33 100 |
| Gastrostomy                       | 18 63 100 | 100 | 100 | 100 |
| Omphalocele                       | 20 60 100 | 100 | 100 | 100 |
| Diaphragmatic hernia              | 18 63 100 | 100 | 100 | 100 |
| Jejunal atresia                   | 33 67 100 | 100 | 100 | 100 |

Abbreviations: ECMO, extracorporeal membrane oxygenation; NEC, necrotizing enterocolitis; PN, parenteral nutrition.
The percent of patients who developed a direct bilirubin concentration >2.0 mg/dl is shown, as related to birth weight, surgical condition and days PN was administered. Data are given only for NICU patients who survived at least 28 days after birth.

<sup>2</sup> Excluding patent ductus arteriosus ligation, inguinal hernia repair, retinopathy of prematurity surgery, and other ‘minor’ surgeries.

<sup>2</sup> No laparotomy.
Which Lipid Emulsion to Choose?

My Logic

1. What is the indication?
   Maintenance *different from* therapeutic
2. What is the goal? (Assuming for now total energy delivery and utilization is the same)
   a. Prevent cholestaticis, PNALD in *non-surgical infant*
      Important to recognize that most preterm infants with short courses of IL, do NOT get Cholestasis/PNALD
      Feed the baby!
      Given trade-offs, short courses of IL may be better than FOLE, to avoid greater AA losses, excess EPA, and lower n-6:n-3 ratios

b. Prevent cholestasis, PNALD in *surgical infant*
   Omegaven has premise in treatment of established PNALD
   SMOF does not – has phytosterols
   ClinicalTrials.gov Identifier: NCT02412566
   Can the neonatal community wait? Trickling in practice has already started
   **Problem**: Underpowered use will not expose the potential rare, but important harms induced by the practice. Role of registries?
Which Lipid Emulsion to Choose?

My Logic

1. What is the indication? Maintenance different from therapeutic
2. What is the goal? (Assuming for now total energy delivery and utilization is the same)
   c. Prevent BPD, ROP....
      Small trials, not enough information
      ** Lofqvist et al., 2018 (ROP); Collins et al., 2017 (BPD) find potential harm **

Which Lipid Emulsion to Choose?

My Logic

1. What is the indication? Maintenance different from therapeutic
2. What is the goal? (Assuming for now total energy delivery and utilization is the same)
   d. Maintain birth levels of fatty acids
      Neither do well. Next, next generation lipid emulsions required.

   As previously, given trade-offs, short courses of IL may be better than FOLE, to avoid greater AA losses, excess EPA, and lower n-6:n-3 ratios for now
A Word of Caution

Intravenous lipid emulsions providing DHA at doses similar to those given in our trial are being used to provide nutritional support during the transition to full enteral feeding in preterm infants, although with limited testing in clinical trials. Our results raise questions about the safety of this strategy and suggest the need for further study.
Summary

✧ Lipids & fatty acids are highly bioactive & are essential for neurodevelopment, cell membrane structure & function, including cell signaling

✧ Lipids are a critical component of parenteral nutrition preventing EFAD, providing a high energy source and an alternative fuel for gluconeogenesis

✧ Fourth generation lipid emulsions offer lipids and fatty acids from a diverse source of oils, but changes are not without potential concerns and the benefits remain unclear

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