Suitable fat emulsions

Bernard Messing
Suitable Fat Emulsions for Long term (H)PN

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Suitable Fat Emulsions for Long term (H)PN

Objectives

Available sources & composition
Doses of administration and liver (RES) complications
Essential fatty acids & Deficiency (EFAD)
Relation PUFAs and antioxidants: Vit E
Peroxidation and liver fibrosis
Potential advantages of new sources
Practical advices to increase tolerance

Full published articles
COMPARISON of FATTY ACID COMPOSITION

1GD/Baxter

Recomm.: DGE, ÖGE, SGE, SVE 2000, Reference values for the nutrient supply
EFAD: Mead acid 20:3 n-9
< 0.2  Arachidonic 20:4 n-6

*n-3 not taken into account
Ratio: n-6/n-3 usual 10, Ideal: ? ≤ 5
n-3>n-6>n-9 substrates for Δ and El

2 Prostanoids

4 Leukotrienes

Inflammation
Immunity
Structures

2BM.ESPEN.04
## Composition of 20% lipidic emulsions

<table>
<thead>
<tr>
<th></th>
<th>Clinoleic</th>
<th>RichW6 MCT/LCT</th>
<th>Structured</th>
<th>MLF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soybean oil</td>
<td>4 g</td>
<td>20 g</td>
<td>10 g</td>
<td>8 g</td>
</tr>
<tr>
<td>Olive oil</td>
<td>16 g</td>
<td>0 g</td>
<td>0 g</td>
<td>//2gFish*</td>
</tr>
<tr>
<td>Coconut oil</td>
<td>0 g</td>
<td>0 g</td>
<td>10 g</td>
<td>10 g</td>
</tr>
<tr>
<td>Egg phospholipids</td>
<td>1.2 g</td>
<td>1.2 g</td>
<td>1.2 g</td>
<td>1.2 g</td>
</tr>
<tr>
<td>PUFA g%</td>
<td>20%</td>
<td>60%</td>
<td>30%</td>
<td>41%</td>
</tr>
<tr>
<td>MUFA g%</td>
<td>63%</td>
<td>23%</td>
<td>12%</td>
<td>13%</td>
</tr>
<tr>
<td>SFA g%</td>
<td>17%</td>
<td>17%</td>
<td>11%</td>
<td>10%</td>
</tr>
<tr>
<td>MCT g%</td>
<td>-</td>
<td>-</td>
<td>46%</td>
<td>36%</td>
</tr>
<tr>
<td>n-6 FA g%</td>
<td>19%</td>
<td>52%</td>
<td>25%</td>
<td>35%</td>
</tr>
<tr>
<td>n-3 FA g%</td>
<td>2%</td>
<td>8%</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Ratio n-6 /n-3 FA</td>
<td>9</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Vit E (α-toco) mg/L</td>
<td>30</td>
<td>27</td>
<td>20 (200°)</td>
<td>12</td>
</tr>
<tr>
<td>α-toco mg/PUFA g</td>
<td>0.75</td>
<td>0.23</td>
<td>0.33 (3.3°)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

*EPA: 3.1, DHA: 2.3g%  ° recently (2004) enriched  (EPA: 2.45, DHA: 2.5g% in 100 ml Omegaven® ≤ 4 wk)
Suitable Fat Emulsions for Long term (H)PN

Objectives

Available sources & composition

*Doses of administration and liver (RES…) deposits*

Essential fatty acids & Deficiency (EFAD)

Relation PUFAs and antioxydants : Vit E

Peroxidation and liver fibrosis

Potential advantages of new sources

Some practical advices to increase tolerance
Fat emulsion (rich w6) phospholipid effect (10% versus 20%) on serum lipoprotein profile during one month of cyclic TPN.

Liver Phospholipidosis Induced by Parenteral Nutrition: Histologic, Histochemical, and Ultrastructural Investigations


EM: phospholipidosis
<table>
<thead>
<tr>
<th>Chronic cholestasis</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short bowel &lt; 50 cm</td>
<td>.009</td>
<td>2.1 (1.2- 3.7)</td>
</tr>
<tr>
<td>IV Lipid &gt; 1 g/Kg/j*</td>
<td>.004</td>
<td>2.3 (1.6- 5.9)</td>
</tr>
<tr>
<td>Energy ≥ 80% DER</td>
<td>.03</td>
<td>NS</td>
</tr>
<tr>
<td>Risk of hepatopathy</td>
<td>.008</td>
<td>3.1 (1.3- 4.1)</td>
</tr>
</tbody>
</table>

90 adult patients
Follow up 5yr HPN


*W6 rich (soybean oil)
### HPN-Associated Liver Disease

#### Liver disease complication

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P</td>
<td>[RR (95%IC)]</td>
</tr>
<tr>
<td>Chronic cholestasis</td>
<td>.0006</td>
<td>4.8 (1.6-13.7)</td>
</tr>
<tr>
<td>IV Lipid &gt; 1 g/Kg/j*</td>
<td>.0001</td>
<td>3.4 (1.6-6.8)</td>
</tr>
<tr>
<td>Energy ≥ 80% DER</td>
<td>.03</td>
<td>NS</td>
</tr>
<tr>
<td>Glucose ≥ 4 g/Kg/j</td>
<td>.04</td>
<td>NS</td>
</tr>
</tbody>
</table>

90 adult patients
Follow up 5yr HPN


* W6 rich (soybean oil)
PROBABILITY OF BEING FREE OF LIVER COMPLICATIONS ACCORDING TO IV LIDOINTAKE

HPN-Associated Liver Disease

- Risk of HPNALD in intestinal failure adult patients increased 3 fold when 20% IV lipid (w6 LCT) was provided ≥ 1 g/Kg/j, even with a non hyper-caloric regimen which was equivalent to 0.88 ± 0.13 DER.
- HPNALD was not linked in this study to liver macro-steatosis and to the amount of Glucose 3.99 ± 1.20 g/Kg/j.

MICROSTEATOSIS IN HPN-LD

OIL RED O
MACROPHAGE PROLIFRATION/ACTIVATION IN HPN-LD
(Long-term) PN Associated liver disease

(Chronic) Cholestasis
? decreased mdr-2 gene expression

PN-dependent
LCT (w6) emulsion: hepatocytes/macrofages

Macrophages (Kupffer):
decreased bacterial clearance

Tauro-Conjugates BS

Patient-dependent

**microsteatosis, phospholipidosis**

**ductular lesions**

Excluded segment(s):
bacterial translocation

Very short bowel/no ileum

extensive fibrosis, cirrhosis
Bone marrow, Macrophages, Black Soudan

Prevalence of clinico-biological abnormalities according to the degree of SBH infiltration

<table>
<thead>
<tr>
<th></th>
<th>absent or mild</th>
<th>moderate or important</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jaundice</td>
<td>0%</td>
<td>40%</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>0%</td>
<td>60%</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>25%</td>
<td>40%</td>
<td>NS</td>
</tr>
<tr>
<td>Anemia</td>
<td>83%</td>
<td>100%</td>
<td>NS</td>
</tr>
<tr>
<td>Leucopenia</td>
<td>16%</td>
<td>0%</td>
<td>NS</td>
</tr>
<tr>
<td>Thrombopenia</td>
<td>0%</td>
<td>30%</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

NS : non significant

Chronic cholestasis and related Cirrhosis can be associated with RES lipid deposits in liver, spleen and bone marrow « Lipidic Thesaurismosis »
LIPIDIC THESAURISMOSE (RES) & HPN

CONDITION:
- IVLE in A-I-O mixtures TCL-rich in PUFA (Black soudan).

CLINICAL FATE:
Slow occurrence of:
- Jaundice with conjugated and non-conjugated bilirubin,
- Hépatosplénomégaly with hypersplenism,
- Pancytopenia with possible hemorrhagic syndrome.

DIAGNOSIS
- Targeted Hématies &/ou platelets
- Bone marrow biopsy: **blue histiocytes (Giemsa)** & activation macrophages (Ac CD 68)

TRAITEMENT:
- Long term interruption of TCL-rich in PUFA.
Suitable Fat Emulsions for Long term (H)PN

Objectives

Available sources & composition
Doses of administration and liver complications

*Essential fatty acids & Deficiency (EFAD)*

Relation PUFAs and antioxidants : Vit E
Peroxidation and liver fibrosis
Potential advantages of new sources
Some practical advices to increase tolerance
FIGURE 1. Relation between the sum of nonessential $n-7$ and $n-9$ fatty acids and the sum of essential $n-6$ and $n-3$ fatty acids. $\bigcirc$, Patients receiving home parenteral nutrition; $\bullet$, patients receiving home parenteral nutrition with a Holman index $> 0.2$; $\triangle$, healthy control subjects.
Conversion rate of linoleic to arachidonic (20:4n-6/18:2n-6)
P < 0.001 in LTPN patients with intestinal failure

*IV input with soya bean oil: 18:2n-6 = 10.8±6.7g/d (52%); 18:3n-3 = 1.2±0.7 g/d (5%)*

Conversion rate* of linolenic to DHA (22:6n-3/18:3n-3) 
P = 0.071 in LTPN patients with intestinal failure

IV input with soya bean oil: 18:2n-6 = 10.8±6.7g/d (52%); 18:3n-3 = 1.2±0.7 g/d (5%)

Specific plasma PL Changes in Fatty Acid Metabolism in LTPN Patients With Chronic Intestinal Failure

• Stimulation of the n-6 pathway: 
  *increased arachidonic with low linoleic due to severe malabsorption*

• Inhibition of the n-3 pathway: 
  *decreased DHA with nl Linolenic due to very SBS*

• Possible EFAD deficiency with W6 rich emulsion (IL 20%) in SBS: 
  *47 g per Infusion (4 infusion/wk) = 24±13g/d*
  *i.e., % Energy as fat: 25% in SBS; 21% in other patients*

Hypothesis: Delta 5 and 6 competition between n-6 & n-3 (Liver; small bowel)

EFAD (Holman Index°) & LTPN (intestinal insufficiency)

- Between 2 and 6 months to document EFAD in IV fat free regimen*
- 1.2-2.4 g/Fat (w6 rich)/Kg biweekly to normalize Index*
- 100 g Fat (w6 rich)/ week sufficient to prevent increased index**
- Index not correlated to dry skin problems…**

<table>
<thead>
<tr>
<th>In % of Energy</th>
<th>linoleic</th>
<th>W6 rich</th>
<th>DHA</th>
<th>LOW</th>
</tr>
</thead>
<tbody>
<tr>
<td>- minimum/insufficient°</td>
<td>4%</td>
<td>(10%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- seems to be sufficient</td>
<td>6%</td>
<td>(15%)*,**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- still lower than controls</td>
<td>7-10%</td>
<td>(15-20%)°°</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

° Mead acid: 20:3 n-9
Arachidonic: 20:4 n-6
n-3 not taken into account

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Studies with Soya oil (W6 rich)

* Fleming CR et al AJCN 1976; 29: 976-83
** Jeppesen et al AJCN 1998; 68: 126-33
EFA in HPN PATIENTS

However, in none of these groups was the intravenous lipid supply able to increase the plasma phospholipid concentration of 18:2n-6 to a concentration similar to that of control subjects.

If one wishes to adjust biochemical plasma phospholipid profiles, our study indicates that almost all patients receiving HPN should be supplemented with lipids. Dose recommendations would have to be adjusted according to repeated blood tests, but this study indicates that large amounts of lipids would be required to normalize plasma phospholipid profiles.

Suitable Fat Emulsions for Long term (H)PN

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Essential fatty acids & Deficiency (EFAD)
Relation PUFAs, Vit E and peroxidation
Peroxidation and liver fibrosis
Potential advantages of new sources
Some practical advices to increase tolerance
• Ideal ratio results in the lowest level of lipid peroxide
• Ideal ratio is ~ 0.6 mg Tocopherol/g PUFA
• The ratio varies depending on the degree of unsaturation of lipids eaten (or infused)


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<td>α-toco mg/PUFA g</td>
<td>0.75</td>
<td>0.23</td>
<td>0.33(3.3°)</td>
<td>0.15</td>
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</table>
100 mL Nutralipid 10% over 30 min

Van Gossum et al

Breath Pentane (pmol/kg/min) vs. Plasma α-tocopherol (μmol/L)

$r = -0.58$
$p < 0.01$

Nl plasma Se and Se-GSHPx levels
Lipid peroxidation and antioxidant status in adults receiving lipid-based (soybean)* HPN

12 HPN GE adult patients of 60(4-100) mo duration
Intralipid 20% 50(0 -100) g/d; 1(0 -1.8)g/Kg/d
(2 patients with 1.2 and 2 with 1.8g). LFT not reported

Lipid peroxidation and antioxidant status in adults receiving lipid-based (soybean) HPN

Plasma $\alpha$-toc/chol+trigl (µmol/mmol)

$\begin{align*}
\text{Duration of HPN (months)} & \\
0 & 10 & 20 & 30 & 40 & 50 & 60 & 70 & 80 & 90 & 100 \\
0 & 1 & 2 & 3 & 4 & 5 & 6 & 7 & 8 & 9 & 10 \\
\end{align*}$

$p = 0.74$

$p < 0.02$

12 HPN GE adult patients of 60(4-100) mo duration
Intralipid 20% 50(0 -100) g/d; 1(0 -1.8)g/Kg/d
(2 patients with 1.2 and 2 with 1.8g). LFT not reported

Increase in Lipid peroxidation in AIO Nutritive Mixtures

• Greater *in vitro* increase (Peroxides & MDA)*:
  - in binary than in ternary (AIO) mixtures
  - Related to PUFA : positive correlation
  - Related to Vit E : PUFA ratio : negative correlation
    - *Soya > Soya/MCT > Olive Oil*

• *In vivo* Long term LTPN with rich soya oil PUFA°:
  - MDA and plasma alpha-tocopherol (Vit E) : r = -0.59
  - Lowering of vit E : related to PUFA load & PN duration

Pironi et al Nutrition 2003;19: 784-8
Pironi et al AJCN 1998; 68 :888-93
Lemoyne et al AJCN 1988; 88;48:1310-5
Jonas et al AJCN 2000; 72: 181-9
Vitamin E (alpha tocopherol) & LT HPN

- Tocopherols in W6 rich emulsions poorly bioavailable °
- Competition between alpha-tocopherol° and less active esters (beta, gamma) of IV lipids
- Exchange very active during metabolism of chylomicrons
- Usual recommendation (~ 10-15 mg/d) inadequate *°
- 25-50 mg in fat free or more if IV fat **
- Ideal ratio ≥ 0.6 mg alpha-Tocopherol / g PUFA°°
- Route of supplementation: ? both oral and IV

** Thurlow , Grant. Ann N Y Acad Sci. 1982;393:121-32
Vitamin E, EFAD and (LT)HPN

- Platelet hyperaggregation correlated significantly with EFAD
- EFAD was observed in patients with an associated platelet hyperaggregation independent of vitamin E deficiency
- Supplementation with all-rac-alpha-tocopherol corrected platelet hyperaggregation and H2O2-induced hemolysis;
- Intravenous fat emulsion (rich w6) did not correct the platelet and red blood cell abnormalities

Thurlow PM, Grant JP. Ann N Y Acad Sci. 1982;393:121-32
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HPN-Associated Liver Disease

Explicative analysis: multifactorial

I) HPN regimen matters:

- Solution:
  - Promote oral feeding with « hyperphagia »
  - Avoid exclusive (total) HPN
  - Avoid hyper Patenteral nutrition
  - No more than 1 g/Kg/j of 20% W6TCL/Soja
  - Quid of other IV lipids MCT, Olive Oil, W3?
α-tocopherol reduces peroxidation of MCT(50%)/LCT(50%)* Lipidic emulsion

• Enriched α-tocopherol group% *:
  120 min TBARs:
  Basal : 66±34 nmol MDA/mg LDL and VLDL-cholesterol
  5 d     : 39±25
  10 d    : 42±17

  \[ \text{P} < 0.02 \text{ vs controls} \]

• no change in the Control group (IL20% no added α-tocopherol)

* 200 mg/L of α-tocopherol, i.e. : 3.4 mg α-tocopherol /g of PUFA vs 0.2 in C

Randomized study of 2x 12 patients (internal medicine, 14 cancer)
50% calories as lipids 20% in all-in-one (500 ml / d)

Manuel-y-Keenoy B et al Europ J Clin Nutr 2002; 56: 121-8
Effect of MCT/LCT LE on plasma EFA in 11 HPN patients

- **Plasma PL linoleic acid (18:2n-6)**
- **alpha linolenic acid (18:3n-3)**
- **arachidonic acid (20:4n-6)**
- **DHA (22:6n-3)**

IVLE 2.85 ± 1.55 g.kg⁻¹.week 3(2-5) /wk A-I-O mix (50 g/infusion)/ 4 months

C.Chambrier et al JPEN 2004; 32: 7-12
Effect of MCT/LCT LE on plasma FA in 11 HPN patients

"MCT/LCT lipid substitution of LCT did not change most of essential plasma fatty acid concentrations:

<table>
<thead>
<tr>
<th></th>
<th>LCT</th>
<th>MCT/LCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>22:4n-6</td>
<td>0.50 ± 0.12%</td>
<td>0.63 ± 0.11% P = 0.022</td>
</tr>
<tr>
<td>22:5n-6</td>
<td>0.32 ± 0.11%</td>
<td>0.48 ± 0.15% P = 0.011</td>
</tr>
</tbody>
</table>

Did not induce EFAD nor improved the fatty acid disturbances usually observed in LTPN patients “

IVLE :2.85 ± 1.55g.kg⁻¹.week (50 g per infusion)
3(2-5) cycle per week in A-I-O mixtures
4-month substitution

C.Chambrier et al JPEN 2004; 328: 7-12
Changes of LFT under long-term use (6 yr) of Clinoleic®

**1A**

Long term HPN (13 yr) SBS type II (10 cm j + 85% colon)  
Necrotizing small bowel (01.1991) in a 19 yr-old man

Changes of LFT under long-term use (6 yr) of Clinoleic®

Alkaline phosphatases (IU/L)

$\text{r} = 0.83$  
$P < 0.001$

Long term HPN (13 yr) SBS type II (10 cm $\text{j} + 85\%$ colon)  
Necrotizing small bowel (01.1991) in a 19 yr-old man

Changes of LFT under progressive increase of Clinoleic
Parallels the changes in AGE and vit E status

Long term HPN (13 yr) VSBS type II
since 01.1991 in a 19 yr-old young man

**before**

<table>
<thead>
<tr>
<th>Lipid/CHO ratio</th>
<th>6%</th>
<th>20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>20:3n-9/20:4n-6</td>
<td>0.052±0.023</td>
<td>0.025±0.012 (p&lt;0.01)</td>
</tr>
</tbody>
</table>

Substitution of LCT (n=6) or MCT/LCT (n=8) By Olive Oil: a 3 mo-study in LTHPN patients

**Conclusion:** ClinOleic® 20% is safe and efficient in adult HPN patients. It maintains a normal EFAs status and did not influence systemic inflammatory parameter concentrations. By contrast to studies in preterm infant or pediatric patients,* no effect on vitamin E concentration or lipid peroxidation could be observed.

Standard IV infusion of vit E in Reimund & Goulet studies

Reimund et al (submitted) 2004
* Goulet et al AJCN 1999;70: 338-45
° Vahedi et al : 13 HPN, 3-mo study
(submitted 2004) (added oral Vit E)
Safe and efficacious prolonged use of an olive oil-based lipid emulsion (ClinOleic®) in chronic intestinal failure

- 6-mo observation periods (W6 rich) before & after vs Olive
- Lipids: 500 ml/2 or 3 times/week
- 12 patients completed
- LFT & platelets unchanged
- Retrospective analysis:
  - Same numbers of infections or line sepsis
  - Thrombotic events: 9 patients intent to treat
    7 events versus 0 (11% B, 55% A versus 0% with Olive)

° Peroxides, Vit E, Vit K and platelet hyperaggregability...

Olive oil (Clinoleic\textsuperscript{R}) versus Soja W6 oil (i.e., Intralipid\textsuperscript{R})

In non-hypercalorie HPN

- Is -supposed- better liver tolerance directly or indirectly Oil related?
- Improvement in EFA status without PUFA loading
- Improvement in tolerance of TG delivery
- Better balance in CHO/Lipid energy ratio (? ideal 30%)
- Higher Vit E supply inducing:
  - less lipid peroxydation*
  - less or no abnormal (RES / Liver) lipid deposits
  - a protective effect in non alcoholic steato hepatitis°

* McDonald GA et al J Gastro Hepatol 2001; 16: 599-606
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Fat Emulsions for Long term (H)PN:
Storage & delivery influence ‘suitability’

- * Oversized fat globule (> 5µm) increase (> 0.1%) after 5 days of storage in All-in-one containing LCTs but not MCT/LCT:

  \[\text{This can increase trapping in RES and peroxidation}\]

- ° Vit E (\(\alpha\)-tocopherol) losses/degradation occurs in A-I-O mixtures stored in EVA but not in multi-layered bags:

  \[\text{Peroxidation may be not decreased by added vitamin E}\]

- Light-induced peroxidation can be prevented by dark delivery tubing (limiting vitamins A, C losses):

  \[\text{Emulsions are susceptible to light-induced peroxidation}\]

* Driscoll DF. Clin Nutr 2001, 20 (suppl 4) 8-10
** Silvers K et al Acta Paediatr 2001; 90: 242-9
Suitable Fat Emulsions for Long term (H)PN
In adult patients

- Suitable gallenic A-I-O bags (with separate chamber for E)
- No more than 1g/Kg/d of any type of lipid emulsion - in adults -
- 50% of energy as lipids is too high (30% seems OK)
- Do not forget multivitamin preparations
- Check and Increase $\alpha$-tocopherol, according to PUFA content in A-I-O
- Do not forget that hidden vit K in lipid emulsions modifies coagulation
- MCT/LCT better in cirrhosis
- MCT/LCT might be better in hyperlipoproteinemic patients (Renal…)
- Fish oil component might be better in « proinflammatory diseases »
- Olive oil is a good source, neutral, and suitable for many patients
- Large clinical multicentre prospective trials are needed to conclude
Suitable Fat Emulsions for Long term (H)PN
In adult patients

collection of data benefited from:

- academic sources: C Chambrier, O Corriol,
  AM Badran, F Joly
  KN Jeejeebhoy, L Pironi, JM Reimund

- Pharmaceutical companies:
  G Dutot        Baxter
  C Mauriac      B Braun
  C Yvon         Fresenius Kabi

BM has no source of conflict to declare
Fat Emulsions, Vitamin K in Long term (H)PN
Is K1* supplementation necessary?

° In patients receiving IV lipids (50g/Infusion 4-5 times a wk) (except for Eurolip® and Clinoleic®), a normal K1 status can be maintained during long term HPN without added K1.
K1 concentration ranges from 179 ± 39 to 353 ± 78 ng.l-1 in batches. K supplementation cannot be abandoned until specification of the vitamin K content of emulsions by manufacturers.
A weekly supply of 250 to 400 µg of vitamin K1 (1L of IVlipids) is enough to observe a normal vitamin K1 status in (H)°°PN patients.

°°The vit K content of emulsions should be specified by manufacturers because increased amount of vit K could lead to “warfarin” resistance

* not included in multivitamin preparations
normal K1 values: 150 - 900 ng.l-1

BM.ESPEN.04

°° Duerksen D, Papineau N. JPEN 2004; 28:30-3.
<table>
<thead>
<tr>
<th>? EXCESS OF</th>
<th>? DEFICIENCY IN</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Vit. A</td>
<td>• Selenium</td>
</tr>
<tr>
<td>• Cu.</td>
<td>• Vit E.</td>
</tr>
<tr>
<td>• Fe.*</td>
<td>• Sulfur AA (glutathion)</td>
</tr>
<tr>
<td>• Mn.</td>
<td>• Carnitine</td>
</tr>
<tr>
<td>• Alu.</td>
<td>• Choline</td>
</tr>
<tr>
<td>• <strong>Phospholipids</strong>°</td>
<td>• Others</td>
</tr>
<tr>
<td>• <strong>P.U.F.A.</strong>°</td>
<td><strong>micronutrients</strong></td>
</tr>
<tr>
<td>• <strong>Phytosterols</strong></td>
<td></td>
</tr>
</tbody>
</table>

Peroxidation: * indpd of vit E, ° dpd of vit E
Potential advantages of Fish oil

- Decrease inflammatory response:
  Decreased TNF production
- Reduce blood viscosity & platelet aggregation:
  Reduced production of 2 series of PG and TXs
- Reduced diet induced hepatic TG content:
  Inhibits de novo synthesis of FA
  Oral: yes, IV: paradoxical risk of Hyper TG
- Less accumulation of lipid peroxidation products?
  Suggested by lower Liver SOD, GPX
  But not adjusted in α-toc /g PUFA

α-tocopherol reduces in vitro peroxidation of MCT(50%)/LCT(40%)/FO(10%)* Lipidic emulsion

• Peroxidation induced by TG (not by PL) rich particles
• In vitro peroxides increase with storage of emulsions
• α-tocopherol (100 mg, i.e. 2mg/g of PUFA) reduces in vitro peroxide concentration (at 2hr):
  by 40% (from 500 to 300 µM) versus « no added α-toc  »
  by 30% (from 500 to 350 µM) with 1mg α-toc /g PUFA
• Addition of 2 fold vit E (200mg, i.e. 4 mg α-toc /g of PUFA) did not further reduce peroxidation

* Lipoplus