Improved fatty acid and leukotriene pattern with a novel lipid emulsion in surgical patients

Summary
Objective We assessed the effects of a novel lipid emulsion with reduced content of n-6 fatty acids (FA), increased share of MUFA and n-3 FA and supplemental vitamin E on fatty acid and leukotriene pattern in surgical patients. Methods In a double-blind, randomized study 33 patients received isonitrogenous, isocaloric TPN over 5 postoperative days following major abdominal surgery. 19 patients received the new SMOFlipid® 20% and 14 patients a standard soybean oil emulsion (Lipovenoes® 20%, both Fresenius Kabi), each 1.5 g fat/kg body weight (BW)/d. Routine lipid biochemistry, plasma tocopherol, fatty acid pattern in plasma phospholipids, as well as leukotriene (LT) release in leukocytes were assessed. Additionally, fatty acid pattern in leukocyte and platelet phospholipids were analysed, but results are not presented. Results On day 6, plasma α-tocopherol (34.2 ± 10.3 μmol/L) and, in plasma PL, total n-3 FA were higher (11.1 ± 1.9 vs. 4.9 ± 0.9 mol%; p < 0.05) and total n-6 FA lower (23.8 ± 2.2 vs. 31.8 ± 1.7 mol%; P < 0.05); the ratio n-3/n-6 FA being elevated (0.5 ± 0.1 vs. 0.2 ± 0.0 p < 0.05) with SMOFlipid compared to the soybean oil emulsion. The shares of EPA (3.3 ± 1.0 vs. 0.4 ± 0.2 mol%; p < 0.05) and DHA (6.9 ± 1.8 vs. 3.7 ± 0.8 mol%; p < 0.05) were highly increased but that of arachidonic acid (AA) was unchanged with SMOFlipid while the ratio EPA/AA was increased (0.7 ± 0.2 vs. 0.1 ± 0.0 p < 0.05). LTB5 release was enhanced on day 6 (8.1 ± 5.3 vs. 1.8 ± 3.8 pmol/107 PMN, p < 0.05) and liberation of LTB4 was lowered, yet not significantly with SMOFlipid (124.0 ± 51.2 vs. 152.1 ± 68.8 pmol/107 PMN). Length of hospital stay was significantly shorter with SMOFlipid (13.4 ± 2.0 vs. 20.4 ± 10.0 days, p < 0.05). Conclusion Treatment with the new emulsion SMOFlipid is well tolerated and modulates FA and leukotriene pattern suggesting favourable anti-inflammatory effects and further clinical benefits.

Key words lipid emulsion – TPN – fish oil – olive oil – vitamin E – immunomodulation

Introduction
In clinical nutrition, lipids are more than sources of energy and building blocks for cell membranes. They may also be considered as pharmacological agents provided by nutrition, thus emphasising the major role of the quality of lipid intake in the clinical context [1, 2]. Excessive intake of polyunsaturated fatty acids (PUFA), especially linoleic acid, impairs synthesis of long-chain...
PUFA by inhibiting their desaturation pathways [3, 4], resulting in imbalanced synthesis of eicosanoids. In addition, suppressive effects of PUFA on immune cell function have been reported [4–6]. Indeed, increased susceptibility to infection is to be seriously considered as a disadvantage especially in patients at risk of sepsis and SIRS. There is, however, a substantial uncertainty about the mechanisms whereby lipids modulate inflammation; certainly lipids modulate the composition of plasma membranes both in cells producing pro-inflammatory cytokines and in those which are targets of their action [7].

Recently, a NIH working group recommended that the amount of dietary n-6 fatty acids (FA) should be reduced and the share of n-3 FA increased [8]. These measures were considered as mandatory for optimal brain and cardiovascular health and function. Furthermore, it was recommended that the majority of FA should be obtained from monounsaturated fatty acids (MUFA) [8]. The question might be raised whether this public health related recommendation can be implicated in clinical nutrition.

In the present study we investigated the effects of a newly developed lipid emulsion made of a physical mixture of soybean oil (long-chain), medium-chain, olive oil and fish oil triglycerides (SMOFlipid 20%). The new emulsion contains an increased amount of vitamin E (approx. 200 mg per litre) in order to counteract peroxidation but also to avoid immunosuppression due to decreased antioxidant capacity [9].

We hypothesised that the novel emulsion with reduced content of n-6 FA, increased amount of n-3 FA and MUFA, might exert beneficial antiinflammatory and immunomodulatory effects.

**Material and methods**

- **Patients and nutrition**

In a randomised, double blind study 33 patients derived from two centres [University hospitals Münster (n = 12, centre 1) and Gießen (n = 21, centre 2), respectively] received isonitrogenous (1.5 g amino acids/kg body weight (BW) isoenergetic (33 kcal/kg BW) total parenteral nutrition over 5 postoperative days following major abdominal surgery. Patient characteristics are given in Table 1. All patients were apparently well nourished. Patients with manifest metabolic diseases (e.g. diabetes mellitus, hyperlipidaemia), overweight (body mass index > 30 kg/m²), chronic renal, liver or heart diseases, acute or life-threatening diseases, history of drug abuse or chronic alcoholism, or concomitant corticosteroid therapy were excluded. The study was approved by the local Ethical Committees according to German law and the procedures followed were in accordance with the Helsinki Declaration of 1975 as revised in 1996. Written informed consent of each patient was obtained before commencement of the investigation.

The novel emulsion (SMOFlipid® 20%, Fresenius Kabi, Bad Homburg, Germany) is a physical mixture of soybean oil (60 g/L), MCT (60 g/L), olive oil (50 g/L) and fish oil (30 g/L). The emulsion was supplemented with vitamin E which is important for antioxidant protection, and contained about 200 mg/L vitamin E. Nineteen patients received the new emulsion, and 14 patients a standard soybean long-chain triglyceride emulsion (Lipovenoes® 20%, Fresenius Kabi, Bad Homburg, Germany), which contains 200 g soybean oil/L and 57 mg vitamin E/L [10]. Each fat regimen corresponded to 1.5 g lipids/kg BW/day. The fatty acid composition of SMOFlipid and Lipovenoes are given in Table 2.

During the study, all patients were monitored daily for vital signs (arterial blood pressure, heart rate, body temperature and body weight) and complicating factors like allergic reactions, nausea, dysfunction of the gastrointestinal tract, signs of infection, cardiac discomforts, pulmonary affections, renal or hepatic dysfunction, haematological signs or behavioural disorders. Concomitant medications, fluid input and blood substitution were carefully monitored. For clinical outcome assessment, length of postoperative hospital stay was monitored.

Heparin blood was drawn before and the day after operation and on the subsequent days of infusion in order to monitor lipid metabolism (serum triglycerides, total cholesterol, phospholipids), before start of infusion and on the 6th postoperative day to screen FA profiles and vitamin E concentrations, and before infusion and on the 4th and 6th postoperative days to measure stimulus-induced eicosanoid release by leukocytes.

- **Analytical methods**

Serum triglycerides, total cholesterol, and phospholipids were assayed using commercially available kits (Boehringer, Mannheim, D) using a Hitachi 717 autoanalyser.

**Table 1** Patient characteristics

<table>
<thead>
<tr>
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<th>Lipovenoes 20%</th>
<th>SMOFlipid 20%</th>
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</thead>
<tbody>
<tr>
<td>Number of patients (n)</td>
<td>14</td>
<td>19</td>
</tr>
<tr>
<td>Male/female</td>
<td>12/2</td>
<td>12/7</td>
</tr>
<tr>
<td>Mean age (years ± SD)</td>
<td>61.1±10.5</td>
<td>63.1±14.2</td>
</tr>
<tr>
<td>Mean weight (kg ± SD)</td>
<td>77.7±11.9</td>
<td>72.9±11.3</td>
</tr>
<tr>
<td>Mean height (cm ± SD)</td>
<td>176.9±7.7</td>
<td>168.9±9.4</td>
</tr>
<tr>
<td>Duration of surgery (hours ± SD)</td>
<td>3.58±1.40</td>
<td>3.47±1.25</td>
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SD standard deviation.