Evaluation of clinical safety and beneficial effects of a fish oil containing lipid emulsion (Lipoplus, MLF541): Data from a prospective, randomized, multicenter trial*

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Objective: **To prove safety and effectiveness of a lipid emulsion enriched with n-3 fatty acids from fish oil (Lipoplus) within the setting of parenteral nutrition of patients after major abdominal surgery and to determine whether there are effects on outcome parameters.**

Design: **Prospective, randomized, double-blind, multicenter trial.**

Setting: **University and surgical teaching hospitals.**

Patients: **After obtaining informed consent, 256 patients undergoing major abdominal surgery were randomized. Parameters of safety, effectiveness, and outcome were routine laboratory parameters, complication rates, length of stay in the intensive care unit, and length of hospital stay. In addition we determined in patient subgroups of 30 patients each, the changes of the content of selected long-chain polyunsaturated fatty acids, the leukotriene synthetic capacity and the antioxidant α-tocopherol.**

Interventions: **Participating patients were randomized to receive either Lipoplus (group I; n = 127 patients) or Intralipid (group II; n = 129 patients). Parenteral nutrition was initiated immediately after surgery and ended on day 5 after surgery.**

Measurements and Main Results: **No significant differences between groups I and II were observed when comparing routine laboratory parameters during the perioperative period. Plasma levels of eicosapentaenoic acid, leukotriene B_5, and antioxidant content were significantly increased in group I. Furthermore, there was a significantly shorter length of hospital stay of ≈21% (17.2 vs. 21.9 days; $p = .0061$) in group I.**

Conclusions: **Our findings indicate that the administration of Lipoplus in the postoperative period after major abdominal surgery is safe and results in a significantly shorter length of hospital stay. Administration of n-3 polyunsaturated fatty acids in the postoperative period can be considered a valuable choice for patients requiring parenteral nutrition after major abdominal surgery. (Crit Care Med 2007; 35:700–706)**

Key Words: omega-3 fatty acids; fish oil; prospective randomized clinical study; nutrition; surgery

The potential health benefits of long-chain (n-3) polyunsaturated fatty acids (PUFA) have been described by Kromann and Green (1) in 1980, at which time they reported a very low incidence of death from ischemic heart disease in Greenland Eskimos. This observation was related to the high (n-3) PUFA intake by these people and subsequent studies confirmed the protective role of (n-3) PUFA in fish oils, i.e., eicosapentaenoic acid (20:5 [n-3]; EPA) and docosahexaenoic acid (22:6 [n-3]) against cardiovascular and inflammatory disease states (2–6). Moreover, a meta-analysis of the available data on clinical trials providing an (n-3) PUFA-supplemented enteral nutrition product suggested an immunomodulating effect represented by a significant reduction of infection rates and a trend toward reduced mortality (7).

Nonetheless, there have also been reports of potential adverse effects of consuming a diet rich in (n-3) PUFA on host immunity. This diet has been shown to suppress *in vivo* and *in vitro* immune responses and elements of T- and B-cell function in humans, including a reduced lymphocyte proliferation in conjunction with impaired interleukin-2 biosynthesis as well as a reduced production of proinflammatory cytokines (e.g., tumor necrosis factor-α and interleukin-1β) (review in references 8, 9). However, the beneficial effects of enteral (n-3) PUFA on immune competence and patient outcome have been reported too (10, 11).

The observed immunomodulating effects of (n-3) PUFA lead to the conclusion that these substrates should not only be considered as energy sources but also possess the additional potential to influence the healing processes and patient outcome in the clinical setting. So far, only limited information is available from clinical trials focusing on the use of parenteral fish oil, which is rich in EPA and docosahexaenoic acid, as an adjunct for

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***See also p. 951.**

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improvement of outcome after major surgery (12). A recent retrospective study analyzed the effects of routine peri- and/or postoperative parenteral application of fish oil in critical illness (13). Tsekos et al. (13) reported a significantly decreased mortality rate (3% vs. 15%; $p < .02$), as well as a significantly shorter hospital stay (22 days vs. 29 days; $p < .05$), in patients receiving pre- and postoperative fish oil when compared with patients receiving standard total parenteral nutrition. The authors concluded from their retrospective data that the perioperative provision of parenteral fish oil beneficially influences patient outcome, probably by modulating the immune response.

So far, there is limited information in respect to the safety and effectiveness of parenterally administered n-3 PUFA-enriched lipid emulsions. The main objective of this study, hence, was to determine the safety and effectiveness of Lipoplus.

PATIENTS AND METHODS

A total of 256 patients from four surgical departments undergoing elective abdominal surgery were recruited to receive total parenteral nutrition during a 5-day period after major abdominal surgery. Mean patient age was 59.3 ± 11.5 yrs (group I, 59.6 ± 11.6 yrs; group II, 59.1 ± 11.5 yrs); benign and malignant conditions were equally distributed in both patient groups (benign: group I, 25%, group II, 29%; malignant: group I, 75%, group II, 71%) (see Table 1 for demographic data). The study was performed under permission of the responsible Committee on Ethics in Clinical Research of every individual participating university hospital. Written informed consent was obtained from all participating patients before they were randomized to receive either supplementation of a fat emulsion composed of 50% medium-chain triglycerides, 40% long-chain triglycerides and 10% fish oil (MLF541 = Lipoplus, group I; n = 127 patients), or a fat emulsion composed of 100% long-chain triglycerides (Intralipid, group II; n = 129 patients). The test drug and the reference drug were administered as lipid components of total parenteral nutrition, which was infused at a constant rate (controlled by an infusion pump) via a central venous catheter for 22–24 hrs per day. The daily dosage was 0.7 g fat/kg body weight on the first and second postoperative days and 1.4 g of fat/kg of body weight on 3rd to 5th postoperative days (see Table 2 for the composition of both fat emulsions). Both drugs were supplied by the hospital pharmacy and were "blinded" in the pharmacies of the participating hospitals.

The nutritional status of both study groups was comparable with regard to body mass index as well as plasma protein levels (body mass index was 25 in both groups; total plasma protein content, 68.7 ± 9.3 g/L for group I and 68.1 ± 8.9 g/L for group II). The intra-abdominal surgical sites were comparable in both patient groups, and most patients underwent surgery in the lower abdomen (67% and 62%, respectively).

Morbidity, Mortality, and Complication Rates. During the perioperative period, the following parameters of morbidity were recorded: elevated body temperature (>38.0°C), catheter-related sepsis (positive culture from catheter tip and fever >39.0°C), pneumonia (clinical and/or radiologic finding), cardiac complications (arrhythmia, brachy-/tachycardia, atrial fibrillation, myocardial ischemia/infarction), and days receiving artificial ventilation. Mortality was recorded during a 30-day period after surgery. Moreover, the length of intensive care unit stay was recorded prospectively.

Length of Stay. The length of stay was defined as the time between the day of surgery and hospital discharge.

Clinical Chemistry. Clinical safety was evaluated by repeated determination of the following parameters: white blood cell count, blood differential (including monocytes, lymphocytes), hemoglobin, reticulocytes, hematocrit, platelet count, prothrombin time [Quick's test], partial thromboplastin time, fibrinogen, aspartate transaminase, alanine amino transaminase, γ-glutamyle transferase, alkaline phosphatase, triglycerides, total protein, low-density lipoprotein, high-density lipoprotein, blood gases, sodium, potassium, calcium, chloride, blood glucose, urea, creatinine, bilirubin, and C-reactive protein. Not all of these parameters are shown.

In patient subgroups, we determined the content of PUFAs (amino acid [AA], EPA) in plasma phospholipids, the leukotriene synthetic capacity (LTB_5 and LTB_4 plus isomers), and the α-tocopherol content (30 patients each analysis) during the postoperative period.

Plasma Phospholipids and Leukotriene Synthetic Capacity. These parameters were determined by chromatography (thin layer and gas) as described by Schulte and Weber (14). Leukotriene release was determined in 2×10^7 whole blood leukocytes per milliliter stimulated with the calcium ionophore A23187 (5 μmol/L) (Sigma, Deisenhofen, Germany) by reverse-phase high-performance liquid chromatography.

α-Tocopherol. α-Tocopherol was determined using the high-performance liquid chromatography assay previously described by Hess (15).

Statistical Analysis

All parameters were measured preoperatively as well as on days 1 and 6 after surgery. For statistical analysis data were entered into an Oracle database (v. 7.02), and analyses were done with SAS 9.1. Graphs were plotted using STATISTICA 7.1.30. Fisher's exact test was used for comparison of dichotomous variables. Categorical variables with more than two categories were analyzed with the Pearson's chi-square test. Variables of at least ordinal scale were analyzed with the nonparametric Wilcoxon-Mann-Whitney-test. Findings for categorical variables are presented as percentages per group. Variables that are at least ordinal scaled are given as medians, along with the 10th and 90th percentiles, and are tabulated according to the analysis used. Variables that are interval scaled are presented as mean and SD. $p < .05$ was considered significant.

RESULTS

Both treatment regimens were well tolerated. With regard to the laboratory parameters listed in Table 3, we observed comparable trends in both treatment groups; moreover, no significant differences in postoperative morbidity were detected. Differences between groups are always within the reference ranges of the

Table 1. Demographic data

	Group I		Group II	
	Male	Female	Male	Female
Gender (%)	71 (56)	56 (44)	73 (57)	56 (43)
Body weight, kg	76.4 ± 11.3	67.0 ± 13.3	78.9 ± 11.9	65.3 ± 12.2
Body mass index	24.9 ± 3.1	25.2 ± 4.7	26.1 ± 4.0	24.6 ± 3.9

Results are presented as absolute numbers (gender) or as mean ± SD (body weight, body mass index).

Table 2. Composition of lipid solutions used for total parenteral nutrition

Content per 1000 mL Emulsion	MLF 541 (Lipoplus)	LCT (Intralipid)
Medium-chain triglyceride	100.0 g	—
Soybean oil	80.0 g	200.0 g
Fractionated fish oil	20.0 g	—
Phospholipids derived from egg	12.0 g	12.0 g
Glycerol	25.0 g	22.5 g
α-Tocopherol	200 mg	—

Table 3. Morbidity and laboratory findings

	Group I	p Value	Group II
Elevated body temperature (>38.0°C)	17.3%	.207	24.0%
Catheter-related sepsis	3.1%	.752	3.9%
Pneumonia	0.8%	.102	3.9%
Cardiac complications	2.4%	.320	4.7%

	Group I Preoperative	Group I Postoperative, Day 1	Group I Postoperative, Day 6	p Day 1 vs. Day 6	Group II Preoperative	Group II Postoperative, Day 1	Group II Postoperative, Day 6	p Day 1 vs. Day 6
WBC, G/L[a]	6.5 (4.1–10.2)	11.0 (7.2–16.4)	9.6 (6.0–16.1)	.0004	6.9 (4.4–11.2)	11.7 (7.5–18.3)	9.4 (5.9–15.7)	<.0001
RBC, T/L	4.4 (3.6–5.1)	3.8 (3.1–4.7)	3.7 (3.1–4.4)	.0315	4.3 (3.4–5.1)	3.7 (3.2–4.4)	3.7 (3.2–4.3)	.5311
Platelets, G/L[b]	241.0 (171.0–369.0)	227.0 (148.0–325.0)	275.5 (185.0–402.0)	<.0001	278.0 (180.0–416.0)	212.0 (115.0–324.0)	292.0 (181.0–432.0)	<.0001
PT (Quick), %	97.5 (82.0–121.0)	78.0 (59.0–94.0)	94.0 (78.0–112.0)	<.0001	100.0 (83.0–119.0)	77.0 (61.0–95.0)	94.0 (74.0–112.0)	<.0001
AST, U/L	11.0 (7.3–19.3)	14.7 (7.3–36.7)	15.3 (7.8–41.3)	.538	10.0 (6.0–17.7)	15.0 (8.0–48.0)	14.7 (7.3–33.7)	.244
γGT, U/L	13.3 (6.7–43.3)	9.8 (3.3–26.7)	49.3 (13.3–146.7)	<.0001	13.3 (6.7–39.3)	9.0 (3.3–26.7)	51.0 (18.0–110.0)	<.0001
Bilirubin, mg/dL	0.58 (0.29–1.11)	0.76 (0.41–1.55)	0.55 (0.29–1.29)	.0001	0.52 (0.23–0.94)	0.70 (0.41–1.40)	0.58 (0.25–1.29)	.0003
Creatinine mg/dL	0.87 (0.62–1.11)	0.88 (0.58–1.18)	0.72 (0.50–0.98)	<.0001	0.87 (0.60–1.12)	0.83 (0.59–1.20)	0.75 (0.54–1.09)	<.0001
Triglycerides, mg/dL[c]	113.8 (61.3–210.0)	70.0 (35.0–129.0)	146.0 (78.8–259.0)	<.0001	113.8 (76.0–201.3)	63.0 (35.0–113.8)	106.0 (66.0–182.0)	<.0001
Cholesterol, mg/dL	208.8 (116.0–266.8)	123.7 (69.6–181.7)	149.0 (104.4–194.0)	<.0001	208.8 (135.3–263.0)	116.0 (81.0–172.0)	139.2 (100.6–188.0)	<.01
Lymphocytes, %	23.5 (14.0–38.0)	8.0 (4.0–14.0)	13.0 (7.0–25.0)	<.0001	22.0 (11.0–33.0)	8.0 (4.0–14.0)	11.0 (5.0–21.0)	<.0001
CRP, mg/L	6.0 (2.0–32.0)	83.0 (43.0–157.0)	44.0 (30.0–125.0)	<.0001	7.0 (2.0–55.0)	93.0 (54.0–163.0)	49.0 (16.0–117)	<.0001
Glucose, mg/dL	97.2 (76.0–127.9)	149.6 (100.9–214.4)	124.3 (93.7–192.8)	.0004	97.3 (77.5–156.8)	148.8 (106.0–241.0)	115.0 (84.0–232.5)	<.0001

WBC, white blood cell count; RBC, red blood cell count; PT, prothrombin time; AST, aspartate transaminase; γGT, γ-glutamyle transferase; CRP, C-reactive protein.

[a] $p = .0371$ between treatment groups for changes from postoperative day 1 to day 6 (Wilcox-Mann-Whitney test [WMW]); [b] $p = .0081$ between treatment groups for changes from postoperative day 1 to day 6 (WMW); [c] $p = .0027$ between treatment groups for changes from postoperative day 1 to day 6 (WMW). Values are provided as median, including 10th and 90th percentiles.

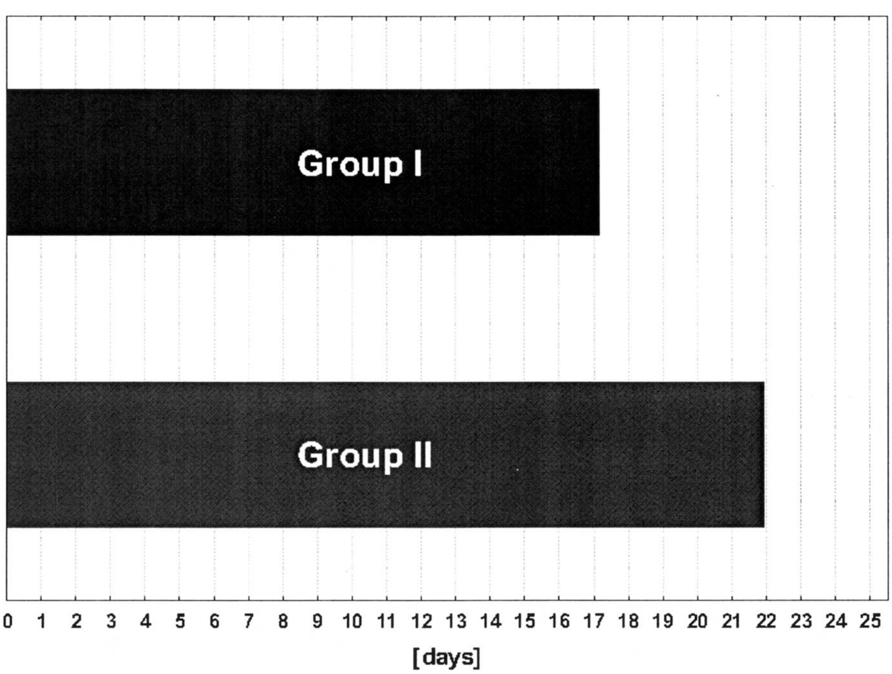

Figure 1. Length of hospital stay ($p = .0061$ group I vs. group II).

respective parameters. No significant differences between groups I and II were detected for mortality (4.7% vs. 1.6%; $p = .1445$) and length of intensive care unit stay (4.1 days vs. 6.3 days; $p = .364$).

Regarding length of hospital stay, leukotriene synthetic capacity (LTB4 and LTB5), antioxidative capacity (α-tocopherol), and polyunsaturated fatty acids in plasma phospholipids patients (EPA, AA) group I showed a significantly different and clinically relevant treatment effect compared with group II.

Length of Hospital Stay

Following major abdominal surgery, we observed a significantly shorter length of hospital stay of ≈21% in group I when compared with group II (17.2 days vs. 21.9 days; $p = .0061$). Twelve percent of patients in group I and 9% of the patients in group II were discharged within 10 days, and 47% of the patients in group I and 57% of the patients in group II stayed in the hospital longer than 15 days (Fig. 1).

Leukotriene Synthetic Capacity

LTB_5+Isomers. On day 6 after surgery, significantly higher levels of LTB_5 and isomers were detected in group I when compared with early postoperative values ($p = .0098$), as well as with group II ($p = .0035$) (Fig. 2).

LTB_5 + Isomers/LTB_4 + Isomers Ratio. We observed a higher LTB5/LTB4 ratio in patients receiving Lipoplus on day 6 after surgery. The ratio was significantly increased when compared with early postoperative values in group I ($p = .0020$), as

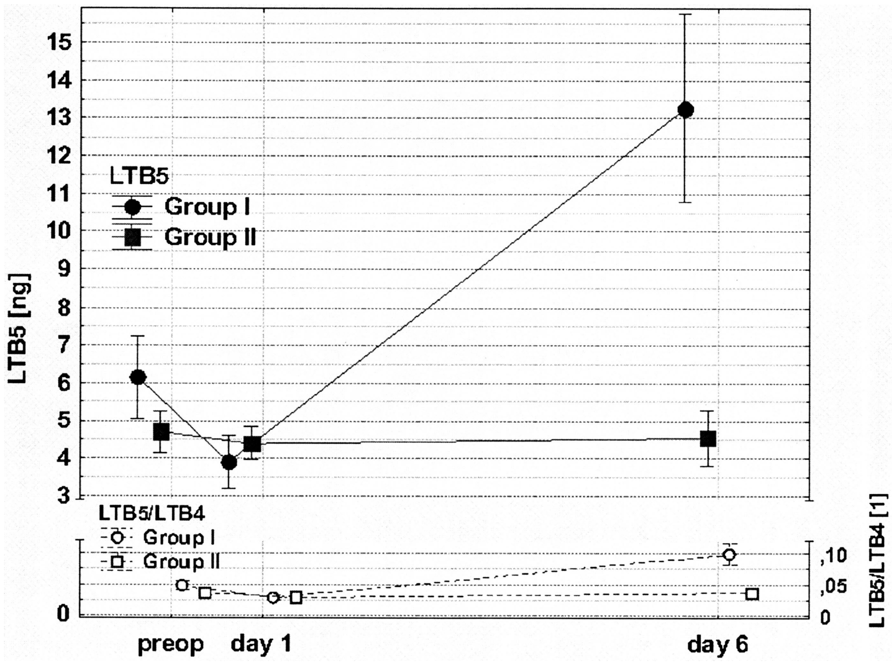

Figure 2. Leukotriene synthetic capacity—(LTB_5) + isomers (p = .0098 group I postoperative day 1 vs. day 6; p = .0035 group I vs. group II; leukotriene synthetic capacity—ratio of LTB_5 + isomers/LTB_4 + isomers; p = .0020 group I postoperative day 1 vs. day 6; p = .0017 group I vs. group II). *preop*, preoperative.

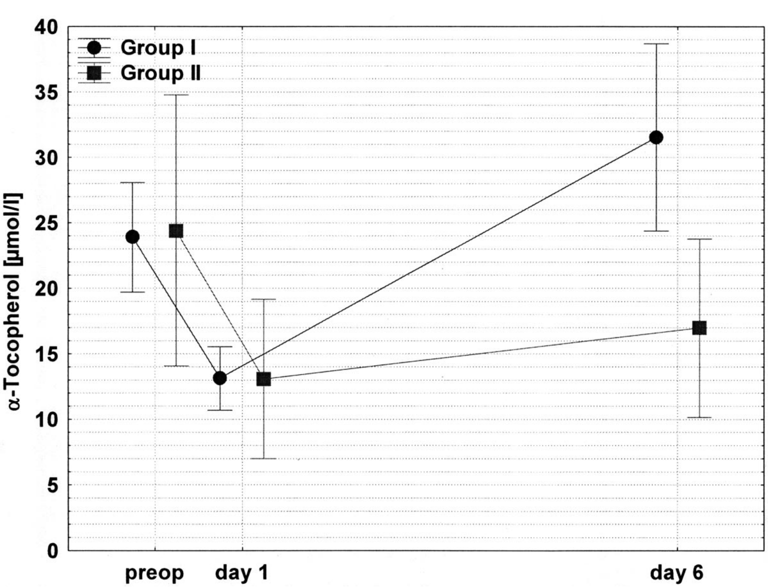

Figure 3. Antioxidant capacity—α-tocopherol (p = .0001 group I postoperative day 1 vs. day 6; p = .0256 group II postoperative day 1 vs. day 6; p < .0001 group I vs. group II). *preop*, preoperative.

well as with values in group II, on day 6 after surgery (p = .0017).

Antioxidant Capacity

α-Tocopherol. Patients receiving Lipoplus during the postoperative period showed significantly higher levels of α-tocopherol on day 6 after surgery when compared with group II (p < .0001) and with early postoperative values in group I (p = .0001). In group II, a significant depression of α-tocopherol was observed in the postoperative period (p = .0256 vs. preoperative values) (Fig. 3).

Polyunsaturated Fatty Acids in Plasma-Phospholipids

EPA. During the postoperative period, no changes of EPA were observed in group II, whereas administration of Lipoplus resulted in a significant increase of the EPA content of plasma phospholipids on day 6 after surgery when compared with early postoperative values (p = .0009) and with the findings in group II (p = .0012) (Fig. 4).

AA. The content of AA in plasma phospholipids decreased significantly in groups I and II (p = .0002 and p = .0125, respectively) but did not differ between both patient groups.

EPA/AA Ratio. We detected a significantly increased EPA/AA ratio in study patients on day 6 after surgery when compared with early postoperative values (p = .0003) and with group II (p = .0023).

DISCUSSION

Surgical trauma induces a general inflammatory response associated with a stimulation of the innate immune system and a depression of cell-mediated immunity (16–19). In parallel with the proinflammatory response, compensating mechanisms with antiinflammatory activity are generated (18, 20). An overwhelming proinflammatory state may ultimately lead to organ dysfunction and multiorgan failure (18). With regard to this, Weiss et al. (21) recently reported a significant down-regulation of the proinflammatory response in patients after abdominal surgery if these patients were treated with fish oil emulsion during the perioperative period. Fish oil contains the long-chain n-3 PUFAs, EPA, and docosahexaenoic acid. Especially, EPA appears to be the most potent when included in the human diet and down-regulates the T-lymphocyte response; nonetheless, the immunologic effects of fish oil supplementation are complex (22). Studies by Calder et al. and other groups (for a review, see reference 22) suggest that dietary fish oil diminishes the cell-mediated immune response by decreasing the activity of antigen presenting cells and by decreasing the sensitivity of macrophages to T-lymphocyte–derived cytokines. These fatty acids, therefore, exert beneficial effects in diseases with a hyperinflammatory character (23). It has been observed that PUFAs of the n-3 series enhance the production of prostaglandin E_3 and decrease the production of prostaglandin E_2. Thus, they have a major impact on the function of many components of the immune system and exert their effects through changes of membrane lipid composition, the binding of

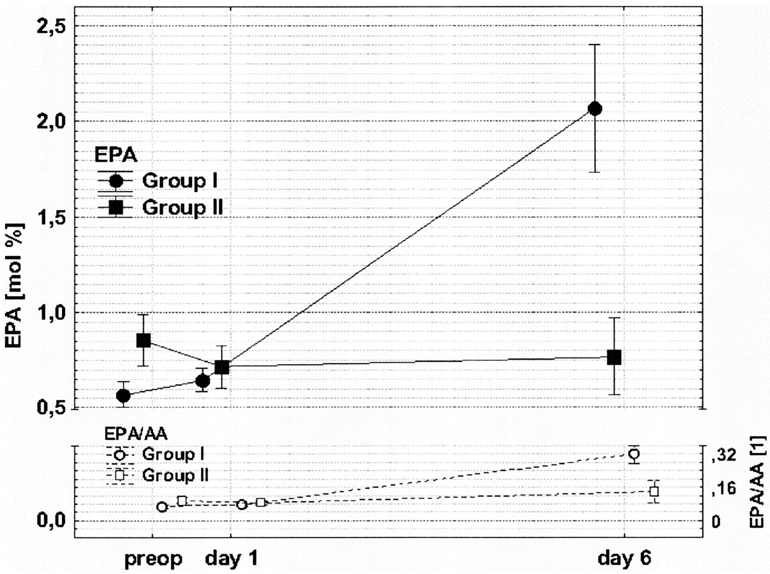

Figure 4. Eicosapentaenoic acid (*EPA*) content of plasma phospholipids (p = .0009 group I postoperative day 1 vs. day 6; p = .0012 group I vs. group II; ratio of EPA/amino acid (*AA*) content of plasma phospholipids; p = .0003 group I postoperative day 1 vs. day 6; p = .0023 group I vs. group II). *preop*, preoperative.

cytokines, the formation of membrane-generated cellular signals, and effects on gene expression (24). Results from animal studies led to the conclusion that the provision of n-3 PUFAs in combination with other immunomodulating nutrients enhances the immune function (24) and in cancer patients, supplementation of n-3 PUFAs leads to prolonged survival (25). The effects of n-3 PUFAs on the inflammatory response can be induced by free fatty acids, triglyceride fatty acids, after incorporation into the membrane phospholipid bilayer or following metabolism to eicosanoids, thereby affecting components of both natural and acquired immunity, including the production of key inflammatory mediators (22, 23). So far, only limited information is available from clinical trials focusing on the use of parenteral fish oil as an adjunct for the improvement of clinical results after major surgery (12). Three studies analyzed the effects of perioperative parenteral application of fish oil supplements on patient outcome and/or patient immune functions during the early postoperative period (13, 21, 26). Tsekos et al. (13) reported a significantly decreased mortality rate (3% vs. 15%; $p < .02$), as well as a significantly shorter hospital stay (22 vs. 29 days; $p < .05$), in patients receiving pre- and postoperative fish oil supplements when compared with patients receiving standard total parenteral nutrition. Schauder and colleagues (26) reported that perioperative administration of fish oil did not result in immunosuppression but an increase of interleukin-2, tumor necrosis factor-α, and interferon-γ production by lymphocytes. Finally, Weiss et al. (21) showed in a small (24 patients) single-center study that n-3 fatty acids may have favorable effects on postoperative length of stay (significant reduction of hospital stay from 23.5 days to 17.8 days) after major surgery via modulation of the postoperative immune response.

The findings published so far led us to evaluate the safety and effectiveness of an (n-3) PUFA-enriched parenteral nutrition (Lipoplus, MLF541) in a prospective, randomized, multicenter study, including 256 surgical patients.

Our findings indicate that parenteral administration of n-3 PUFA in a double-blinded randomized study allows for a faster recovery of patients undergoing major abdominal surgery. This is illustrated by a significantly shorter length of hospital stay. The length of stay reported here was reduced by ≈21% in the treatment compared with the control group. These time periods compare well with those reported by Senkal and colleagues (10) who used an oral formula of n-3 PUFA and also observed a significant reduction of postoperative length of stay. A recent review by Calder (27) showed beneficial effects of enteral nutrition containing fish oil on length of hospital stay in some but not all of the reviewed studies. Daly and coworkers (28) described a mean length of stay of 15.8 ± 5.1 days in their immunonutrition group and 20.2 ± 9.4 days in their control group.

The average length of hospital stay is fairly long in both patient groups (17 days in the treatment group and 22 days in the control group). This observation may in part be explained by the complexity of surgical procedures, with 36% of patients in both study groups undergoing extended resections involving more than one organ within the same surgery. Another contributing factor to this prolonged length of stay was the advanced disease state of the patients, with 50% to 55% of the study population suffering from disseminated cancer (lymph node positive and/or distant metastases). In total 47% of the study patients (Lipoplus) and 57% of the control patients (Intralipid) were in the hospital for >15 days, and 12% and 9% were discharged within 10 days, respectively.

As far as the postoperative inflammatory response is concerned, both patient groups suffered from a sustained depression of circulating lymphocytes during the postoperative period. We have previously reported a similar depression of circulating immune competent cells in a different patient group undergoing rectal cancer surgery, with and without preoperative chemo-radiotherapy (29). The posttraumatic depression of circulating lymphocyte subpopulations has also been reported by other groups (30, 31). The postoperative increases of circulating C-reactive protein concentrations did not differ significantly between both study groups (32).

Patients receiving parenteral nutrition during the postoperative course showed a comparably significant increase of blood glucose levels up to a peak level of 155 mg/dL in the drug study group and 166 mg/dL in the reference drug group. This increase returned to levels comparable with preoperative values by day 6 after surgery.

It has been reported that long-chain n-3 fatty acids may be useful antiinflammatory agents and may be of benefit in patients at risk of developing sepsis (33). This antiinflammatory potential of long-chain n-3 fatty acids may be of clinical relevance in our patients. The observed increase of EPA and LTB_5 at the end of the study period supports the notion of a smaller degree of proinflammation in the study group.

Group I received a fat emulsion with a ratio of n-3 to n-6 fatty acids of 1:2.7. This mixture was chosen to warrant a relative increase of EPA within the membrane phospholipids without depriving the membrane of AA. As we were able to show herein, this goal was achieved because the EPA content of the membrane phospholipids increased during the postoperative period in the study population, and the content of AA in both patient groups showed comparable changes during the postoperative period. Furthermore, the EPA/AA ratio changed toward a relative increase of EPA in the study population. These beneficial effects of Lipoplus administration on the EPA/AA ratio may well contribute to altered immune function in surgical patients after major abdominal interventions. This notion is supported by the fact that EPA and docosahexaenoic acid serve as alternative lipid precursors for both cyclooxygenase and lipoxygenase pathways, with the formation of trienoic prostanoids (instead of the 2-series originating from AA) and 5-series leukotrienes (instead of the 4-series leukotrienes derived from AA) (34). Arachidonic acid metabolites lead to activation of the inflammatory processes and an attenuation of cell-mediated immune function. This effect is reduced by an increased EPA content of the membrane phospholipids, because n-3 fatty acids compete with n-6 fatty acids for metabolism and EPA is known to be the preferred substrate for the lipoxygenase pathways (21, 35). Moreover, the n-3 fatty acid-derived metabolites, including 5-series cysteinyl-leukotrienes, leukotriene B_5, and thromboxane A_3 possess reduced inflammatory and vasomotor potencies when compared with the AA-derived lipid mediators (36). Administration of fish oil in the postoperative period can, therefore, ameliorate the known suppression of cell-mediated immunity after surgery and also leads to an increased level of leukotriene B_5 in group I, as well as an increased LTB_5/LTB_4 ratio. Our study results show that short-term administration of n-3 PUFA not only alters the substrate content of the membrane phospholipids, but also changes the pool of fatty acid-derived metabolites toward the less inflammatory n-3 fatty acid derived metabolites.

We also observed that the antioxidant capacity during the postoperative period is markedly increased in patients receiving Lipoplus. This is indicated by a significant increase in circulating alpha tocopherol in group I and is due to its concentration of 200 mg/L in the lipid emulsion. α-Tocopherol is a very active form of the tocopherols and is of importance for the prevention of oxidation of tissue PUFA (37). This increase of antioxidant capacity in patients receiving Lipoplus also is in favor of the postulated beneficial immunomodulating potential of n-3 fatty acids.

CONCLUSION

This study compares a new lipid formula containing long-chain triglycerides/middle-chain triglycerides/n-3 fatty acids with a conventional emulsion for parenteral nutrition containing long-chain triglycerides fatty acids. The clinical importance of this study so far is restricted to patients who require prolonged parenteral nutrition after abdominal surgery. Nonetheless, the findings reported here indicate that the administration of Lipoplus in the postoperative period after major abdominal surgery is safe and results in a significantly shorter length of hospital stay. Administration of Lipoplus in the postoperative period, therefore, can be considered a valuable choice for patients requiring parenteral nutrition after major abdominal surgery.

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