B BRAUN
SHARING EXPERTISE

Clinical Nutrition

Omega-3

Influence of n-3 Polyunsaturated Fatty Acids Enriched Lipid Emulsions on Nosocomial Infections and Clinical Outcomes in Critically Ill Patients: ICU Lipids Study

Grau-Carmona T, Bonet-Saris A, García-de-Lorenzo A, Sánchez-Alvarez C, Rodríguez-Pozo A, Acosta-Escribano J, Miñambres E, Herrero-Meseguer JI, Mesejo A; Crit Care Med. 2015 Jan;43(1):31-9.

Objective

Omega-3 enriched lipid emulsions have shown a positive influence on infection rate and clinical outcome in surgical patients, but studies on administration of omega-3 enriched lipids in critical ill patients showed controversial results. This prospective, randomized, comparative, double-blind multicenter study, investigates in 159 medical and surgical intensive care patients the effect of n-3 polyunsaturated fatty acids on the prevalence of nosocomial infections and clinical outcome in medical and surgical critically ill patients.

Interventions

Patients received total parenteral nutrition for at least 5 days, prepared either with a lipid emulsion contains 10% n-3 polyunsaturated fatty acids derived from fish oil (Lipoplus) or a standard lipid emulsion (Lipofundin MCT/LCT). Incidence of nosocomial infections was evaluated for 28 days of ICU stay, as well as length of hospital stay, hospital mortality and 6-month mortality.

Results

The number of patients with nosocomial infections was significantly lower in the treatment group than in the control group (21.0% vs 37.2%, p = 0.035) (Fig. 1). The predicted time free of infection was 5 days longer in the treatment group, than in the control group (21 ± 2 vs 16 ± 2 d, p = 0.03) (Fig. 2). No significant differences were detected for ICU, hospital, and 6-month mortality.

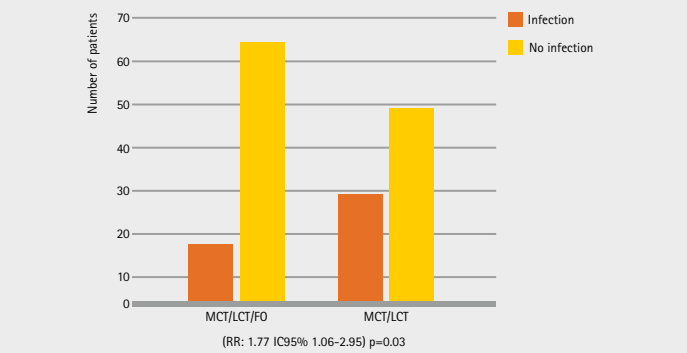

Fig. 1: Cumulative incidence of nosocomial infections. Bar chart showing the number of patients with and without infection in treatment and control groups. RR = risk ratio (modified from Grau 2015)

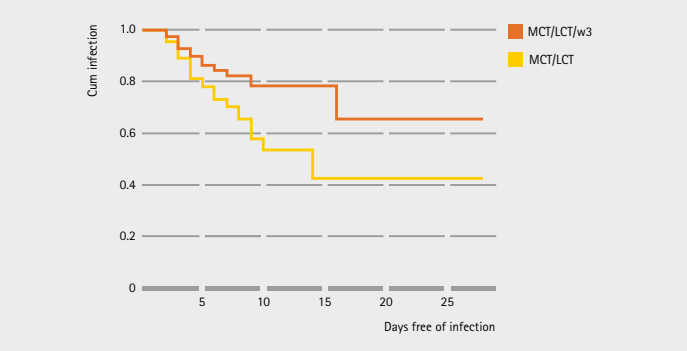

Fig. 2: Time free of infection (TFI) in treatment and control groups. TFI was estimated for patients without signs of infection on 1st and 2nd days after study enrolment (n = 68) for treatment group and (n = 71) control group. TFI was significantly longer in the treatment group (21 vs 16 d, p = 0.03). (modified from Grau 2015)

Author's Conclusion

In conclusion, the study results presented here suggest that administration of ~ 0.1 g FO*/kg BW per day in combination with MCT and LCT in a lipid emulsion reduces the risk of nosocomial infections and increases the predicted time free of infections in critically ill medical and surgical ICU patients. Length of hospital stay was reduced close to significance. The administration of a MCT/LCT/FO* parenteral lipid emulsion in critically ill patients was shown to be safe.

*The term "FO" was used by the author in the original publication

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Lipoplus®/Lipidem®

Composition
1000 ml of emulsion contains:

Medium-chain triglycerides:	100.0 g
Soybean oil, refined:	80.0 g
Omega-3-acid triglycerides:	20.0 g
Essential fatty acid content per liter:	
Linoleic acid (omega-6):	48.0 - 58.0 g
Alpha-linolenic acid (omega-3):	5.0 - 11.0 g
Eicosa-pentaenoic acid and docosahexaenoic acid:	8.6 - 17.2 g
Caloric content per liter:	7900 kJ ≈ 1910 kcal
Osmolality:	approx. 410 mOsm/kg
Titration acidity or alkalinity (to pH 7.4):	less than 0.5 mmol/l NaOH or HCl
pH:	6.5 - 8.5

Indications:
Source of calories and essential omega-6 fatty acids and omega-3 fatty acids as a component of a Parenteral Nutrition regimen for adults.

Contraindications:
Lipoplus® must not be used in any of the following conditions:
- Severe hyperlipidemia
- Serious blood clotting disorders
- Acidosis
- Intrahepatic cholestasis
- Severe liver failure
- Severe kidney failure
- Acute phase of myocardial infarction or stroke
- Acute thromboembolic disease, fat embolism
- Known hypersensitivity to egg, fish, or soybean protein

The following conditions are general contraindications to Parenteral Nutrition.
- Unstable hemodynamic status with compromised vital functions (conditions of collapse and shock)
- Fluid overload
- Acute pulmonary edema

Special warnings and precautions for use
Before infusing a fat emulsion together with other solutions via a Y connector or bypass set, the compatibility of these fluids should be checked, especially when co-administering carrier solutions to which drugs have been added. Particular caution should be exercised when co-infusing solutions that contain divalent electrolytes (such as calcium).

The emulsion should always be brought to room temperature prior to infusion.

If filters are used, these must be permeable to fat emulsions.

Serum triglycerides should be monitored during the infusion of Lipoplus®. In patients with suspected disorders of lipid metabolism, fasting lipemia should be ruled out before the start of the infusion. Hypertriglyceridemia 12 hours after the administration of fat is also indicative of abnormal lipid metabolism.

Transient hypertriglyceridemia or elevated blood glucose levels may arise from the patient's metabolic status. If the plasma triglyceride concentration rises to more than 3 mmol/l during administration of the fat emulsion, it is recommended to reduce the infusion rate. If the plasma triglyceride concentration still remains higher than 3 mmol/l, the infusion should be stopped until the plasma triglyceride concentration normalizes.

Electrolytes, water balance or body weight, acid-base balance, blood glucose levels, and, during long-term administration, blood counts, coagulation status, and liver function should be monitored.

There is as yet no clinical experience of the use of Lipoplus® in children, and there is only limited experience of its use in patients with diabetes mellitus or renal impairment.

There is as yet only limited experience of the use of Lipoplus® for periods longer than seven days.

Caution should be exercised in patients with conditions associated with impaired lipid metabolism, such as renal insufficiency, uncontrolled diabetes mellitus, pancreatitis, hepatic insufficiency, hypothyroidism (in the presence of hypertriglyceridemia), and sepsis.

Lipids may interfere with certain laboratory tests (such as bilirubin, lactate dehydrogenase, oxygen saturation) when the blood sample is taken before the lipids have been eliminated from the bloodstream. In most patients this takes 5 to 6 hours beyond the end of the infusion.

The use of fat emulsions as the sole source of calories may give rise to metabolic acidosis. This may be avoided by the concurrent infusion of carbohydrates. It is therefore recommended to infuse an adequate quantity of intravenous carbohydrates or an amino acid solution containing carbohydrates along with the fat emulsion.

Vitamin E can interfere with the effect of vitamin K in clotting factor synthesis. This should be borne in mind in patients with blood clotting disorders or suspected vitamin K deficiency.

Subject to sale by pharmacists only.

B. Braun Melsungen AG, 34209 Melsungen, Germany, Please refer to local Summary of Product Information, before prescribing. Status of latest information: 2009-02-012

NuTRIflex® Omega

Composition
NuTRIflex® Omega plus emulsion for infusion/NuTRIflex® Omega special emulsion for infusion (mixed and ready for use 1.250 ml).

Active ingredients of:
NuTRIflex® Omega plus emulsion for infusion/NuTRIflex® Omega special emulsion for infusion. Glucose monohydrate 165.0 g/198.0 g, equivalent to anhydrous glucose 150.0 g/180.0 g, Sodium dihydrogen 2.340 g/3.120 g, Zinc acetate dehydrate 6.580 mg/8.78 mg, Medium-chain triglycerides 25.0 g/25.0 g, Soya-bean oil refined 20.0 g/20.0 g, Omega-3-acid triglycerides 5.0 g/5.0 g, Isoleucine 2.82 g/4.11 g, Leucine 3.76 g/5.48 g, Lysine hydrochloride 3.41 g/4.98 g, equivalent to Lysine 2.73 g/3.98 g, Methionine 2.35 g/3.42 g, Phenylalanine 4.21 g/6.15 g, Threonine 2.18 g/3.18 g, Tryptophan 0.68 g/1.00 g, Valine 3.12 g/4.51 g, Arginine 3.24 g/4.73 g, Histidine hydrochloride monohydrate 2.03 g/2.96 g, equivalent to Histidine 1.50 g/2.19 g, Alanine 5.82 g/8.49 g, Aspartic acid 1.80 g/2.63 g, Glutamic acid 4.21 g/6.14 g, Glycine 1.98 g/2.89 g, Proline 4.08 g/5.95 g, Serine 3.60 g/5.25 g. Sodium hydroxide 0.976 g/1.464 g, Sodium chloride 0.503 g/0.473 g, Sodium acetate trihydrate 0.277 g/0.313 g, Potassium acetate 3.434 g/4.611 g, Magnesium acetate tetrahydrate 0.858 g/1.137 g, Calcium chloride dehydrate 0.588 g/0.779 g, Amino acid content (g) 48/70.1, Nitrogen content (g) 6.8/10, Carbohydrate content (g) 150/180, Lipid content (g) 50/50, Electrolytes (mmol): Sodium 50/67, Potassium 35/47, Magnesium 4.0/5.3, Calcium 4.0/5.3, Zinc 0.03/0.04, Chloride 45/60, Acetate 45/60, Phosphate 15/20, Energy in the form of lipid [kJ (kcal)] 1990 (475)/1990 (475), Energy in the form of carbohydrate [kJ (kcal)] 2510 (600)/3015 (720), Energy in the form of amino acids [kJ (kcal)] 800 (190)/1170 (280), Non-protein energy [kJ (kcal)] 4500 (1075)/5005 (1195), Total energy [kJ (kcal)] 5300 (1265)/6175 (1475), Osmolality (mOsm/kg) 1540/2090, pH 5.0 - 6.0/5.0 - 6.0, Theoretical osmolarity (mOsm/l) 1215/1545.

List of excipients:
Citric acid monohydrate, Egg lecithin, Glycerol, Sodium oleate, all-rac-α-tocopherol, Sodium hydroxide for pH adjustment, Water for injections.

Therapeutic indications:
Supply of energy and essential fatty acids including omega-3 and omega-6 fatty acids, amino acids, electrolytes and fluids in the setting of parenteral nutrition of patients in states of moderate to severe catabolism when oral or enteral nutrition is impossible, insufficient or contraindicated.

Posology and method of administration:
The dosage is adapted to the patients' individual requirements. It is recommended that NuTRIflex® Omega be administered continuously. A stepwise increase of the infusion rate over the first 30 minutes up to the desired infusion rate avoids possible complications. *Paediatric population* NuTRIflex® Omega is contraindicated in newborn infants, infants and toddlers < 2 years of age. Safety and efficacy in children > 2 years and adolescents have not been established. *Patients with renal/hepatic impairment:* The doses should be adjusted individually in patients with hepatic or renal insufficiency. *Duration of treatment:* The duration of treatment for the indications stated is not limited. During long-term administration of NuTRIflex® Omega plus it is necessary to provide for appropriate supply of trace elements and vitamins. *Method of administration:* Intravenous use. For central venous infusion only.

Contraindications:
This product must not be administered in the presence of the following conditions: hypersensitivity to the active substances, to egg, fish, peanut or soya protein or to any of the excipients, congenital disorders of amino acid metabolism, severe hyperlipidaemia, hyperglycaemia not responding to insulin doses of up to 6 units insulin/hour, acidosis, intrahepatic cholestasis, severe hepatic insufficiency, severe renal insufficiency in absence of renal replacement therapy, aggravating haemorrhagic diatheses, acute thrombo-embolic events, lipid embolism, on account of its composition NuTRIflex® Omega must not be used in newborn infants, infants and toddlers under 2 years of age. General contraindications to parenteral nutrition include: unstable circulatory status with vital threat (states of collapse and shock), acute phases of cardiac infarction and stroke, unstable metabolic condition (e.g. severe postaggression syndrome, coma of unknown origin), inadequate cellular oxygen supply, disturbances of the electrolyte and fluid balance, acute pulmonary oedema, decompensated cardiac insufficiency.

Special warnings and precautions for use:
Caution should be exercised in cases of increased serum osmolarity. Disturbances of the fluid, electrolyte or acid-base balance, must be corrected before the start of infusion. Too rapid infusion can lead to fluid overload with pathological serum electrolyte concentrations, hyperhydration and pulmonary oedema. Any sign or symptom of anaphylactic reaction (such as fever, shivering, rash or dyspnoea) should lead to immediate interruption of the infusion. The serum triglyceride concentration should be monitored when infusing NuTRIflex® Omega. Depending on the patient's metabolic condition, occasional hypertriglyceridaemia may occur. If the plasma triglyceride concentration rises to above 3 mmol/l during administration of lipids, it is recommended that the infusion rate be reduced. Should the plasma triglyceride concentration remain above 3 mmol/l, the administration should be stopped until the level normalises. Like all solutions containing carbohydrates, the administration of NuTRIflex® Omega can lead to hyperglycaemia. The blood glucose level should be monitored. If there is hyperglycaemia, the rate of infusion should be reduced or insulin should be administered. If the patient is receiving other intravenous glucose solutions concurrently, the amount of additionally administered glucose has to be taken into account. An interruption of administration of the emulsion may be indicated if the blood glucose concentration rises to above 14 mmol/l (250 mg/dl) during administration. Intravenous infusion of amino acids is accompanied by increased urinary excretion of the trace elements, especially copper and, in particular, zinc. This should be considered in the dosing of trace elements, especially during long-term intravenous nutrition. Refeeding or repletion of malnourished or depleted patients may cause hypokalaemia, hypophosphataemia and hypomagnesaemia. Adequate supplementation of electrolytes according to deviations from normal values is necessary. NuTRIflex® Omega should not be given simultaneously with blood in the same infusion set due to the risk of pseudoagglutination. Controls of the serum electrolytes, the water balance, the acid-base balance and – during long-term administration – of blood cell counts, coagulation status and hepatic function are necessary. Substitution of electrolytes, vitamins and trace elements may be necessary as required. As NuTRIflex® Omega contains zinc and magnesium, care should be taken when it is co-administered with solutions containing these elements. As with all intravenous solutions strict aseptic precautions are necessary for the infusion of NuTRIflex® Omega. *Paediatric population:* There is as yet no clinical experience of the use of NuTRIflex® Omega in children and adolescents. *Elderly patients:* Basically the same dosage as for adults applies, but caution should be exercised in patients suffering from further diseases like cardiac insufficiency or renal insufficiency that may frequently be associated with advanced age. *Patients with diabetes mellitus, impaired cardiac or renal function:* Like all large-volume infusion solutions, NuTRIflex® Omega should be administered with caution to patients with impaired cardiac or renal function. There is only limited experience of its use in patients with diabetes mellitus or renal failure. *Patients with impaired lipid metabolism:* NuTRIflex® Omega should be administered cautiously to patients with disturbances of lipid metabolism, e.g. renal insufficiency, diabetes mellitus, pancreatitis, impaired hepatic function, hypothyroidism (with hypertriglyceridaemia) and sepsis. If NuTRIflex® Omega is given to patients with these conditions, monitoring of serum triglycerides is necessary. The presence of hypertriglyceridaemia 12 hours after lipid administration also indicates a disturbance of lipid metabolism. Special warnings/precautions regarding excipients: Vitamin E (α-tocopherol) can interfere with the effect of vitamin K in clotting factor synthesis. This should be considered in patients with blood coagulation disorders or suspected vitamin K deficiency and in patients treated with coumarin anticoagulants. Interference with laboratory tests: The fat content may interfere with certain laboratory measurements (e.g. bilirubin, lactate dehydrogenase, oxygen saturation) if blood is sampled before fat has been adequately cleared from the blood stream.

B. Braun Melsungen AG, 34209 Melsungen, Germany, Please refer to local Summary of Product Information, before prescribing. Status of latest information: February 2013

Specific Product Information may differ from country to country.