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SHARING EXPERTISE

Changes in plasma and erythrocyte omega-6 and omega-3 fatty acids in response to intravenous supply of omega-3 fatty acids in patients with hepatic colorectal metastases

Omer Al-Taan, James A Stephenson, Laura Spencer, Cristina Pollard, Annette L West, Philip C Calder, Matthew Metcalfe and Ashley R Dennison; Lipids in Health and Disease 2013, 12:64

OBJECTIVE

This study was part of a double blind randomized controlled trial examining the effect of fish oil on human colorectal metastases. The trial is registered at www.clinicaltrials.gov with identifier NCT00942292.

Twenty patients were rendomised to receive a 72 hour infusion of total parenteral nutrition with (treatment group) or without (control group) omega-3 PUFAs.

EPA, DHA, ARA and linoleic acid were measured in plasma phosphatidylcholine (PC) and erythrocytes at several time points up to the end of infusion and 5 to 12 days (mean 9 days) after stopping the infusion.

RESULTS

The treatment group showed increases in plasma PC EPA and DHA and erythrocyte EPA and decreases in plasma PC and erythrocyte linoleic acid, with effects most evident late in the infusion period. Plasma PC and erythrocyte EPA and linoleic acid all returned to baseline levels after the 5–12 day washout. Plasma PC DHA remained elevated above baseline after washout.

DISCUSSION

This current study shows that intravenous infusion of omega-3 PUFAs in the form of Lipoplus®/Lipidem® (B. Braun, Melsungen, Germany) induces a fairly rapid and marked increase in EPA and DHA in plasma PC and a small increase of EPA in erythrocytes. Amongst these changes, the elevation of EPA in plasma PC occurred the earliest.

CONCLUSION

Intravenous supply of omega-3 PUFAs results in a rapid increase of EPA and DHA in plasma PC and of EPA in erythrocytes. These findings suggest that infusion of omega-3 PUFAs could be used to induce a rapid effect especially in targeting inflammation.

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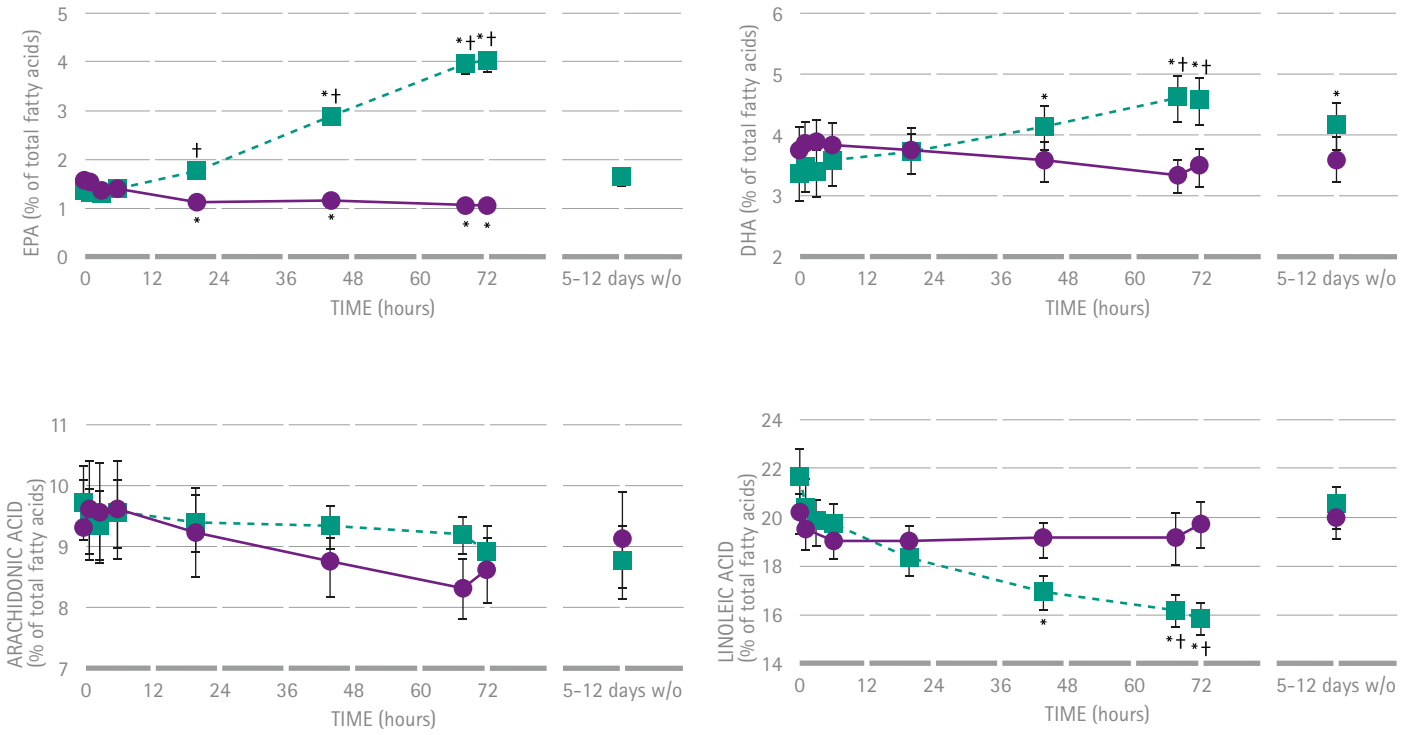

FIGURE 1

Plasma PC eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), arachidonic acid and linoleic acid before (baseline), during (1 hr to 72 hr) and 5–12 days after stopping infusion of a mixture of medium-chain triglycerides and soybean oil (control: violet circles joined by solid lines) or medium-chain triglycerides, soybean oil and fish oil (fish oil: green squares joined by dashed lines).

Data are mean ± SEM. * indicates significantly different from baseline value in the same group. † indicates significantly different from control group at the same timepoint. 5–12 days w/o indicates the samples collected 5 to 12 days after stopping the infusions.

Modified from Al Taan 2013

Acknowledgements: The study was part funded by an educational grant for research from B. Braun, Melsungen, Germany.

Literature

Lipoplus® 200 mg/ml emulsion for infusion

COMPOSITION
1000 ml of emulsion contains:

Medium-chain triglycerides	100.0 g
Soya-bean oil, refined	80.0 g
Omega-3-acid triglycerides	20.0 g
Content of triglycerides	200 mg/ml (20 %)
Content of essential fatty acids	
Linoleic acid (omega-6)	38.4 - 46.4 g/l
Alpha-linolenic acid (omega-3)	4.0 - 8.8 g/l
Eicosapentaenoic acid and docosahexaenoic acid (omega-3)	8.6 - 17.2 g/l

Excipient with known effect:
1000 ml emulsion contains 2.6 mmol sodium (as sodium hydroxide and sodium oleate).

Excipients:
Egg phospholipids for injection, glycerol, sodium oleate, ascorbyl palmitate, all-rac-α-Tocopherol, sodium hydroxide (for pH adjustment), water for injections.

THERAPEUTIC INDICATIONS
Supply of energy, including a readily utilisable lipid component (medium-chain triglycerides) and essential omega-6 fatty acids and omega-3 fatty acids, as part of parenteral nutrition when oral or enteral nutrition is impossible, insufficient or contraindicated. Lipoplus® is indicated in adults, preterm and term neonates, infants and toddlers, children and adolescents.

CONTRAINDICATIONS
Hypersensitivity to the active substances, to egg, fish, peanut or soya protein or to any of the excipients. Severe hyperlipidaemia characterised by hypertriglyceridaemia (≥ 1000 mg/dl or 11.4 mmol/l); severe coagulopathy; intrahepatic cholestasis; severe hepatic insufficiency; severe renal insufficiency in absence of renal replacement therapy; acute thromboembolic events; fat embolism; acidosis. General contraindications to parenteral nutrition include unstable circulatory status with vital threat (states of collapse and shock); acute phases of cardiac infarction or stroke; unstable metabolic conditions (e.g. decompensated diabetes mellitus, severe sepsis, coma of unknown origin); inadequate cellular oxygen supply; disturbances of the electrolyte and fluid balance; acute pulmonary oedema; decompensated cardiac insufficiency.

UNDESIRABLE EFFECTS
The following listing includes a number of systemic adverse reactions that may be associated with the use of Lipoplus®. Under the conditions of correct use, in terms of dosing, monitoring, observation of safety restrictions and instructions, most of them are very rare (<1/10 000).

Undesirable effects are listed according to their frequencies as follows:

Rare: (≥ 1/10000 to < 1/1000)
Very rare: (< 1/10000)
Not known: (cannot be estimated from the available data)

Blood and lymphatic system disorders
Very rare: Hypercoagulation
Not known: Leucopenia, thrombocytopenia

Immune system disorders
Very rare: Allergic reactions (e.g. anaphylactic reactions, dermal eruptions, laryngeal, oral and facial oedema)

Metabolism and nutrition disorders
Very rare: Hyperlipidaemia, metabolic acidosis. The frequency of these adverse reactions is dosedependent and may be higher under conditions of absolute or relative overdose
Very rare: Hyperglycaemia

Nervous system disorders
Very rare: Headache, drowsiness

Vascular disorders
Very rare: Hypertension or hypotension, flush

Respiratory, thoracic and mediastinal disorders
Very rare: Dyspnoea, cyanosis

Gastrointestinal disorders
Very rare: Nausea, vomiting, loss of appetite

Skin and subcutaneous tissue disorders
Very rare: Erythema, sweating

Hepatobiliary disorders
Not known: Cholestasis

Musculoskeletal and connective tissue disorders
Rare: Back, bones, chest and lumbar region pain

General disorders and administration site conditions
Very rare: Elevated body temperature, feeling cold, chills, fat overload syndrome (see below)

Should adverse reactions occur, the infusion must be stopped.

Should the triglyceride level rise to above 11.4 mmol/l (1000 mg/dl) during infusion, the infusion must be stopped. With levels above 4.6 mmol/l (400 mg/dl), the infusion may be continued at a reduced dosage. If the infusion is restarted, the patient should be carefully monitored, especially at the beginning, and serum triglycerides should be determined at short intervals.

Information on particular undesirable effects
Nausea, vomiting and lack of appetite are symptoms often related to conditions for which parenteral nutrition is indicated, and may be associated with parenteral nutrition at the same time.

Fat overload syndrome
Impaired capacity to eliminate triglycerides can lead to "fat overload syndrome" which may be caused by overdose. Possible signs of metabolic overload must be observed. The cause may be genetic (individually different metabolism) or the fat metabolism may be affected by ongoing or previous diseases. This syndrome may also appear during severe hypertriglyceridaemia, even at the recommended infusion rate, and in association with a sudden change in the patient's clinical condition, such as renal function impairment or infection. The fat overload syndrome is characterised by hyperlipidaemia, fever, fat infiltration, hepatomegaly with or without icterus, splenomegaly, anaemia, leucopenia, thrombocytopenia, coagulation disorder, haemolysis and reticulocytosis, abnormal liver function tests and coma. The symptoms are usually reversible if the infusion of the fat emulsion is discontinued. Should signs of a fat overload syndrome occur, the infusion of Lipoplus® must be discontinued immediately.

WARNINGS
Keep out of the sight and reach of children. For single use only. Any unused emulsion should be discarded.

MARKETING AUTHORIZATION HOLDER
B. Braun Melsungen AG, 34209 Melsungen, Germany

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Prescription only

Not all products are registered and approved for sale in all coutries or regions. Indications of use may also vary by country and region. Please contact your country representative for product availability and information.

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