Clinical Nutrition Supplements (2005) 1, 17–24

Clinical Nutrition Supplements

http://intl.elsevierhealth.com/journals/clnu

ORIGINAL ARTICLE

Benefits of ω-3 fatty acids in parenteral nutrition

Thea Koch*, **Axel R. Heller**

Department of Anesthesiology and Critical Care Medicine, University Hospital Carl Gustav Carus, University of Technology, Dresden, Germany[1]

KEYWORDS
ω-3 Fatty acids;
Fish oil;
Soybean oil;
Immunonutrition;
Inflammation;
Acute phase response;
Parenteral nutrition;
Abdominal surgery;
Sepsis

Summary Apart from energy supply, ω-3 fatty acids (FA) exert immune modulating and organ protective effects. This has been particularly shown for eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) contained in fish oil. Depending on nutritional intake, ω-3 fatty acids are incorporated in the phospholipid pool of cellular membranes and replace the ω-6 FA thereby increasing membrane fluidity and influencing lipid mediator and cytokine production. Furthermore, ω-3 FA modify the function of membrane-linked enzyme systems, signal transduction and receptor functions. There is a large body of experimental data showing that ω-3 FA attenuate inflammatory reactions, ameliorate host defence, improve splanchnic blood flow and gut barrier function in septic states and prevent tumor growth. These different biologic properties of ω-3 FA offer promising prophylactic and therapeutic potential in different clinical settings, which seem to be attainable by supplementation of parenteral nutrition with ω-3 FA. Clinical trials over the last decade suggest beneficial effects of ω-3 FA in parenteral nutrition on recovery and outcome in patients with severe surgical interventions and in the critically ill by lowering the magnitude of inflammatory response and improving host defense. Recent clinical data support the hypothesis that an optimal preoperative composition of cell membranes, before initiation of the inflammatory cascade, is more effective with respect to modulation of cytokine biology and patient recovery than mere postoperative nutrition therapy. This review gives an outline on current developments in the field of polyunsaturated ω-3 FA in parenteral nutrition.

Introduction

Since the epidemiological studies of Dyerberg et al.[1] in the early 1970s, demonstrated that the Greenland Inuit, eating diets high in fish oil, have lower incidences of thrombosis, coronary heart disease and myocardial infarction, interest has been focused on ω-3 polyunsaturated fatty acids (FA). Since then, numerous studies have been

*Corresponding author. Klinik für Anaesthesiologie und Intensivtherapie, Universitätsklinikum Carl Gustav Carus, Fetscherstrasse 74, 01307 Dresden, Germany. Tel.: +49 351/458 2785; fax: +49 351/458 4336.
E-mail address: thea.koch@uniklinikum-dresden.de (T. Koch).
[1]A Harvard Medical International Associated Institution.

1744-1161/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.clnu.2005.05.010

carried out in vitro as well as in vivo that showed that ω-3 FA exhibited fewer inflammatory properties when compared to ω-6 FA.[2] Besides the beneficial effects of long-term intake of ω-3 FA on the development of cancer and cardiovascular diseases, encouraging results were obtained also in critically ill patients after short-term supplementation with long-chain ω-3 FA.[3] Compared to the delayed bioavailability of enterally administered ω-3 FA, the intravenous route allows for a fast onset of the beneficial effects in acute diseases.

Consequently, in recent years increased research activities in clinical nutrition of the critically ill were concentrated on ω-3 FA as a supplement for optimized parenteral nutrition with adjunctive therapeutic effects. With the introduction of fish oil into parenteral nutrition the evolution of lipid emulsions resulted in a mixture of oils with a reduced ω-6 FA share and an optimized ω-6 to ω-3 FA ratio of about 3:1–2:1.[4–6]

The mechanisms of action of this fascinating immunomodulatory concept in the critically ill patient will be outlined and the current experimental and clinical data will be presented.

Metabolism and biologic effects of ω-3 FA

Apart from energy supply, polyunsaturated ω-3 FA exert immune modulating and organ protective effects.[2,7] Depending on nutritional intake, ω-3 FA are incorporated in the phospholipid pool of cellular membranes and replace the ω-6 FA thereby increasing membrane fluidity and influencing lipid mediator and cytokine production.[9,10] The concept that nutritional supplementation with ω-3 FA exerts immunomodulatory and organ protective effects that are based on the multiple interactions of ω-3 FA is summarized in Fig. 1.

While the impact of ω-3 FA on lipid mediator generation has been greatly clarified, up to now the understanding of subcellular effects is limited. ω-3 FA affect biophysical characteristics of cellular membranes by alteration of the membrane phospholipid composition and the content of cholesterol, which improves membrane fluidity. The associated increase in the deformability of blood cells might account for improvement of blood rheology after fish oil intake. Furthermore, ω-3 FA modify the function of membrane-linked enzyme systems, signal transduction and receptor functions (Fig. 2). Recent work of Lee et al.[11] demonstrated that activation of general proinflammatory pathways, such as NFκB and cyclooxygenase-2 expression by saturated FA and the inhibition of this induction by polyunsaturated FA are mediated through a common signaling pathway derived from toll-like receptor (TLR)-4. TLR-4 conveys signals as a part of innate immunity from the endotoxin receptor (CD14) on the surface of macrophages to the inner cell and may, likewise, be activated by saturated FA. In addition, TLR-2 is activated by bacterial cell surface components. Activated TLR-4 and TLR-2, respectively, activate the enzyme IκB-kinase resulting in a diminished blockade-function of inhibitory factor kappa B (IκB). Thus, NFκB may translocate into the nucleus to setup transcription activity of inflammatory DNA-gene loci. Consequently, inflammatory receptors, enzymes and cytokines are expressed.

ω-3 FA modify cellular receptor functions[12] and downstream signal transduction features[13] until the level of NFκB and beyond.[14,15] As a result of down regulation of nuclear transcription factors, formation of cytokines such as TNFα and IL-1[16] in monocytes was reduced after fish oil administration. Taken together, ω-3 FA seem to interfere with early inflammatory signal transduction processes and, thus, are capable of blunting hyperinflammation. A large body of experimental data confirms that ω-3 FA attenuate inflammatory reaction,[17] ameliorate host defense,[18,19] improve splanchnic blood flow and gut barrier function in septic states,[20] and prevent tumor growth.[21] These different biologic properties of ω-3 FA offer a promising prophylactic and therapeutic potential in different clinical settings which seems to be attainable by supplementation of parenteral nutrition with ω-3 FA even after short-term administration.[10]

Effects of short-term infusion of ω-3 FA

In view of the clinical consequences in acutely ill patients, more recent interest was focused on the question of whether or not ω-3 FA are integrated into the phospholipid pool even after short-term intravenous application, and whether they induce organ protective effects by means of their metabolites after inflammatory stimulation. Recent studies in humans by Mayer et al.[22] have shown that several hours of parenteral nutrition with ω-3 FA significantly decreases the ω-6/ω-3 FA ratio in the plasma-free FA fraction and in the monocyte membrane lipid pool which was associated with a suppression of monocyte generation of proinflammatory cytokines (TNFα, Interleukin-1, -6, -8) in response to endotoxin. Additionally, adhesive