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### Omega-3 Fatty Acids in the ICU - A Remunerative Investment?

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Omega-3 fatty acids improve recovery and patient outcome by lowering the overwhelming self-destructing inflammatory response but at the same time improving host defence. Despite higher costs, this strategy seems to be a remunerative investment.

#### Introduction

Most recent recommendations of the "surviving sepsis campaign" by the Society of Critical Care Medicine and others set the goal of devising a single concept (Levy et al. 2004). In the light of the "PIRO" concept therapeutic options of critical illness should be intensively investigated regarding individual Pre-existing disease, type of Infection, Response of the organism and the respective degree of Organ failure. Our group and others have been working on the cutting edge of omega-3 fatty acid (FA) research for more than a decade, beginning in animal models of acute illness

and then further developing and introducing concepts into clinical practice (Heller et al. 2003, 2004 & 2005). Commercially available omega-3 FA enriched solutions are available for an optimal clinical (enteral and parenteral) nutrition therapy. Present data indicate definitive dose-related beneficial effects of omega-3 FA on outcome in PIRO-selected patients in various diseases (Heller et al. 2005).

#### The Gordian Knot

The key issue in the development of systemic inflammatory response syndrome (SIRS) and septic organ failure is the complex pathophysiologic sequelae, characterized by a pro-inflammatory and simultaneous compensatory anti-inflammatory response. This, to a degree, represents a sort of chaos within the mechanisms of host response termed Mixed Antagonistic Response Syndrome (MARS). The net effect depends on the predominance of either anti-inflammatory or pro-inflammatory reactions and may vary time dependently (Bone 1996).

We know today that critical illness may be beneficially modulated by augmentation of distinct defence mechanisms, while other mechanisms need to be suppressed simultaneously. The nutritional state of man is determined by the constituents of nutrition (see figure 1). Concerning Lipids, the ratio between omega-3 and omega-6 FA determines the type and intensity of the inflammatory reaction, in terms of lipid mediators and cytokine production. While arachidonic acid (AA)- metabolites (black boxes in figure 1) may induce hyperinflammation, eicosapentaenoic acid (EPA)-derived mediators are more immunoneutral. The magic solution to this multiplicity of tasks, reducing overwhelming systemic inflammatory reaction and preventing organ failure, has still to be found. However, the effects of omega-3 FAs supplementation may be one key (Heller et al. 2005).

#### Putting Pieces Together to Improve Patient Care

During the last decade pharmacological aspects of omega-3 FA have been intensively investigated (Mayer et al. 2002; Pacht et al. 2003) and

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have contributed to a better understanding of the effects associated with FA administration (see table 1). Besides being compact energy carriers and membrane components, lipids hold crucial functions as modulators of biochemical processes (Heller et al. 2003). Therefore the combination of energetic, pharmacological, and essential properties must be the object of an optimized individual nutritional concept.

Accordingly, a down-regulation of the inflammatory response, and, simultaneously, a smaller postoperative immune suppression was associated with less severe infections after omega-3 FA. In addition, a shorter ICU- and hospital stay has been observed after perioperative fish oil supplementation (see figures 2 and 3). In the critically ill, on the other hand, early use is advisable, before complex inflammatory host actions and overshooting reactions during SIRS and sepsis commencing (Heller et al. 2005).

Consequently, lipids should cover 30-50% of the energy demand. They can be infused after securing haemodynamic stability of the patient (about 15-30 hours after trauma). New concepts of fat nutrition therapy should aim to reduce arachidonic acid precursors (omega-6 FAs) to their level of essentiality. Fish oil should be added up to 0.1-0.2 g/kg/d. To what extent olive oil, a monounsaturated FA, may play a role in the future cannot not be assessed at the moment. Nevertheless, an ideal FA combination still needs to be defined. Future combinations administered in patients could consist of 30-40% LCTs with 40-50% MCTs (ideally as structured lipids), 15-20% fish oil and possibly 15-20% olive oil.

#### **Outlook**

Several recent studies suggest beneficial effects of omega-3 FA on recovery- and outcome-parameters in patients with major surgical interventions and in critically ill patients by lowering the extent of overwhelming self-destructing inflammatory response (Gadek et al. 1999; Grecu et al. 2003; Mayer 2002), but at the same time improving host defence. Furthermore, increasing clinical data supports the hypothesis that an optimum 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 (Tsekos et al. 2004; Weiss et al. 2002). According to the most recent recommendations, we found omega- 3 FA to be a valuable nutritional additive to improve outcome in patients with peritonitis, trauma, abdominal SIRS and sepsis, but also to reduce infections and complication rates in postoperative patients. Despite higher costs for omega-3 FA emulsions in clinical nutrition, in our view this strategy is a remunerative investment.

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