

## Fatty acids and enteral nutrition in the critically ill



Dutch researchers performed a systematic review and meta-analysis of randomised controlled trials of fish oil-containing enteral nutrition addressing relevant clinical outcomes in critically ill patients. Based on the results, they conclude that enteral fish oil supplementation cannot be recommended for these patients as strong scientific evidence for improved clinical benefits could not be found.

"There is a signal of mortality benefit in patients with acute respiratory distress syndrome; however, results are based on low-quality studies. Further research should focus on the relation between the individual critically ill patients' immune response, the administration of fish oil, and clinical outcomes," according to the review published in the journal Nutrition.

Fish oil (FO) has gained great interest as dominant source of  $\omega$ -3 polyunsaturated fatty acids, more specifically eicosapentaenoic acid (EPA; 20:5  $\omega$ -3) and docosahexaenoic acid (DHA; 22:6  $\omega$ -3). FO exerts anti-inflammatory and immunomodulatory properties that may be beneficial for critically ill patients. However, controversy remains as to whether fish oil-enriched enteral nutrition can improve clinical outcomes in adult critically ill patients in intensive care units (ICUs).

The Dutch research team systematically reviewed 24 eligible RCTs evaluating the effects of enteral FO supplementation in ICU patients (n = 3,574). The primary outcome was 28-day mortality. Secondary outcomes were ICU and hospital mortality, ICU and hospital length of stay (LOS), ventilation duration, and infectious complications. Predefined subgroup and sensitivity analyses were performed. The assessment of risk for bias showed that most of included studies were of moderate quality.

The overall results revealed no significant effects of enteral FO supplementation on 28-day, ICU or hospital mortality. However, ICU LOS and ventilation duration were significantly reduced in patients receiving FO supplementation. In addition, subgroup analysis revealed a significant reduction in 28-day mortality, ICU LOS, and ventilation duration in patients with acute respiratory distress syndrome (ARDS) but not in other subgroups. "These results should be interpreted with caution because six of the seven ARDS studies were of low methodological quality," the review team noted.

When comparing high- and low-quality trials, significant reductions in 28-day mortality and ventilation duration in low-quality trials only were observed. Regarding ICU LOS a significant reduction was observed in high-quality trials; whereas only a trend was observed in low-quality trials. No significant effects on hospital LOS or infectious complications were observed in overall or subgroup analyses.

"Contemplating the results of recent meta-analyses, including our own, it remains unclear whether FO supplementation is beneficial," according to the review team, who added that the conflicting results may be, at least partially, explained by two factors:

- Study populations were heterogeneous and ranged from general ICU patients to specific groups like elective surgical patients admitted to the ICU, severe trauma patients, and patients with sepsis or ARDS.

- Study designs are variable as demonstrated by differences in method of administration (i.e., parenteral versus enteral, continuous versus bolus, FO as a component of nutrition versus a separate supplement), amount and composition of the (par)enteral nutrition studied, and the composition of the control feeds.

The reviewers further said that the consequently reported immunologic response to FO supplementation may be the key to the differences in clinical outcomes found in individual trials. They explain: "The (patho) physiological immunologic response to critical illness is different between individual patients and over time, ranging from an extensive hyperinflammatory response to severe immunosuppression."

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