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The role of ω-3 supplemented parenteral nutrition in critical illness in adults: a systematic review & meta-analysis

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Many forms of critical illness are characterised by the systemic inflammatory response syndrome (SIRS). In this syndrome, deregulation of the immune system results in massive pro-inflammatory cytokine release and incongruous immune suppression, resulting in the clinical manifestations of organ dysfunction and sepsis. Important secondary mediators of the SIRS include the eicosanoid family of fatty acids (FA), which are derived from the ω-6 FA, arachidonic acid. There is considerable interest in the supplementation of parenteral lipid emulsions with ω-3 FAs. The rationale is that eicosanoids derived from ω-3 FAs are less inflammatory, inactive or even anti-inflammatory. Thus ω-3 supplemented total parenteral nutrition (TPN) may dampen the hyper-inflammatory state which defines the SIRS and improve patient outcomes [(1)]. This review examines the evidence from randomised controlled trials (RCT) in critically ill adult patients receiving ω-3 supplemented TPN on mortality, infections and length of intensive therapy unit (ITU) and hospital stay.

We performed computerized searches for relevant articles on MEDLINE (1996 to June 2011), EMBASE (1996 to June 2011) and the Cochrane register of controlled trials (2nd quarter 2011). We included RCT looking at critically ill patients admitted who received ω-3 supplemented TPN, compared to lipid emulsions without ω-3 FA. We limited all studies to man. No language limit was set. In addition we searched reference lists of studies and review articles, and abstract proceedings of scientific meetings from 2005 through to 2011.

Over 12,000 reports of potential studies were found. Both reviewers independently assessed reports of trials and, as a result of mutual agreement, 6 fully published trials and 3 trials published in abstract form with 467 randomised participants have been included. Both reviewers independently extracted data and assessed trial quality, with differences resolved by consensus. Authors of trials were contacted for further information as necessary.

Overall, the quality of the trials, as reported, was poor. The availability of outcome data was limited and trials were small. Thus the results must be interpreted with caution.

Mortality data were pooled for meta-analysis from 9 studies with 467 participants. No appreciable differences were found in terms of mortality for patients receiving ω-3 supplemented TPN with a risk ratio (RR) for death of 0.85 (95% CI 0.58 to 1.23; $P = 0.38$). Data relating to infectious complications was available from 5 studies with 321 participants. Again no appreciable differences were found, with a RR for infection of 0.75 (95% CI 0.38 to 1.47; $P = 0.4$). Data relating to length of ITU and hospital stay was available from 6 and 3 studies with 305 and 117 participants respectively. With respect to ITU length of stay, no appreciable differences were observed with a mean difference of 0.59 days in favour of the ω-3 group (95% CI −5.07 to 3.90; $P = 0.80$). However, a significant reduction in length of hospital stay of 9.49 days (95% CI −16.52 to −2.46; $P = 0.008$) was observed for those receiving ω-3 supplemented TPN. No significant heterogeneity between studies was observed in any analyses.

In conclusion, there is inadequate evidence to recommend supplementation of parenteral lipid emulsions in critically ill patients with ω-3 FAs. Large trials are required which overcome the defects of the reviewed studies, particularly with respect to methodology.

1. AR Heller, S Rossler, RJ Litz, SN Stehr, S Heller, R Koch & T Kock (2006) *Critical Care Medicine* **4** (4), 972–978.