Abstract

The combination of intestinal failure and parenteral nutrition is a condition associated with mild chronic inflammation and organ injury, the most significant of which is hepatic injury. This crossover-controlled trial investigated the effects of different intravenous lipid emulsions (IVLE) enriched with increased doses of omega-3 polyunsaturated fatty acids (n-3 PUFA) from fish oil (FO) in patients on home parenteral nutrition (HPNP) for chronic intestinal failure. Twelve patients were consecutively given three different IVLEs, with an FO emulsion added after each IVLE. The study also included twelve paired healthy controls for comparison. The aim of this study was to investigate how long-term administration of these IVLEs affected primarily the erythrocyte and plasma fatty acid (FA) spectrum, as well as the inflammatory response, antioxidant status, markers of liver function and bile acid spectrum in HPNP, and how these changes differed from healthy subjects.

We demonstrated successful incorporation of n-3 PUFA into erythrocyte phospholipids and corresponding changes in the plasma FA spectrum, characterized in particular by significant increases in n-3 versus n-6 PUFA, with a decrease in the n-6/n-3 PUFA ratio. We also found a more prolonged effect on these changes with high dose FO administration.

We observed increased serum cytokine concentrations and *in vitro* lipopolysaccharide (LPS)-stimulated cytokine production in HPNP, despite lower n-6/n-3 PUFA levels relative to healthy controls. Furthermore, the study showed an effect of FO on lower *in vitro* leukocyte reactivity, as expressed by reduced LPS-stimulated cytokine production. LPS-stimulated IL-6 production was also negatively correlated with parenteral dose of n-3 PUFA in the cohort, but also with their proportion in erythrocyte phospholipids, suggesting their anti-inflammatory effect.

All IVLE administration regimens were associated with increased superoxide dismutase 1 (SOD1) activities, probably related to increased oxidative stress (OS) and mild inflammation. Intervention by adding FO significantly reduced SOD1 levels to HC levels, which may have contributed to the reduction in OS. We observed impaired bile acid metabolism in terms of increased bile acid synthesis and decreased fibroblast growth factor 19 and a slight increase in alkaline phosphatase in HPNP. However, we did not demonstrate any effect of escalated dose of FO on their metabolism.

Keywords: Home parenteral nutrition, lipid emulsions, omega-3 fatty acids, intestinal failure, cytokines, inflammation, oxidative stress, antioxidant enzymes, superoxide dismutase 1, intestinal failure associated liver disease, fibroblast growth factor 19