SMOFLipid® is a commonly used fat emulsion for parenteral nutrition. We investigated how enrichment of SMOFLipid® with n-3 polyunsaturated fatty acids (PUFA) in a form of second fat emulsion, Omegaven®, changes fatty acid composition of total plasma phospholipids and erythrocyte phospholipids, cytokine concentrations in serum and in supernatant from in vitro whole blood culture stimulated with lipopolysaccharide (LPS) and we evaluated also changes in oxidoreductive balance. Eight patients on long-term home parenteral nutrition received both emulsions, SMOFLipid® (6 weeks) and SMOFLipid®+Omegaven® (4 weeks), one by one. We observed no significant differences in common laboratory and clinical parameters between these two types of diet. Enrichment of SMOFLipid® with Omegaven® led to an increase in eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) in total plasma phospholipids and there was also an increase in proportion of EPA in erythrocyte phospholipids, while proportion of DHA remained unchanged. These changes were in both phospholipids of plasma and erythrocyte compensated for a decrease in proportion of linoleic and arachidonic acid (n-6 PUFA). There were elevated IL-6 and TNF-α serum concentrations in patients after both diets. There was a decrease in IL-6 production by 36% with SMOFLipid®+Omegaven® diet after stimulation of in vitro whole blood culture with LPS, production of TNF-α decreased even more, by 60%. There was no difference between SMOFLipid® and SMOFLipid®+Omegaven® in the extent of lipid peroxidation. Despite expectations, superoxid dismutase activity (as a marker of antioxidant capacity) decreased with the diet rich in n-3 PUFA.