#23: Lipid Emulsions, Rich in n-3 or n-9 Fatty Acids, Reverse Hepatic Steatosis in Lean Mice, After its Induction by Feeding Parenteral Nutrition Formula

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Hepatic steatosis occurs in the early stage of the parenteral nutrition (PN)-associated liver disease. Previously we reported that Intralipid®, a lipid emulsion (LE) rich in n-6 fatty acids (FA), reduced hepatic triacylglycerol (TG) accumulation and markers of inflammation, once lipid accumulation has begun. However, it remains unclear whether other LEs (Omegaven®, rich in n-3 FA, and ClinOleic®, rich in n-9 FA), can reverse hepatic steatosis. Here, we compared 3 LE –Intralipid®, Omegaven® and ClinOleic® --for their ability to reverse hepatic TG accumulation after the onset of steatosis. Male C57BL/6 mice, n=8-9/group, were fed chow for 5 weeks (reference group) or a PN diet (Clinimix-E® with vitamins and minerals, and 3% Intralipid® for sufficient essential FA) for 2.5 weeks and tissues were collected from the PN2.5 group to establish that hepatic steatosis had developed. The remaining mice were then randomized into 4 groups: continuation of PN alone (PN5), or change to PN with 13.5% (en-%) of either Omegaven® (fish oil LE, FOLE), ClinOleic® (olive oil LE, OOLE), or Intralipid® (soybean oil LE, SOLE) and fed for another 2.5 weeks (end of wk 5). Transcripts of genes associated with lipogenesis and lipid mobilization, and liver total FA composition, were analyzed. FOLE and OOLE reduced TG vs. PN2.5 and PN5 ($P<0.001$); SOLE lowered hepatic TG vs. PN5 ($P<0.01$). FOLE mice had the lowest hepatic TG, not different from chow-fed mice, and the lowest transcripts for lipogenesis-associated genes and Srepbf, Ppar-α, and -γ ($P<0.001$). FOLE, OOLE, and SOLE lowered hepatic palmitic, palmitoleic, and vaccenic acids, while FOLE resulted in the lowest concentration of arachidonic acid but highest concentration of docosahexaenoic acid and eicosapentaenoic acid vs. PN2.5 and PN5 mice ($P<0.001$). Genes associated with lipid mobilization were also reduced by FOLE, including Acox1, Cpt-1, Acad1, and Mttp, all $P<0.0001$, while OOLE and SOLE lowered Acox1 ($P<0.001$). Overall, the inclusion of lipid in the form of 13.5 en-% LE, especially as FOLE, into the PN formula reversed the progression of hepatic lipid accumulation in mice with preexisting PN diet-induced hepatic steatosis.