TACSM Abstract

Fish-Oils Protect Against Hepatic Inflammation Following LPS Stimulation

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ABSTRACT

Omega-3 polyunsaturated fatty acids (ω-3 FA) have shown to possess anti-inflammatory properties; however, it remains unclear if ω-3 FA can provide protection against LPS induced inflammation in hepatic tissue. **PURPOSE:** To determine the effects of dietary fat on hepatic cytokine gene expression and secretion following LPS stimulation. **METHODS:** Male C57Bl/6J mice were randomly assigned to one of four diet groups for 32 weeks: low-fat lard (LFL, 10% fat), low-fat fish-oil (LFFO, 10% fat), high-fat lard (HFL, 41% fat), or high-fat fish-oil (HFFO, 41% fat). Hepatic gene expression and release of cytokines were induced by incubating liver tissue (100 mg) with or without LPS (25 μg/mL media) for 20 hours. The cytokines interferon-γ (IFN-γ), interleukin-1β (IL-1β), IL-6, IL-10, monocyte chemoattractant protein-1 (MCP-1), and tumor necrosis factor-α (TNF-α) were evaluated. A 2-way factorial ANOVA was performed to identify significant ($p<0.05$) differences between fat amount (low-fat vs. high-fat) and fat type (lard vs. fish-oils) on cytokine gene expression and release. **RESULTS:** In samples without LPS, only IL-1β expression was significantly ($p=0.044$) greater (2-fold) in high-fat compared to low-fat diets, matching a 2.7-fold higher ($p=0.004$) IL-1β media concentration. When comparing fat type in samples without LPS, IL-10 and TNF-α expression were 5-fold ($p=0.006$) and 2-fold higher ($p=0.014$), respectively, in lard-based diets leading to 1.5-fold ($p=0.007$) and 2-fold ($p=0.014$) higher media concentrations compared to fish-oil diets. Following LPS stimulation, MCP-1 and TNF-α mRNA expression were 3-fold ($p=0.045$) and 71% ($p=0.023$) higher, respectively, in high-fat when compared to low-fat groups. In contrast to samples without LPS, LPS stimulation increased the mRNA expression of IL-1β such that it was 47% higher ($p=0.008$) in the low-fat groups when compared to the high-fat groups. When comparing fat type following LPS, expression of IFN-γ and TNF-α were 2.3-fold ($p=0.033$) and 2-fold ($p=0.007$) lower, respectively, in the fish-oil diets when compared to lard diets. In contrast, IL-6 mRNA expression was 5-fold ($p=0.044$) higher in fish-oil diets following LPS stimulation. No difference in media concentrations of IFN-γ, TNF-α, and IL-6 were observed between diet types. **CONCLUSION:** The higher basal (untreated LPS samples) cytokine gene expression and secretion of IL-1β in high-fat diets showed that IL-1β response is independent to fat type. In contrast, IFN-γ and TNF-α expression were more sensitive to fat type versus amount of fat consumed, exemplified by lower cytokine activities post-LPS stimulation. These results display the protective role of fish-oils against chronic hepatic inflammation associated with obesity.