Abstract

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Docosahexaenoic acid induces an anti-inflammatory profile in lipopolysaccharide-stimulated human THP-1 macrophages more effectively than eicosapentaenoic acid.

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OBJECTIVE: A number of studies have investigated the effects of fish oil on the production of pro-inflammatory cytokines using peripheral blood mononuclear cell models. The majority of these studies have employed heterogeneous blends of long-chain n-3 polyunsaturated fatty acids (PUFA), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), which preclude examination of the individual effects of LC n-3 PUFA.

METHODS: This study investigated the differential effects of pure EPA and DHA on cytokine expression and nuclear factor kappaB (NF-kappaB) activation in human THP-1 monocyte-derived macrophages.

RESULTS: Pretreatment with 100 microM EPA and DHA significantly decreased lipopolysaccharide (LPS)-stimulated THP-1 macrophage tumor necrosis factor (TNF) alpha, interleukin (IL) 1beta and IL-6 production (P<.02), compared to control cells. Both EPA and DHA reduced TNF-alpha, IL-1beta and IL-6 mRNA expression. In all cases, the effect of DHA was significantly more potent than that of EPA (P<.01). Furthermore, a low dose (25 microM) of DHA had a greater inhibitory effect than that of EPA on macrophage IL-1beta (P<.01 and P<.04, respectively) and IL-6 (P<.003 and P<.003, respectively) production following 0.01 and 0.1 microg/ml LPS stimulation. Both EPA and DHA down-regulated LPS-induced NF-kappaB/DNA binding in THP-1 macrophages by approximately 13% (P< or =.03). DHA significantly decreased macrophage nuclear p65 expression (P< or =.05) and increased cytoplasmic IkappaBalpha expression (P< or =.05). Although similar trends were observed with EPA, they were not significant.

CONCLUSIONS: Our findings suggest that DHA may be more effective than EPA in alleviating LPS-induced pro-inflammatory cytokine production in macrophages - an effect that may be partly mediated by NF-kappaB. Further work is required to elucidate additional divergent mechanisms to account for apparent differences between EPA and DHA.

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