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EPA and DHA Reduce LPS-induced Inflammation Responses in HK-2 Cells: Evidence for a PPAR-gamma-dependent Mechanism

Hang Li [1], Xiong Z Ruan, Stephen H Powis, Ray Fernando, Wint Y Mon, David C Wheeler, John F Moorhead, Zac Varghese

Affiliations

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Abstract

Background: Recent studies have shown that fish oil, containing omega-3 polyunsaturated fatty acids (omega-3 PUFAs) eicosapentaenoic acid (EPA) (C20:5 omega 3), and docosahexaenoic acid (DHA) (C22:6 omega 3) retard the progression of renal disease, especially in IgA nephropathy (IgAN). Despite increasing knowledge of the beneficial effects of fish oils, little is known about the mechanisms of action of omega-3 PUFAs. It has been reported that activation of peroxisome proliferator-activated receptors (PPARs) inhibits production of proinflammatory cytokines. Both EPA and DHA have been shown to activate PPARs. The aim of this study was to examine if omega-3 PUFAs have anti-inflammatory effects via activation of PPARs in human renal tubular cells.

Methods: An immortalized human proximal tubular cell line [human kidney-2 (HK-2) cells] was used in all experiments. Conditioned media was collected from omega-3 PUFAs- treated cells and subjected to enzyme-linked immunosorbent assay (ELISA). Total cellular RNA was isolated from the above cells for real-time quantitative polymerase chain reaction (PCR). Nuclear Extracts were prepared from the HK-2 cells for transcription factor activation assay.

Results: Both EPA and DHA at 10 micromol/L and 100 micromol/L concentrations effectively decreased lipopolysaccharide (LPS)-induced nuclear factor-kappaB (NF-kappaB) activation and monocyte chemoattractant protein-1 (MCP-1) expression. EPA and DHA also increased both PPAR-gamma mRNA and protein activity (two- to threefold) in HK-2 cells. A dose of 100 micromol/L bisphenol A diglycidyl ether (BADGE) abolished the PPAR-gamma activation induced by both EPA and DHA and removed the inhibitory effect of EPA and DHA on LPS-induced NF-kappaB activation in HK-2 cells. Overexpression of PPAR-gamma further inhibited NF-kappaB activation compared to the control cells in the presence of EPA and DHA.

Conclusion: Our data demonstrate that both EPA and DHA down-regulate LPS-induced activation of NF-kappaB via a PPAR-gamma-dependent pathway in HK-2 cells. These results suggest that PPAR-gamma activation by EPA and DHA may be one of the underlying mechanisms for the beneficial effects of fish oil.

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