Anti-inflammatory properties of omega-3 fatty acids in critical illness: novel mechanisms and an integrative perspective.

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INTRODUCTION: Fish oil-based nutrition is protective in severe critical care conditions. Regulation of the activity of transcription factor NF-kappaB is an important therapeutic effect of the major omega-3 fatty acids in fish oil, eicosapentaenoic and docosahexaenoic acid (EPA and DHA). METHODS AND RESULTS: Using the articles obtained by a Pubmed research, this article reviews three aspects of NF-kappaB/inflammatory inhibition by fish oil. (1) Inhibition of the NF-kappaB pathway at several subsequent steps: extracellular, free omega-3 inhibits the activation of the Toll-like receptor 4 by endotoxin and free saturated fatty acids. In addition, EPA/DHA blocks the signaling cascade between Toll-like/cytokine receptors and the activator of NF-kappaB, IKK. Oxidized omega-3 also interferes with the initiation of transcription by NF-kappaB. (2) The altered profile of lipid mediators generated during inflammation, with production of the newly identified, DHA-derived inflammation-resolving mediator classes (in addition to the formation of less pro-inflammatory eicosanoids from EPA). Resolvin D1 and Protectin D1 are potent, endogenous, DHA-derived lipid mediators that attenuate neutrophil migration and tissue injury in peritonitis and ischemia-reperfusion injury. Their production is increased in the later stages of an inflammatory response, at which time they enhance the removal of neutrophils. (3) Modulation of vagal tone with potential anti-inflammatory effects: vagal fibers innervating the viscera down-regulate inflammation by activating nicotinic receptors upon infiltrating and resident macrophages. Stimulation of the efferent vagus is therapeutic in experimental septic shock. Fish oil supplementation increases vagal tone following myocardial infarction and in experimental human endotoxinemia. CONCLUSION: It remains to be shown whether these pleiotropic actions of EPA/DHA contribute to fish oil's therapeutic effect in sepsis.