Oxidized omega-3 fatty acids inhibit pro-inflammatory responses in glomerular endothelial cells.

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BACKGROUND: Omega-3 fatty acids have beneficial effects in chronic inflammatory diseases that are characterized by accumulation of leukocytes and leukocyte-mediated tissue injury. Accumulation of leukocytes occurs, in part, due to pro-inflammatory responses in endothelial cells, such as increase in expression of leukocyte adhesion receptors and chemokines, such as MCP-1 and IL-8. METHODS: omega-3 fatty acids, such as EPA, are highly polyunsaturated and readily undergo auto-oxidation. We studied the effect of oxidized EPA and unoxidized (native) EPA on leukocyte-glomerular endothelial cell interactions using adhesion assays, ELISA assays and transmigration assays. We used electrophoresis mobility shift assays to determine the effect of oxidized and unoxidized EPA on cytokine-induced nuclear factor-kappaB (NF-kappaB) activation. RESULTS: Oxidized EPA but not unoxidized EPA dose-dependently inhibits cytokine-induced leukocyte adhesion receptors on glomerular endothelial cells, which correlates with inhibition of leukocyte-glomerular endothelial cell interactions. Oxidized EPA but not unoxidized EPA inhibits cytokine-induced glomerular endothelial and mesangial cell expression of MCP-1, and to a lesser extent IL-8. Transmigration assays show that oxidized EPA but not unoxidized EPA inhibits leukocyte transmigration across glomerular endothelial cells. Oxidized EPA but not unoxidized EPA potently inhibited cytokine-induced activation of NF-kappaB in glomerular endothelial and mesangial cells. CONCLUSIONS: These studies show that the beneficial effects of fish oil in chronic inflammatory diseases, including IgA nephropathy, may result from the inhibitory effects of oxidized omega-3 fatty acids on pro-inflammatory events in endothelial cells via inhibition of NF-kappaB activation.