

Abstract

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Acute changes in dietary omega-3 and omega-6 polyunsaturated fatty acids have a pronounced impact on survival following ischemic renal injury and formation of renoprotective docosahexaenoic acid-derived protectin D1.

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BACKGROUND: Exacerbated inflammation plays an important role in the pathogenesis of ischemic renal injury (IRI), which is the major cause of intrinsic acute renal failure. Clinical studies suggest that long-term treatment with omega-3 polyunsaturated fatty acids (PUFA) improves renal function and lowers the risk of death or end-stage renal disease. Docosahexaenoic acid, a principle omega-3 PUFA of fish oils, is of particular interest as it is found in most human tissues and is converted to protectin D1 (PD1), which exhibits antiinflammatory and proresolving bioactions.

OBJECTIVE AND METHODS: We set out to investigate the impact of acute dietary modulation of omega-3 or omega-6 PUFA on IRI and renal lipid autacoid circuits, using an established mouse model and liquid chromatography-mass spectroscopy/mass spectroscopy-based lipidomics.

RESULTS: Thirty minutes of renal ischemia significantly elevated serum creatinine in the omega-6 diet group while renal function remained normal in the matched omega-3 diet group. Notably, extending ischemia to 45 min caused 100% mortality in the omega-6 group, in sharp contrast to 0% mortality in the omega-3 group. Protection against IRI in the omega-3 group correlated with decreased polymorphonuclear leukocyte recruitment, chemokine and cytokine levels, abrogated formation of lipoxygenase- and cyclooxygenase-derived eicosanoids, and increased renal levels of PD1. Systemic treatment with PD1 reduced kidney polymorphonuclear leukocyte influx and, more importantly, amplified renoprotective heme-oxygenase-1 protein and mRNA expression in injured and uninjured kidneys.

CONCLUSIONS: These findings suggest therapeutic or dietary amplification of PD1 circuits restrains acute renal injury and that short-term changes in dietary omega-3 and omega-6 PUFA dramatically impacts renal lipid autacoid formation and outcome of IRI.

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