

Differential effects of eicosapentaenoic acid and docohexaenoic acid on septic shock induced arterial dysfunction in rats

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Scope: Immunonutrition includes long chain n-3 fatty acid (n-3 PUFA) supplementation, which may modulate septic shock-induced hyper-inflammatory state and immune response to pathogen. We aimed at determining the respective effects of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in septic shock-induced vascular dysfunction.

Methods and results: In a peritonitis-induced septic shock model, rats were infused with EPA, DHA, an EPA/DHA mixture or 5% dextrose (D5) during 22 hours. From H18, rats were resuscitated and monitored during 4 hours. At H22, aorta and mesenteric resistance arteries were collected to perform *ex vivo* experiments. We have shown that septic rats needed an active resuscitation with fluid challenge and norepinephrine treatment, while SHAM rats did not. In septic rats, norepinephrine requirements were significantly decreased in DHA and EPA/DHA groups (10.6 ± 12.0 and 3.7 ± 8.0 $\mu\text{g}/\text{kg}/\text{min}$ respectively *versus* 17.4 ± 19.3 $\mu\text{g}/\text{kg}/\text{min}$ in D5 group, $p < 0.05$) and DHA infusion significantly improved contractile response to phenylephrine through nitric oxide pathway inhibition. DHA moreover significantly reduced vascular oxidative stress and nitric oxide production, phosphorylated I κ B expression and vasodilative prostaglandin production.

Conclusions: DHA infusion in septic rats improved hemodynamic dysfunction through decreased vascular oxidative stress and inflammation.