

Peroxynitrite scavenger improves intestinal epithelial barrier dysfunction induced by polymicrobial sepsis

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Aim: To investigate the role of peroxynitrite in intestinal epithelial barrier dysfunction induced by polymicrobial sepsis.

Methods: Mice were treated with a peroxynitrite scavenger FeTPPS (1 or 5mg/kg, *i.p.*) or saline immediately after cecal ligation and puncture (CLP) or sham surgery. At 24h post-surgery, analysis including ileal permeability by injection of dextran-FITC (FD4; 5mg/mL); microbiological quantification in blood, peritoneal lavage and mesenteric lymph node; and determination of cytokines in serum and ileal mucosa were investigated.

Results: Septic animals (3,39±0,52) showed increased plasma FD4 concentration when compared to controls (1,23±0,18), demonstrating an increase in ileal permeability, which was attenuated in mice treated with FeTPPS 1mg/kg (1,43±0,27) and 5mg/kg (1,31±0,26). Septic mice showed increased bacterial counts in blood, peritoneal lavage and mesenteric lymph nodes when compared to control groups. However, FeTPPS treatment decreased the bacterial translocation and increased the resistance to infection in septic mice. Concentrations of pro-inflammatory mediators were higher in the serum (IL-6 and TNF- α) and in the ileal mucosa (IL-6, TNF- α and IFN- γ) of septic animals when compared to the control groups, however the FeTPPS treatment reduced their synthesis. On the other hand, serum IL-10 concentrations were higher in septic animals when compared to control groups, and treatment with FeTPPS only at the highest dose stimulated the synthesis of this anti-inflammatory cytokine.

Conclusion: Our findings demonstrated that peroxynitrite promotes the epithelial barrier dysfunction in ileum, associated with bacterial translocation and increased inflammatory response during polymicrobial sepsis.