OXIDATIVE STRESS AND MITOCHONDRIAL DYSFUNCTION DURING SEPSIS DEVELOPMENT

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Sepsis is a complex syndrome characterized by an imbalance between pro-inflammatory and anti-inflammatory response to pathogen. Some of the postulated molecular mechanisms of sepsis and its progression are linked with the imbalance between reactive oxygen species (ROS) production and its degradation by cellular antioxidants pathways. The pro-inflammatory effects of ROS include endothelial damage, formation of chemotatic factors, neutrophil recruitment, TNF and IL-1 release and mitochondrial impairment. To date the major sources of ROS during sepsis are the NADPH oxidase system, xanthine oxireductase and dysfunction in the mitochondrial electron transport chain. Using a well established animal model of polimicrobial sepsis we determined that superoxide dismutase (SOD)/catalase (CAT) ratio was increased in septic animals and this presented a strong correlation with oxidative damage and organ dysfunction. Antioxidant treatment was able to reduce both the SOD/CAT ratio, organ damage and mortality in this model. In addition, it seemed that plasma SOD levels were related to response to antioxidant treatment. ROS were related to mitochondrial dysfunction, mitochondrial swelling and cell death. These results support a role for ROS in sepsis progression and an opportunity to the use of antioxidants as adjuvant treatment in sepsis.
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