

Effects of hyperoxia on the pulmonary inflammatory response in murine peritoneal sepsis.

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Sepsis triggers a systemic inflammatory response that may produce multiple organ dysfunction. Impaired oxygen extraction and cellular hypoxia are key mechanisms of target organ involvement in this condition. We evaluated the effects of hyperoxia on the pulmonary inflammatory response in rats 20h and 48h after cecal ligation and puncture (CLP). Six groups were studied: 1) control (anesthesia only), 2) sham operated (all surgical procedures without CLP; air ventilation), 3) CLP and ambient air, 4) CLP and continuous inhalation of 100% oxygen for 20 h, 5) CLP and continuous inhalation of 70% oxygen for 48h, 6) CLP and intermittent inhalation of 100% oxygen (6h/day) for 48h. Macromolecular (FITC-albumin) flux into the lungs was evaluated by intravital video-microscopy. Myeloperoxidase staining and morphometry were used to quantify pulmonary leukocyte infiltration. The ratio of lung solid tissue area to alveolar spaces area was calculated by imagepro software. Expression of the adhesion molecules, CD18/CD11b and L-selectin, on peripheral blood neutrophils was analyzed by Fluorescence-activated cell sorting (FACS). Nitric oxides (NO), IL-10 and TNF- α concentrations were determined in the serum and lung lavage fluid. CLP caused marked increases in neutrophil count, expression of CD11b adhesion molecules, pulmonary sequestration of leukocytes, macromolecular leak, and lung solid tissue area ratio. Continuous inhalation of 100% oxygen for 20h or intermittent exposure (6h/d) for 48h reduced leukocyte infiltration in the lungs ($P<0.01$), attenuated the increase in pulmonary macromolecular leak ($P<0.01$) and diminished the increase in lung tissue to alveolar spaces area ratio ($P<0.01$). Intermittent inhalation of 100% oxygen for 48h also attenuated the increase in CD11b expression ($P<0.001$) and increased NO concentrations ($P<0.01$). Inhalation of 70% oxygen for 48h did not exert beneficial effects on pulmonary leukocyte infiltration, macromolecular leak, or lung tissue area ratio. Our data support favorable dose dependent effects of normobaric hyperoxia that attenuate the pulmonary inflammatory response in abdominal sepsis. It is suggested that increased production of NO and decreased expression of leukocyte adhesion molecules may mediate the anti-inflammatory effect of hyperoxia.