

European Respiratory Society Annual Congress 2012

Abstract Number: 4642

Publication Number: P1493

Abstract Group: 8.2. Transplantation

Keyword 1: ALI (Acute Lung Injury) **Keyword 2:** Sepsis **Keyword 3:** ARDS (Acute Respiratory Distress Syndrome)

Title: Creatine supplementation attenuates systemic and pulmonary effects of acute lung injury induced by pulmonary ischemia-reperfusion in rats

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Body: Creatine supplementation (CS) presents prophylactic and therapeutic effects for some muscular, cardiovascular and neurological disorders. In case of temporary ischemia, CS improves the capacity to generate ATP reducing cell damage. Ischemia and reperfusion (IR) injury is partially attributed to decreased intracellular ATP turnover, but also to increased oxidative stress and reduced IGF-1. Thus, this study evaluated the effects of 5 days of CS prior 90 minutes ischemia of left pulmonary artery followed by 120 minutes of reperfusion in 40 male Wistar rats divided in 4 groups: Sham-operated, Creatine+Sham, Ischemia/Reperfusion, Creatine+Ischemia/Reperfusion. Lung mechanics, exhaled nitric oxide, cellularity in systemic circulation and in bronchoalveolar lavage (BAL), neutrophils and edema in lung tissue, total proteins in BAL, the levels of IL-1beta, IL-4, IL-6, IL-17, KC, MCP-1 and TNF-alpha in serum and in bronchoalveolar lavage were evaluated by ELISA, as well as the expression of IGF-1, iNOS and caspase-3 in lung tissue. Compared with IR group, CS supplementation (CS+IR group) resulted in a reduction of exhaled nitric oxide ($p<0.05$), tissue damping (GTIS) and tissue elastance (HTIS) ($p<0.05$), total cells and neutrophils number in systemic circulation, in BAL and also in lung tissue ($p<0.01$), BAL levels of total proteins ($p<0.05$) and edema index in lung tissue ($p<0.05$), and systemic and pulmonary IL-1beta levels ($p<0.05$). In addition, CS resulted in increased expression of IGF-1 in lung tissue. CS presents protective effects for the development of pulmonary and systemic manifestations of acute lung injury caused by pulmonary IR.