

Insulin attenuates endotoxin-induced acute lung injury in conscious rats

高尚志

Chen HI;Yeh DY;Liou HL;Kao SJ

摘要

Abstract

OBJECTIVES: To investigate the effects of insulin on the acute lung injury induced by lipopolysaccharide using a conscious rat model. **DESIGN:** Prospective, randomized, controlled animal study. **SETTING:** University research laboratory. **SUBJECTS:** A total of 190 adult male Sprague-Dawley rats weighing 250-300 g. **INTERVENTIONS:** Endotoxemia was induced by intravenous infusion of lipopolysaccharide. Lipopolysaccharide at various doses (0, 1, 5, 10, 20, and 30 mg/kg, n=10 for each dose) was administered intravenously in 20 mins. Insulin infusion at doses of 0.5, 1, and 5 microU/kg/min was given 5 mins before lipopolysaccharide administration. Plasma glucose was clamped at 90-110 mg/dL by infusion of 10-80% glucose solution. Insulin and glucose infusion (0.01 mL/min) was started 5 mins before lipopolysaccharide and continued for 120 mins. The rats received a total of 60, 120, and 600 microU/kg insulin as well as 0.12, 0.36, and 0.96 g of glucose in respective groups. The animals were then observed for 4 hrs. **MEASUREMENTS AND MAIN RESULTS:** The extent of acute lung injury was evaluated by lung weight/body weight ratio, lung weight gain, protein concentration in bronchoalveolar lavage, and exhaled nitric oxide. We also measured plasma nitrate/nitrite and methyl guanidine. In addition, histopathologic changes of the lung were examined. Lipopolysaccharide caused systemic hypotension and severe acute lung injury with increases in plasma nitrate/nitrite and methyl guanidine. Pretreatment with insulin infusion at doses of 0.5, 1, and 5 microU/kg/min mitigated or prevented systemic hypotension and the development of acute lung injury, depending on the dose. Insulin also attenuated the lipopolysaccharide-induced increases in nitrate/nitrite and methyl guanidine. **CONCLUSIONS:** Insulin is effective in reducing or preventing the lipopolysaccharide-induced increases in plasma nitrate/nitrite and methyl guanidine and the occurrence of acute lung injury.