Captopril decreases plasminogen activator inhibitor-1 in rats with ventilator-induced lung injury

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摘要.

Abstract

OBJECTIVE: To test the hypotheses that high tidal-volume ventilation increases plasminogen activator inhibitor (PAI)-1, and the angiotensin-converting enzyme inhibitor, captopril (CAP), may attenuate these effects. SETTING: University research facility. SUBJECTS: Twenty adult male Sprague-Dawley rats. INTERVENTIONS: All rats were randomized to receive two ventilation strategies for 2 h: 1) a high-volume zero positive end-expiratory pressure (PEEP) (HVZP) group at a tidal volume of 40 mL/kg, a respiratory rate of 25 breaths/min, and an FiO2 of 0.21; and 2) an HVZP + CAP group which received an intraperitoneal injection of CAP (100 mg/kg) 30 min before HVZP ventilation. Another group that was not subjected to ventilation served as the control. MEASUREMENTS AND MAIN RESULTS: Total protein recovered from bronchoalveolar lavage fluid was significantly higher in rats ventilated with the HVZP protocols than in control rats. Rats treated with HVZP ventilation had significantly higher lung angiotensin (ANG) II and PAI-1 messenger RNA expression levels and a higher plasma active PAI-1 level than did the control and HVZP + CAP groups. Lung ANG II levels were positively correlated with plasma PAI-1. Representative lung tissue of the HVZP + CAP group showed mild inflammatory cell infiltration and less hemorrhage and fibrin deposition than did the HVZP group. The HVZP and HVZP + CAP groups had significantly higher lung injury scores than did the control group and rats treated with HVZP + CAP ventilation exhibited significantly lower lung injury scores than did the HVZP group. CONCLUSIONS: Mechanical ventilation with a high tidal volume and no PEEP increases alveolar fibrin deposition and systemic PAI-1 activity, which are attenuated by captopril, an angiotensin-converting enzyme inhibitor. These results imply that local ANG II is involved in the pathogenesis of disordered coagulation in ventilator-induced lung injury (VILI) and suggest that the protective mechanism of captopril's attenuation of VILI is related to a reduction in PAI-1.