

Category : **Respiratory: mechanical ventilation**

A275 - Combined ACE and aminopeptidase inhibition reduces inflammation and maintains normal blood pressure in ventilation induced lung injury

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Introduction:

Patients in need of mechanical ventilation may suffer additional damage to the lungs from ventilator-induced lung injury (VILI) [1]. ACE inhibition was found to be beneficial, but its hypotonic effect impedes clinical application [2]. Here we tested, whether additional manipulation of the renin-angiotensin-system (RAS) by blocking aminopeptidases can alleviate this undesired effect.

Methods:

Anesthetized mice (C57/BL6, 18-28 g, 8-10 weeks) were mechanically ventilated with low or high tidal Volume (LV_T , 6ml/kg; HV_T , 30ml/kg) for 4 hours, and treated with the ACE inhibitor Lisinopril (0.15 ug/kg/min) with or without aminopeptidase inhibitor (ALT00) at 2.7, 10 or 100 ug/kg/min. BALF was analyzed for inflammatory cytokine levels (IL-6, KC, MIP-2 and IL-1 β) by ELISA. Mean arterial pressure (MAP) was measured continuously in the right carotid artery. Equilibrium concentrations of RAS metabolites in plasma were measured by LC tandem MS.

Results:

ACE inhibition decreased ventilation-induced inflammatory cytokines and MAP. Co-treatment with ALT00 reduced inflammation and increased dose dependently levels of Ang 1-7, an anti-inflammatory and anti-fibrotic RAS metabolite. Various doses had mixed effects of normalizing MAP and reducing cytokine secretion.

Conclusion:

Combined manipulation of the RAS system might represent a promising new treatment strategy for VILI requiring further mechanistic exploration.

References:

1. Baumgardner JE, et al. Am J Respir Crit Care Med 166: 1556-1562, 2002;
2. Jiang JS et al. J Appl Physiol 102: 2098–2103, 2007.