The Effect of Angiotension-(1-7) to Experimental Acute Lung Injury Rat

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Background: Acute lung injury was common in operative theatre and intensive care unit while still with 30-40% mortality. The rennin-angiotensin system (RAS) played an important role in the pathogenesis of acute lung injury (ALI), the overexpression of angiotensin II in RAS contributed to the pathogenesis of inflammation and fibrogenesis. As a natural antagonist of angiotensin II, angiotension-(1-7) may block the effects of angiotensin-II. This study was aimed to evaluating the potential for angiotension-(1-7) to reduce lung injury, inflammation and fibrosis in an experimental model of ALI.

Methods: LPS (0.2mg/kg) was given to the Sprague Dawley rats (male) by i.v. which were also suffered the high-volume ventilation (10ml/kg) for 4h in acute lung injury study, and then the rats were randomized to receive an intravenous infusion of either angiotension-(1-7) (50pmol/kg/min), the antagonist of angiotensin II (AVE0991, 500pmol/kg/min), the agonist D-pro-angiotension-(1-7) (100pmol/kg/min) or vehicle (saline), starting simultaneously with injury till 2h afterwards. Mean artery pressure and mean pulmonary artery pressure were recorded during the 2h, artery blood gas analysis was also collected at the same time, bronchoalveolar lavage (test of white blood cell) and hematoxylin-eosin staining of the lung tissue were performed to assess the injury. The counts of IL-8, IL-10, TNF- α and MCP-1 from peripheral blood was measured to access the inflammatory. The wet/dry weight ratio (W/D) of the lung was also compared among the three groups.

Results : In this study, Angiotension-(1-7) and its' agonist D-pro-angiotension-(1-7) led to a improvement in MAP while no difference in PAP compared to its anagonist AVE0991 ($p>0.05$, two-way repeated measures ANOVA, Figure 1). There's no difference of PaO₂ among the four groups, MCP-1 in BAL was less in Angiotension-(1-7) and D-pro-angiotension-(1-7) groups (Figure2). Worst injury was found in AVE0991 group from the HE staining of the lung tissue (Figure 3), the white blood cells counts reduced with the treatment of Angiotension-(1-7) and D-pro-angiotension-(1-7) (Figure 3).

Conclusion: Angiotension-(1-7) played an protective role in acute lung injury while further study still needed to confirm the precise dose.

Figure 1A : The MAP changes from the drug administration to 120 minutes afterwards in three groups

Figure 1B : The mPAP changes from the drug administration to 120 minutes afterwards in three groups

Figure 3: HE staining of lung tissue (emphysema)

Ang-(1-7) group (×100)

AVE0991 group (×100)

D-pro-Ang-(1-7) (×100)

Figure 2: The difference of MCP-1, monocyte, lymphocyte and neutrophile in BALF of the three groups

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