EFFECTS OF HEXARELIN IN A MODEL OF ARDS

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Acute Respiratory Distress Syndrome (ARDS) is an acute form of diffuse lung injury characterized by an intense inflammatory response, increased pulmonary vascular permeability and lung weight, and loss of aerated lung tissue. The clinical hallmarks are hypoxemia and bilateral radiographic opacities, associated with decreased lung compliance. The morphological hallmark of the acute phase is diffuse alveolar damage, and macrophages could play a critical role contributing to lung remodelling. No drug has proven beneficial in the prevention or management of acute respiratory distress syndrome. Although no specific therapy has been approved for ARDS, treatment of the underlying condition is essential, along with supportive care, noninvasive ventilation or mechanical ventilation using low tidal volumes, and conservative fluid management.

The aim of this work was to explore the therapeutic potential of hexarelin, a synthetic GH secretagogue (GHS), in an experimental model of ARDS.

Hexarelin is an agonist of ghrelin receptor (GHS-R1a), shows effects similar to those of ghrelin but is more stable in biological fluids. Its beneficial actions on the cardiovascular system, including inhibition of cardiomyocyte apoptosis, anti-atherosclerosis, cardiac output increase, and suppressing cardiac fibrosis have been previously reported.

Male mice received an instillation of 0.1 M HCl, 1.5 ml/kg into the right bronchus. They were treated with hexarelin 320 µg/kg ip or vehicle control, 2 days before and on the same day of HCl challenge. Respiratory system compliance, blood gas analysis and differential cell counts in a selective broncho-alveolar lavage (BAL) were determined 24 h after HCl. In a parallel experiment, mice were observed for 14 days to assess lung fibrosis.

The treatment with Hexarelin showed a significant improvement of lung compliance and a reduction of the number of total immune cells in BAL. 24 hour after challenge with HCl there was a lower recruitment of neutrophils compared to the control group, with no differences in macrophage number. At day 14 hexarelin group showed a decreased collagen deposition in lung tissue.

In conclusion, our data suggest that hexarelin can inhibit the early phase of the inflammatory response in a mouse model of HCl-induced ARDS, which may modulate lung remodeling at a late phase, preventing a fibrotic evolution. These results suggest a potential role for Hexarelin in ARDS therapy.