PHARMA Pharmacologia

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Gelsolin(GSN) Attenuated LPS-Induced Acute Lung Injury in Rats

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Acute Respiratory Distress Syndrome (ARDS), also known as Acute Lung Injury (ALI), is a syndrome that develops because of severe shock, infection, trauma, and burns. It causes diffuse pulmonary interstitial and alveolar oedema of pulmonary capillary endothelial cells and alveolar epithelial cells, which results in acute hypoxic respiratory insufficiency or failure. A chemical component of the active tissue found in the cell wall of Gram-negative bacteria is lipopolysaccharide (LPS), also known as endotoxin. It can cause ALI by directly triggering alveolar macrophages to release a range of inflammatory factors. Injured pulmonary endothelial cells will release a certain quantity of Reactive Oxygen Species (ROS), which will cause an imbalance of oxidation and antioxidation in the lung. Numerous proteins will enter the alveolar cavity directly, causing pulmonary oedema and even respiratory failure.

An essential part of the cytoskeleton is gelsolin (GSN). It is a crucial actin-binding protein that can bind to actin and control the polymerization and depolymerization of actin. To establish an experimental foundation for GSN to be used as a clinically effective treatment for ALI/ARDS or to create a novel class of drugs that specifically target GSN, the goal of this work was to investigate the effect of GSN on LPS-induced ALI/ARDS and its potential mechanism.

Sigma Chemical Co. supplied LPS (Escherichia coli 055: B5) (St. Louis, MO, USA). Biyuntian Biotechnology Research Institute supplied the mouse TNF-", IL-6, IL-1$, MPO, MDA, and SOD ELISA kits. Male SD rats weighing 200–230 g were bought from Liaoning Changsheng Biological Co., Ltd.: Sixty mice were randomized into five groups at random (n = 12) as follows: LPS+GSN (0.1, 0.3, and 0.9 mg kg^{-1}) groups, control group, and LPS group. LPS was administered intratracheally once a day for two days to the rats in the LPS group and the LPS+GSN (0.1, 0.3, 0.9 mg kg^{-1}) groups at a dose of 2 mg kg^{-1} body weight. One hour after the final intratracheal instillation of LPS, GSN received an intravenous injection. After 24 hrs of injection, rats in each group were killed.

The alveolar structure and alveolar cavity were both completely in the control group, and there was no apparent oedema or inflammatory cell infiltration in the alveolar septum. Red blood cell leakage, inflammatory exudation of lung tissue, better alveolar structure, and relief from pulmonary interstitial oedema were all considerably reduced after intervention with various concentrations of GSN. A common form of respiratory failure known as acute lung injury is characterized by acute increasing hypoxemia and respiratory distress brought on by a variety of pathogenic causes. Diffuse alveolar injury, capillary endothelial injury, high protein alveolar and interstitial oedema, and increased alveolar

membrane permeability are its main characteristics. A well-known multifunctional protein, gelsolin (GSN), is a crucial part of the cytoskeleton. It can cut, obstruct, or cause actin filaments to nucleate and is controlled by calcium ions. It also plays a crucial purpose in controlling cell shape and metabolism while taking part in cell motility, apoptosis, and phagocytosis. The findings indicated that different doses of GSN intervention significantly decreased the gene and protein expression of TLR4, MyD88, TRAF6, IRAK1, TAK1, and NF-B p65 in lung tissue of ALI rats, suggesting that GSN may reduce the severity of LPS-induced ALI by inhibiting TLR4/MyD88/NF-B pathway activation.

The modulation of the TLR4/MyD88/NF-B signalling pathway may play a role in GSN's ability to lessen lung damage in LPS-induced ALI mice. A fresh concept for the clinical treatment of ALI is offered by the intervention effect of GSN on LPS-induced ALI.

JOURNAL REFERENCE

Fu, H.Y., Z.S. Hu, X.T. Dong, R.B. Zhou and H.Y. Du, 2021. Gelsolin attenuates lipopolysaccharide-induced acute lung injury in rats by modulating TLR4/Myd88/NF-κB signaling pathway. Int. J. Pharmacol., 18: 511-521.

KEYWORDS

Gelsolin, acute lung injury, lipopolysaccharide, TLR4/MyD88/NF-κB, signalling pathway