Effect That Ganlu Qingwen Formula on Acute Lung Injury Protection in Rats via the Nrf2/GPX4 Ferroptosis Pathway

Li Jiang-tao[1], Li Xiang-peng[1], Liang Qian-qian[1], Liao Chun-yan[2], Li Feng-sen[1, 2, *], Li Zheng[2, *]

[1]The Fourth Clinical Medical College of Xinjiang Medical University, Urumqi, China

[2]Affiliated Hospital of Traditional Chinese Medicine of Xinjiang Medical University, Xinjiang National Clinical Research Base of Traditional Chinese Medicine, Xinjiang Respiratory Obstructive Disease Clinical Medical Research Center, Xinjiang Key Laboratory of Respiratory Disease Research, Urumqi, China

Email address:

530443341@qq.com (Li Jiang-tao), fengsen602@163.com (Li Feng-sen), 149668116@qq.com (Li Zheng)

[*]Corresponding author

Abstract

Ganlu Qingwen Formula (GLQWF) is a prescription based on years of clinical experience by experts in respiratory diseases who integrate traditional Chinese and Western medicine. It is widely used to regulate immunity, reduce inflammation and improve symptoms of pulmonary infection, but its mechanism of action is unknown. In this study, rats model of ALI induced by LPS was used to simulate ALI caused by pulmonary infection. The effects of different doses of GLQWF on rats were observed to explain its underlying mechanism. Thirty-six SD rats were randomly divided into the normal group, the model group, and the dexamethasone group, low, medium, and high groups of GLQWF, after continuous administration by gavage for 3 d, except for the normal group, LPS was instillated into the trachea of the remaining rats to establish the ALI inflammation model. Serum and lung tissue were collected 24 h later. The content of TNF-α, IL-1β and IL-6 in rat serum was detected by ELISA, the pathological changes of lung tissue were observed by HE staining, and Fe2+ , MDA and GSH in lung tissue was detected by biochemical methods. The results of detecting the expression levels of Nrf2, SLC7A11 and GPX4 protein and mRNA by Western blot or RT-qPCR. Results showed that, Compared with normal group, the model group displayed increased serum TNF-α, IL-1β, IL-6 levels, pathological injury score of lung tissue and levels of MDA and Fe^{2+} in lung tissue (P<0.05) , decreased GSH level , Nrf2, SLC7A11 and GPX4 protein and mRNA expressions in lung tissue (P<0.05), Compared with the model group, the Ganluqingwen formula medium and high dose groups displayed decreased levels of serum TNF-α, IL-1β, IL-6, pathological injury score of lung tissue, MDA and Fe^{2+} in lung tissue (P<0.05), decreased GSH level, Nrf2, SLC7A11 and GPX4 protein and mRNA expressions in lung tissue (P<0.05). Studies have shown that GLQWF can induce LPS by by improving inflammatory response and oxidative stress in rats. The mechanism may be related to activation of Nrf2/GPX4 signaling pathway and inhibition of ferroptosis.

Keywords

Acute Lung Injury, Traditional Chinese Medicine Network Pharmacology,
Nuclear Factor Erythroid 2- related Factor 2 (Nrf2), Glutathione Peroxidase 4 (GPX4), Ferroptosis