

Oral Presentation - 16

Rosiglitazone Exerts Protective Activity against Paraquat Induced Acute Lung Toxicity by Modulating Nrf-2 and NF-κB Signaling

Zhenning Liu, Min Zhao, Yu Wang, Hongyu Zhao

Shengjing Hospital of China Medical University, Shenyang, China

Abstract

Objectives: To investigate the effects and potential mechanisms of rosiglitazone, an agonist of PPAR-γ, on paraquat-induced acute lung injury.

Method: Male Sprague-Dawley rats were given rosiglitazone (3 mg/kg, 10 mg/kg) by intraperitoneal injection 1 hour prior to exposure to PQ. After PQ exposure for 4 h, 8 h, 24 h, 72 h, peripheral blood was collected for detection of MDA level, SOD activity, levels of TNF-alpha and IL-1β. After PQ exposure for 72 h, lung tissues were collected for detection of W/D ratio, lung injury score and protein expression of NF-κBp65, PPAR-γ, Nrf2, IκB-α and pIκB-α.

Results: Our results showed that with pre-treatment of rosiglitazone, the PQ-induced lung edema and lung histopathological changes were attenuated significantly. In addition, the excessive secretion of TNF-alpha and IL-1β, the increased level of MDA and the reduced activity of SOD induced by PQ were significantly reversed by rosiglitazone in peripheral blood of PQ poisoning rats. Additionally, immunohistochemistry and western blotting results implied that rosiglitazone could efficiently activate PPAR-γ, induce the expression of Nrf2 and inhibit the activation of NF-κB in lung tissue of PQ poisoned rats. Western blotting also showed it was by inhibiting the degradation and phosphorylation of IκB-α that rosiglitazone could have the ability to inhibit the activation of NF-κB.

Conclusions: The results and indications suggest that rosiglitazone presented protective effects on PQ-induced acute lung injury in rats by activating PPAR-γ, inducing the expression of Nrf2 and inhibiting the activation of NF-κB.