Oral Abstracts

5B-01

LIVER X RECEPTOR AGONIST TO901317 ATTENUATES PARAQUAT-INDUCED ACUTE LUNG INJURY THROUGH INHIBITION OF NF-KB AND JNK/P38 MAPKS SIGNAL PATHWAYS

Xiao Hu, Haitao Shen, Yu Wang, Min Zhao

Department of Emergency Medicine, Shengjing Hospital of China Medical University, Shenyang 110004, China

Objectives: To investigate the effects and possible underlying mechanisms of TO901317, a potent Liver X receptors(LXRs) receptor ligand,againstparaquat(PQ)-induced acute lung injury(ALI) in mice.

Methods: Male C57BL/6J mice were injected with PQ (28 mg/kg, ip).TO901317 (5 or 20 mg/kg, ip) was administered 30 minutes after PQ exposure. Bronchoalveolar lavage fluid (BALF) was collected at 6, 12, 24 and 72 h after PQ exposure for protein concentration and cytokines measurement. Lung tissues were collected at 72 h after PQ exposure to determine the wet-to-dry (W/D) ratios ,histopathologychangs, antioxidant capacity, cell apoptosis as well as the protein levels of LXRα, LXRβ, NF-κBp65,IκB-α, JNK,p38 MAPK,Bax and Bcl-2.

Results: PQ exposure induced ALI characterized by significant tissue damage and edema , neutrophils(PMNs) infiltration and increased production of proinflammatory cytokine ,such as tumor necrosis factor-α(TNF-α) and interleukin-1β(IL-1β),in the BALF.PQ administration also decreased the antioxidant capacity by reducing superoxidedismutase(SOD), catalase (CAT) and glutathioneS-transferases(GSTs) activities ,as well as increasing lipid peroxidation damage evaluated by malondialdehyde(MDA) levels. Furthermore, PQ administration induced upregulation of pro-apoptotic gene Bax and downregulation of anti-apoptotic gene Bcl-2,which leads to significantly increased cell apoptosis in the lung tissues.However,TO901317 pretreatment reversed all these parameters via inhibition of PQ-induced NF-κB and JNK/p38 MAPKs activation.

Conclusion: Our results imply that LXR agonists TO901317 showed potent antioxidant, anti-inflammatory and anti-apoptotic effects against PQ-induced ALI.