MINI ORAL 8 [ID#45]

Exogenous Hydrogen Sulfide Attenuated Paraquat-induced Acute Liver Injury in Rats by Enhancing Keap1/Nrf2-Mediated Antioxidation, Regulating SIRT3/IDH2 Signaling Pathway, and Suppressing NLRP3 Inflammasome Activation

Zhenning Liu and Min Zhao
Shengjing Hospital of China Medical University

OBJECTIVE: In addition to lung, liver is considered as another major target for paraquat (PQ) poisoning. Hydrogen sulfide (H2S) has been shown to be effective in the inhibition of oxidative stress and inflammation. The aim of this study was to investigate the protective effect of H2S against PQ-induced acute liver injury.

METHODS: The acute liver injury model was established by a single intraperitoneal injection of PQ, evidenced by histological alternation and elevated serum aminotransferase. Different doses of NaHS were administered intraperitoneally one hour before prior to exposure to PQ.

RESULTS: Our data showed that exogenous H2S attenuated the PQ-induced liver injury and oxidative stress in a dose-dependent manner. Exogenous H2S significantly suppressed the elevation of malondialdehyde content and increased the contents of antioxidases including SOD, GSH-Px, HO-1, and NQO-1. H2S markedly enhanced translocation of Nrf2 to the nucleus via S-sulfhydration of Keap1 and promoted the downstream cytoprotective genes transcription. Besides, H2S resulted in the increase of IDH2 activity by regulating S-sulfhydration of SIRT3. Moreover, H2S significantly suppressed the expression of NLRP3, cleaved caspase-1 (p20), and IL-1β in PQ-induced acute liver injury. The protective effect of H2S was weakened by knockdown of Nrf2. Conclusions: H2S attenuated PQ-induced acute liver injury by enhancing Keap1/Nrf2-mediated antioxidation, regulating SIRT3/IDH2 signaling pathway, and inhibiting NLRP3 inflammasome activation. Thus, H2S supplementation could represent a promising novel therapeutic strategy for PQ-induced acute liver injury.