Role of Farnesoid X Receptors in Chlorine-Induced Pulmonary Injury

Jaden He, Khushi Desai, Elena V. Abramova, Kinal Vayas,
Rama Malaviya, Jeffrey D. Laskin, Debra L. Laskin
Rutgers, the State University of New Jersey

Chlorine (Cl2) gas is a highly toxic irritant that causes acute injury to the respiratory tract. Farnesoid X Receptor (FXR) is a nuclear receptor involved in lipid metabolism; it exerts anti-inflammatory activity. In these studies, the role of FXR in Cl2-induced injury and inflammation was assessed. Male WT and FXR-/- mice were exposed to air or Cl2 (300 ppm, 25 min) in a whole-body exposure chamber. Bronchoalveolar lavage (BAL) and lung tissue were collected 24 h later and analyzed for markers of injury and oxidative stress. Cl2 exposure caused necrosis of proximal bronchiolar epithelial cells and an accumulation of epithelial cell debris in in the lungs of both WT and FXR-/- mice; proximal peribronchial edema and mononuclear inflammatory cells were also observed. These structural changes were associated with increases in total BAL protein and cell content, demonstrating alveolar-epithelial barrier dysfunction. Immunohistochemistry revealed that Cl2 upregulated FXR expression in alveolar macrophages in lungs of WT mice. Oxidative stress, assessed by expression of heme oxygenase (HO)-1 and Ym-1 were also increased in WT as well as FXR-/- mice. However, no differences were noted in the response of FXR-/- and WT mice to Cl2. These findings suggest that FXR does not play a role in acute lung injury or oxidative stress induced by inhaled Cl2. Supported by NIH Grants U54AR055073, P30ES005022, R25ES020721, and the American Society for Pharmacology and Experimental Therapeutics.