Ghrelin ameliorates bleomycin-induced acute lung injury by protecting alveolar epithelial cells and suppressing lung inflammation

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Body: Acute lung injury (ALI) is a critical illness syndrome consisting of acute respiratory failure with bilateral pulmonary infiltrates that is refractory to current therapies. ALI is characterized by injury of the alveolar capillary barrier, neutrophil accumulation, and induction of pro-inflammatory cytokines followed by devastating lung fibrosis. Ghrelin, an acylated peptide produced in the stomach, increases food intake and growth hormone secretion, suppresses inflammation, and promotes cell survival. We investigated the pharmacological potential of ghrelin in the treatment of ALI by using a bleomycin-induced ALI model in mice. Ghrelin or saline was given to mice daily starting 1 day after bleomycin administration. Ghrelin-treated mice showed a definitively higher survival rate than saline- treated ones. They also had smaller reductions in body weight and food intake. The amelioration of neutrophil alveolar infiltration, pulmonary vascular permeability, induction of pro-inflammatory cytokines, and subsequent lung fibrosis were notable in ghrelin-treated mice. Additionally, ghrelin administration reduced the injury-induced apoptosis of alveolar epithelial cells. Our results indicate that ghrelin administration exerts a protective effect against ALI by protecting the alveolar epithelial cells and regulating lung inflammation, and highlight ghrelin as a promising therapeutic agent for the management of this intractable disease.