β2 Adrenergic Receptor Agonists And Steroids Inhibit Cafo Dust-Mediated Bronchial Epithelial Inflammation In Vitro

D. J. Romberger¹, K. Palm¹, A. J. Heires², T. M. Nordgren², M. L. Toews², T. A. Wyatt²,

¹VA Nebraska-Western Iowa Healthcare System, Omaha, NE, ²University of Nebraska Medical Center, Omaha, NE

Corresponding author's email: dromberg@unmc.edu

and are susceptible to inflammatory lung diseases including COPD. Aqueous extracts of agricultural dust collected from swine CAFOs (HDE) have been shown to be potent inflammatory stimulators in human cells and in vivo mouse models. HDE exposure augments proinflammatory cytokine release, ICAM-1 expression, PKC activation, and lymphocyte and neutrophil adhesion to airway epithelial cells. Because 2 adrenergic receptor agonists (β-agonists) alone, and in combination with corticosteroids, have been used to treat COPD, we examined the ability of these agents to diminish the inflammatory effects of HDE in human epithelial cells and mouse lungs in vitro. **Methods:** Immortalized human bronchial epithelial cells (Beas-2B) were grown in serum-free medium lacking the growth supplements hydrocortisone and epinephrine (LHC-7HE). Mouse lung slice cultures were prepared by making precise 150-μm sections through agarose-infused intact mouse lungs, and cultured for up to two weeks in serum-free medium. Cultured cells or lung slice cultures were pretreated with one of several -agonists [salbutamol,10 M, (SB); salmeterol, 0.01–10 M, (SM)) alone or in combination with the steroid fluticasone propionate (1 M, (FP)] for one hour prior to challenge with a 5% solution of HDE for an additional 24 hours. Supernatant medium was assayed for human IL-6 and IL-8, or for murine IL-6, KC, MIP-2, and TNF- by ELISA. Cells were harvested for ICAM-1 expression

Rationale: Agricultural workers employed in concentrated animal feeding operations (CAFOs) are repeatedly exposed to aerosolized dust,

Results: Pretreatment of epithelial cells with the long-acting -agonist SM significantly inhibited the HDE-induced release of inflammatory cytokines both time- and dose-dependently (63%, IL-8; and 72%, IL-6, at 10 M SM; from 12 to 24 hours). Pretreatment with the steroid FP in combination with SM further decreased the proinflammatory effect. Likewise, mouse lung slice cultures treated with SM or the short-acting SB, alone and in combination with FP, exhibited a blunted response to subsequent 24-h HDE challenge for all four cytokines measured (a 48-71% decrement, depending on the cytokine measured). In addition, SB pretreatment markedly decreased the HDE-enhanced ICAM-1 surface expression on Beas-2B cells, whereas intracellular PKA activity was significantly increased.

Conclusions: Long-acting β-agonists alone, or in combination with steroids, are a potentially useful therapy for the treatment or prevention of chronic inflammatory lung disease in workers exposed to dust from CAFO buildings.

This abstract is funded by: R01OH008539 (DJR) & R0AA017993 (TAW)

by flow cytometry, and cell lysates were analyzed for protein kinase A (PKA) activity.

Am J Respir Crit Care Med 185;2012:A4656 Internet address: www.atsjournals.org

Online Abstracts Issue