Hydrogen Sulfide Prevents Cigarette Smoke-Induced Development of Hallmark Features of COPD in Mice and Interleukin-8 Production in Human Primary Bronchial Epithelial Cells

V. Kumar[1], J. Horvat[1], M. Whiteman[2], P. Hansbro[3]; [1]University of Newcastle, Newcastle, Australia, [2]University of Exeter Medical School, Exeter, United Kingdom, [3]School of Life Sciences, University of Technology Sydney, Sydney, Australia.

Corresponding author's email: vinodkumar@uon.edu.au

RATIONALE: The major risk factor in the development of chronic obstructive pulmonary disease (COPD) is cigarette smoke (CS). CS causes chronic lung inflammation that results in progressive and irreversible lung damage which consequently leads to the development of hallmark features of COPD. Thus, interventions preventing CS-induced inflammation could offer a novel treatment option for COPD and related lung diseases. COPD patients exhibit reduced levels of anti-inflammatory agents such as Hydrogen sulfide (H_2S) in serum and lung tissue. H_2S is produced endogenously through enzymatic reactions and maintains homeostasis by regulating inflammation and oxidative stress. CS exposure reduces the expression of H_2S synthases and consequently lower levels of H2S in mice. Inhibition of endogenous H_2S synthases exacerbates lung inflammation and injury, indicating that H_2S is essential for regulating lung inflammation. Additionally, in vitro supplementation of H_2S from an exogenous source prevents oxidative stress and release of pro-inflammatory mediators. We therefore propose that restoration of H_2S would prevent the development of CS-induced COPD in mice and release of pro-inflammatory mediators in human primary bronchial epithelial cells (hpBECs). To investigate this, we used hydrogen sulfide donor (H_2SD; AP39) in CS-induced mouse model of experimental COPD and differentiated hpBECs. METHODS: Female BALB/c mice were exposed to CS (12 cigarettes, 2x/day, 5 days/week) or air for 10 weeks and treated with (1.0 mg/kg/day, intranasal) of AP39. HpBECs obtained from healthy individuals were differentiated in culture conditions at air-liquid interface and treated with cigarette smoke extract (CSE; 10%) and AP39 (1μM) for 24 h, and media and CSE only served as controls. Lung inflammation was assessed by differential enumeration of leukocytes in bronchoalveolar lavage fluid. Pro-inflammatory mediators in lung tissue homogenate and culture supernatant were quantified using ELISA. Lung function was assessed using forced oscillations and forced manoeuvre techniques. RESULTS: Supplementing H_2S with AP39 significantly prevented CS-induced lung inflammation and aberrant lung function in mice. CSE-induced IL-8 production was significantly attenuated with AP39 treatment in hpBECs. CONCLUSION: Supplementation of H_2S from an exogenous source can be a potential treatment strategy against inflammation associated lung diseases.

This abstract is funded by: National Health and Medical Research Council (Australia)