Poster Number 77

Abstract 0240_0346_000059

Mechanisms for oxidative stress in response to allergen challenge

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Background:

Asthma is a chronic inflammatory disorder of the airways that affects over 16% of children under the age of 12 in Canada. Asthma is characterized by airway inflammation, remodelling, and oxidative stress. Although the lung has many antioxidant systems to blunt the negative effects of oxidative stress, these systems are overwhelmed in severe disease and we currently have no therapy's designed to support them. The glutathione system is an antioxidant vital to attenuating oxidative stress, which is altered in asthma and may play a role in the pathogenesis of the disease.

Objective:

Allergen induces oxidative stress that dysregulates the glutathione system in airway structural cells.

Methods:

Human airway epithelial, Calu-3, cells were incubated with increasing doses of house dust mite (HDM) and levels of reactive oxygen species (ROS) and oxidized lipids were measured using fluorescent markers. Abundance of key glutathione genes was measured using qPCR, in human airway smooth muscle (HASM) and Calu-3 cells after 24 hour incubation with HDM or oxidized lipids (OxPAPC). Total glutathione protein levels in HASM and Calu-3 cells were measured after a 4 hour incubation with OxPAPC. All experiments were completed in triplicate at minimum.

Results:

HDM induced rapid accumulation of ROS and lipid peroxides in Calu-3 cells with a 62.9% ($p<0.001$) and 26.9% ($p<0.001$) increase after 2 hours, respectively. While HDM didn't alter the abundance of genes for key glutathione enzymes after 24 hours, its product, OxPAPC significantly does. Furthermore, OxPAPC dose dependently decreased abundance of reduced glutathione with a 34% decrease at the highest dose, 160 µg/ml ($p<0.01$).

Conclusion:

HDM induces oxidative stress in structural cells of the airway, but has no effect, acutely, on the glutathione system, but a product of oxidative stress, OxPAPC resulted in large changes. This highlights a potential therapeutic avenue that augments the glutathione system ability to remove the oxidative stress products.