Airway Epithelial Paraoxonase-2 in Obese Asthma

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Background

Problem statement: Mitochondrial dysfunction is thought to play an important role in airway injury from oxidative stress in patients with asthma and obesity.

- Excessive production and insufficient clearance of mitochondrial reactive oxygen species (mtROS) produced in the TCA cycle is thought to lead to oxidative damage in this patient population
- Paraoxonase-2 (PON2), a mitochondrial matrix-bound antioxidant enzyme, potentially protects cell from excessive ROS production
- Quercetin, a naturally occurring flavonoid, has been shown to upregulate the expression of PON2 in vitro

Hypothesis: quercetin supplementation can increase levels of PON2 in bronchial airway cells, which can then provide therapeutic effects in patients with obesity and asthma by preventing oxidative damage.

Aims:

1) To determine if there is a significant difference in the levels of PON2 expression between patients with asthma and obesity and healthy controls.

2) To determine if there is any association between quercetin supplementation and PON2 expression and ROS production in bronchial airway cells.

Methods

- Bronchoscopy was performed to obtain bronchial epithelial cells from healthy volunteers and patients with asthma and obesity
- Cells were cultured for 21 days allowing them to differentiate into ciliated, mucosal cells
- PON2 levels were measured via Western Blot analysis
- ROS injury was induced by exposing cells to hydrogen peroxide and napthoquinone, before and after quercetin supplementation, and ROS production was measured by fluorescence and spectrophotometric analysis

Results

PON2 Levels In Bronchial Epithelial Cells

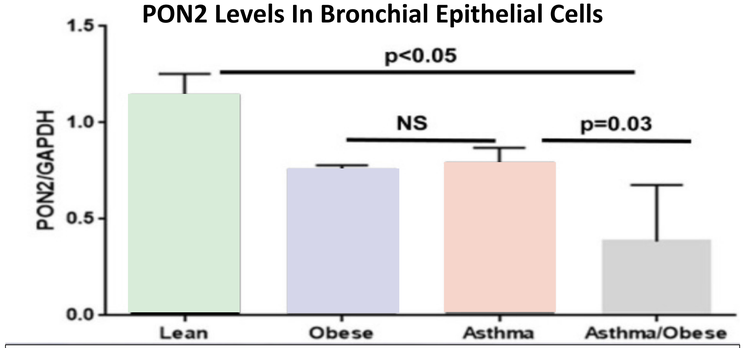

Figure 1. PON2 levels measured from patient's bronchial epithelial cells. Cells from patients with both asthma and obesity have the lowest PON2 levels

PON2 Levels After Quercetin Treatment

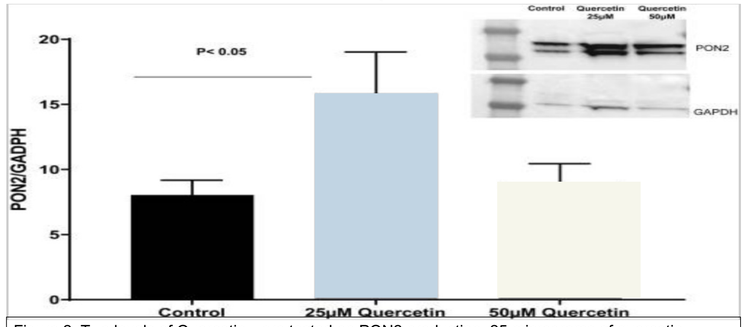

Figure 2. Two levels of Quercetin were tested on PON2 production. 25 micrograms of quercetin significantly increased PON2 levels as compared to control.

ROS Levels After Quercetin Treatment

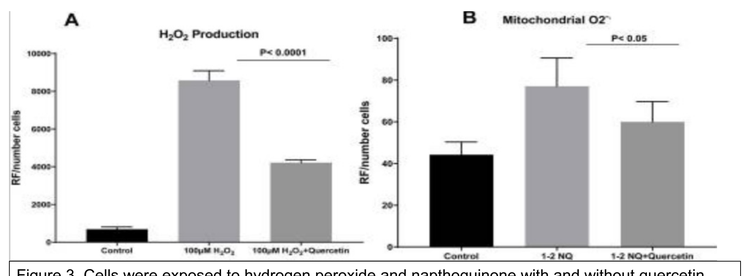

Figure 3. Cells were exposed to hydrogen peroxide and napthoquinone with and without quercetin supplementation. Cells with quercetin produced significantly less ROS

Summary

Person with Asthma / Obesity

- Mitochondrial Dysfunction
- ↓ PON2 production
- ↑ Mitochondrial ROS production

Quercetin supplementation

- ↑ PON2 production
- ↓ Mitochondrial ROS production

Oxidative stress and airway epithelial damage

Conclusion and Implications

- Patients with asthma and obesity have significantly decreased levels of PON2
- PON2 is important to mitigate the effects of ROS and protect against oxidative stress
- Quercetin can augment PON2 expression in bronchial epithelial cells
- Further studies are needed to determine a clinical correlation between quercetin supplementation and oxidative stress in patients with asthma and obesity
- These data with further research can lead to improved pharmacologic strategies to treat oxidative lung injury in patients with asthma and obesity
- Limitations: small sample size, results limited to in vitro data

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