Soluble Antioxidant Modulation of Ozone Induced Responses and Uptake Kinetics During Exercise.

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Background

- Ozone is a common pollutant in photochemical smog and is known to induce rapid shallow breathing, reduce respiratory capacity and increase breathing discomfort in humans.
- Response to ozone has been attributed to a number of factors including O3 distribution in airways, 1,2, reaction of O3 with the constituents of the respiratory tract lining fluid, 3 interaction of oxidized products with the lung epithelium, and the resulting release of inflammatory mediators due to oxidative stress induced by reactive oxidative products. 4,5

Hypothesis

- Supplementation with soluble anti-oxidants will attenuate the magnitude of the dose at onset of symptoms (DOS) in response to ozone (O₃) challenge and there will be a reduction in the pulmonary function decrements induced by O₃ exposure.
- Attenuation of the O₃ response is related to the contribution of these anti-oxidants in increasing the ability of the airway epithelium to withstand oxidative damage with no differences in the measured O₃ uptake between non-supplemented and anti-oxidant supplemented protocols.

Methods

- Subjects first provide consent and undergo preliminary pulmonary function testing in order to obtain medical clearance.
- Subjects take part in 4 exercise protocols: exercise workload determination, O₃ characterization to determine O₃ sensitivity, O₃ exposure with Placebo treatment, O₃ exposure with vitamin c and uric acid, "ANTiox", treatment
- 10 ozone-sensitive subjects will be identified as meeting all the inclusion criteria and continue to the exposure phase of the study.
- Study is double blinded and treatments are unmasked post-data analysis

Results

- Five subjects (n=5) have participated in the study to date. This includes completion of a workload protocol, an Ozone sensitivity characterization protocol, and both placebo and treatment protocols.
- Unmasking of the treatment order did not take place until after all protocols had been completed and final data analysis had been organized and completed.

Table 1. Preliminary baseline data as collected during the O₃ sensitivity characterization protocol for all subjects (n=5). Data is reported as the mean ± standard deviation of all participants.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Age (years)</th>
<th>Height (in)</th>
<th>Weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>27±10.71</td>
<td>165.68±17.07</td>
<td>63.76±16.34</td>
</tr>
<tr>
<td>Antioxidant</td>
<td>56.31±17.61</td>
<td>652.59±295.85</td>
<td>16.01±11.63</td>
</tr>
<tr>
<td>%ΔFEV₁, %ΔFVC</td>
<td>%ΔFEV₁/FVC</td>
<td>%ΔA FEV₁/FVC</td>
<td>%ΔA FVC</td>
</tr>
<tr>
<td>Placebo</td>
<td>-13.51±4.45</td>
<td>-16.87±4.36</td>
<td>4.04±4.33</td>
</tr>
<tr>
<td>Antioxidant</td>
<td>1260.88±268.73</td>
<td>680.33±142.38</td>
<td>64.45±13.53</td>
</tr>
</tbody>
</table>

Table 2. Comparison of the % change in FEV₁, FVC, and FEV₁/FVC from subjects calculated from pre and post protocol spirometry. The % change in frequency of breathing between pre- and post- DOS is also reported. Data represents mean ± SD.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Total O₃ Dose (µg)</th>
<th>DOSₙ₁</th>
<th>V₁ (l/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>1260.88±268.73</td>
<td>680.33±142.38</td>
<td>64.45±13.53</td>
</tr>
<tr>
<td>Antioxidant</td>
<td>1134.19±196.72</td>
<td>817.51±234.37</td>
<td>58.57±8.76</td>
</tr>
</tbody>
</table>

Table 3. Comparison of the Total Inhaled O₃ dose, the calculated dose at the onset of symptoms (DOSₙ₁) and the average minute ventilation (VE) during protocols. Data represents mean ± SD.

Figure 1. Schematic of the proposed two compartment model. Compartment 1 represents airway lining fluid while compartment 2 represents the production and elimination of inflammatory mediators of airway epithelium involved in neural activation.

Figure 2. Subjects ingest either the “Placebo” drink mix or the Vit-C containing “ANTiox” drink one hour prior to exercise. Spirometry data is collected before and after each protocol. Tidal volume Tᵥ, Breathing Frequency (fᵥ), and subjective symptoms are collected throughout the protocols.

Figure 3. Representative data analysis method from a single subject ozone characterization protocol. Figure 3a is a plot of cumulative breaths versus cumulative O₃ dose. Figure 3b represents the linear regression analysis as fitted to the data in 3a. Figure 3c represents the statistical comparison of the resulting linear regression output.

Figure 4. Example of treatment data comparison for one subject. Graphical data in a. and b. coincide with placebo treatment where an infection in the breathing response was identified as significant and occurred with a DOS of 449.35µg. Data in c. and d. represent a non-significant relationship where the infection identified at DOS = 130.79µg (interpreted due to noise in data). Visual inspection reveals an infection in the data in plot c. at ~900µg.

Conclusions

- Data suggests that the ANTIox treatment increases the dose of ozone at the onset of symptoms (DOS).
- Modification of the linear regression analysis may reveal infections in cumulative breath data that occur late in exposures.

References


Acknowledgements

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