

Airway Antioxidant Responses to Oxidative Air Pollution and Vitamin Supplementation

av

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Akademisk avhandling

som med vederbörligt tillstånd av rektorsämbetet vid Umeå universitet för
avläggande av medicine doktorsexamen
framläggs till offentligt försvar i Sal B, 9 trappor, Tandläkarhögskolan,
fredagen den 21 april 2006, kl.9.00.
Avhandlingen kommer att försvaras på engelska.

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Cuernavaca, Mexico



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Umeå University
Umeå 2006

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Document name

DOCTORAL DISSERTATION

Date of issue

April 21, 2006

Title

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Abstract

Air pollutants, such as ozone (O₃) and diesel exhaust particles, elicit oxidative stress in the lung. Antioxidants within the respiratory tract lining fluid (RTLFL) protect the underlying tissue from oxidative injury. Supplementation with vitamins has been shown to modulate the acute ozone-induced effects, but the mechanisms behind this have not been fully clarified.

The aim of this thesis was to investigate the airway responses to diesel exhaust and ozone exposure in healthy humans, with the emphasis on inflammatory and antioxidant responses. Furthermore, to study whether oral supplementation with vitamin C could increase ascorbate concentration in the RTLFL and whether vitamin supplementation could modulate the negative effects induced by ozone exposure. Diesel exhaust (100 µg/m³ PM₁₀ for 2h), evaluated 18 hours post exposure (PE), induced a neutrophilic airway inflammation and an increase in bronchoalveolar (BAL) urate and reduced glutathione. During O₃ exposure (0.2 ppm for 2h), significant losses of nasal RTLFL urate and ascorbate concentrations were observed. Six hours PE, a neutrophilic inflammation was evident in the bronchial wash (BW), together with enhanced concentrations of urate and total glutathione. In the bronchoalveolar lavage (BAL), where vitamin C, urate and glutathione concentrations were augmented, no inflammatory response was seen. In alveolar lavage leukocytes, there was a significant loss of glutathione and cysteine, whereas an increase in ascorbate was found in bronchial tissue samples.

Following supplementation with increasing doses of vitamin C (60-1,000 mg/day, for 14 days), evaluated 24 hours after the last dose, ascorbate concentrations were unchanged in the nasal RTLFL, despite elevated concentrations in plasma and urine. In contrast, following a single dose of 1g of vitamin C, vitamin C concentrations increased significantly in both plasma and nasal lavage two hours post supplementation, before returning to baseline levels at 24 hours. Notably, dehydroascorbate (DHA) accounted for the largest part of RTLFL vitamin C and a number of control experiments were performed to ensure the authenticity of this finding. Healthy O₃ responders were exposed to O₃ (0.2 ppm for 2 h) and air, following seven days of supplementation with vitamin C and E or placebo. No protective effect on lung function or airway inflammation was observed following supplementation. BW and BAL-DHA were enhanced after O₃, with further increases following supplementation.

In conclusion, oxidative air pollutants induce airway inflammation, as well as a broad spectrum of antioxidant adaptations, which could ultimately limit the airway inflammatory responses. Oral vitamin supplementation was shown to augment RTLFL-vitamin C concentrations, but it did not provide protection from the ozone-induced airway responses following a single insult of ozone. The finding of high concentrations of DHA in the RTLFL could indicate that DHA represents an important transport form of vitamin C onto the surface of the lung.

Key words: air pollution, ozone, diesel exhaust, airway inflammation, antioxidants, vitamin C, dehydroascorbate, vitamin supplementation.

Language: English

ISBN: 91-7264-040-5

Number of pages: 93 + 5 papers

Signature:

Date: March 31, 2006