

Lung permeability, antioxidant status and NO₂ inhalation: a selenium supplementation study in rats.

de Burbure C.Y.¹, Heiliger J.-F.¹, Nève J.², Becker A.³, Albrecht C.³, Borm P.J.A.³, Gromadzinska J.⁴, Wasowicz W.⁴, Ryzdinski K.⁴, Bernard A.M.¹

Introduction

Little is known about antioxidant status, selenium status in particular, and lung response to NO₂ which acts as a proinflammatory air pollutant. In this study, the effects of a low selenium diet (1.3µg Se/day) with or without selenium supplementation were studied in 128 two-month old male Wistar rats exposed to various concentrations of NO₂.

Materials and methods

Groups of Se-normal and Se-deficient rats were exposed to 1 or 10 ppm NO₂ 6 h/day, 5 days/week for 4 weeks (Groups I and II respectively, long-term exposures), 5 ppm for 6 h/day for 5 days (Group III, sub-acute exposure), 50 ppm for 30 minutes (Group IV, acute exposure) or used as controls breathing normal atmospheric air (Group V). Rats were sacrificed immediately after the experiment or 48 hours later in order to estimate recovery (see Table 1).

Table 1: NO₂ exposure conditions

NO ₂ Exposure conditions	Groups of rats	Total exposure to NO ₂		Se status	Recovery
		ppm	ppm days		
1ppm 28d 6h/d 5d/wk	I (4x8rats)	28	5	Se ⁺ /Se ⁻	0/48h
10ppm 28d 6h/d 5d/wk	II(4x8rats)	280	50	Se ⁺ /Se ⁻	0/48h
5ppm 5d 6h/d	III(4x8rats)	25	6.25	Se ⁺ /Se ⁻	0/48h
50ppm 30min	IV(2x8rats)	1.04	1.04	Se ⁺ /Se ⁻	0
Controls	V(2x8rats)	0	0	Se ⁺ /Se ⁻	0

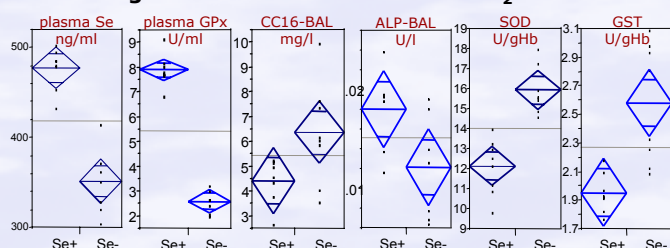
Se⁺: diets with normal selenium content
Se⁻: diets with low selenium

Along standard measurements of lipid peroxidation (TBARS, chemiluminescence), antioxidative enzymes (GPx, SOD, GST, Cp), lung damage (alkaline and acid phosphatases), lung permeability (total protein, albumin) and inflammation markers (cell populations), new biomarkers such as CC16 (Clara cell protein) were also determined, both in serum and in broncho-alveolar lavage fluid (BAL).

Results

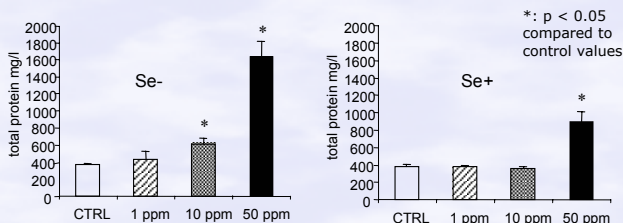
Selenium status did not only significantly influence GPx, SOD, GST, and even ALP activity prior to any NO₂ inhalation experiments, CC16 also showed unexpected changes, decreasing following selenium supplementation (Fig. 1).

Figure 1: Changes in plasma and BALF composition according to Selenium status before NO₂ inhalation.



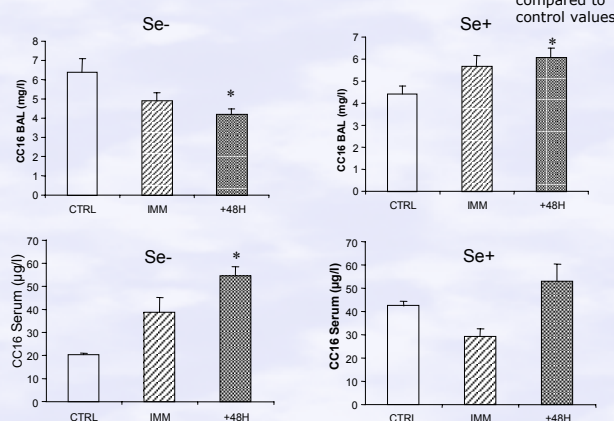
The protective role of normal selenium status with respect to NO₂ lung toxicity was evident both for long-term and acute exposures (Groups II and IV), as the increase in BALF-total proteins (and corresponding decrease in serum), indicating increased lung permeability, was significantly more pronounced in selenium-deficient animals compared to rats receiving adequate selenium (Figure 2).

Figure 2: Total protein concentrations found in BALF immediately following NO₂ inhalation experiments according to Selenium status.



Serum CC16 further confirmed its key role as an early marker of increased lung permeability during the various inhalation experiments (Figure 3).

Figure 3: CC16 mirror levels in BAL and serum following exposure to 1ppm NO₂ for 28 days and according to Selenium diet.



Conclusions

These findings confirm the important role of antioxidant status, and selenium status in particular, in the lung's own defense mechanisms such as the integrity of the alveolo-capillary barrier and the production of anti-oxidants like

CC16 when challenged by air pollutants such as NO₂.

However, in view of the unexpected decreased CC16 secretion observed in selenium-supplemented rats, further corroborated in the human studies of the BIOART project, one should exert caution when advocating selenium supplementation.

Further studies on the complex interactions of selenium and CC16 in their protective antioxidant properties in the lung are required as these would shed light on the important fields of lung disease, asthma and allergy.

¹ Unit of Industrial Toxicology and Occupational Medicine, Université Catholique de Louvain, 1200 Brussels, Belgium

² Institute of Pharmacy, Université Libre de Bruxelles, 1050 Brussels, Belgium

³ Particle Toxicology, Institut für Umweltmedizinische Forschung gGmbH (IUF), 40021 Düsseldorf, Germany

⁴ Department of Toxicology and Carcinogenesis, The Nofer Institute of Occupational Medicine, 90-950 Lodz, Poland

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