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ORIGINAL ARTICLE

Low alveolar and bronchial nitric oxide in severe uncomplicated obesity

Mauro Maniscalco[a,*], **Anna Zedda**[a], **Stanislao Faraone**[a], **Stefano Cristiano**[b], **Matteo Sofia**[c], **Andrea Motta**[d]

[a] *Section of Respiratory Medicine, S. Maria della Pietà Hospital, Casoria, Naples, Italy*
[b] *Department of Surgery, S. Maria della Pietà Hospital, Casoria, Naples, Italy*
[c] *Department of Respiratory Medicine, Monaldi Hospital, University Federico II of Naples, Italy*
[d] *Institute of Biomolecular Chemistry, National Research Council, Pozzuoli, Naples, Italy*

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KEYWORDS
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Summary
Background: Fractional concentration of exhaled nitric oxide (FeNO) is a recognized biomarker of the lower respiratory tract, where it is produced by the proximal conducting airways and the expansible peripheral bronchoalveolar compartment. We have previously shown that large increase in body mass decreases FeNO. Here we evaluated bronchial and alveolar components of the NO output of the lower respiratory tract in subjects with severe uncomplicated obesity (OB).
Methods: Fifteen OB subjects (BMI $45.3 \pm 5.6\,kg/m^2$), 15 healthy controls (HC) (BMI $22.4 \pm 2.4\,kg/m^2$) and 10 obese subjects who experienced weight loss after bariatric surgery (OBS) (BMI $31.2 \pm 3.4\,kg/m^2$), were examined. Anthropometry and respiratory lung tests were performed. Exhaled NO was assessed using multiple single-breath NO analysis at different constant expiratory flow rates. From the fractional NO concentration measured at each flow-rate, the total NO flux between tissue and gas phase in the bronchial lumen (J'awNO), and the alveolar NO concentration (CANO) were extrapolated.
Results: Measured FeNO levels at 50 mL/s were lower in OB compared with HC and OBS (11.6 ± 2.8 ppb, 18.0 ± 4.1 ppb and 17.6 ± 2.9 ppb, respectively, $p < 0.05$). In OB, both J'awNO and CANO resulted significantly lower than OBS and HC values.
Conclusions: Respiratory NO output is decreased in severe uncomplicated obesity for the reduction of both large/central airway maximal NO flux and alveolar NO

* Corresponding author at: Largo delle Mimose 1, 80131 Naples, Italy. Tel.: +39 0817411457; fax: +39 0817411457.
E-mail address: mauromaniscalco@hotmail.com (M. Maniscalco).

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concentration. The pathophysiological relevance of airway NO abnormalities in severe obese phenotype remains to be investigated.

Introduction

Fractional exhaled nitric oxide (FeNO) concentration is recognized as a useful biomarker of airway inflammation for many pulmonary diseases [1]. FeNO can be partitioned in its bronchial and alveolar components, which may represent the contribution to the NO respiratory output from both the proximal non expansible conducting airways compartment and the expansible alveolar small airways compartment [2]. Mathematical models and measurement of NO at different exhalation flow rates [2,3] partitioned peripheral (peripheral/small airway/alveolar NO concentration [CANO])and central (large/central airway maximal NO flux [J'awNO]) airways NO production. This approach requires a minimum of three exhalation flows, and both J'awNO and CANO are calculated by a linear regression analysis. The results provided information on abnormalities of the respiratory NO output in several diseases including asthma, allergic alveolitis, cystic fibrosis, scleroderma, allergic rhinitis, chronic obstructive pulmonary disease, and Sjögren's syndrome [3].

Some of the above diseases are often associated with obesity [4], which may influence single breath FeNO by interacting with changes in conducting airway and lung volumes [5,6]. Two main reasons are put forward: impaired systemic NO production and sub-clinical low-grade inflammation, and change in both airway and alveolar compartments with consequent changes in respiratory NO output. However, studies on exhaled NO in obesity have shown controversial results [7—9]. These results might be due to the reduction of NO concentration in lung periphery due to the large ''sink effect'' of the pulmonary circulation, and the high affinity of NO for haemoglobin [10], which may cancel out any change in NO production by the lung parenchyma.

To assess the origin of that abnormality within the respiratory tract, we performed extended FeNO analysis by multiple flow in severe obese subjects.

Materials and methods

Fifteen consecutive severe obese patients (OB), evaluated for bariatric surgery (Table 1) were studied. Exclusion criteria included: current smoking, respiratory infection within the past 3 weeks; atopy and/or chronic respiratory diseases; FEV_1/FVC ratio < 0.7; heart disease; sleep apnea syndrome; regular medications. Ten obese patients fulfilling the same exclusion criteria, who had undergone gastric banding for weight reducing at least 1 year before (OBS), and 15 healthy controls (HC) were also studied (Table 1). The study was approved by the local Ethic Committee and informed written consent was obtained from each patient. Patients were evaluated the first day with anthropometry, spirometry and pulse oximetry, and the second day with measurement of exhaled NO.

All anthropometric measurements were determined in the morning with the subjects wearing very light clothing. The body mass index (BMI) was calculated as the ratio of weight to height squared (kg/m^2).

Lung volumes and flow rates were determined using automated equipment (V Max 22 System SensorMedics, Milan, Italy) as previously described [8]. Recommendations for standardized procedures for various lung function tests were followed [11].

Exhaled NO measurement

Exhaled NO concentrations were measured by chemiluminescence (280 NOA Sievers Instruments, Boulder, Sensor Medics, Milan, Italy). Daily 2-point calibration was performed with an external zero filter (Zero Air Filter, Sievers) and a certified NO gas mixture at 1.01 ppm (SIAD Osio, Italy).

NO was exhaled using a 'restricted breath technique' following the method recommended for online measurement of the fractional exhaled NO concentration in adult [12]. All subjects performed a vital capacity manoeuvre and then a slow (20 s) exhalation against three separate resistances in turn while maintaining the same expiratory