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Titel:

Nitric Oxide Exchange in Central and Peripheral Airways: Determinants in Health and Respiratory Disease

Abstract:

Background: Exhaled nitric oxide (NO) is a marker of eosinophilic steroid-sensitive inflammation in the airways of patients with respiratory disease. Moreover, information about the localization of inflammation in the respiratory tree is obtained by estimates of bronchial and alveolar contributions to exhaled NO.

Aims: The main aim of this thesis was to identify the determinants of exhaled NO, as well as determinants of bronchial and alveolar contributions to exhaled NO in health and disease. Smoking history, degree of IgE sensitization and effects of modulating the pharyngo-oral tract production of NO were specifically studied in this context. Other specific aims were to determine the association of exhaled NO with the presence of asthma and pulmonary hypertension (PH).

Methods: Both population-based studies and experimental studies have been performed within the frame of the thesis. The population-based studies are based on data from the European Community Respiratory Health Survey II. NO measurements at several exhalation flow rates were performed in order to estimate alveolar and bronchial contributions to exhaled NO.

Results: Both current and previous smoking were associated with decreased exhaled NO and bronchial NO flux levels. Alveolar NO concentrations were decreased in current smokers. The degree of IgE sensitization was positively related to the levels of exhaled NO and its bronchial contribution. Exhaled NO appeared to be a more specific marker of allergic inflammation than of rhinitis or asthma. Both allergic and non-allergic asthma were associated with increased exhaled NO levels, but only in never-smoking persons. The estimated alveolar NO increased after ingestion of nitrate in individuals with high nitrate turnover in the pharyngo-oral tract. Pulmonary arterial hypertension, but not other forms of PH, was associated with decreased bronchial NO flux, whereas PH of all etiologies was related to increased alveolar NO concentrations.

Conclusion: Smoking history and IgE sensitization, that are known determinants of exhaled NO, affected the bronchial and alveolar contributions to exhaled NO differently. The limitations of the simple NO pulmonary exchange models were highlighted by the paradoxical effects on estimated alveolar NO when modulating the NO production proximally, in the pharyngo-oral tract. Predominance of non-eosinophilic inflammation in ever-smoking patients with asthma could explain the poor association between the presence of asthma and exhaled NO in these patients. Different pathophysiological changes in terms of bronchial NO production and exchange were related to the etiology of pulmonary hypertension.

Disputation:
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