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ORIGINAL ARTICLE

Comparison of Nasal Nitric Oxide Levels between the Inferior Turbinate Surface and the Middle Meatus in Patients with Symptomatic Allergic Rhinitis

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ABSTRACT

Background: Because of the anatomical complexity and the high output of the human nose, it has been unclear whether nasal nitric oxide (NO) serves as a reliable marker of allergic rhinitis (AR). We examined whether nasal NO levels in the inferior turbinate (IT) surface and the middle meatus (MM) differ in symptomatic AR patients.

Methods: We measured fractional exhaled NO (FeNO) and nasal NO in normal subjects (n = 50) and AR patients with mild symptoms (n = 16) or moderate or severe symptoms (n = 27). Nasal NO measurements were obtained using an electrochemical analyzer connected to a catheter and an air-suction pump (flow rate 50 mL/sec).

Results: Compared to the normal subjects, the AR patients showed significantly higher nasal FeNO and nasal NO levels in the IT area. No significant difference in the MM area was observed among the three groups. The MM area showed higher NO levels than the IT area in all three groups. The ratio of nasal NO levels of the MM area to the IT area (MM/IT ratio) was significantly lower in the AR groups. The moderate/severe AR patients showed significantly higher nasal NO in the IT area (104.4 vs. 66.2 ppb) and lower MM/IT ratios than those in the mild AR patients. The analysis of nasal brushing cells revealed significantly higher eosinophil cationic protein and nitrotyrosine levels in the AR groups.

Conclusions: Nasal NO assessment in the IT area directly reflects persistent eosinophilic inflammation and may be a valid marker to estimate the severity of AR.

KEY WORDS

allergic rhinitis, exhaled nitric oxide, inferior turbinate, nasal nitric oxide, nitrotyrosine

ABBREVIATIONS

AR, allergic rhinitis; ECP, eosinophil cationic protein; FeNO, fractional exhaled nitric oxide; IT, inferior turbinate; MM, middle meatus; NO, nitric oxide; NT, nitrotyrosine; NOS, nitric oxide synthase; ppb, parts per billion.

INTRODUCTION

The standardization of measuring techniques by the American Thoracic Society/European Respiratory Society (ATS/ERS) has opened the way for the collection of comparable airway data on nitric oxide (NO) in normal subjects and those with disease states.[1,2] Allergic rhinitis (AR) has been considered to be asso-

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ciated with increased NO levels. However, it has not yet been determined whether nasal NO serves as a reliable index of disease severity, or to what extent NO concentrations inside the nose contribute to pathologies of AR.[3-5] Nasal NO is not routinely measured in daily clinical practice. One reason may be the heterogeneous results found in previous studies, mainly due to the complexity of the anatomical and physiological features of the human nose and the lack of consensus concerning the suitable measurement technique.[6-8]

In the present study, the fractional exhaled nitric oxide (FeNO) and nasal NO levels were examined in a population of normal subjects and AR patients. We used a newly designed method to measure nasal NO locally based on the anatomical features of the nasal cavity. For this purpose, the NO analyzer was connected to a suction catheter and a fixed-quantity suction pump in an out-patient clinic setting. The handheld device with an electrochemical sensor for nasal NO measurement has been shown to be reliable and simple to use at a lower cost.[9,10]

Here we examined whether local gradients of NO concentration in different areas inside the nasal cavity differ among normal subjects and AR patients classified by subjective symptom severity. We also obtained nasal brushing cells from the surface of the inferior turbinate mucosa and analyzed the concentrations of the extracted inflammatory mediators related to eosinophil activation and NO metabolism. We note that the nasal NO assessment described here is noninvasive, quickly performed, and may directly reflect the degree of allergic inflammatory conditions adjacent to the surface mucosa of the inferior turbinate.

METHODS

SUBJECTS

Ninety-three subjects were included in this cross-sectional, between-group and method comparison study. The subjects were 43 patients with perennial AR without bronchial asthma (28 males and 15 females; mean age 27.7 years) and 50 normal volunteers without nasal symptoms (30 males and 20 females; mean age 32.1 years). The AR patients were recruited on an outpatient setting and subdivided into two groups based on disease severity: the group of 16 patients with mild symptoms (mild group) and the group of 27 patients with moderate or severe symptoms (moderate/severe group).

The diagnosis of AR was based on clinical history, the presence of subjective nasal symptoms together with positive nasal eosinophil tests, and positive skin reactions or serum allergen-specific IgE antibody measurements against house dust mites. Nasal endoscopy was performed for all subjects before measuring nasal NO in order to assess the degree of nasal septum deviation and patency of middle meatus, and to exclude the presence of nasal polyposis. We excluded current-smokers and patients who had been treated with any allergen-specific immunotherapy. The patients did not receive any anti-allergic medication in the 30 days before the study. The patients' subjective symptoms were recorded at the time of the NO measurement. They include the average number of paroxysmal sneezing, episodes of nose blowing, and the degree of nasal blockage. The severity of the disease was then determined as mild, moderate or severe based on the classification proposed by the Japanese guideline for allergic rhinitis.[11]

The study protocol was approved by the Institutional Review Board at the Hiroshima University School of Medicine (Project approval #181-1). The purpose of the research and experimental protocols was explained to all participants, and written informed consent was obtained prior to the study.

NITRIC OXIDE MEASUREMENTS

The subjects' NO levels were measured using a handheld electrochemical analyzer (NObreath®, Bedfont Scientific, Rochester, UK) according to the ATS/ERS guidelines.[1] For the oral FeNO measurements, the subjects exhaled at a flow rate of 50 mL/s through a mouthpiece assisted by visual cues. For the nasal FeNO measurements, the subjects were instructed to exhale transnasally with their mouth closed into a nose adaptor at the same flow rate, as described.[12] The nasal FeNO measurements were carried out for the right and left nasal cavities separately, with the other nostril closing in turn. We also measured nasal NO in all of the subjects by directly aspirating air from the nasal cavity. For this purpose, the NO analyzer was connected to a suction catheter via a sterile syringe filter and a portable air-suction pump (MP-Σ300N, Sibata Science, Saitama, Japan), which could be set at constant flow levels (Fig. 1). The aspiration flow rate was fixed at a rate of 50 mL/sec, and the tip of the catheter was placed inside the nasal cavity under direct vision during the sampling period. Two different target areas were set based on the anatomical features of the nasal cavity, i.e., near the anterior surface of the inferior turbinate (IT area) and the front of the middle meatus (MM area). The subjects were advised to breathe through the mouth with their soft palate elevated to cease the choanal airflow. Nasal NO levels were measured separately for the left and right side, leaving the other nostril open, in alignment with ATS recommendations.[1] The measurements were performed in the same clinic under constant environmental conditions. The measurement was repeated three times and the mean value was used for analysis.

NASAL CELL SAMPLING

Nasal brushing cell specimens were obtained for an enzyme-linked immunosorbent assay (ELISA) from 27 of the 50 normal subjects and 31 of the 43 AR pa-