

Allergen avoidance is associated with a fall in exhaled nitric oxide in asthmatic children

Giorgio L. Piacentini, MD,^a Alessandro Bodini, MD,^a Silvia Costella, PhD,^b Lucia Vicentini, PhD,^a Diego Peroni, MD,^a Luisa Zanolla, MD,^c and Attilio L. Boner, MD^a
Verona and Belluno, Italy

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In allergic asthmatic children the efficacy of allergen avoidance is reflected by improvement of disease indicators, including symptoms, medication requirements, pulmonary function, and bronchial hyperresponsiveness.¹

The aim of this study was to evaluate whether exhaled nitric oxide (FE_{NO}), a marker of airway inflammation in asthma,² can be used for evaluating the effect of house dust mite (HDM) avoidance in allergic asthmatic patients.

METHODS

Patients

Twenty asthmatic children (6 to 15 years) sensitized to HDM were evaluated at the Istituto Pio XII (Misurina BL, Italy) at 1756 m on the Italian Alps. None of them had respiratory infections in the 2 months before and during the study period.

The study was approved by the local ethics committee, and both children and their parents gave informed consent.

Study design

The children had been living with their families for at least 3 months before admission to the residential home (T0). FE_{NO} was measured daily, always at the same hour, for 2 weeks after T0 (day 15 = T1), after 3 months at the residential home (T2), and, in 10 of the 20 patients, 2 weeks after their return to sea level (T3). FEV₁ and forced expiratory flow, midexpiratory phase were measured at T0, T1, T2, and T3. Serum eosinophil cationic protein (ECP) was measured at T0, T2, and T3.

Thirteen of the 20 patients were receiving regular courses of inhaled steroids at T0. Treatments were kept constant until T1 and then gradually withheld in all subjects in the month after T1.

FE_{NO} measurement

FE_{NO} measurements were performed by using a chemiluminescence analyzer (Logan LR 2149; Rochester, Kent, UK),² which was calibrated daily. The subjects performed a slow exhalation against a

Abbreviations used

FE_{NO}: Exhaled nitric oxide
HDM: House dust mite
T0: Before admission to residential home
T1: Two weeks after T0
T2: Three months at residential home
T3: Two weeks after return to sea level

resistance at 5 to 6 L/min steady flow. Nitric oxide value was measured at the plateau of the end-exhaled reading and expressed in parts per billion.²

ECP measurement

ECP was measured in duplicate by means of Pharmacia CAP System R ECP FEIA (Pharmacia & Upjohn, Uppsala, Sweden). The interassay and intra-assay coefficients of variation were less than 8%, and the detection limit was 0.5 µg/L.

Statistical analysis

Because FE_{NO} data presented significant deviation from normality ($P < .0001$), as determined by the Shapiro-Wilk test, they were log-transformed. After log-transformation, FE_{NO} values did not deviate from normal values. The comparison among the values at times T0, T1, and T2 was performed by using a repeated-measures ANOVA (SAS GLM Procedure, Version 6, SAS Institute Inc), with a profile transformation for testing within-subject variations. The comparison for ECP was performed by using the Wilcoxon signed-rank test. The comparison between values at T2 and T3 was performed by using the paired *t* test with log-transformed values of FE_{NO}.

RESULTS

The mean levels of HDM group 1 (Der p 1 and Der f 1) antigen in the dust from beds were 13.8 and less than 0.05 µg/g of dust in the family houses and in the residential home, respectively, as measured by means of ELISA.³

FE_{NO} decreased ($P = .014$ at T1) with a significant effect of the time in the first 2 weeks ($P = .0026$), remained unchanged from T1 to T2, and at T3 returned approximately to T0 level ($P = .004$, T2 vs T3; Fig 1).

FEV₁ improved gradually (T0 = 2.006 ± 0.42 L/min; T1 = 2.0075 ± 0.43 L/min; T2 = 2.112 ± 0.63 L/min; at T2 $P = .0017$) and continued after T2 (T3 = 2.496 ± 0.63 L/min; $P = .0035$, T2 vs T3).

No change in serum ECP level was observed throughout the study period (T0 = 16.175 ± 12.699 µg/L; T2 = 16.017 ± 13.558 µg/L; and T3 = 14.355 ± 7.09 µg/L).

From ^aClinica Pediatrica, Università di Verona, Verona; ^bIstituto Pio XII, Misurina, Belluno, ^cthe Department of Cardiology, Università di Verona, Verona.

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Reprint requests: Giorgio L. Piacentini, MD, Clinica Pediatrica, Policlinico Borgo Roma, 37134 Verona, Italy.

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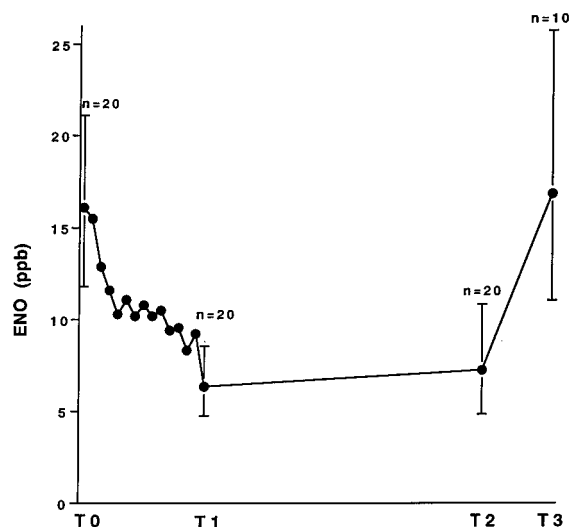


FIG 1. Changes in FE_{NO} levels (geometric mean and upper and lower limits of confidence intervals) during the periods of antigen avoidance and exposure. *n*, Number of subjects at each time of the study.

DISCUSSION

The results of this study suggest that FE_{NO} is modifiable by changes in environmental conditions in asthmatic children. A reduction in other inciters of asthma (eg, air pollution, passive smoke exposure, viral infection, or stress) could also have caused the fall in FE_{NO}, although we believe that HDM reduction is the major factor.

After a significant reduction in the first 2 weeks of avoidance, FE_{NO} did not significantly change from T1 to T2, despite the withdrawal of steroids. Because FE_{NO} is modulated in a dose-response fashion by inhaled steroids,⁴ it is tempting to speculate that the expected increase in FE_{NO} after stopping steroid treatment could

have been opposed by the beneficial effect of HDM avoidance in our study.

FEV₁ required a longer period of avoidance to be modified. Furthermore, the ongoing improvement in FEV₁ during re-exposure while nitric oxide levels increased strengthen the idea that FEV₁ should not be considered a promptly modifiable indicator of antigen avoidance.

To our knowledge, this is the first study suggesting that FE_{NO} can represent a sensitive marker of antigen avoidance in allergic asthmatic children.

In the case of allergen avoidance strategies, the most critical question is whether these strategies can reduce the severity of the disease and not just whether the actual level of allergen is reduced. Because airway inflammation is the most characteristic feature of asthmatic patients, and FE_{NO} is considered to reflect the level of airway inflammation,^{2,5} we believe that this marker could be proposed to predict the outcome of allergy avoidance regimens.

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