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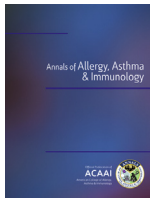

The importance of atopy on exhaled nitric oxide levels in African American children

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ABSTRACT

Background: For physicians to be maximally effective in managing asthma in minority populations, a better understanding of the factors that affect fractional exhaled nitric oxide (FeNO) measurements in African Americans is needed.

Objective: To examine demographic, environmental, and physiologic factors that influence FeNO measurements in African American children with and without asthma.

Methods: A cross-sectional study of 128 African American children aged 7 to 18 years (44% with asthma) was conducted. FeNO measurements, skin prick tests (as a measure of atopy), spirometry, and questionnaire data were obtained from all participants. Regression models were constructed after identifying factors significantly associated on univariate analysis.

Results: Among all study participants, the mean FeNO measurement at baseline was 24.4 ppb. Children with asthma had a higher level than those without (30.9 vs 19.3 ppb, $P = .002$). When examining all children through logistic regression analysis, an elevated FeNO level was significantly associated with atopy, lower spirometric values, and current asthma ($P < .05$ for all). Among asthmatic children, univariate analysis revealed that an elevated FeNO level was associated with inhaled corticosteroid use, recent respiratory infection, and atopy ($P < .05$ for all). However, only atopy remained significant after regression analysis. For asthmatic and nonasthmatic children, FeNO levels were directly correlated with the number of positive skin test results.

Conclusion: In African American children with and without asthma, FeNO levels are strongly influenced by atopy. Guidelines for FeNO measurements that incorporate atopic status are needed.

Introduction

Fractional exhaled nitric oxide (FeNO) has emerged as a potential biomarker for eosinophilic airway inflammation. Eosinophils are thought to release cytokines and additional inflammatory mediators, which in turn stimulate epithelial cells to produce nitric oxide.[1–3] Patients with eosinophilic asthma often have elevated FeNO levels during an exacerbation, and these levels may normalize after treatment with glucocorticoids.[4–6] Compared with spirometry and peak expiratory flow readings, some studies have found that FeNO may be a better predictor of response to corticosteroid treatment.[7,8] In addition, FeNO measurements are noninvasive and can be readily obtained in clinical practice.

Despite its potential advantages, appropriate clinical application of FeNO measurements remains ambiguous. The American Thoracic Society has recommended specific FeNO levels to guide patient care in asthma management.[9] Clinical use of exhaled nitric oxide, however, has yielded conflicting results. Although some studies have found no benefit in using FeNO measurements,[10,11] another trial found that using an FeNO-based algorithm lowered exacerbation rates and mean dose of inhaled glucocorticoids.[12] Although varying study designs may have contributed to the inconsistent results, confounding factors likely influenced FeNO measurements and outcomes. Previous studies have suggested that age, atopy, cigarette smoking, air pollution exposure, and upper respiratory tract infections (URIs) may affect FeNO levels.[13] Differences in race and ethnicity may also influence FeNO levels in both children and adults.[14,15] Therefore, a better understanding of specific factors that influence FeNO levels is critical to enhance its clinical value.

Some authors have suggested that an incomplete understanding of airway pathophysiology and genetics contributes to inadequate, incorrect, and ineffective asthma treatment strategies.[16–18] This knowledge gap amplifies the health disparities seen in asthma because minority populations may have different pathophysiologic properties and therapeutic responses.[18–20] The prevalence rates for current asthma in the United States indicate that 9.3% of children have asthma, although this rate is 16.0% among African American

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Table 1
Characteristics of the study participants[a]

Characteristic	All children (n = 128)	Asthmatic children (n = 56)	Nonasthmatic children (n = 72)	*P* value[b]
Age, mean (SD), y	11.8 (3.1)	11.5 (3.1)	12.1 (3.0)	.26
Female	66 (51.6)	19 (33.9)	47 (65.3)	<.001
BMI, mean (SD)	21.9 (5.9)	21.1 (5.4)	22.5 (6.2)	.21
Overweight or obese	33 (25.8)	11 (20.8)	22 (31.0)	.20
Allergies or hay fever	47 (36.7)	34 (60.7)	13 (18.1)	<.001
Eczema	44 (34.4)	28 (50.0)	16 (22.2)	.001
URI in 2 weeks	40 (31.3)	20 (35.7)	20 (27.8)	.34
Home smoke exposure	47 (36.7)	22 (39.3)	25 (34.7)	.60
Atopic sensitivity	79 (61.7)	43 (76.8)	36 (50)	.002
FEV_1, mean (SD), % predicted	97.4 (17.7)	95.7 (17.7)	98.7 (17.7)	.36
FEV_1/FVC, mean (SD)	87.3 (7.7)	86.3 (8.1)	88.0 (7.4)	.20
FeNO, mean (SD)	24.4 (20.7)	30.9 (26.0)	19.3 (13.0)	.002
Elevated FeNO	15 (11.7)	11 (21.2)	4 (6.0)	.01

Abbreviations: BMI, body mass index; FeNO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; URI, upper respiratory tract infection.
[a]Data are presented as number (percentage) of children unless otherwise indicated.
[b]*P* value is for comparison between those with and without asthma.

children.[21] Unfortunately, severity and disease control are also significantly worse in this group. For example, the 2010 age-adjusted hospitalization rate among whites in Michigan was 11.2 per 10,000 people, whereas for blacks it was 45.1 per 10,000.[22] A more complete understanding of the factors that influence FeNO measurements in African American children is needed for physicians to be maximally effective in its treatment. The goal of this study was to examine demographic, environmental, and physiologic factors that influence FeNO measurements in African American children and adolescents and specifically in those with asthma.

Methods

Participants and Protocol

Participants were self-identified African American children (with and without asthma) seen at a general pediatric clinic in Ypsilanti, Michigan (a city where one-third of the population is African American, and the median income is $31,469). Children were 7 to 18 years old at the time of enrollment. Participants with any known cardiac or pulmonary condition other than asthma were excluded. Children and their parents or guardians were provided a questionnaire (see below) and underwent FeNO measurement, skin prick testing for common inhalant allergens, and spirometric testing. Participants were recruited through the use of flyers posted throughout the clinic. The entire study protocol was approved by the University of Michigan Institutional Review Board, and written informed consent was obtained from all participants.

Baseline Measurements

A questionnaire administered to all study participants assessed the following information: sex, home smoke exposure, weight, body mass index (BMI), URIs within the past 2 weeks, and physician diagnosis of allergy, asthma, or eczema. Patient with current asthma also provided asthma-specific information: current medications, prior history of intensive care unit stay or intubation for asthma, and hospitalization, emergency department, or urgent care visits in the previous year for an asthma exacerbation. Asthma quality of life was assessed with the Mini Pediatric Asthma Quality of Life Questionnaire (PAQLQ),[23] and asthma control was determined by the Asthma Control Questionnaire (ACQ).[24]

All study patients with and without asthma performed spirometric measurements. The test was performed according to the American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines.[25] Both the forced expiratory volume in 1 second (FEV_1) and the ratio of FEV_1 to forced vital capacity (FVC) were recorded as percent predicted for age, height, sex, and ethnic origin. Skin prick testing was also performed for all study participants. This was accomplished using a panel of common allergens: house dust mite mix, grass mix, tree mix, weed mix, mold mix, and cockroach, cat, and dog epithelia. ComforTen lancets were used (Hollister-Stier Allergy, Spokane, Washington). The wheal diameter was recorded at 15 minutes, and the test result was interpreted positive if the wheal was at least 3 mm greater than the saline control.[26] Participants were classified as atopic if any of the 8 allergens were apparent on skin prick testing.[27]

To obtain FeNO measurements, the online single-breath method was used with the NIOX MINO device (Aerocrine Inc, Morrisville, North Carolina), according to ATS/ERS guidelines.[28] This device uses a dynamic flow controller to ensure an exhalation flow rate of 50 mL/s. Each participant underwent coaching of the proper method before taking the measurements. As specified by the ATS guidelines, an FeNO measurement was considered elevated if the value was 35 ppb or more for children between the ages of 7 and 11 years and 50 ppb or more for children between the ages of 12 and 18 years.[9]

Statistical Analysis

Bivariate calculations for demographic information between those with and without asthma were obtained using a *t* test or Mann-Whitney test as appropriate. Next, associations with FeNO levels analyzed as a continuous variable were made using Pearson correlations or *t* tests for variables that were continuous or dichotomous, respectively. FeNO was also analyzed as a dichotomous outcome (elevated or normal), using a χ^2 test or *t* test for

Table 2
Asthma features

Feature	No (%) of asthmatic children (n = 56)[a]
Use of ICS	21 (37.5)
Use of ICS and LABA	7 (12.5)
Use of montelukast sodium	11 (19.6)
ACQ score, mean (SD)	1.3 (1.23)
PAQLQ, mean (SD)	5.4 (1.4)
History of ICU stay	7 (12.5)
History of intubation	5 (8.9)
Hospitalization, ED visit, or UC visit in past year	15 (26.8)
Has asthma action plan	37 (66.1)

Abbreviations: ACQ, Asthma Control Questionnaire; ED, emergency department; ICS, inhaled corticosteroid; ICU, intensive care unit; LABA, long-acting β-agonist; PAQLQ, Pediatric Asthma Quality of Life Questionnaire; UC, urgent care.
[a]Data are presented as number (percentage) of children unless otherwise indicated.