Race is associated with differences in airway inflammation in patients with asthma

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Background: African American subjects have a greater burden from asthma compared with white subjects. Whether the pattern of airway inflammation differs between African American and white subjects is unclear.

Objective: We sought to compare sputum airway inflammatory phenotypes of African American and white subjects treated or not with inhaled corticosteroids (ICSs; ICS+ and ICS−, respectively).

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Methods: We performed a secondary analysis of self-identified African American and white subjects with asthma enrolled in clinical trials conducted by the National Heart, Lung, and Blood Institute–sponsored Asthma Clinical Research Network and AsthmaNet. Demographics, clinical characteristics, and sputum cytology after sputum induction were examined. We used a sputum eosinophil 2% cut point to define subjects with either an eosinophilic (≥2%) or noneosinophilic (<2%) inflammatory phenotype.

Results: Among 1018 participants, African American subjects (n = 264) had a lower FEV_1 percent predicted (80% vs 85%, $P < .01$), greater total IgE levels (197 vs 120 IU/mL, $P < .01$), and a greater proportion with uncontrolled asthma (43% vs 28%, $P < .01$) compared with white subjects (n = 754). There were 922 subjects in the ICS+ group (248 African American and 674 white subjects) and 298 subjects in the ICS− group (49 African American and 249 white subjects). Eosinophilic airway inflammation was not significantly different between African American and white subjects in either group (percentage with eosinophilic phenotype: ICS+ group: 19% vs 16%, $P = .28$; ICS− group: 39% vs 35%, $P = .65$; respectively). However, when adjusted for confounding factors, African American subjects were more likely to exhibit eosinophilic airway inflammation than white subjects in the ICS+ group (odds ratio, 1.58; 95% CI, 1.01-2.48; $P = .046$) but not in the ICS− group ($P = .984$).

Conclusion: African American subjects exhibit greater eosinophilic airway inflammation, which might explain the greater asthma burden in this population. (J Allergy Clin Immunol 2017;140:257-65.)

Key words: *Asthma, race, eosinophil, airway inflammation, African American, body mass index, corticosteroid, induced sputum, clinical trial*

African American subjects have a higher prevalence of asthma than white subjects and a greater burden of morbidity and mortality, with rates of asthma-related emergency department visits, hospitalizations, and death being approximately 2 to 3 times the rates observed in white subjects.[1,2] Many factors, including asthma severity, differences in access to health care, and environmental exposures, have been implicated as causes of race-related variations in asthma burden.[3-8] Studies that have controlled for these factors have still found higher asthma-related emergency department visits, hospitalizations, and death from asthma among African American subjects.[9-11] Results of some studies suggest that African American subjects can have reduced responsiveness to some asthma therapies, including inhaled corticosteroids (ICSs), compared with white subjects, suggesting biological differences in asthma between these groups.[12-15] The basis for race-related differences in asthma burden and treatment responsiveness is not well understood.

Airway inflammation is a key cornerstone of asthma pathogenesis and is mediated by numerous inflammatory cells that infiltrate the airways, including eosinophils, neutrophils, type 2 lymphocytes, basophils, and mast cells.[16] By counting these inflammatory cells in induced sputum, airway inflammation in asthmatic patients has been characterized as either eosinophilic (≥2% eosinophils) or noneosinophilic (<2% eosinophils).[17-19] Emerging evidence suggests that differences in airway inflammatory phenotype can affect response to asthma therapies.[20-22] In one study subjects with noneosinophilic asthma had an impaired response to treatment with oral and high-dose ICSs compared with those with eosinophilic asthma.[20] Relatively few African American patients with asthma (21/158 patients) were included in this study, and therefore it remains unclear whether differences in airway inflammation could explain, at least in part, the observed race-related disparities in asthma burden.[20]

These considerations led us to ask the following question: Are there differences in the prevalence of eosinophilic versus noneosinophilic airway inflammatory phenotypes in African American versus white patients with asthma? Because ICS use can improve asthma control and modify the observed airway inflammatory phenotype, we compared the clinical characteristics and airway inflammation phenotypes in African American and white subjects separately in patients receiving (ICS+) and off (ICS−) ICS treatment.

Abbreviations used

ACQ: Asthma Control Questionnaire
ACRN: Asthma Clinical Research Network
ACT: Asthma Control Test
BMI: Body mass index
ICS: Inhaled corticosteroid
SLIMSIT: Salmeterol and Leukotriene Modifiers vs. Salmeterol and ICS Treatment
SMOG: Smoking Modulates Outcomes of Glucocorticoid Therapy in Asthma
SOCS: Salmeterol Off Corticosteroids

METHODS

Study population

The study population consisted of self-reported African American or white patients with asthma enrolled in 10 clinical trials conducted by the National Heart, Lung, and Blood Institute–sponsored Asthma Clinical Research Network (ACRN) and AsthmaNet (see Fig E1 and Table E1 in this article's Online Repository at www.jacionline.org) that included at least 1 sputum induction as part of the study protocol.[23-32] The data were collected as part of the clinical trials that had been reviewed and approved by institutional review boards at all participating ACRN and AsthmaNet centers, and all subjects provided written informed consent. The University of Illinois Institutional Review Board deemed the secondary analyses in this report to be exempt from human subject review.

All subjects were aged 12 years or older; met the criteria for mild or moderate persistent asthma, as defined by the National Asthma Education and Prevention Program Guidelines for the Diagnosis and Management of Asthma; were current nonsmokers with a lifetime history of smoking no greater than 10 pack years; and had not smoked within the past 12 months (see Table E1).[33] In addition, all subjects had to have either (1) a positive methacholine challenge result with a provocative concentration for a 20% decrease in FEV_1 of less than or equal to 16 mg/mL in ICS+ subjects or less than or equal to 12 mg/mL in ICS− subjects or (2) a postbronchodilator increase in FEV_1 of 12% or greater. Sputum eosinophils were the chosen inflammatory marker for this study because evidence supports that differences in airway inflammatory phenotype affect asthma exacerbations and response to asthma therapies.[20,21] Sputum induction data and corresponding clinical data were only included when ICS use or nonuse was known and standardized as part of the study protocols. Subjects in the ICS+ group were receiving ICSs (fluticasone equivalent dose range, 80-400 μg/d) for at least 4 weeks before sputum assessment. Those in the ICS− group had not been treated with ICSs for at least 6 weeks before the time of sputum assessment. In the ICS− group patients using a leukotriene-modifying agent in the 4 weeks before sputum induction or clarithromycin