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Ethnic Variation in Response to IM Triamcinolone in Children With Severe Therapy-Resistant Asthma

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BACKGROUND: Although ethnicity may influence response to treatment of patients with asthma, this approach is controversial. The objective of this study was to determine if ethnicity influences the response to IM steroid use (eliminating adherence as an issue).

METHODS: Children with severe therapy-resistant asthma who had previously undergone a detailed assessment (including a nurse-led hospital and home visit in which potentially modifiable factors had been identified and addressed) were admitted for further evaluation; this evaluation included assessment of steroid response. Children were classified as white, black, Asian, or mixed white/black. Steroid responsiveness was defined according to symptoms (Asthma Control Test), inflammation (sputum eosinophil count and exhaled nitric oxide), and spirometry (FEV_1); these variables were measured before and 4 weeks after IM triamcinolone use. Data were collected regarding exacerbations. Fractional exhaled nitric oxide (FENO) response was defined as a decrease to < 24 parts per billion (ppb).

RESULTS: Seventy-nine subjects were identified (white, n = 54 [68%]; black, n = 16 [20%]; Asian, n = 5 [6%]; and mixed white/black, n = 4 [5%]). After administration of triamcinolone, there was a significant drop in median FENO in white children (46.8 to 23.1 ppb; $P < .001$) but not in black children (52.2 to 34.5 ppb; $P = .58$). More black children than white children (86.7%) were FENO nonresponders (86.7% vs 45.3%; $P < .05$), and more black children had exacerbations compared with white children (61% vs 17%; $P < .05$).

CONCLUSIONS: Black children with asthma were less likely to report an FENO response and had more exacerbations 4 weeks after administration of triamcinolone than white children. Further research is needed to understand the mechanisms of these differences, but they cannot be due to differences in adherence or access to care.

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KEY WORDS: corticosteroids; ethnicity; pediatric asthma

ABBREVIATIONS: ACT = Asthma Control Test; ETS = environmental tobacco smoke; FENO = fractional exhaled nitric oxide; ICS = inhaled corticosteroids; ppb = parts per billion; SES = socioeconomic status; STRA = severe therapy-resistant asthma

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Problematic severe asthma is an umbrella term that is used to describe those children with frequent symptoms and exacerbations despite treatment with high-dose inhaled corticosteroids (ICS), long-acting β-agonists, and trials of other controller medications.[1] After addressing basic management factors, including adherence, the environment, and psychological issues, children with improved symptom control are considered to have "difficult asthma" and those with ongoing, poorly controlled symptoms have genuine "severe therapy-resistant asthma" (STRA). Those with difficult asthma have been shown to have a better medium term outcome, with reductions in prescribed asthma medications.[2] The basic mechanisms underlying true STRA are unknown, although previous studies have proposed that non-T-helper type 2 cell-driven airway eosinophilia is important.[3]

Previous studies have attempted to delineate the ethnic differences in asthma severity. It has been shown that ethnic minorities have higher mortality, hospitalizations, and emergency department and urgent care visits related to asthma.[4] Ethnic disparities in asthma are unlikely to be solely explained by socioeconomic status (SES) because there can also be differences in genetic composition and gene-environment interactions.[5] Ethnicity may also influence the response to treatment in patients with asthma, but this assertion is controversial. Black subjects are twice as likely as white subjects to experience treatment failure with a long-acting β-agonist, but albuterol is equally efficacious between the two groups.[5-7] Black patients may have a diminished response to glucocorticoids,[4] but the evidence regarding ethnic variations in response to steroid treatment is limited.

We hypothesized that ethnicity influences the response to systemic steroids in children with STRA. An IM depot corticosteroid was used to eliminate adherence and access to care as possible causes of any differential responses.

Materials and Methods

The study was conducted at the Royal Brompton Hospital, London, United Kingdom. Children with STRA who had previously undergone a detailed assessment (including a nurse-led hospital and home visit in which potentially modifiable factors had been identified and addressed[8]) were admitted for further evaluation that included bronchoscopy and an assessment of steroid response. Only those children with ongoing, poorly controlled asthma despite attention to the basics of asthma management, including adherence, allergen avoidance, and prescription of high-dose ICS plus at least one other controller medication, were included. Full details of the methods have been published elsewhere.[9]

This evaluation protocol was approved by the ethics committee of the Royal Brompton Hospital. Data were retrieved from the database for children with STRA from 2005 to 2011. Children were classified as white, black (African or Afro-Caribbean), Asian (including Chinese), or mixed white/black. Asthma Control Test (ACT) results, fractional exhaled nitric oxide (F_{ENO}), spirometry (FEV_1), and sputum eosinophil levels were measured before and 4 weeks after administration of IM triamcinolone. The dose of IM triamcinolone was 40 mg and 80 mg for children with weight < 30 kg and ≥ 30 kg, respectively.

Steroid responsiveness was measured according to three domains[10]: (1) symptom response: an increase in ACT to ≥ 20 or by ≥ 5; (2) inflammatory response: a decrease in sputum eosinophil count to $\leq 2.5\%$ (if paired samples were available) or, if unavailable, a decrease in F_{ENO} to < 24 parts per billion (ppb); and (3) lung function response: an increase in FEV_1 to ≥ -1.96 z score or by $\geq 15\%$ (Table 1).

Data regarding exacerbations were collected over the 4 weeks following triamcinolone administration. An exacerbation was defined as a deterioration in symptoms requiring a course of oral steroids and/or emergency department visit and/or hospital admission.[11]

Because there are no published data to enable a power calculation, sample size was opportunistic. Descriptive analyses were used to delineate the baseline characteristics. The Fisher exact test or χ^2 test was used to assess the ethnic differences in the proportion of nonresponders, partial responders, and complete responders, as well as the ethnic differences in the proportion of responders in each domain (symptom, lung function, and inflammatory [F_{ENO} and sputum eosinophil count]) and children having exacerbations. For parametric and nonparametric data, Student t tests and Mann-Witney U tests were used, respectively, to compare the

TABLE 1] Criteria for Steroid Responsiveness in Children With Severe Asthma

Domain	Requirement
Symptom response	Asthma control test rises to a score of ≥ 20/25 or by at least five points
Lung function response	FEV_1 rises to normal (≥ −1.96 z score) or by ≥ 15% No residual bronchodilator response
Inflammatory response (if paired induced sputum samples available)	Sputum eosinophil count normal (≤ 2.5%)
Inflammatory response (if paired induced sputum samples not available)	Fractional exhaled nitric oxide[a] normal (< 24 parts per billion)

[a]Measured at a flow rate of 50 mL/s.