Impact of Race on the Severity of Acute Episodes of Asthma and Adrenergic Responsiveness

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Rationale: African Americans acutely ill with asthma come to emergency departments more frequently and are admitted to hospital more often than whites but the reasons are unclear.

Objectives: To determine whether such phenomena represent racial differences in attack severity or limited effectiveness of β_2 -agonist therapy.

Methods and Main Results: We contrasted clinical features, airflow limitation, and albuterol responsiveness in adults acutely ill with asthma, 155 of whom were African American and 140 white, as they presented to eight emergency departments. Assessments were standardized across institutions using a care path, and admission and discharge decisions were made according to predetermined criteria. The degree of obstruction was measured by peak expiratory flow rates. The clinical features of both groups were similar. The African Americans, however, had lower flow rates ($p = 0.002$), and more of them experienced severe or potentially life threatening episodes ($p < 0.001$). Albuterol was equally efficacious in both populations and there were no differences in the post-treatment flow rates achieved irrespective of the initial attack intensity. There were no racial differences in admission/discharge ratios.

Conclusions: Our data indicate that African Americans with asthma tend to present with somewhat more intense attacks than whites, but they respond equally well to routine treatment. Similarly, there were no racial disparities in hospitalizations when standard criteria are employed.

Keywords: acute bronchial obstruction; albuterol; β_2 -agonists; racial disparities

Bronchial asthma is a common disorder that affects perhaps as many as 31 million people in the United States (1, 2). Despite continuous advances in preventive therapy, acute exacerbations remain frequent occurrences. The most recently available national statistics indicate that in 2002 there were 1.9 million emergency department (ED) visits nationwide requiring approximately 450,000 hospital admissions (1, 2). Minorities, particularly African Americans, seem to bear a disproportionate burden of the disease. They have a greater frequency of urgent care visits, are hospitalized more often than whites, and have a higher death rate (1, 2). The reasons for these disparities are not yet completely understood, but socioeconomic issues such as the availability of health care resources and the adequacy of medical

management have been suggested as playing a role (3–6). Although such factors are likely quite important, they do not readily explain the entire problem. One area that has not been satisfactorily examined is the possibility that there are inherent racial differences in the severity of acute decompensations or inadequate responses to routinely used reliever treatment. The existence of either of these factors could readily contribute to the untoward outcomes reported in the literature.

To explore these two possibilities, we contrasted the presenting signs, symptoms, and degree of airway obstruction in adults, African American and white, acutely ill with asthma as they sought emergency care in eight hospitals in a university health system. We also examined their immediate response to standardized treatment regimens with albuterol (7–11). Our observations form the basis of this report.

METHODS

Whites and African Americans with asthma, 18 yr of age or older, who came to EDs of eight hospitals with an acute exacerbation of their illness were eligible for enrollment. Three of the participating institutions were urban based, with patients predominantly coming from the inner city; three were in regional communities with patients drawn from suburban areas; and two were in rural areas. Because the communities served by the university health system contained few Hispanics, only African Americans and whites were studied. Participants were prospectively accrued over a 3-mo period. Recruitment was based on patient-reported physician-diagnosed histories of asthma and the assessments of the urgent-care provider. The presence of asthma was defined according to the recommendations of the National Asthma Education and Prevention Program of the National Institutes of Health (12). Each volunteer gave a history of reversible airway obstruction associated with episodes of cough, dyspnea, and wheezing interspersed with symptom-free periods. Only individuals in whom the index ED visit was for the treatment of an acute asthma attack were studied. Patients with histories suggestive of congestive heart failure, pneumonia, chronic bronchitis, or emphysema were excluded.

The identical treatment protocol was used in all EDs. On presentation, the subjects entered into a care path in which they underwent clinical and physiologic evaluations and received treatment according to a tested algorithm (7–11). Demographics, symptoms, signs, past medical histories, and routine medication use for the previous month were recorded on an intake sheet. The race of each subject was determined by self-report in response to written inquiries on the clinical questionnaire. Oxygen saturation was determined by pulse oximetry on room air and supplemental oxygen was administered as necessary for values less than 90%. Before treatment, the best of three peak expiratory flow rates (PEFRs) was taken as representing the patient's initial state of flow limitation. The initial flow limitation was recorded in absolute terms as well as a percentage of predicted normal (13). If a patient's airway obstruction prevented him or her from achieving the minimum level on the peak flow meter, a value of 10 was arbitrarily assigned to avoid dividing by zero when the percentage improvement following albuterol was calculated (7–11). The presenting PEFR levels were also used to characterize attack severity using consensus international guidelines (12, 14–16). Initial PEFR values greater than 50% of predicted were considered to represent mild attacks, while those 50% or less

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were classified as being severe. Within the severe group, PEFR values of 35% or less were categorized as potentially life threatening (14–16). The subjects received either 2.5 mg of nebulized albuterol every 20 min for three doses or two doses of 5.0 mg of albuterol 20 min apart (8, 9). At the end of each schedule, PEFRs were repeated and the patient was reexamined.

Admission and discharge decisions were made according to predetermined criteria (7–11). Patients were considered ready to be sent home if they were asymptomatic, free of accessory muscle use, had absent or diminished wheezing, and had achieved a peak flow $\geq 60\%$ of predicted. Those not meeting these requirements were given further treatment with adrenergic and anticholinergic bronchodilators and glucocorticoids at the discretion of the ED physician and reassessed hourly. If they subsequently met the discharge criteria, they were released. If not, they were admitted to hospital. The false-positive admission rate with these algorithms has been found to be less than 1% and the 24-h relapse rate less than 2% (7).

The information sheets generated in the EDs were collected weekly and copied. At the end of the study, the patients from each institution were pooled and segmented into African American and white racial groups. Enrollment was based on consecutive ED presentations to each institution. When a patient who was not African American or white presented, the next African American or white person who came was registered. Data compilation and analysis were performed by investigators who were not involved in the delivery of care to the study subjects. The primary variables of interest were the presenting signs, symptoms, and PEFR values as well as the improvement achieved after the initial 7.5 and 10 mg albuterol regimens in the ED. Secondary endpoints included the admission–discharge ratios and the pretreatment clinical treatments used by the patients.

The trial was powered to detect a 15 to 20% difference in initial PEFR between groups with an α of 0.05 and a β of 0.20. To accomplish this goal, approximately 138 subjects per population were required. Statistical comparisons were made with paired and unpaired *t* tests, two-factor analysis of variance, and χ^2 analysis. A two-tailed *p* value of 0.05 was considered significant.

The Institutional Review Boards for Human Investigation of the participating institutions approved the investigation. Every subject was given a written and oral description of the study and its purpose, but because we were only examining possible differences between the presenting features of African Americans and whites and their response to standard therapeutic modalities (7–11), the respective committees believed that it was not necessary to obtain an additional signed consent form beyond that permitting emergency treatment.

RESULTS

A total of 295 individuals acutely ill with asthma, 155 African Americans and 140 whites, served as subjects. All of the institutions provided care to both African Americans and whites, but the distribution of patients was different. Most African Americans were treated in the inner-city hospitals and most whites were treated in the suburban and rural EDs (urban = 165 participants: 129 African Americans, 36 whites; suburban = 106 participants: 24 African Americans, 82 whites; rural = 24 participants: 2 African Americans, 22 whites). There were no relationships between the hospital type or specific institutions and the initial PEFR observed (*p* = 0.38 and 0.34, respectively).

The demographic and pretreatment clinical data and the medications taken for the previous month for both populations are presented in Table 1. The subjects ranged in age from 18 to 82 yr (mean African American = 37.1 ± 1.2 yr; mean white = 39.5 ± 1.4 yr). Women predominated (African Americans = 69%, whites = 77%). All of the participants had the typical signs and symptoms of acute airway obstruction, such as tachycardia and tachypnea, and came to the ED seeking relief from dyspnea. The average values for pulse oximetry ranged between 95 and 96%. Most subjects were wheezing on examination and about 25% in each group were using their accessory muscles of respiration. Diaphoresis was uncommon (3 to 6%) and cyanosis was

TABLE 1. DEMOGRAPHIC AND CLINICAL DATA ON PRESENTATION

Variable	AA	C	<i>p</i> Value
<i>n</i>	155	140	—
Age, yr*	37.1 ± 1.2	39.5 ± 1.4	0.21
Female, n/%	107/69	108/77	0.15
Pulse, beats/min*	97 ± 1	97 ± 1	0.59
Respiration, breaths/min*	22 ± 1	23 ± 1	0.11
SpO ₂ , %*	96 ± 0.5	95 ± 0.3	0.12
Wheezing, n/%	124/80	121/87	0.04
Accessory muscle use, n/%	42/27	37/26	0.38
Diaphoresis, n/%	5/3	8/6	0.79
Cyanosis, n/%	0/0	1/0.7	0.48
Medications†			
β_2 -agonists			
Both forms, %	95.5	79.4	< 0.001
Short-acting, %	94.2	76.2	< 0.001
Long-acting, %	18.1	24.6	0.19
Glucocorticoids			
Inhaled, %	31.6	42.1	0.13
Oral, %	11.0	6.4	0.21
Antileukotrienes, %	11.6	21.4	0.03
Anticholinergics, %	7.7	3.2	0.12

Definition of abbreviations: AA = African Americans; C = whites; F = female; *n* = number of observations; SpO₂ = arterial saturation measured by pulse oximetry.

* Mean $\pm$ SEM.

† Percentages of subjects taking each class of drug. Because many patients were using more than one type of medication simultaneously, the total percentage figure exceeds 100%.

rare (< 1%). There were no significant differences between populations for any of these variables except that wheezing was more often observed in whites (*p* = 0.04).

Most of the participants were using multiple therapies for control of their asthma and there were no differences between populations in the total number of drugs prescribed before entrance into the study. Similarly, there was no relationship between the presenting PEFR and the amount or type of medication routinely used (*p* = 0.61). The African Americans were taking 1.6 drugs per person on average and the whites, 1.5 per person (*p* = 0.06). There were, however, notable distinctions in patterns of consumption. The African Americans used β_2 -agonists more frequently (African Americans = 95.5%, whites = 79.4%; *p* = 0.001), particularly the short-acting forms (94.2% African American vs. 76.2% white; *p* = 0.001). Overall, only 30–40% of the participants were using inhaled steroids. Whites were prescribed these agents more often than were blacks, but the differences did not reach statistical significance. More of the African Americans were taking oral glucocorticoids, but here, too, there were no statistically significant differences. The two groups used equal amounts of anticholinergic agents, but more whites received antileukotrienes (*p* = 0.03).

Only eight African Americans and eight whites had initial PEFR values less than the lower limit on the PEFR meter. The African Americans tended to present with more obstruction. The mean PEFR in this group was 175 ± 8 versus 203 ± 8 L/min in the whites (*p* = 0.01). On average, this translates into a 19.6% difference when the data are expressed as a percentage of predicted normal (African Americans = $34.1 \pm 1.4\%$ predicted, whites = $40.8 \pm 1.7\%$ predicted; *p* = 0.002; Figure 1). The distribution of attack intensity was also skewed toward increased severity in the African Americans. There were more African Americans with attacks in the severe and life-threatening categories and fewer in the mild range (Figure 1). Of the African Americans, 83% had PEFR values $\leq 50\%$ of predicted and

Figure 1. Comparison of the intensity of acute episodes of asthma in African Americans (AA) and whites (C). The left panel displays the presenting values for the peak expiratory flow rate (PEFR) expressed as a percentage of normal. The heights of the bars are mean values and the brackets represent 1 SEM. The right panel contrasts the pattern of intensity found. The heights of the bars are the percentages of the populations. Mild = PEFR > 50%; severe = PEFR ≤ 50% of predicted; life-threatening = PEFR ≤ 35% of predicted. The statistical probabilities for the comparisons are shown below the panels.

56.8% had levels ≤ 35%. The corresponding numbers for whites were 66.4 and 40.7%, respectively ($p < 0.001$). Twice as many whites presented with mild attacks (16.7 vs. 33.4%, $p = 0.001$). Although the proportion of subjects in each classification was different, the levels of obstruction were equivalent (Table 2). This observation holds true whether the data are presented as percent of predicted or in absolute terms.

The African Americans and whites responded similarly to standard doses of albuterol. The mean PEFR increased significantly for each set of subjects in both absolute terms (African Americans Δ PEFR initial to final = 106.1 L/min, $p = 0.001$; whites Δ PEFR initial to final = 93.8, L/min, $p = 0.001$; African American vs. white Δ PEFR, $p = 0.27$) and as a percentage of predicted normal (Figure 2). For the latter, the mean percentage improvement from baseline in the African Americans was 77.4 ± 10.8 and it was $57.9 \pm 5.7\%$ in the whites ($p = 0.10$). Similarly, the magnitude of the pretreatment obstruction in the African Americans and whites did not seem to be a critical variable. There were no discrepancies in the degree of improvement in the African-American and white patients whether their episodes were mild, severe, or life threatening (Figure 3).

The admission rates were identical for both populations (African Americans = 21.3%, whites = 24.6%; $p = 0.60$). The majority of hospitalizations came from the severe and life-

threatening groups and there were no differences between African Americans and whites.

DISCUSSION

The reasons why inequalities exist in long-term outcomes with asthma between African Americans and whites are complex and likely involve many factors. Our findings indicate that excessively severe, unremitting acute episodes do not appear to be one of them. The results of the present study demonstrate that, although African Americans tend to present with more intense airflow limitation than do whites, the effect is relatively small and readily alleviated with routine treatment. The initial PEFR in the African Americans was approximately 20% lower and more of the attacks fell into the severe and life-threatening ranges, but these differences were rapidly eliminated with standardized therapeutic approaches. There were no racial distinctions in either the immediate response to albuterol or in the ultimate need for hospitalization. As such, we believe that these data provide the critical first steps in understanding the elements involved in the production of ethnic disparities in asthma.

To our knowledge, there are no previous studies that have been specifically designed to assess attack intensity and therapeutic responsiveness between racial groups. However, the validity of our observations can be evaluated from published compendiums,

TABLE 2. INTENSITY OF PRESENTING AIRFLOW OBSTRUCTION

Population	AA		C		p Value
	No.	PEFR, % predicted (absolute)	No.	PEFR, % predicted (absolute)	
All subjects	155	34.1 ± 1.4 (175 ± 8)	140	40.8 ± 1.7 (203 ± 8)	0.002
Subgroups					
Mild	26	60.06 ± 2.3 (312 ± 15)	47	61.1 ± 1.4 (297 ± 8)	0.68
Severe	129	28.7 ± 1.2 (147 ± 6)	93	30.3 ± 1.5 (156 ± 8)	0.41
Life-threatening	88	22.6 ± 1.2 (117 ± 6)	57	22.1 ± 1.6 (115 ± 8)	0.76

Definition of abbreviations: AA = African Americans; C = whites; PEFR = peak expiratory flow rates as a percentage of predicted.

The data are mean values $\pm$ SEM; the data in parentheses are the absolute values in L/min. Mild = acute episodes with an initial PEFR $\geq 50\%$ of predicted, severe = an initial PEFR value $\leq 50\%$ of predicted, life-threatening = an initial PEFR value $\leq 35\%$ of predicted.

Figure 2. Effect of albuterol in African Americans (AA) and whites (C). The *left panel* displays the absolute increase from the pretreatment baseline after albuterol in the two populations. The *right panel* displays the percent improvement for each group. The heights of the bars are mean values and the brackets are 1 SEM. I = Initial value; F = final value. The statistical probabilities for the comparisons are shown below the panels.

such as the Multicenter Airway Research Collaboration (MARC), which represents more than 1,800 patients seen in 64 EDs (17–19). In one MARC analysis, Bordeaux and colleagues (18) found that African-American and Hispanic adults came to the ED with values for PEFRs that were 10% lower than those of whites. This phenomenon was not seen in the children in the cohort when a pulmonary severity index was used (19). It should be noted, however, that such scoring systems rely only on signs and symptoms and do not include any direct measures of airflow limitation. Consequently, they are subject to false impressions

Figure 3. Effect of albuterol in African Americans (AA) and whites (C) with different attack intensities. The heights of the bars are mean values and the brackets = 1 SEM. Mild = PEFR > 50% of predicted, severe = PEFR ≤ 50%; life-threatening = PEFR ≤ 35%. The statistical probabilities for the comparisons are shown below the panels.

as to attack severity (20, 21). As reemphasized in a recent review, the relationship between the clinical and physiologic manifestations of acute asthma is imprecise (21). Surrogate markers such as pulse and respiratory rates, accessory muscle use, wheezing, and inspiratory/expiratory ratios lack sufficient selectivity and specificity to quantitate the intensity of a given attack or reliably detect difference in severity between individuals (21). Table 1 demonstrates that abnormalities in these clinical indices were present with equal frequency in both the African Americans and whites, and none of them, either in isolation or in combination, reflected the differences found in PEFR. Only direct measures of obstruction can serve this purpose.

The reasons why African Americans present for care with more severe attacks are not yet established. Because African Americans with asthma die more frequently than do whites (22), it is assumed that their disease is more aggressive. Although this may be so, there are no data conclusively demonstrating fundamental differences in disease progression or pathophysiology. Collaborative cross-sectional investigations have found African Americans to have lower values for the FEV₁ and a higher rate of skin test allergies to cockroach than do whites (22), but the long-term implications of such observations for morbidity and mortality remain uncertain. It may be that other factors such as socioeconomic or cultural issues are at work.

We did not collect information on smoking status, so we do not know if there were differences between whites and African Americans. Since initiation of the current study, data have appeared indicating that exposure to tobacco smoke may worsen asthma severity in Latinos with CD14 genotypes (23). This gene, which is part of the receptor complex for endotoxin (24), not only can adversely modulate atopic features and airway hyper-responsivity (25, 26) but may also contribute to cigarette smoke-induced respiratory disorders (27). It is not yet established if similar events occur in African Americans or if there are differences between African Americans and whites in this regard.

The frequency of ED visits by African Americans with asthma is two to three times that of whites (1, 2) and it has been suggested that limited use, or availability, of health care resources as well as inadequate medical management may be root causes (3–6). Murray and associates (3) found that, in comparison to whites, African Americans had fewer outpatient encounters with health care providers and prescription refills. In a similar vein, Haas and colleagues (5) reported an inverse relationship between socioeconomic status and the intensity of ambulatory treatment for asthma after hospital discharge. Patients with low incomes and limited education received less follow-up and less intensive treatment than did those of higher socioeconomic status. All of these possibilities could have been operational in our study.

Inadequate use of antiinflammatory therapy by inner-city residents with asthma has also been implicated as a cause for severe attacks (6). Although only 30 to 40% of our patients were prescribed inhaled steroids, this is not an uncommon finding in large series dealing with ED care (7–11, 17–19). Most important, because there were no significant differences between African Americans and whites in utilization, this factor cannot explain our results.

The higher use of β_2 -agonists by the African Americans could also have conceivably contributed to any difference. Hartert and associates (6) reported overuse of adrenergic drugs to be recurrent among inner-city residents with asthma admitted to the hospital. Most patients experiencing acute episodes delay seeking care until their rescue medications no longer work (28). In so doing, they run the risk of experiencing progressively worsening obstruction while consuming increasing quantities of drugs. Although the impact of such behavior has not yet been studied formally, many of our urban patients assert that they

prefer a "wait and see" course of action when acutely ill. In this fashion they hope to avoid incurring additional medical expense and the inconvenience of prolonged delays in busy inner-city EDs.

Interestingly, the failure of adrenergic agonists to relieve attacks at home appears to be related to acute disease-induced problems in patient-delivery device interactions and not to drug tachyphylaxis (29, 30). The identical medications that have been unsuccessful when self-administered in an outpatient setting readily resolve acute episodes when given by a health care professional using appropriate delivery techniques (29, 30).

The finding of equal admission rates for African Americans and whites with asthma in our data seems to be in conflict with previous publications (2, 17), but such differences may relate more to the manner in which the need for hospitalization is determined than to intrinsic features of the disease. We used pretested objective criteria for decision making (7–11) and did not find any racial differences. In contrast, multicenter assessment of ED care indicates that the judgment to admit is often based on historical considerations such as the number of previous ED visits, hospitalizations, or accounts of the need for ventilatory support, rather than an assessment of the resolution of the particular episode being treated or the final value of the PEFR (17). In fact, objective measures of obstruction are not frequently obtained by treating ED physicians, and if available are not used in decision making (17). It is also possible that the racial distribution of individuals with asthma using an ED determines the frequency of admission. For example, in the MARC data two times more African American adults and four times more African American children were admitted than corresponding whites, but two and four times more African Americans than whites came to the ED (18, 19). As percentages, the admission rates in both children and adults ranged between 19 and 25% and exactly matched ours. Similarly, there were no differences in relapses. Once again composite data indicate that recurrence rates average about 17% in the 2 wk following an ED visit and there are no differences between African Americans, Hispanics, and whites (31).

We do not believe that issues such as patient selection or treatment modalities influenced our findings. Our subjects were typical demographically, clinically, and physiologically to those in other studies (7–11, 17–19, 31). Furthermore, our observations were derived from consecutive presentations to the EDs and there were no relationships found between the pretreatment PEFRs in either the hospital region or specific institutions; thus, sampling bias seems unlikely. In addition, the albuterol regimens we employed to achieve the primary endpoint had been documented to produce maximally effective results and there are no major differences between the effects of 10 and 7.5 mg (8, 9). Finally, although the medications in the second phase of the care path were left to the discretion of the treating physicians, the same drugs and dose intervals tended to be used by all, and the disposition criteria were predetermined (7–11).

We think it unlikely that our description of the racial disparities in initial attack intensity were distorted by the use of predicted data. We appreciate that there are limited published pulmonary reference values for minorities so precise quantitation of normalcy might not be possible. However, because we focused primarily on the pattern of differences between and within populations, we do not believe that major bias was introduced by following usual custom and normalizing the results (7–11, 15, 17–19). This supposition is readily borne out by the fact that our principal findings hold true whether we use untransformed raw PEFR readings in L/min or express them as a percentage of predicted.

We also followed precedent by assessing obstruction with PEFR (7–11, 15, 17–19), but this, too, is unlikely to have influenced the conclusions. Our approach was undertaken with the full understanding that this index provides only a limited clinical and physiologic snapshot of the relevant events and that errors can result if the resulting data are not considered in context. Peak flow is, however, a functionally useful tool. As frequently pointed out, it can certainly be normal in a patient with multiple other functional abnormalities (7, 20, 21, 32) and as such can lead to erroneous assumptions about attack intensity and disease severity. Nonetheless, in circumstances where PEFR is reduced as a result of intrathoracic airflow limitation as herein, it invariably signals that all other spirometric indices as well as measures of gas exchange are compromised (7, 20, 21, 32). It is in the evaluation of patients with minimal impairment that PEFR tends to fail and that other techniques are required.

In summary, our findings demonstrate that acutely ill African Americans with asthma present for emergency care with more severe obstruction than whites. The underlying reasons for this behavior remain to be determined. Selective therapeutic responses do not appear to be an issue. African Americans and whites respond equally well to albuterol and there are no racial differences in immediate outcomes or hospitalizations when standardized treatments are used.

Conflict of Interest Statement: None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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