Airway responsiveness as a direct factor contributing to the dyspnoea perception in asthma

Y. I. KOH, I. S. CHOI AND H. LIM

Division of Allergy, Department of Internal Medicine, Chonnam National University Medical School and Research Institute of Medical Science, Kwangju, Korea

It is not clear whether airway responsiveness is directly related to the perception of bronchoconstriction in asthma. The purpose of this study is to directly compare the perception of induced bronchoconstriction among the groups classified according to the degree of airway responsiveness. Two hundred and twenty-seven patients with the definitive or suspected asthma underwent a methacholine provocation test. During the test, the degree of dyspnoea was assessed by a modified Borg scale. The perception of induced bronchoconstriction was indicated by the slope in the linear regression analysis between changes in Borg score and the reduction in forced expiratory volume in 1 sec (FEV$_1$) as a percentage of baseline value. The provocative concentration of methacholine resulting in 20% fall in FEV$_1$ (PC$_{20}$) was calculated. The degree of airway responsiveness to methacholine was categorized as moderate to severe airway hyper-responsiveness (AHR) if PC$_{20}$ was $<1$ mg ml$^{-1}$, mild AHR if PC$_{20}$ was $1$ but $<4$ mg ml$^{-1}$, borderline AHR if PC$_{20}$ was $>4$ but $\leq 16$ mg ml$^{-1}$, and normal airway responsiveness (negative AHR) if PC$_{20}$ was $>16$ mg ml$^{-1}$. Positive AHR was defined as PC$_{20}$$\leq 4$ mg ml$^{-1}$. Another index of bronchial responsiveness (BR index) was calculated as the log [(% decline in FEV$_1$/log final methacholine concentration as mg dl$^{-1}$)$+10]$. We found that the geometric mean of the slope was lower in subjects with positive AHR (0 $\pm$ 12, $n=115$) than in subjects with negative AHR (0-17, $n=72$; $P<0.01$). The geometric mean of the slope in subjects with borderline AHR (0-14, $n=40$) was between the two groups. Furthermore, the slope was decreased in asthmatics with moderate to severe AHR compared with mild AHR ($P<0.05$), although the baseline FEV$_1$ did not differ between the two groups. In multiple regression analysis, airway responsiveness expressed as BR index had a significant effect on the perception of bronchoconstriction. We conclude that the perception of bronchoconstriction is diminished in patients with AHR and the degree of airway responsiveness may be directly related to the perception of bronchoconstriction in asthmatic subjects.

Key words: perception; dyspnoea; asthma; airways responsiveness.

Introduction

It has been known that some patients perceive the severity of asthma rather poorly. This may put the patient at a disadvantage because it may lead to under-treatment and be potentially dangerous because the severity of an exacerbation may be under-estimated. Detection of the determinants of the ability of perceiving bronchial obstruction might be helpful therefore in protecting ‘poor perceivers’ from a severe asthmatic attack.

Airway hyper-responsiveness (AHR) has been found to be a possible factor in influencing the perception of asthma symptoms (1,2). The AHR describes the tendency of the bronchi to narrow too much and too easily in response to provocative stimuli (3). Bijl-Hofland et al. (4) have suggested that patients with AHR experience airway constriction due to increased inflammation relatively more often and therefore may be more used to the sensation of breathlessness and more inclined to disregard the severity of the airway obstruction. Although these above studies have found that airway responsiveness may be related to the perception of dyspnoea, they did not directly compare the perception of breathlessness among the groups with the different degree of airway responsiveness. Furthermore, the relationship between AHR to direct stimuli and respiratory symptoms is not strong; about 50% of subjects with AHR report no respiratory symptoms (5). A few previous studies have failed to show any influence of the severity of airway responsiveness on the perception of airway obstruction (6, 7). Therefore, it is not clear whether airway responsiveness is directly related to the perception of airway obstruction in patients with asthma.
We studied the perception of bronchoconstriction by using a Borg score (8) during a methacholine provocation test in subjects with respiratory symptoms to investigate the relationship of the airway responsiveness to methacholine, one of direct stimuli, with the perception of dyspnoea. We directly compared the perception of methacholine-induced bronchoconstriction among the three groups classified according to the degree of airway responsiveness. Specifically, the perception of dyspnoea in asthmatics with moderate to severe AHR was compared with the perception of asthmatics with mild AHR.

## Materials and methods

### SUBJECTS

We studied 136 patients with definitive asthma and 91 patients with suspected asthma who visited our Allergy Clinic at Chonnam National University Hospital from November 1996 to December 1999 for the investigation of their respiratory symptoms such as breathlessness, wheezing, cough and/or sputum. There were 104 male and 123 female subjects, aged 14–80 years (mean ± SEM: 41.6 ± 1.1). All subjects with definitive asthma met the American Thoracic Society's diagnostic criteria (9) and had a PC₂₀ methacholine equal to or less than 8 mg ml⁻¹ (3). Suspected asthma was recorded if a subject had a history of episodic dyspnoea or wheezing and PC₂₀ methacholine of more than 8 mg ml⁻¹. All subjects had a baseline FEV₁ > 60% of predicted value. The subjects were studied during a clinically stable period, without symptoms of an upper respiratory tract infection for 6 weeks prior to the study. All subjects took no anti-asthmatic medications except for 29 subjects who had inhaled short-acting β₂-agonists on demand as rescue medication. The inhaled β₂-agonists were withheld for at least 8 h. Subject characteristics are summarized in Table 1. The study was approved by the Hospital Medical Ethics Committee, and informed consent was given by all subjects.

### METHACHOLINE INHALATION CHALLENGE TEST

Methacholine challenge tests were performed according to a standardized tidal breathing method (3). Methacholine in isotonic saline was aerosolized at room temperature by a DeVilbiss 646 nebulizer (DeVilbiss Co., Somerset, PA, U.S.A.; output 0.13 ml min⁻¹). Dilution increments were: 0.075, 0.15, 0.31, 0.62, 1.25, 2.5, 5.0, 10, and 25 mg ml⁻¹. The aerosols were inhaled by tidal breathing during 2 min at 5-min intervals through the mouth with the nose clipped. Measurements of FEV₁ were made in triplicate before the test (baseline) and in duplicate (30 and 90 sec) after each increasing dose with a spirometer (Spiro Analyzer ST-250, Fukuda Sangyo, Tokyo, Japan). The challenge test was discontinued if FEV₁ dropped 20% or more from baseline or if the maximal concentration of methacholine was administered. The provocative concentration of methacholine resulting in 20% fall in FEV₁ (PC₂₀) was calculated by linear interpolation of the log-dose-response curves. The degree of airway responsiveness to methacholine was categorized as moderate to severe AHR if PC₂₀ was <1 mg ml⁻¹, mild AHR if PC₂₀ was ≥1 but ≤4 mg ml⁻¹, borderline AHR if PC₂₀ was >4 but ≤16 mg ml⁻¹, and

---

### Table 1. Clinical characteristics of subjects

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Definitive asthma (n=136)</th>
<th>Suspected asthma (n=91)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>39.8 ± 1.5</td>
<td>44.5 ± 1.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Female†</td>
<td>73 (53.7)</td>
<td>50 (54.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Height (cm)*</td>
<td>162.6 ± 0.8</td>
<td>162.4 ± 1.0</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>25 (18.4)</td>
<td>12 (13.2)</td>
<td></td>
</tr>
<tr>
<td>Ex</td>
<td>9 (6.6)</td>
<td>9 (9.9)</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>102 (75.0)</td>
<td>70 (76.9)</td>
<td>NS</td>
</tr>
<tr>
<td>FEV₁ (l)*</td>
<td>2.7 ± 0.1</td>
<td>3.0 ± 0.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FEV₁ (% of predicted)*</td>
<td>79.8 ± 0.9</td>
<td>94.6 ± 2.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PC₂₀ (mg ml⁻¹)†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>61 (44.9)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1–4</td>
<td>54 (39.7)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4–16</td>
<td>21 (15.4)</td>
<td>19 (20.9)</td>
<td>—</td>
</tr>
<tr>
<td>&gt;16</td>
<td>—</td>
<td>72 (79.1)</td>
<td>—</td>
</tr>
</tbody>
</table>

* Values were mean ± SEM and comparisons were carried out with a Student’s t-test.
†Values were the number of subjects (percentages in parentheses) and comparisons were carried out done with a χ² test.
FEV₁: forced expiratory volume in 1 sec; PC₂₀: the provocative concentrations of methacholine resulting in 20 % fall in FEV₁; NS: non-significant.
normal airway responsiveness (negative AHR) if PC20 was >16 mg ml⁻¹. Positive AHR was defined as PC20 ≤4 mg ml⁻¹ (10). Another index of bronchial responsiveness (BR index) was calculated as the log [(% decline in FEV1/log final methacholine concentration as mg dl⁻¹)] (11). The BR index was introduced only to provide a number available to use in regression analyses and other parametric statistical tests in all subjects including those with negative methacholine challenges.

**ASSESSMENT OF PERCEPTION OF DYSPNOEA**

The severity of dyspnoea during the methacholine challenging tests was assessed by a modified Borg scale, at 20 sec after inhalation of each dose, just before the measurement of the FEV1 curves. Each subject was instructed to record the degree of dyspnoea they felt at that moment. Dyspnoea was described to the subjects as shortness of breath or breathlessness. The modified Borg scale is a vertical list with labelled categories (0–10) describing increasing intensities of breathlessness (0 = ‘nothing at all’, 10 = ‘maximal’) (8). During the tests the subjects were blinded to their lung function response.

**ANALYSIS OF PERCEPTION OF DYSPNOEA**

A patient’s perception of bronchoconstriction was determined by the relationship between the absolute changes in Borg score and the reduction in FEV1 as a percentage of the baseline value in each patient. This relationship was analysed by means of a linear regression coefficient (slope) between these two parameters in which the change in FEV1 was the independent variable and was placed on the x-axis. The change in Borg score, being the dependent variable, was put on the y-axis. Each (ΔBorg score/ΔFEV1) slope indicates the perception of airway obstruction of that patient, the steeper the slope the more sensitive is the subject to signals of bronchoconstriction (Fig. 1).

**STATISTICAL ANALYSIS**

Data were expressed as means ± SEM for the continuous variables or number of subjects (percentages in parentheses) for dichotomous variables. The values of slope (ΔBorg score/ΔFEV1), which were positively skewed (skewness index of 1.8), were log transformed before this parameter was entered in the analysis. This transformation reduced the skewness index to −0.5. Comparisons were made using χ²-test for dichotomous variables, and unpaired Student’s t-test or a post-hoc Scheffe’s test for continuous variables. Multiple regression analysis was performed, with the perception of bronchoconstriction (slope) as the dependent variable and BR index, baseline FEV1, baseline Borg score, sex, age, and current smoking habits as predictor variables. A P-value of <0.05 was regarded as statistically significant.
subjects, the geometric mean of the slope in 28 asthmatics with an increase in diurnal peak flow variations, in 52 patients with allergic rhinitis, in seven patients with chronic bronchitis, and in four patients with bronchiectasis were 0.13, 0.16, 0.22 and 0.32, respectively, without statistical differences between them.

When all subjects were classified into the three groups according to the degree of methacholine airway responsiveness. The subjects with positive AHR were younger than those with negative AHR. There were no differences in sex and current smoking habits among the three groups. The baseline FEV₁ was significantly lower in subjects with positive or borderline AHR than in subjects without AHR. The mean maximal % fall in FEV₁ was greater in groups with positive or borderline AHR than in negative AHR (Table 2). The geometric mean of the slope (AHR than in patients with negative AHR (Table 2). The score was higher in patients with positive or borderline among the three groups. However, the mean maximal Borg score was higher in patients with positive or borderline AHR than in subjects without AHR. The mean maximal % fall in FEV₁ was greater in groups with positive or borderline AHR than in negative AHR (0.14) was between positive and negative AHR groups, although it did not significantly differ from that in positive or negative AHR group (Fig. 2).

When the analyses were limited to positive AHR group, there were no significant differences in age, sex, current smoking habits, baseline FEV₁, and baseline Borg score between moderate to severe AHR group and mild AHR group. However, the mean maximal % fall in FEV₁ in moderate to severe AHR group was greater than in mild AHR group, whereas the mean maximal Borg score was higher in mild AHR group than in moderate to severe AHR group (Table 3). The geometric mean of the slope (ΔBorg score/dFEV₁) was significantly lower in moderate to severe AHR group (0.10) than in mild AHR group (0.14, *P* < 0.05), indicating that the perception of dyspnoea is decreased in asthmatics with moderate to severe AHR as compared with asthmatics with mild AHR (Fig. 3).

For all subjects, BR index and baseline Borg score were significant factors contributing to the perception of bronchoconstriction when the multiple regression analysis of the perception of bronchoconstriction according to BR index, baseline FEV₁, baseline Borg score, sex, age and

![Fig. 2. The perception of bronchoconstriction quantified by the linear regression slope of the relationship between changes in Borg score and the reduction in FEV₁ as a percentage of the baseline value for the subjects with positive airway hyperresponsiveness (AHR) (*n* = 115), borderline AHR (*n* = 40), and negative AHR (*n* = 72). The slope was calculated as shown in Fig. 1 and the values, which were skewed, were log-transformed (log-slope). Data were expressed as mean ± SEM. Statistical analyses were performed by a post-hoc Scheffe’s test.](image)

**Table 2. Comparisons of characteristics among the three groups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Positive (<em>n</em> = 115)</th>
<th>Borderline (<em>n</em> = 40)</th>
<th>Negative (<em>n</em> = 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)†</td>
<td>39.0 ± 1.6*</td>
<td>41.1 ± 3.0</td>
<td>45.9 ± 1.8</td>
</tr>
<tr>
<td>Female‡</td>
<td>61 (53-0)</td>
<td>21 (52.5)</td>
<td>41 (56-9)</td>
</tr>
<tr>
<td>Current smokers‡</td>
<td>21 (18-3)</td>
<td>7 (17-5)</td>
<td>9 (12-5)</td>
</tr>
<tr>
<td>Baseline FEV₁ (% of predicted)†</td>
<td>79.6 ± 1.1*</td>
<td>83.8 ± 1.9*</td>
<td>96.6 ± 2.5</td>
</tr>
<tr>
<td>Maximal % fall in FEV₁‡</td>
<td>26.9 ± 0.7*</td>
<td>24.8 ± 0.7*</td>
<td>14.9 ± 0.6*</td>
</tr>
<tr>
<td>Baseline Borg score‡</td>
<td>0.7 ± 0.1</td>
<td>0.6 ± 0.2</td>
<td>0.4 ± 0.1</td>
</tr>
<tr>
<td>Maximal Borg score‡</td>
<td>4.3 ± 0.2*</td>
<td>4.5 ± 0.4*</td>
<td>3.5 ± 0.2</td>
</tr>
</tbody>
</table>

* †P < 0.05 and ‡P < 0.001 compared with negative airway hyper-responsiveness.

* †Values were mean ± SEM and comparisons were carried out with a post-hoc Scheffe’s test.

* ‡Values were the number of subjects (percentages in parentheses) and comparisons were carried out with a *χ²*-test. FEV₁: forced expiratory volume in 1 sec.
current smoking habits was performed. The baseline FEV1, sex, age and current smoking habits had no significant effect on the perception of bronchoconstriction (Table 4). When the multiple regression analyses were limited to definitive asthmatics or suspected asthmatics, only BR index had a significant effect on the perception of bronchoconstriction. The regression coefficients for BR index in definitive subjects and suspected asthmatic subjects were $-0.93$ and $-2.82$ with $P$-values of $<0.001$ and $0.002$, respectively. In definitive asthmatic subjects, PC$_{20}$ was a significant predictor even when PC$_{20}$ in place of BR index entered the regression.

**Discussion**

This study demonstrates that induced bronchoconstriction is less well perceived by patients with AHR as compared with patients without AHR. In addition, in asthmatics with severe to moderate AHR, the perception of bronchoconstriction is impaired as compared with asthmatics with mild AHR, although baseline FEV1 values did not differ between the two groups. In the regression analysis, airway responsiveness is a significant factor contributing to the perception of bronchoconstriction. The results suggest that airway responsiveness may be directly related to the perception of induced bronchoconstriction in asthmatic subjects. Some previous studies (1,2,4) have also shown that airway responsiveness is associated with the perception of dyspnoea, although they did not directly compare the perception of bronchoconstriction among subjects with the different airway responsiveness.

However, two earlier reports showed no relationship between airway responsiveness and the intensity of breathlessness for a given fall in FEV1 (6,7). Possible reasons for this different result might be an inhaled and oral steroid taken during their study (6) or a smaller sample size in their study (7). It has been suggested that corticosteroids improve the perception of bronchoconstriction by reducing the airway inflammation or via the central nervous system (12). Ottanelli et al. (13) reported that airway hyper-responsiveness did not play a major role in perceived breathlessness in patients without airway obstruction, and even less of a role in patients with obstruction. However, they showed that the PC$_{20}$ was related to the Borg score at a 20% reduction in initial FEV1 when considering all subjects.

It has been known that asthmatic subjects with AHR have more severe asthma, greater improvement after

---

**TABLE 3. Comparisons of characteristics between the two groups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Moderate to severe $(n=61)$</th>
<th>Mild $(n=54)$</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>$39.1 \pm 2.2$</td>
<td>$38.9 \pm 2.3$</td>
<td>NS</td>
</tr>
<tr>
<td>Female†</td>
<td>32 (52.5)</td>
<td>29 (53.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Current smokers†</td>
<td>11 (18.0)</td>
<td>10 (18.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Baseline FEV1 (% of predicted)*</td>
<td>$78.3 \pm 1.3$</td>
<td>$81.0 \pm 1.7$</td>
<td>NS</td>
</tr>
<tr>
<td>Maximal % fall in FEV1*</td>
<td>$29.2 \pm 1.2$</td>
<td>$24.4 \pm 0.5$</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Baseline Borg score*</td>
<td>$0.7 \pm 0.2$</td>
<td>$0.6 \pm 0.2$</td>
<td>NS</td>
</tr>
<tr>
<td>Maximal Borg score*</td>
<td>$3.9 \pm 0.2$</td>
<td>$4.8 \pm 0.3$</td>
<td>$&lt;0.05$</td>
</tr>
</tbody>
</table>

*Values were mean±SEM and comparisons were carried out with a Student’s $t$-test.
† Values were the number of subjects (percentages in parentheses) and comparisons were carried out with a $\chi^2$-test.

FEV1: forced expiratory volume in 1 sec; NS: non-significant.

**Fig. 3.** Comparison of the perception of bronchoconstriction quantified by the linear regression slope of the relationship between changes in Borg score and the reduction in FEV1 as a percentage of the baseline value between asthmatic subjects with moderate to severe airway hyper-responsiveness (AHR) $(n=61)$ and those with mild AHR $(n=54)$. The slope was calculated as shown in Fig. 1 and the values, which were skewed, were log-transformed (log-slope). Data were expressed as mean ± SEM. Statistical analyses were performed by Student’s $t$-test.
bradypnoea, greater diurnal variation (14), greater
tolerance to other bronchoconstrictor stimuli (15–17) and
greater response to treatment. These might mean that
asthmatic patients with the lowest PC20 are likely to have
greater response to treatment. These might mean that
response to other bronchoconstrictor stimuli (15–17) and
bronchodilators, greater diurnal variation (14), greater
response to other bronchoconstrictor stimuli (15–17) and
greater response to treatment. These might mean that
asthmatic patients with the lowest PC20 are likely to have
increased frequency and, perhaps, also severity of
episodes of bronchospasm. With repeated episodes the
subject’s tolerance to comparable amounts of stimulation
may result in reduction of symptoms. However, the
opposite conclusion might be considered—namely, that
the subjects with a poor perception did not demand
sufficient treatment in the past, which might have resulted in
a more severe degree of asthma. Transient AHR may be
caused by some components of the airway inflammatory
response (18,19). Roisman et al. (12) found that the
perception of bronchoconstriction induced by bradykinin
was inversely related to the number of eosinophils in
bronchial biopsies. Veen et al. (20) showed that the
perception of bronchoconstriction was inversely correlated
with the percentage of eosinophils in induced sputum in
patients with severe asthma. From these above findings, it is
possible that eosinophilic airways inflammation contributes
to the increased airway responsiveness, which reduces the
perception of breathlessness. Further studies are needed to
investigate this theory.

Bill-Hofland et al. (4) showed that low baseline FEV1 was
associated with a low degree of the perception of
bronchoconstriction. Similarly, we found that positive
AHR group with a lower baseline FEV1 had a lower
perceptiveness than negative AHR group with a higher
baseline FEV1. However, baseline FEV1 was not a
significant predictor in the regression analysis. In our study
the degree of baseline FEV1 in asthmatics with moderate to
severe AHR did not differ from that in asthmatics with mild
AHR, although there was a significant difference in the
perception of bronchoconstriction between the two groups.
Some studies have shown that there is either no correlation
or a very small correlation between baseline FEV1 and
histamine or methacholine PC20 in asthmatics (21,22). This
finding in our study indicates that airway responsiveness
may be a factor contributing to the perception of
bronchoconstriction, independently of the baseline FEV1.
We did not find that the perception of induced
bronchoconstriction was influenced by age and sex. This
is in agreement with the results of a large study in which age
and sex had no significant effect on the symptoms (23).
However, a few studies have found that younger patients
are more likely to perceive their dyspnoea (2,24) and
women report more dyspnoea than men (2). We observed
that the baseline Borg score influenced the perception of
dyspnoea. Brand et al. (2) have showed that the change in
Borg score is higher when the initial Borg score was lower.
Further investigations will be needed to understand the
factors that influence perception of asthma.

From this observation, impaired perception in some
asthmatic subjects with moderate to severe degree of AHR
may lead to under-estimation of the severity of asthma,
resulting in under-treatment. This suggests that objective
measurement of airflow obstruction should be encouraged
in asthmatic subjects with moderate to severe degree of
AHR.

References

4. Bijl-Hofland ID, Cloosterman SG, Folgering HT, Akkermans RP, van Schayck CP. Relation of the

---

**Table 4. Multiple regression analysis with the perception of bronchoconstriction as the dependent variable***

<table>
<thead>
<tr>
<th>Variable</th>
<th>Regression coefficient</th>
<th>t-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BR index†</td>
<td>−0.911</td>
<td>−4.691</td>
<td>0.000</td>
</tr>
<tr>
<td>Baseline FEV1 (% of predicted)</td>
<td>−0.002</td>
<td>−1.555</td>
<td>0.121</td>
</tr>
<tr>
<td>Baseline Borg score</td>
<td>−0.040</td>
<td>−2.228</td>
<td>0.027</td>
</tr>
<tr>
<td>Sex (male=0, female=1)</td>
<td>−0.027</td>
<td>0.570</td>
<td>0.569</td>
</tr>
<tr>
<td>Age (years)</td>
<td>−0.0001</td>
<td>−0.083</td>
<td>0.934</td>
</tr>
<tr>
<td>Smoking (ex or never=0, current=1)</td>
<td>−0.019</td>
<td>0.318</td>
<td>0.751</td>
</tr>
</tbody>
</table>

*The perception of bronchoconstriction was indicated by the slope in the linear regression analysis between the change in Borg score and the reduction in FEV1 as percentage of baseline value. The slope was calculated as shown in Fig. 1 and the values, which were skewed, were log-transformed.

†BR index was calculated as the log [(% decline in FEV1/log final methacholine concentration as mg dl⁻¹) + 10] (11).

FEV1: forced expiratory volume in 1 sec; BR index: bronchial responsiveness index.


