Asian Pacific Journal of Allergy and Immunology (1996) 14 : 1-4

Bronchial Responsiveness of Aged Asthmatic Patients to Bronchodilator and Methacholine

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SUMMARY **Geriatric asthma is characterized by prolonged illness, lower remission rate, poor response to therapy and higher mortality rate. We studied bronchodilator response and methacholine challenge in 25 aged non-smoking asthmatic patients; thirty-two young asthmatic patients were included as control. The elderly patients had poorer baseline pulmonary function and were more responsive to a bronchodilator than the younger patients. The response to bronchoprovocation did not show any difference between the two groups. Our findings suggested that the airways of elderly asthmatics are as sensitive as those of younger patients and should not be under-treated.**

Pediatric asthma is characterized by episodic attack, good response to drug therapy, and rare sequelae.[1] On the contrary, geriatric asthma is a prolonged illness, has a lower remission rate, poor response to therapy and higher mortality rate.[2] Patients usually have evidence of emphysematous changes in their chest X-ray film as well as poor pulmonary function.

It was our plan to compare the bronchial reactivity between geriatric asthmatic patients and younger ones. The reversibility of pulmonary function following bronchodilator inhalation may predict the pulmonary capacity for improvement,[3] and the degree of function impairment following methacholine challenge test may predict the severity of disease in case of an asthma attack.[4] By taking advantage of the functional improvement from bronchodilator and impairment from bronchoprovocation, one may elucidate the mechanism of the poorer therapeutic response in geriatric asthmatic patients. Hence, we studied the bronchial response to a bronchodilator and a bronchoconstrictor in both elderly and young groups of asthmatic patients.

PATIENTS AND METHODS

Patients

Patients were selected from the Allergy Clinic of the Veterans General Hospital, Taipei. All were life-long non-smokers and suffered from asthma for at least 5 years. Their clinical diagnosis of bronchial asthma was made according to the criteria of the ACCP-ATS Joint Committee on Pulmonary Nomenclature.[5]

Fifty-seven asthmatic patients were included in the study (Table 1). They were divided into two groups: Group 1 were older than or equal to 55 years of age (N = 25, mean age 60.6 ± 4.5), there were 12 males and 13 females. The duration of the disease was 20.9 ± 15.3 years. Group 2 were younger than or equal to 35 years of age (N = 32, mean age 26.5 ± 7.6), there were 20 males and 12 females. The duration of the disease was 14.6 ± 8.2 years. Drugs required to control their symptoms included beta-2 adrenergic agonists (oral or inhaled) and theophylline. A few patients had been receiving corticosteroids for years, some others required several short courses of corticosteroids occasionally to control acute exacerbation of asthma. All

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Table 1. Patient groups.

	Elderly	Young
Age (yrs)	60.6 ±4.5*	26.5 ±7.6
Sex (M/F)	12/13	20/12
Duration of asthma (yrs)	20.9 ±15.3	14.6 ±8.2

*mean ± SD

Table 2. Baseline pulmonary function.

	Elderly	Young	p value
1. FVC(L)	1.25 ±0.38*	2.29 ±0.76	< 0.01
% predicted	46.68 ±12.85	66.25 ±17.88	< 0.01
2. FEV_1 (L/sec)	1.06 ±0.39	2.12 ±0.66	< 0.01
% predicted	59.12 ±22.33	70.91 ±16.50	< 0.01
3. $FEF_{25-75\%}$	70.28 ±46.19	179.25 ±68.11	< 0.01
% predicted	43.00 ±27.19	80.15 ±30.88	< 0.01

*mean ± SD

medication was withdrawn 12 hours before test for bronchodilator responses and methacholine challenge test, which were performed on separate days.

Bronchodilator responses

FEV_1 (forced expiratory volume in one second), FVC (forced vital capacity), and $FEF_{25-75\%}$ (forced expiratory flow rate between 25–75% of FVC) were measured by using a vitalograph dry spirometer (Vitalograph Ltd, Buckingham, England). Isoproterenol (twice inhalation of 0.2 mg each) was delivered to patients via a metered dose inhaler using the conventional inhalation technique. FEV_1, FVC, and $FEF_{25-75\%}$ were again measured three minutes later. The percent improvement in FEV_1 and $FEF_{25-75\%}$ was calculated. The normal values obtained from a report of Quanjer *et al.*[6]

Methacholine challenge test

The method of bronchial provocation used in the study was according to the method of Tsai *et al.*[7] Briefly, bronchial challenge was performed provided that a patient's baseline FEV_1 was more than 50% predicted. Normal saline was delivered using the nebulizer, and FEV_1 was measured 3 minutes later. Unless FEV_1 had fallen by 10% from the baseline level, the first dose of 0.075 mg/ml methacholine was inhaled 5 times. Thereafter, 0.31, 1.25, 5.0, 10, and 25 mg/ml of methacholine were likewise administered. The end point being a fall in FEV_1 of more than 20% or $FEF_{25-75\%}$ of more than 25% from the post-saline control level. On completing the test, twice inhalation of bronchodilator (isoproterenol 0.2 mg/dose) was given to reverse any bronchoconstriction. Dose response curves were plotted and $PD_{20}FEV_1$ and $PD_{25}FEF_{25-75\%}$ were obtained by linear interpolation. The percent improvement in FEV_1 and $FEF_{25-75\%}$ were calculated. The total inhaled methacholine was expressed as breath unit (BU). One BU of methacholine is equal to one inhalation of 1 mg/ml of methacholine. Dose response curves were plotted and the reversibility of FEV_1 and $FEF_{25-75\%}$ were calculated.

Statistics

For statistical analysis, student's *t*-test was used for comparison by Statistical Analysis System on an IBM-compatible personal computer.[8]

RESULTS

The comparison of basic pulmonary function between young and elderly asthmatics

Fifty-one patients completed bronchodilator tests and 54 patients completed methacholine challenge tests.

The results of baseline pulmonary function tests are shown in Table 2. For FVC, % predicted FVC, FEV_1, % predicted FEV_1, $FEF_{25-75\%}$ and % predicted $FEF_{25-75\%}$, elderly asthmatic patients were less than the younger group.

The comparison of airway reversibility and hyperreactivity between young and elderly asthmatic patients

The results of test for bronchodilator responses are shown in

Table 3. Test for bronchodilator responses (% reversibility).

	Elderly	Young	p value
FEV_1	18.6 ±15.7*	12.3 ±11.2	0.11
$FEF_{25-75\%}$	37.9 ±33.2	20.0 ±19.1	0.02

* mean ± SD

Table 4. Methacholine challenge tests.

	Elderly	Young	p value
1. $PD_{20}FEV_1$ (BU)	8.35 ±8.87*	7.37 ±10.23	0.72
2. $PD_{25}FEF_{25-75\%}$ (BU)	6.54 ±13.26	5.27 ±5.58	0.65

* mean ± SD

Table 3. There was no significant difference in % reversibility of FEV_1 between both groups although the average was greater in the elderly (18.58 ± 15.73) than the young patients (12.25 ± 11.24). The percent reversibility of $FEF_{25-75\%}$ was significantly greater ($p = 0.02$) in elderly (37.9 ± 33.2) than in young asthmatic patients (20.0 ± 19.1).

The results of methacholine challenge test are shown in Table 4. There was no difference in PD_{20} FEV_1 and $PD_{25}FEF_{25-75\%}$ between groups.

DISCUSSION

Asthmatic patients have a feature of greater variability in airway caliber than normal subjects in response to a variety of stimuli, either endogenous or exogenous. This concept of asthma as a condition of increased airway responsiveness is embodied in the definition proposed by the American Thoracic Society.[5] In 1942, Curry reported that histamine and acetyl-beta-methylcholine may provoke airway narrowing in asthmatic but not in normal subjects.[9] This has confirmed the earlier observation that the airway of asthmatics is abnormally sensitive to these agents. Subsequently, bronchial provocation by inhaled methacholine or histamine has been widely used in the assessment of airway disease, and it has been generally assumed that the reactivity to these agents reflects the natural phenomenon of hyperresponsiveness in asthmatics. The measurement of airway reactivity has been used in cross-sectional epidemiological studies to estimate the prevalence of asthma. In the clinical context, it has been used to assess the severity of asthma, and it has been asserted that a reduction in reactivity should be the principal aim of treatment.[10]

The pulmonary function declines faster in asthmatics than in the normal subjects. Peat *et al.*[11] have reported that the mean yearly loss of FEV_1 in males of 1.7 m height is 50 ml/year in nonsmoking asthmatics, whereas it is only 35 ml/year in the normal subjects. However, the effect of asthma is variable and not all subjects with asthma may have a steep rate of decline.[11] We found that most parameters of baseline pulmonary function were poorer in the elderly than in the young asthmatics, which included FVC, % predicted FVC, FEV_1, % predicted FEV_1, $FEF_{25-75\%}$ and % predicted $FEF_{25-75\%}$. These results suggest that the elderly asthmatic patients have poorer lung function than the young asthmatics, even when the % predicted values are taken into account.

The reversibility of pulmonary function following bronchodilator inhalation may predict the pulmonary capacity for improvement. In our study,the average degree of reversibility was greater in the elderly than in the young asthmatic patients both in FEV_1, and $FEV_{25-75\%}$, and the latter reached a statistical significant level ($p = 0.02$). It seems that bronchodilator treatment may improve the function of small airway of the elderly group, although they had poorer baseline pulmonary function. It is suggested that optimal treatment with bronchodilators of the elderly asthmatics is crucial. Isoproterenol has a short onset of action, and is suitable for use in the diagnostic procedure in this study.

The degree of pulmonary functional impairment following methacholine challenge will predict the severity of the disease in case of acute asthmatic attack. Brook *et al* have found no statistically significant correlation between $PD_{20}FEV_1$ and the age of subject, duration of asthma or other host characteristics.[12] The same results were found in this study. The elderly patients

had the same degree of bronchial hyperresponsiveness as young patients (Table 4). These results suggest that the bronchial airways of elderly patients are as sensitive as that of young patients. All allergens and irritants should be avoided.

ACKNOWLEDGEMENTS

This work was supported by a grant from Chin-Lin Medical Center, Taiwan.

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