◎原 著

Characteristics of ventilatory function in clinical types of bronchial asthma in the elderly

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Abstract : Ventilatory function was examined in 55 patients with asthma (25 older patients over the age of 60 and 30 younger patients under the age of 59) in relation to four clinical types classified by clinical symptoms and signs.

1. Regarding cellular composition of bronchoalveolar lavage (BAL) fluid, number of BAL neutrophils was significantly increased in type II, bronchiolar obstruction type, of older and younger patients compared to that in type Ia-1 and type Ia－2 of same patients. In contrast, BAL eosinophilia was observed in type Ia－2 of both older and younger patients and in type Ib of younger patients.
2. The values of %FVC, $FEV_{1.0\%}$ and %PEFR were not significantly different among four clinical types of asthma and between older and younger patients, although the values of these ventilatory parameters in type II asthma showed a tendency to be lower compared to other clinical types.
3. The values of %MMF, $\%\dot{V}_{50}$ and $\%\dot{V}_{25}$, showing ventilatory dysfunction of small airways, were lowest in type II asthma of both older and younger patients among four clinical types. A significant difference in these ventilatory parameters of type II asthma compared to type Ia－1 asthma was observed in younger patients, but not in older patients.

These results show that ventilatory dysfunction of small airways is related to clinical asthma types in younger patients, and to aging rather than asthma types in older patients.

Key words : Ventilatory function, Clinical asthma type, BAL cells, aging

Introduction

In asthma in the elderly, qualitative and quantitative changes of allergic reaction can be observed with aging[1,2]. Furthermore, functional and organic changes of the airways have been demonstrated in asthma in the elderly. Thus, onset mechanisms and pathphysiology of asthma in the elderly have been thought to be different from those of younger patients. Regarding allergic reaction, it has been clarified that IgE-mediated immediate allergic reaction participates in onset mechanisms of asthma[3-5]. The allergic reaction is also affected by aging[6]. In contrast, functional and organic changes of the airways in general lead to decrease in ventilatory function in the elderly.

Our previous studies have shown that asthma is classified into three types, Ia simple bronchoconstriction type, Ib bronchoconstriction + hypersecretion type and II bronchiolar obstruction type, by clinical findings and signs[7-11], and by a score calculated by clinical findings and examinations[12,13]. Decrease in ventilatory function in older asthma patients is related to aging, and also to clinical types of asthma.

In the present study, ventilatory function of each clinical type of asthma in the elderly was compared in relation to that in younger asthma patients.

Subjects and Methods

The subjects in this study were 55 patients (28 female and 27 males) with asthma. The subjects were divided into two groups according to age: group A, older patients over the age of 60 (N=25, mean age ; 65.2 years, range ; 61－74 years. mean serum IgE ; 296 ± 316 IU／mℓ), and group B, younger patients under the age of 59 (N=30, mean age ; 44.9 years, range ; 21－56 years. mean serum IgE ; 509 ± 582 IU／mℓ).

Asthma classification was made according to clinical symptoms based on previously reported criteria[7-11].

Type Ia. Simple bronchoconstriction : patients with symptoms such as wheezing and dyspnea, which are elicited mainly bronchoconstriction. In this study, this type was further divided into two subtypes according to the amount of expectoration／day ; type Ia－1 (0-49 mℓ／day) and type Ia－2 (50－99 mℓ／day).

Type Ib. Bronchoconstriction + hypersecretion : patients with symptoms due to hypersecretion (more than 100 mℓ／day of expectoration), in addition to bronchoconstriction.

Type II. Bronchiolar obstruction : patients with symptoms elicited mainly by bronchiolar obstruction.

The background of each asthma type in both older and younger patients was shown in Table 1. Ventilatory function test was carried out in all subjects at attack-free stage using Box Spiror 81 (Chest Co, Japan). Ventilatory function was evaluated in all subjects by six ventilatory parameters such as %FVC, $FEV_{1.0\%}$, %PEFR, %MMF, $\%\dot{V}_{50}$ and $\%\dot{V}_{25}$.

Table 1. Background of older and younger asthma patients classified into clinical types

	Clinical type	No. of patients	Mean age (years)	Serum IgE (IU/ml)
Older patients	Ia	16	65.6	337±368
	Ib	3	62.7	315±231
	II	6	65.5	178± 92
Younger patients	Ia	17	44.2	467±447
	Ib	4	44.8	763±996
	II	9	49.7	367±353

In this study, to evaluate the diagnosis of clinical types of asthma, cellular composition of bronchoalveolar lavage (BAL) fluid was examined in all subjects. Bronchoalveolar lavage (BAL) was performed in all subjects when they were asymptomatic[12-17]. Informed consent for the BAL examination was obtained from all the subjects. The aspirates obtained by a bronchofiberscope were filtered through sterile steel mesh and centrifuged at 1200 rpm for 10 min at 4 ℃. Smear preparations made from the cell suspension were stained with May-Giemsa. BAL cytology was performed by observing 500 cells, excluding epithelial cells. The results were expressed as a percentage of the total cells.

Results

The BAL cytology in each clinical type in older and younger patients with asthma showed that an increase in number of neutrophils was related to bronchiolar obstruction and that in number of eosinophils to hypersecretion. Regarding BAL neutrophils, the number of BAL neutrophils in type II asthma of older and younger patients was significantly increased compared to the number in type Ia－1 and Ia－2 asthma (in older patients ; $p<0.001$, in younger patients ; $p<0.001$) (Fig. 1－a) In contrast, the number of BAL eosinophils was significantly increased in type Ia－2 asthma of older and younger patients than in type Ia－1 asthma (in older patients ; $p<0.05$, in younger patients ; $p<0.02$). A significant increase in BAL eosinophils was also observed in type Ib asthma of younger patients compared to that in type Ia－1 ($p<0.01$). A significant difference in BAL eosinophils was shown between older and younger asthma patients with type Ib ($p<0.01$), suggesting that an increase in BAL eosinophils in younger patients with type Ib was related to hypersecretion (Fig. 1－b).

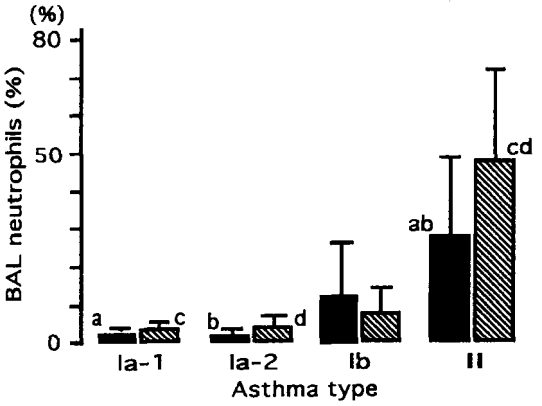

Fig. 1－a. Proportion of BAL neutrophils in older (■) and younger asthma patients (▨). a, b, c and d ; $p<0.001$

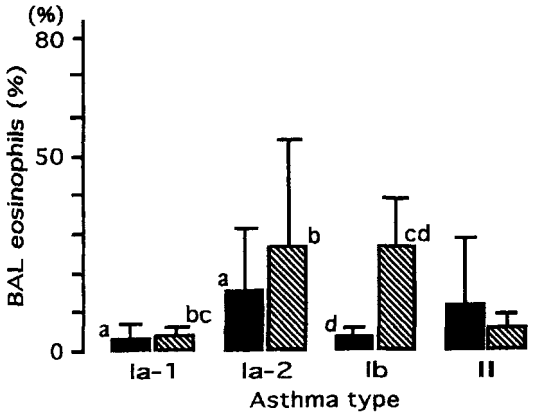

Fig. 1 −b Proportion of BAL eosinophils in older (■) and younger asthma patients (▨). a ; $p<0.05$, b ; $p<0.02$, c and d ; $p<0.01$.

The value of %FVC was not significantly different between older and younger asthma patients as shown in Fig. 2. The value was in general low in type II asthma in both older (75.6%) and younger patients (84.7%), however, there was not significant difference between type Ia− 1 and type II asthma.

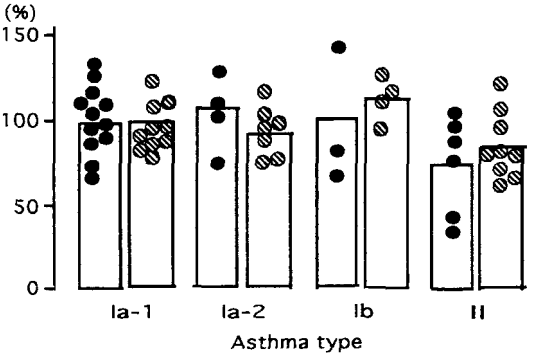

Fig. 2. %FVC value in each clinical type of older (●) and younger patients (⊘) with asthma

Figure 3 showed the value of $FEV_{1.0\%}$ in each clinical type of asthma patients. The mean value in older patients was 67.7% in type Ia− 1, 64.8% in type Ia− 2, 71.4% in type Ib and 57.5% in type II asthma. In contrast, the value in younger patients was 71.2% in type Ia− 1, 74.3% in type Ia− 2, 70.0% in type Ib and 61.3% in type II asthma. The significant difference was not present between older and younger patients. The value was low in type II asthma of both older and younger patients, although there was not significant difference between type Ia− 1 and type II asthma.

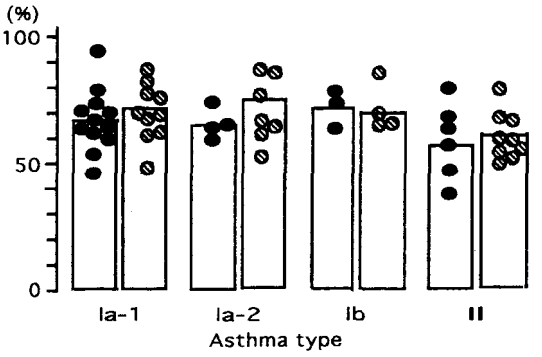

Fig. 3. FEV1.0% value in each clinical type of older (●) and younger patients (⊘) with asthma

Table 2 showed the results of %PEFR value in each clinical type of asthma patients. Any significant difference was not observed in %PEFR value between older and younger asthma patients. The value in type II was low in both older and younger patients, although no significant difference was shown between type Ia− 1 and type II asthma in both older and younger patients.

Table 2. %PEFR value in each clinical type of older and younger patients with asthma

	Asthma type			
	Ia-1	Ia-2	Ib	II
Older patients	73.7 ±24.3%	93.2 ±17.9%	74.9 ±15.8%	69.9 ±21.7%
Younger patients	88.0 ±27.2%	76.2 ±28.4	97.3 ±16.9	57.6 ±21.1

The value of %MMF in type Ia－1, Ia－2 and Ib asthma was in general higher in younger patients than in older patients, however, these were not significant. The value in type II asthma was lower compared to other clinical types. The value of %MMF in type II asthma of younger patients was significantly lower than that in type Ia－1 of same patients ($p<0.01$) (Fig. 4).

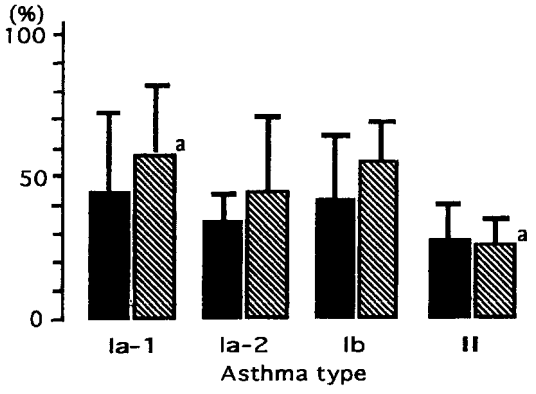

Fig. 4. %MMF value in each clinical type of older (■) and younger patients (▨) with asthma. a : $p<0.01$.

The value of $\%\dot{V}_{50}$ in type Ia－1, Ia－2, and Ib was lower in older patients than in younger patients, although these were not significant. The value was lowest in type II asthma of older and younger patients among four clinical types, and the value of type II asthma of younger patients was significantly lower than that of type Ia－1 ($p<0.001$), as shown in Fig. 5.

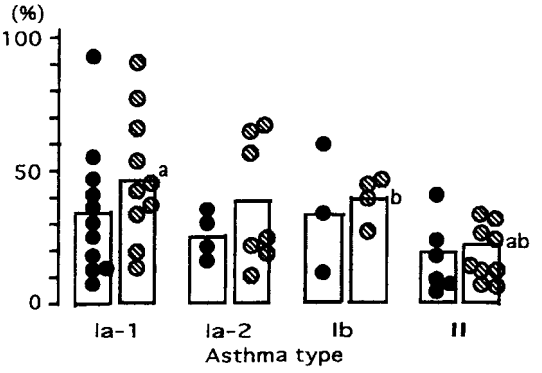

Fig. 5. $\%\dot{V}_{50}$ value in each clinical type of older (●) and younger patients (⊘) with asthma. a : $p<0.01$, b : $p<0.001$.

Figure 6 shows the value of $\%\dot{V}_{25}$ in each clinical type. The value was lower in type Ia－2 and Ib asthma of older patients than in same types of younger patients, however, there was not significant difference between older and younger patients. The value in type II asthma was lower compared to other clinical types in both older and younger patients, and the difference was significant between type Ia-I and type II ($p<0.01$), between Ia－2 and II ($P<0.001$), and between Ib and II ($P<0.001$) in younger patients.

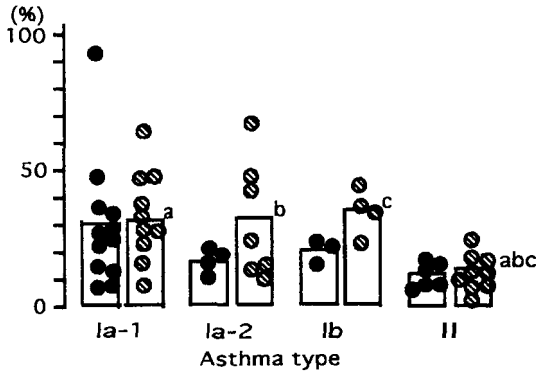

Fig. 6. $\%\dot{V}_{25}$ value in each clinical type of older (●) and younger patients (⊘) with asthma. a : $p<0.01$, b and c : $p<0.001$.

Discussion

In pathological changes in the airways, chemical mediators such as histamine and leukotrienes which are released from tissue mast cells[3-5, 18, 19] and inflammatory cells such as lymphocytes, neutrophils, eosinophils and basophils migrating from blood-stream[20-25] play an important role in onset mechanisms of bronchial asthma. In recent years, airway inflammation has been noticed in adult patients with asthma relating to chronicity and severity of their asthma attacks.

We have reported that asthma can be classified into three (or four clinical types) : Ia) (Ia－1 and Ia－2) simple bronchoconstriction type, Ib) bronchoconstriction + hypersecretion type, and II) bronchiolar obstruction type. Our previous studies also showed that inflammatory cells in the airways shown by analysis of BAL cells are different among three (or four) clinical asthma types. In the present study, a significant increase in number of BAL neutrophils was observed in type II asthma, and of BAL eosinophils in type Ia－2 asthma of both older and younger patients. Furthermore, a significantly increased number of BAL eosinophils was also found in type Ib asthma of younger patients. These results suggest that BAL neutrophilia is closely related to bronchiolar obstruction, and BAL eosinophilia to hypersecretion.

Regarding ventilatory function, the values of %FVC, $FEV_{1.0\%}$, and %PEFR did not show any definite tendency in four clinical asthma types and in two age groups. The results may suggest that the values of these ventilatory parameters are largely affected by disease severity, but not by clinical asthma types and aging. However, it must be noticed that the value of %FVC was more decreased in type II asthma of both older and younger patients compared to other clinical asthma types.

The values of %MMF, $\%\dot{V}_{50}$, and $\%\dot{V}_{25}$ of type II asthma were cleary decreased and significantly lower than the value of type Ia－1 asthma in younger patients. In older patients, the values of %MMF, $\%\dot{V}_{50}$, and $\%\dot{V}_{25}$ in type II asthma were in general lower compared to the value of type Ia－1, however, the differences were not significant. The results may suggest that decreased values of %MMF, $\%\dot{V}_{50}$, and $\%\dot{V}_{25}$, which represent ventilatory dysfunction of small airways, in type II asthma of younger patients are related to pathophysiological changes of airways, bronchiolar obstruction. In contrast, the values of %MMF, $\%\dot{V}_{50}$, and $\%\dot{V}_{25}$ in type II asthma of older patients were not significantly different from those in other clinical asthma types such as type Ia－1, Ia－2, and Ib, suggesting that the values of these parameters show a tendency to decrease with

aging. The results may suggest that a decrease in values of these ventilatory parameters in type II asthma of older patients are affected by aging in addition to pathophysiological changes of airways.

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老年者気管支喘息の各臨床病型における換気機能の特徴

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気管支喘息55例（老年症例－65才以上－25例，若年症例－59才以下－30例）における換気機能の特徴について，各臨床病型別に検討を加えた。

1．まず対象症例の臨床病型の病態的特徴を，気管支肺胞洗浄（BAL）液中の細胞成分で検討すると，Ⅱの細気管支閉塞型の症例では，好中球の増加が，また Ⅰa－2や Ⅰb の過分泌型の症例では好酸球の増加が特徴的であった。

2．%FVC，$FEV_{1.0\%}$，%PEFRなどの換気パラメーターは，Ⅱ型において他の病型に比べ低値を示す傾向は見られたが，各病型間に有意差は見られなかった。

3．%MMF，$\%\dot{V}_{50}$，$\%\dot{V}_{25}$などのどちらかと言えば小ないし細気管支領域の換気障害を示す換気パラメーターの値は，老年および若年症例ともⅡ型（細気管支閉塞型）において最も低い値が示された。そして，若年症例では，Ⅱ型の症例においてこれからの換気パラメーターの値は，Ⅰa－1型（単純性気管支攣縮型）に比べ有意に低い値を示した。しかし，老年症例ではⅡ型におけるこれらの換気パラメーターの値は，他の臨床病型との間に有意の差は見られなかった。

キーワード：換気機能，臨床病型，BAL細胞，加齢