
◎原 著

Decrease in histamine release from bronchoalveolar cells with aging in patients with atopic asthma sensitive to house dust mite

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Abstract : Histamine release from bronchoalveolar cells induced by house dust mite (HDm) was compared in patients with atopic asthma sensitive to HDm in relation to age. 1. Total cell number in bronchoalveolar lavage (BAL) fluid was larger in patients over the age of 40 years (9.10×10^6) than in those aged between 20 and 39 years (6.25×10^6), however, this was not significant. 2. Number of BAL eosinophils was not significantly different between the two age groups. 3. Number of BAL basophilic cells was significantly higher in younger patients (20–39 years) ($1.85 \pm 1.03 \times 10^2 / \text{ml}$) than in older patients (40+ years) ($0.39 \pm 0.24 \times 10^2 / \text{ml}$) ($p < 0.001$). 4. Histamine release from BAL cells induced by HDm was significantly higher in younger patients ($38.1 \pm 24.8\%$) than in older patients (0%) ($p < 0.001$). These results suggest that histamine release from BAL cells in patients with HDm allergy decreases with aging.

Key words : Bronchial asthma, House dust allergy, Histamine release, Bronchoalveolar cells

Introduction

House dust mite is a common allergen in bronchial asthma. In asthma patients with house dust mite (HDm) allergy, bridging of IgE receptors on mast cell membrane is caused by HDm, followed by release of

chemical mediators such as histamine and leukotrienes¹⁻⁸⁾, which induce pathophysiological changes of airways such as bronchoconstriction, mucus hypersecretion and edema of mucous membrane. Thus, histamine is one of the most important mediators participating in onset mechanisms of asthma attacks.

Bronchial asthma is divided into two groups, atopic and non-atopic, based on presence or absence of IgE-mediated allergy, and atopic type is often observed in younger asthma patients, and non-atopic type in older patients. HDm allergy is the most popular one in atopic type asthma. Our previous studies suggest that the role of histamine during triggering events of asthma attacks is different between younger and older patients with asthma⁹⁾.

In the present study, histamine release from bronchoalveolar (BAL) cells was examined in patients with atopic asthma sensitive to HDm to analyze the role of histamine in onset mechanism of asthma attacks.

Subjects and Methods

The subjects in this study were 14 patients (6 females and 8 males) with atopic asthma. The mean age of the subjects was 42.9 years (range; 21–61 years). The mean concentration of total serum IgE was 1012 IU/ml (range; 30–4134 IU/ml). They were all sensitive to house dust mite (HDm) and showed RAST score of 2+ or more for HDm. They were all non-smokers.

Bronchoalveolar lavage (BAL) was performed according to the method previously described^{8, 10–14)} during attack-free stages. Informed consent for the BAL examination was accepted by all subjects. After the aspirates were centrifuged at 300 *g* for 10 min at 4 °C, the cell pellet was resuspended in Tris ACM. A differential cell count was carried out on 1000 cells, excluding epithelial cells, on smear preparations which were made from BAL cell suspensions and stained with May-Giemsa. The number of eosinophils and basophilic cells (basophils and mast cells) was calculated. The results were expressed

as absolute number per ml. In this study, the mean recovery rate at BAL was $28.7 \pm 17.6\%$ (mean \pm SD).

Histamine release from BAL cells was observed by the method previously described^{8, 15)}. After the number of BAL cells was adjusted to 10^6 cells/ml in Tris ACM, house dust extract (8.4 mcg/0.2 ml) was added to the cell suspension. The mixed solution was then incubated for 15 min at 37°C and centrifuged at 300 *g* for 10 min at 4 °C. The histamine content of both the cells and supernatant fluid were analyzed by perchloric acid precipitation and assayed with an automated spectrofluorometric histamine analysis system (Technicon Instruments Co.)¹⁶⁾, as previously reported^{3–5)}. The release of histamine from peripheral blood was observed by a whole blood method, as previously described⁷⁾.

The subjects were divided into two groups according to age: 20–39 years (group A) and 40+ years (group B).

The level of total IgE in sera was measured by radioimmunosorbent test (RIST) and IgE antibodies for HDm were estimated by radioallergosorbent test (RAST).

Results

Table 1 shows the characteristics of subjects divided into two groups, A and B, by age. Recovery rate was higher in group B patients (40+ years) than in group A patients (20–39 years), however the difference was not significant. Total cell number was also larger in group B patients than in group A, as shown in Fig. 1, although this was not significant.

Table 1. Characteristics of subjects studied

Subjects	Age, years	IgE (IU/ml)	Bronchoalveolar lavage Recovery rate	Total cell number ($\times 10^6$)
Group A	30.8 (21-39)	868	26.2% (4.2-56.6%)	6.25 \pm 3.0
Group B	51.9 (41-61)	1120	30.5% (18.6-74.0%)	9.1 \pm 3.8

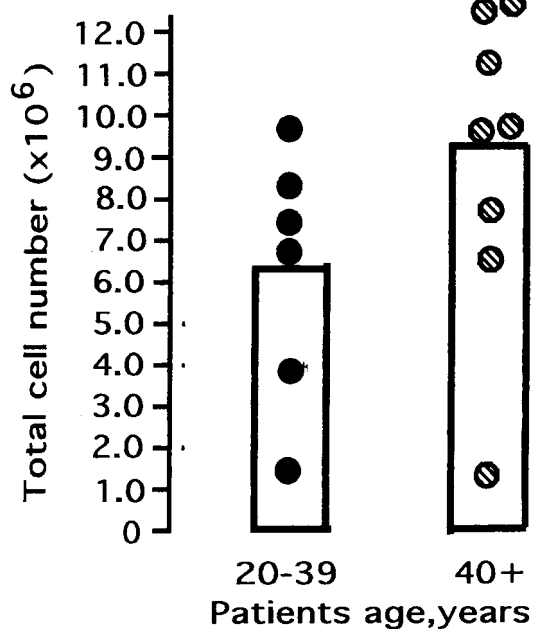


Fig. 1. Total cell number in BAL fluid of patients with atopic asthma classified by age

Number of BAL eosinophils was larger in group A, younger patients ($9.04 \pm 11.8 \times 10^3 / \text{ml}$) than in group B, older patients ($5.32 \pm 4.3 \times 10^3 / \text{ml}$). However, this difference was not significant (Fig. 2).

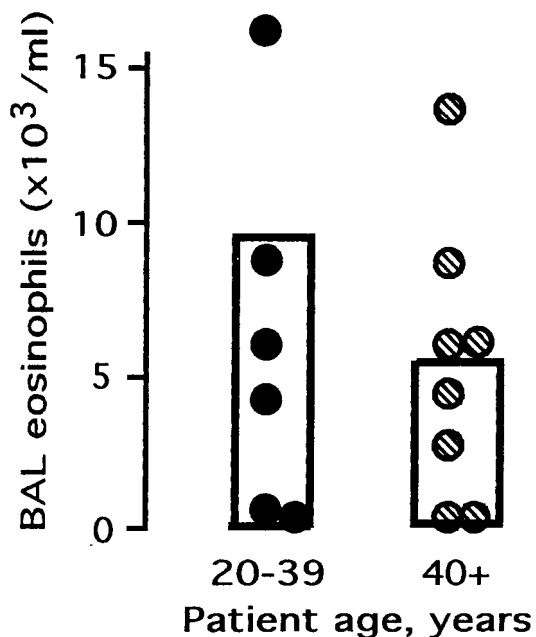


Fig. 2. Number of BAL eosinophils in patients with atopic asthma classified by age

Figure 3 shows number of BAL basophilic cells in the two groups. The number of basophilic cells in BAL fluid was significantly higher in younger patients ($1.85 \pm 1.08 \times 10^2 / \text{ml}$) than in older patients ($0.39 \pm 0.24 \times 10^2 / \text{ml}$) ($p < 0.001$). This suggests that number of basophilic cells in airways decreases with aging.

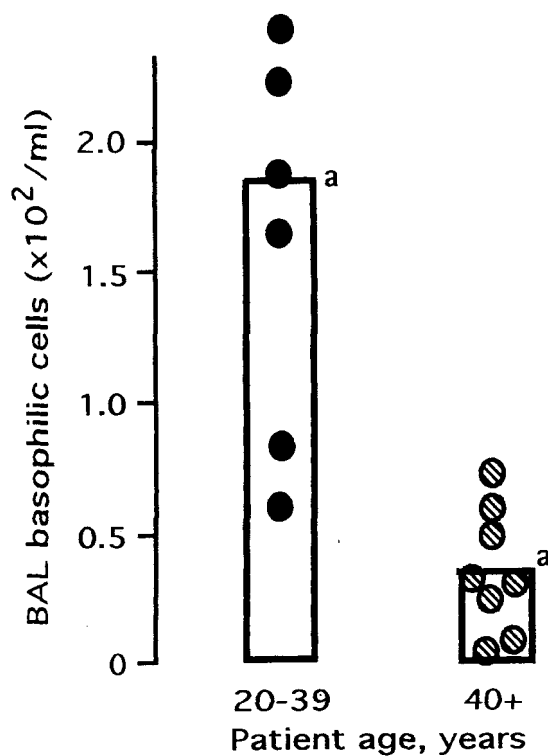


Fig. 3. Number of BAL basophilic cells in patients with atopic asthma classified by age. a ; $p < 0.001$.

Histamine release from BAL cells was significantly higher in group A, younger patient group ($38.1 \pm 24.8\%$) than in group B, older patient group (0%) ($p < 0.001$). The release of histamine from peripheral blood was also higher in younger group ($29.2 \pm 5.3\%$) than in older group ($21.9 \pm 8.5\%$), however this difference was not significant (Fig. 4).

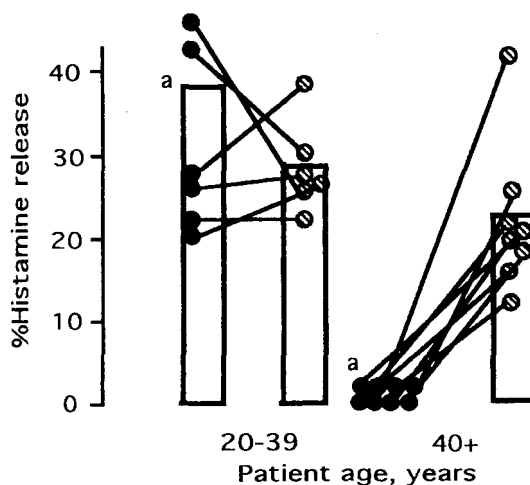


Fig. 4. Histamine release from BAL cells (●) and peripheral blood (⊗) in patients with atopic asthma classified by age. a : $p < 0.001$

Discussion

Asthma is classified by two types, atopic and nonatopic, based on the presence or absence of IgE-mediated allergic reaction. In atopic asthma, bridging of IgE receptors on mast cell by inhalant allergen causes release of chemical mediators such as histamine and leukotrienes from the cell. Thus, the presence of IgE-mediated allergic reactions, positive immediate skin reaction to allergens, elevated serum IgE levels, IgE antibodies against allergen, and release of histamine from basophils and mast cells, can be shown in atopic asthma. Our previous studies have shown that IgE-mediated allergic reactions, particularly, skin reaction and release of histamine from basophilic leucocytes, change with aging^{17, 18)}. However, it is not well known whether IgE-mediated allergic reaction in the airways of atopic asthma changes with aging.

In the present study, effects of aging on IgE-mediated allergic reaction in atopic

asthma was examined by observing number of basophilic cells in the airways and histamine release from the cells. The results obtained here shows that number of basophilic cells in the airways of atopic asthma decreases with aging, and that the release of histamine from bronchoalveolar lavage (BAL) cells^{9, 19)} also decreases with aging.

Chemical mediators such as histamine and leukotrienes, which are released from tissue mast cells during the time of immediate asthmatic reaction (IAR), and from inflammatory cells including basophils during late asthmatic reaction (LAR), play an important role in the onset mechanisms of asthma attacks²⁰⁻²²⁾. It is well known that histamine is released from mast cells and basophils in relation to IgE-mediated allergic reaction^{1, 2)}, and causes bronchoconstriction in asthma patients. The results in the present study demonstrate that histamine is less important in older patients than in younger patients as a triggering factor of asthma attacks.

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ダニ喘息における気道遊走細胞からのヒスタミン遊離の加齢による減少

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ダニ喘息14例を対象に, ハウスダストエキスによる気道遊走細胞からのヒスタミン遊離と加齢との関連について検討を加えた。

1. 気管支肺胞洗浄液 (BALF) 中の総細胞数は, 20-39才の症例群 (6.25×10^6) に比べ, 40才以

上の症例群 (9.1×10^6) でやや多い傾向が見られたが, 推計学的には有意差は見られなかった。

2. BALF中好酸球数は, 20-39才と40才以上の症例群間に差は見られなかった。
3. BALF中好塩基性細胞数は, 40才以上の症例群 ($0.39 \pm 0.24 \times 10^2 / \text{ml}$) に比べ, 20-39才の症例群 ($1.85 \pm 1.03 \times 10^2 / \text{ml}$) において有意に多い傾向が見られた ($P < 0.001$)。
4. ハウスダストエキスによるBALF中細胞からのヒスタミン遊離は, 40才以上の症例群 (0%) に比べ20-39才の症例群 ($38.1 \pm 24.8\%$) において有意に高い結果が得られた ($P < 0.001$)。

これらの結果より, ダニ喘息 (アトピー型喘息) における気道遊走細胞からのヒスタミン遊離は, 加齢とともに減少することが示唆された。