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Yoshiro Tanizaki*

Haruki Komagoe†

Michiyasu Sudo‡

Hiroshi Morinaga**

Hikaru Kitani††

Shinya Tada‡‡

Kiyoshi Takahashi§

Ikuro Kimura¶

*Okayama University,

†Okayama University,

‡Okayama University,

**Okayama University,

††Okayama University,

‡‡Okayama University,

§Okayama University,

¶Okayama University,

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Yoshiro Tanizaki, Haruki Komagoe, Michiyasu Sudo, Hiroshi Morinaga, Hikaru Kitani, Shinya Tada, Kiyoshi Takahashi, and Ikuro Kimura

Abstract

Anti-IgE-induced histamine release from basophils was examined in 46 asthmatic subjects using a whole blood method. Basophils from subjects less than 30 years old released more histamine than those from subjects aged 41 to 50. The age at onset of the disease also affected the reactivity of basophils to anti-IgE: basophils showed a high response in subjects whose age at onset was between 0 and 10 years, and low response in the subjects whose age at onset was between 41 and 50 years. There was a correlation between histamine release and serum IgE levels. However, individual dose-response curves of histamine release varied greatly in whom serum IgE levels were low.

KEYWORDS: histamine release, whole blood, patient age, age at onset, serum IgE levels

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HISTAMINE RELEASE FROM WHOLE BLOOD INDUCED BY ANTI-IGE : RELATIONSHIP TO PATIENT AGE AGE AT ONSET AND SERUM IGE LEVELS

Yoshiro TANIZAKI, Haruki KOMAGOE, Michiyasu SUDO, Hiroshi MORINAGA,
Hikaru KITANI,* Shinya TADA*, Kiyoshi TAKAHASHI* and Ikuro KIMURA*

Department of Medicine, Okayama University Medical School, Misasa Medical Branch, Tottori 682-02,

** Second Department of Medicine, Okayama University Medical School, Okayama 700, Japan*

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Abstract. Anti-IgE-induced histamine release from basophils was examined in 46 asthmatic subjects using a whole blood method. Basophils from subjects less than 30 years old released more histamine than those from subjects aged 41 to 50. The age at onset of the disease also affected the reactivity of basophils to anti-IgE: basophils showed a high response in subjects whose age at onset was between 0 and 10 years, and low response in the subjects whose age at onset was between 41 and 50 years. There was a correlation between histamine release and serum IgE levels. However, individual dose-response curves of histamine release varied greatly in whom serum IgE levels were low.

Key word : histamine release, whole blood, patient age, age at onset, serum IgE levels.

It is well known that blood basophils and tissue mast cells have IgE Fc receptors on the cell membrane. Interaction between anti-IgE and IgE antibodies on the cell membrane causes histamine release from these cells (1). Bridging of IgE molecules induces phospholipid methylation (2, 3) and increase in Ca^{2+} influx (4-6), followed by histamine release.

An automated fluorometric histamine analysis system has been developed by Siraganian (7, 8). The method makes it possible to measure histamine release more easily. Furthermore, Siraganian *et al.* have studied the release of histamine from whole blood to simplify the histamine release assay (9). They showed that maximum histamine release from whole blood correlated closely with the maximum release from washed leucocytes.

Our previous studies (10, 11) demonstrated that there are some differences in anti-IgE-induced histamine release from basophils of asthmatic subjects between whole blood and washed leucocytes. In the present study, anti-IgE-induced histamine release from whole blood of asthmatic subjects was examined in relation to patient age, age at onset and serum IgE levels.

MATERIALS AND METHODS

Forty-six asthmatic subjects were selected for the present study. They were all diagnosed as having bronchial asthma according to their symptoms and clinical findings showing reversible bronchospasm. Histamine release from basophils induced by anti-IgE (Wehringwerke) was performed by a whole blood method, as previously described (10, 11). Whole blood (4 ml) of each subject was incubated with different concentrations of anti-IgE (0.2 ml) at 37°C for 15 min. Histamine released from whole blood was assayed by an automated fluorometric analysis system (7, 8). The results were expressed as a percentage of the total histamine content. All medication was stopped 12 h before the examination. Total serum IgE was measured by a radioimmunosorbent test (RIST).

RESULTS

Histamine release and patient age. The maximum percent histamine release from basophils induced by anti-IgE was highest ($33.8 \pm 9.2\%$) (mean \pm SEM) in the asthmatics aged between 0 and 30 years. On the other hand, the histamine release was lowest ($18.7 \pm 5.9\%$) in the subjects aged between 41 and 50 years, although a significant difference was not present between the two groups. In the asthmatics over 41 years old, anti-IgE-induced histamine release tended to increase with aging. The release of histamine from basophils was rather high ($28.4 \pm 4.2\%$) in the asthmatic subjects over 61 years old (Fig. 1).

Histamine release and age at onset. Anti-IgE caused much more histamine release ($36.6 \pm 4.2\%$) in asthmatic subjects whose age at onset of asthma was between 0 and 10 years than in those whose age at onset was 41 to 50 ($18.1 \pm 4.7\%$). A statistically significant difference in histamine release was present between the two groups ($p < 0.02$). The histamine release was $26.4 \pm 6.9\%$ in the subjects between 51 and 60 years old at onset, and the release was $22.4 \pm 6.1\%$ in the subjects over 61 at onset. The results suggest that anti-IgE-induced histamine release is rather low in 'late onset' asthma (Fig. 2).

Histamine release and serum IgE levels. There was a correlation between histamine release and serum IgE levels. The maximum percent histamine release by anti-IgE was higher with higher serum IgE levels. The percent histamine release was $16.1 \pm 5.0\%$ when serum IgE levels were from 0 to 100 IU/ml. Basophils

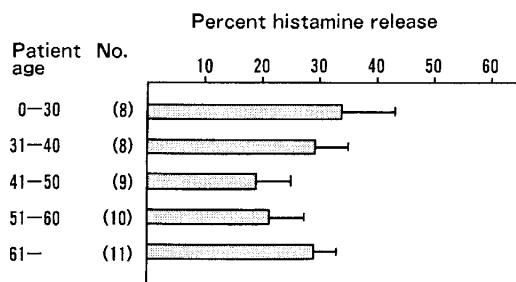


Fig. 1. Maximum percent histamine release from basophils induced by anti-IgE and patient age.

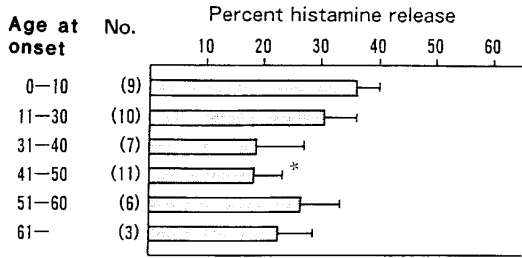


Fig. 2. Maximum percent histamine release from basophils induced by anti-IgE and age at onset of the disease. * $p < 0.02$ compared with the 0-10 group (t test)

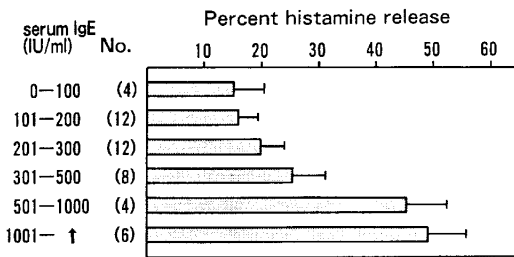


Fig. 3. Maximum percent histamine release from basophils induced by anti-IgE and serum IgE levels.

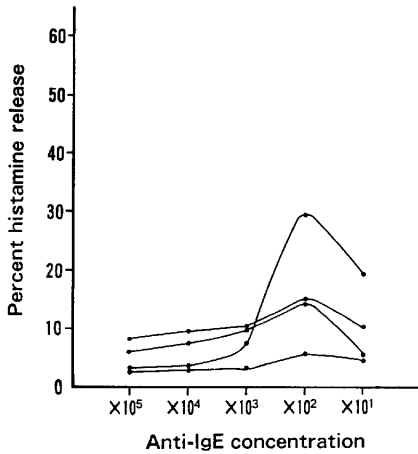


Fig. 4. Dose-response curves of histamine release in asthmatic subjects (serum IgE; 0-100 IU/ml).

stimulated by anti-IgE released more histamine ($45.8 \pm 7.1 \%$) when the levels were from 501 to 1000 IU/ml, and much more histamine ($48.1 \pm 6.7 \%$) when they were more than 1000 IU/ml (Fig. 3).

Dose-response curves of histamine release showed that when serum IgE levels were 0 to 100 IU/ml basophils were less reactive to anti-IgE (Fig. 4). Basophil reactivity to anti-IgE was low in many cases when serum IgE levels were 101 to 200 IU/ml, although basophils in several cases were highly reactive (Fig. 5). The number of cases showing high basophil reactivity increased when the serum IgE

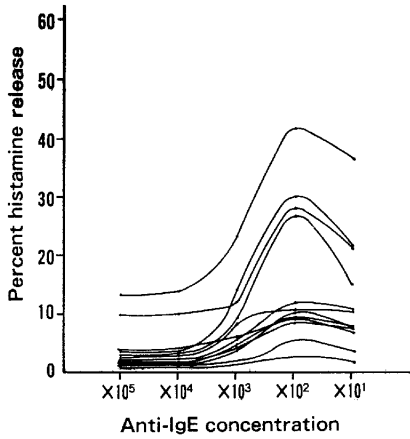


Fig. 5. Dose-response curves of histamine release in asthmatic subjects (serum IgE; 101-200 IU/ml).

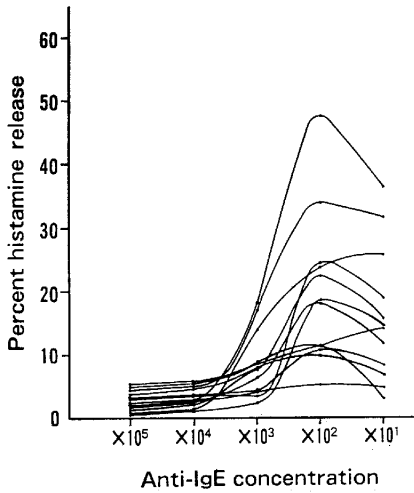


Fig. 6. Dose-response curves of histamine release in asthmatic subjects (serum IgE; 201-300 IU/ml).

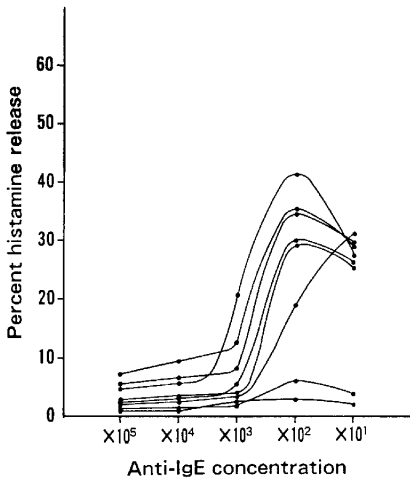


Fig. 7. Dose-response curves of histamine release in asthmatic subjects (serum IgE; 301-500 IU/ml).

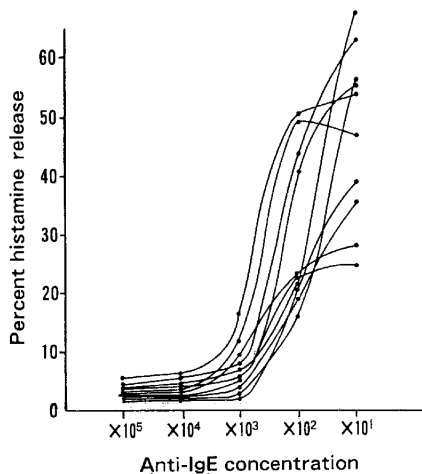


Fig. 8. Dose-response curves of histamine release in asthmatic subjects (serum IgE; over 500 IU/ml).

levels were from 201 to 300 IU/ml (Fig. 6). Basophils highly reactive to anti-IgE were observed in 6 out of 8 cases with levels from 301 to 500 IU/ml, as shown in Fig. 7. The dose-response curves of this group were bell-shaped as in the cases with serum IgE levels less than 300 IU/ml. The curves were symmetric at the concentration causing the maximum percent release. All of the cases with more than 500 IU/ml serum IgE levels showed high basophil reactivity with a consistent increase as the anti-IgE concentrations were increased (Fig. 8).

DISCUSSION

IgE antibodies on the surface of target cells such as basophils and mast cells play an important role in immediate hypersensitivity (12), which mainly participates in pathophysiological changes of bronchial asthma. Antigen (13) and anti-IgE (14) cause IgE-mediated release of histamine from target cells. The interaction between anti-IgE and IgE antibodies on basophils results in the release of chemical mediators such as histamine and SRS-A from the cells.

In the present study, reactivity of basophils from asthmatic subjects to anti-IgE was observed by measuring the release of histamine. The results showed that anti-IgE-induced histamine release correlates to a certain extent with serum IgE levels, as previously reported by several investigators (1, 14). However, the dose-response curves of histamine release varied greatly even in an asthmatic group with the same range of serum IgE levels, especially when serum IgE levels were low (less than 300 IU/ml). Thus the degree of histamine release from basophils due to anti-IgE can not be estimated by serum IgE levels when they are low, though it may be estimated by serum IgE levels when they are greater than 500 IU/ml, because basophils always release a significantly large amount of histamine when the levels are over 500 IU/ml, as shown in Fig. 8.

It was found from the present study that patient age and age at onset of the disease might affect the reactivity of basophils to anti-IgE. Basophils highly reactive to anti-IgE were observed in many subjects between 0 and 30 years old, while less reactive basophils were found in many subjects between 41 and 50. Age at onset affected the basophil reactivity to anti-IgE in almost the same manner as patient age. These factors affecting the reactivity of basophils are important in estimating the degree and type of allergic reaction in patients with asthma.

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