
◎原 著

Total IgE, IgG and IgG₄ levels in sera of patients with bronchial asthma. Changes of serum concentrations in the elderly

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Abstract: The serum levels of total IgE, IgG and IgG₄ were compared among five age groups of patients with bronchial asthma. 1. The level of serum IgE was significantly higher in the patients before the age of 29 than in those between the ages of 30 and 49 ($p < 0.02$), between 50 and 59 ($p < 0.01$) and between 60 and 69 ($p < 0.01$). The serum IgE level tended to increase in the patients over age 70. 2. The serum level of total IgG was significantly higher in the patients over age 70 compared with the level in the 30-49 ($p < 0.05$) and the 60-69 year old groups ($p < 0.05$). 3. The serum IgG₄ level was increased with aging, although no significant difference was found among the five age groups. 4. The IgG₄ level correlated to a certain extent with the level of serum IgE. The results reveal that the levels of total IgE, IgG and IgG₄ are increased in the elderly patients over age 70, and that there is a relationship between serum levels of total IgE and IgG₄.

Key words: Total IgE, IgG, IgG₄, aging, bronchial asthma

Introduction

Lots of studies have shown that allergo-immunological reactions participate in the onset mechanisms of bronchial asthma. Out of various immunoglobulins, IgE antibodies have been well known to play an important role at the initiation stage of asthma attacks. In the immediate allergic reactions induced by IgE antibodies, a release of chemical mediators from mast cells is at

first observed and then pathophysiological changes of the airways are triggered¹⁻³⁾. In the release mechanism of chemical mediators, the release of histamine induced by anti-IgE is correlated to serum IgE levels^{4,5)}. Participation of IgG antibodies in immediate allergic reaction was reported as IgG ST-S⁶⁾ and later as reaginic IgG⁷⁾. The IgG antibody is at the present time identified as IgG₄, subclass of IgG. The role of IgG₄ in allergic reaction is, however, controversial as to whether the

action is anaphylactic or protective⁸⁻¹³. In spite of the findings that these immunoglobulins are related to the pathology of asthma, there are little reports about the changes of serum levels in the elderly patients with bronchial asthma. In the present study, changes in serum levels of total IgE, IgG and IgG₄ were observed in relation to patient age.

Subjects and Methods

The subjects were 72 patients with bronchial asthma (37 females and 35 males). Their mean age was 50.5 years (range, 7 to 80 years). The mean level of serum IgE was 476 IU/ml (range, 9 to 2177 IU/ml). The subjects were divided into five age groups 0-29, 30-49, 50-59, 60-69 and 70+ years of age, to examine the changes in serum levels of IgE, IgG and IgG₄ with aging, particularly in the elderly.

Serum level of IgG was estimated by a turbidimetric immunoassay (TIA), and the level of IgG₄ by an enzyme-linked immunosorbent assay (ELISA). Serum level of IgE was measured by a radioimmunosorbent test (RIST). The results were expressed as mg/dl for IgG and IgG₄, and IU/ml for IgE.

The statistically significant difference of the mean was estimated using the unpaired Student's t test. The values of significance were expressed as a p value.

Results

Serum IgE Levels

The mean level of serum total IgE was highest in the patients before the age of 29. The mean IgE levels of these patients were significantly higher than the levels of those between the ages of 30 and 49 ($p < 0.02$), between 50 and 59 ($p < 0.01$) and between 60

and 69 ($p < 0.01$). The serum levels of IgE tended to decrease with aging. The levels were, however, in the patients over the age of 70, in whom the levels were significantly higher compared with the levels in those between 60 and 69 ($p < 0.05$) (Table 1).

Table 1. Serum levels of total IgE in patients with bronchial asthma in relation to patient age

Age, years	No of cases	Serum IgE level (IU/ml)	
		Mean \pm sd	Range
0-29	16	872 \pm 629 ^{abc}	35-2293
30-49	10	289 \pm 338 ^a	10-1020
50-59	10	217 \pm 189 ^b	27- 712
60-69	20	263 \pm 233 ^{cd}	9- 790
70-	16	632 \pm 757 ^d	10-2177

a, $p < 0.02$; b and c, $p < 0.01$; d, $p < 0.05$.

Serum IgG levels

The mean levels of serum IgG were not different among the patients under the age of 69. The level of IgG in the patients over age 70 was significantly higher compared with that in those between 30 and 49 ($p < 0.05$) and between 60 and 69 ($p < 0.05$). The results show that production of IgG is increased in the patients over age 70 (Table 2).

Table 2. Serum levels of total IgG in patients with bronchial asthma in relation to patient age

Age, years	No of cases	Serum IgG level (mg/dl)	
		Mean \pm sd	Range
0-29	5	1384 \pm 183	1100-1633
30-49	6	1133 \pm 185 ^a	920-1460
50-59	5	1352 \pm 244	1140-1800
60-69	17	1292 \pm 252 ^b	920-1800
70-	12	1531 \pm 347 ^b	1211-2400

a and b, $p < 0.05$.

Serum IgG₄ levels

The mean level of total IgG₄ showed a tendency to increase with aging, and the level was highest in the patients over age 70 ($82.4 \pm 63.6 \text{ mg/dl}$) ($\pm \text{sd}$) and lowest in those before age 29 ($56.8 \pm 40.0 \text{ mg/dl}$). The difference was, however, not significant among the five age groups (Fig. 1).

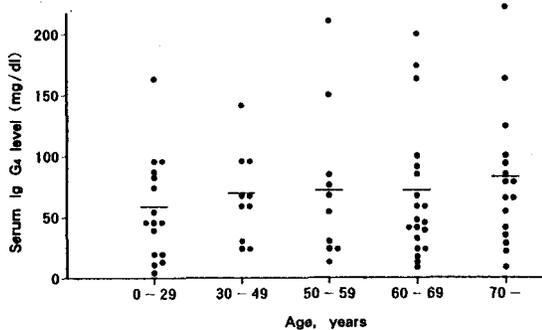


Fig 1. Serum levels of total IgG₄ in patients with bronchial asthma in relation to patient age.

Correlation between the levels of IgE and IgG₄

The mean level of serum IgG₄ was $50.9 \pm 33.2 \text{ mg/dl}$ ($\pm \text{sd}$) in the patients under 100 IU/ml of serum IgE. The mean level of serum IgG₄ showed an increasing tendency with the increase in serum IgE level. The IgG₄ level was highest ($96.0 \pm 79.4 \text{ mg/dl}$) in the patients over 1001 IU/ml of serum IgE and lowest in those under 100 IU/ml of serum IgE. A significant difference was found in the IgG₄ level between the patients under 100 IU/ml and those over 1001 IU/ml of serum IgE ($p < 0.05$) (Fig. 2).

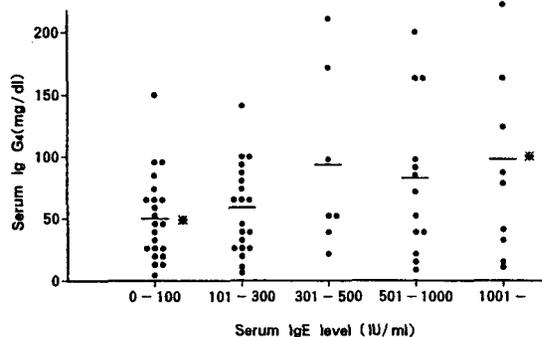


Fig 2. Relationship between serum levels of IgE and IgG₄ in patients with bronchial asthma.

Discussion

Humoral immunity related to IgE, IgG and IgG₄ has been considered to play the role in the pathophysiology of bronchial asthma. Out of these immunoglobulins, IgE is identified as the antibody causing the immediate allergic reactions, and a lot of investigators have observed marked increase of IgE in younger patients with bronchial asthma. There are some attempts to distinguish extrinsic from intrinsic on the basis of the presence or absence of an elevated serum level of IgE¹⁴. There is, however, no agreement about the serum IgE level that exceeds the normal limit¹⁵. Our previous studies have shown that the upper limit of serum IgE in non-allergic healthy subjects is evaluated as 50 IU/ml¹⁶.

It has been suggested that allergic reactions in bronchial asthma change with aging^{17,18}. Extrinsic asthma associated with IgE seems to be the predominant form of the disease among younger subjects, and intrinsic asthma not related to IgE is considered to be more common among elderly subjects, suggesting

that number of patients with asthma related to IgE decreases with aging. There are, however, little reports about the changes in serum levels of these immunoglobulins in the elderly. In this study, the serum level of total IgE was the highest in the patients before age 29, and then tended to decrease with aging. While the serum IgE level was increased in the patients over age 70. The serum levels of IgG and IgG₄ were also increased in the patients over age 70. These results reveal that the serum levels of total IgE, IgG and IgG₄ are elevated in the elderly patients over age 70.

IgE and IgG₄ have been noted to participate in the immediate allergic reaction. The role of IgE in the allergic reaction is well defined, but the role of IgG₄ is not still clear as to whether it is anaphylactic or protective⁹⁻¹³. Recent studies have demonstrated that similar production system is observed between IgE and IgG₄. High serum levels of IgE and IgG₄, but normal levels of the other IgG subclasses have been shown in patients with atopic eczema and bronchial asthma^{19,20}. The T cell derived lymphokine interleukin 4 (IL-4) induces B cells to secrete significant amount of IgE²¹⁻²³. IL-4 also induces IgG₄ production, as well IgE, but not the production of IgG₁, IgG₂ and IgG₃. Thus, IL-4-induced increase in the production of IgE and IgG₄ in B cells is well confirmed^{24,25}.

In the present study, a relationship between serum levels of IgE and IgG₄ was examined in patients with bronchial asthma. The level of total IgG₄ was significantly higher in the patients over 1001 IU/ml of serum IgE compared with those under 100 IU/ml. The results reveal that the production of IgG₄ is in part correlated with the production of IgE in patients with bronchial asthma, and

that increased production of IgE, IgG and IgG₄ is observed in elderly asthmatics over age 70. With regard to the production of IgG₄, a rise of serum IgG₄ seems to be related to serum IgE levels and to aging.

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