

The relationship between anti-IgE auto-antibodies and the IgE response to wasp venom during immunotherapy

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Summary

During immunotherapy with wasp venom, levels of venom-specific IgE antibodies increase and then fall, whereas the concentration of IgG antibodies rises and then remains at a high level. Successful treatment is therefore associated with both increased concentrations of serum IgG and decreased serum IgE antibodies to venom. In this study we have investigated the possible role of auto-antibodies in inducing the decrease in serum IgE antibody. Levels of auto-anti-IgE were measured by a radioimmunoassay. Anti-IgE auto-antibodies were not generated during immunotherapy and there was no significant difference in the levels of anti-IgE auto-antibodies between patients whose venom-specific IgE antibody levels fell more than fivefold after immunotherapy and those patients in whom IgE antibody levels did not change significantly. We conclude that anti-IgE auto-antibodies do not play a part in IgE suppression induced by immunotherapy.

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Introduction

Auto-antibodies directed against specific immunoglobulins have been detected in patients with rheumatoid arthritis [1] and systemic lupus erythematosus [2]. Anti-IgE antibodies have been described in rheumatoid patients [3] and in atopic patients [4–7] but their function and significance are unclear. It has been suggested that anti-IgE auto-antibodies may trigger mediator release from cells by cross-bridging surface-bound IgE. Alternatively, auto-antibodies directed against selected immunoglobulins might regulate B-lymphocyte function. For example, anti-IgM antibodies can modulate the activation and differentiation [8,9] of B cells, and both anti-IgE [10] and IgE–anti-IgE immune complexes [11] have been reported to suppress *in-vitro* IgE synthesis by the human plasmacytoma cells.

The purpose of this investigation was to establish whether there is any relationship between the presence of anti-IgE auto-antibodies *in vivo* and regulation of IgE

antibody responses in humans. We have elected to study patients undergoing wasp venom immunotherapy, because of the falls in venom-specific IgE which accompany successful treatment [12–14].

Subjects and methods

Reagents

Horse serum was purchased from Sera Labs Ltd (Crawley, U.K.) and Tween 20 from Sigma (Poole, U.K.). [¹²⁵I] rabbit anti-human IgE was prepared as described previously. Venoms for skin testing were kindly donated by Pharmacia LKB plc (Milton Keynes, U.K.).

Subjects

Nineteen patients who had received wasp venom immunotherapy were studied. The criteria for diagnosis and the schedule for hyposensitization have been described in detail elsewhere [14]. None of the subjects had suffered from serious adverse reactions to treatment and all individuals received 2 years of maintenance therapy consisting of monthly (100 µg) injections of wasp venom. Eight of the subjects were selected on the basis of a greater

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than fivefold decrease in the serum concentrations of specific IgE to wasp venom after 2 years of immunotherapy. The remainder of the subjects had minimal change in specific IgE levels after 2 years of treatment and they acted as controls. None of the subjects selected for the study reported any adverse reactions to treatment.

Measurement of IgE antibodies to bee venom

Specific IgE antibodies to wasp venom were measured using the radioallergosorbent test [15] with modifications [16]. Wasp venom-coated paper discs (Whatman 541; Maidstone, U.K.) were incubated overnight with 50 μ l of human serum. The next day these were washed in phosphate-buffered saline with 0.05% Tween 20 [17] prior to incubation with 50 μ l [^{125} I]rabbit anti-human IgE [18] diluted in horse serum. After overnight incubation, the discs were washed as before and counts measured in a multichannel Gamma counter (Pharmacia LKB plc, Milton Keynes, U.K.).

Measurement of auto-anti-IgE

Serum samples collected prior to treatment and at the end of 2 years were analysed for the concentrations of anti-IgE auto-antibody as previously described by Nawata *et al.* [19].

Statistical analysis

The levels of wasp venom-specific IgE antibodies and auto-anti-IgE antibodies were compared by a paired *t*-test. All tests were carried out on a Mackintosh II computer using STATVIEW 512+.

Results

Subjects were divided into two groups on the basis of the change in bee venom-specific IgE detected in the serum before and after treatment. In 11 subjects there was a less than fivefold decrease in IgE antibody to wasp venom and in eight subjects there was a fall of greater than fivefold. The changes in the levels of venom-specific IgE antibody in the two groups are shown in Fig. 1.

The concentrations of anti-IgE auto-antibodies before and after 2 years of hyposensitization in the two groups of subjects are shown in Fig. 2. There was no significant change in the concentrations of anti-IgE auto-antibodies following immunotherapy in either group of subjects. Furthermore, there was no correlation between the concentrations of IgE and anti-IgE auto-antibodies after treatment ($r=0.18$, n.s.).

These data do not therefore support the view that anti-IgE auto-antibodies are involved in the decline in IgE

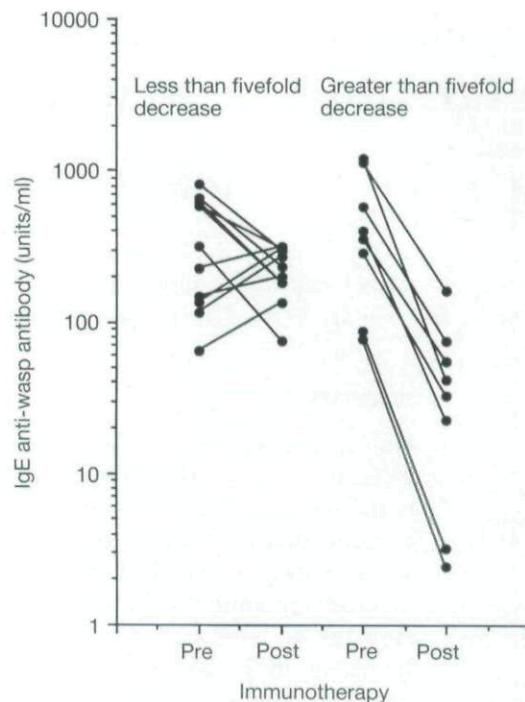


Fig. 1. The levels of wasp venom-specific IgE in the subjects before and after immunotherapy.

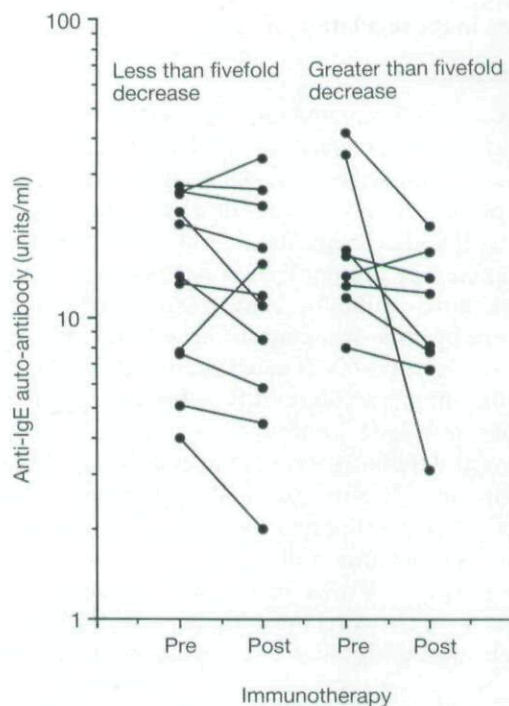


Fig. 2. The levels of anti-IgE auto-antibodies in the subjects before and after immunotherapy.

levels during immunotherapy. Indeed, the level of IgE bore no relationship to the concentration of anti-IgE auto-antibody.

Discussion

Successful immunotherapy with wasp venom is associated with increased IgG antibody levels [12–14], augmented antibody affinity [20], but decreased IgE antibody levels. While increased antigenic stimulation is likely to be responsible for the rise in IgG antibody, the factors which are responsible for falling IgE titres have yet to be identified. It has previously been reported that anti-IgE antibodies can down-regulate IgE synthesis by U266 cells and human peripheral blood mononuclear cells *in vitro* [10,11]. In this study we have investigated the possibility that anti-IgE auto-antibodies could be involved. Subjects were divided into those whose IgE fell markedly (greater than fivefold) and those in whom it fell less than fivefold. There was no relationship between the level of anti-IgE auto-antibodies and the changes in wasp venom-specific IgE antibody. As previous reports have described a correlation between total IgE and anti-IgE auto-antibodies [4–6], we were prompted to analyse the relationship between the level of wasp venom-specific IgE antibody and the concentration of anti-IgE auto-antibodies. We found that there was no correlation between these two variables. Whatever the significance of anti-IgE auto-antibodies we could find no evidence that they were involved in the regulation of IgE during immunotherapy.

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