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Polydesensitisation with reducing elevated serum total IgE by IFN-gamma therapy in atopic dermatitis: IFN-gamma and polydesensitisation (PDS)

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ABSTRACT

Background: AD patients exhibit sensitisation to multiple allergens due to a Th1/Th2 imbalance. Until now, it was impossible to improve the polysensitised status and elevated serum total IgE levels. In this study, the effects of IFN-gamma on systemic polysensitisation to multiple allergens and on serum total IgE levels are investigated.
Methods: A total of 44 AD patients whose food allergies were completely controlled and who were polysensitised to multiple allergens according to the SPT were selected. Twenty-two of these patients received IFN-gamma therapy twice a week for 2 months, and 22 patients did not receive this therapy. The blood eosinophil % and serum total IgE levels were assessed, and a skin prick test for 51 allergens was performed before and after the IFN-gamma therapy.
Results: With IFN-gamma therapy, the polysensitisation status was improved, as demonstrated by a decrease in the positive allergen count and skin reactivity (systemic polydesensitisation). The improvement in the polysensitised status was accompanied by a decrease in serum total IgE levels. The change in serum total IgE levels was significantly correlated with the change in polysensitisation status.
Conclusions: IFN-gamma therapy resulted in systemic polydesensitisation with reduced levels of serum total IgE. IFN-gamma is indicated in AD patients with high serum total IgE levels whose food allergies are well controlled and who are polysensitised to multiple allergens.

1. Introduction

Atopic dermatitis is a chronic relapsing allergic skin disease that is characterised by advanced eczematous skin lesions. The basic immunopathogenesis associated with the development of atopic dermatitis is a Th1/Th2 imbalance with consequent allergy sensitisation and the acquisition of an allergy to a specific allergen, including a food allergen and/or aeroallergen [1]. As a result of an allergenic sensitisation, the skin prick test and allergen-specific IgE levels become positive [2,3].

IFN-gamma is a Th1 cytokine and is known to have anti-allergic properties [1]. During the process of antigen sensitisation, IFN-gamma leads to Th1 immune responses, and Th2 cytokines, including IL-4 and IL-5, lead to Th2 immune responses. Allergen-specific immunotherapy with IFN-gamma has been shown to have tolerogenic effects for certain allergens, including house dust mites and food allergens [4–6]. In this study, we investigated the effects of systemic administration of IFN-gamma on the desensitisation of multiple allergens without the introduction of specific allergens. A new concept of polydesensitisation (PDS) is suggested.

2. Patients and methods

2.1. Subjects and study design

The study subjects consisted of 44 patients who visited the Department of Allergy and Clinical Immunology at the Seoul Allergy Clinic (Seoul, Korea) and met the Hanifin and Rajka criteria [7]. The mean patient age was 19.6 ± 12.7 years (M:F = 23:21) (Fig. 1). The patients' food allergies had been controlled for at least 6 months, as described in the previous report [6], and they were polysensitised to multiple allergens, as demonstrated by the SPT.

Abbreviations: PDS, polydesensitisation; IFN-γ, interferon-gamma; SPT, skin prick test; AD, atopic dermatitis; Dp, dermatophagoides pteronyssinus; Df, dermatophagoides farinae.

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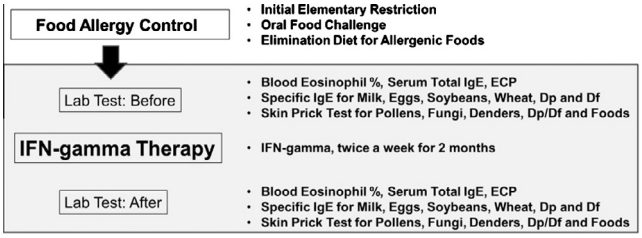

Fig. 1. Study design. Patients whose food allergies were completely controlled and who were polysensitised to multiple allergens, as evidenced by high serum total IgE levels, were selected. Laboratory tests used to determine clinical severity scores were performed before and after IFN-gamma therapy.

Polysensitisation was defined in the previous report as sensitivity to three or more allergens [8]. Among the 44 subjects, 22 patients (mean age = 18.2 ± 9.4 years, M:F = 11:11) received IFN-gamma therapy as scheduled, and the 22 patients (mean age = 20.8 ± 14.3 - years, M:F = 12:10) in the control group were untreated. All subjects received a blood test and skin prick test (SPT) before and after the IFN-gamma therapy. The tests included complete blood counts and an assessment of differential serum total IgE, serum eosinophil cationic protein (ECP) and IgE levels for specific allergens. A SPT was performed for 50 allergens, including pollens, fungi, danders, Dp/Df and food allergens. The clinical severity was evaluated before and after the intervention using the SCORing Atopic Dermatitis (SCORAD) index, which is used worldwide to assess the severity of atopic eczema [9].

The subjects or their parents signed consent forms that included information concerning this study, especially information regarding the possibility of an emergency situation due to acute anaphylactic reactions to the oral challenge tests. The study was approved by the Ethics Committee of Chungnam National University Hospital, Daejeon, Korea.

2.2. Blood tests and SPT

Blood testing on each patient included a CBC with differential counts for the eosinophil fraction, serum total IgE levels, and specific IgE for milk, eggs, soybeans, wheat, Dp and Df. These tests were conducted before and after the tolerance induction. Food-specific IgE levels were measured using the UniCap® (Pharmacia & Upjohn Diagnostics AB, Uppsala, Sweden) method.

The SPTs were conducted on the patients' left forearms using commercial allergen extracts (Bencard, Brentford, England). Histamine hydrochloride (1 mg/ml) (Bencard) was used as a positive control. Physiologic saline, distilled water, and glycerol were used as negative controls. A minimum wheal size of 3 mm was used to indicate a positive reaction to histamine, and the ratios of the wheal sizes resulting from the allergens to the wheal size resulting from histamine were calculated.

2.3. IFN-gamma therapy

Patients received an IFN-γ injection three times a week for 8 weeks. Recombinant IFN-γ (Intermax gamma, LGCI, Seoul, Korea), with a specific activity of 2×10^6 IU (50 mg), was administered by subcutaneous injection at a dose of 3×10^6 IU/m^2 according to the body surface area, as previously reported [10]. Although the patients were instructed to take oral acetaminophen (10 mg/kg, up to a maximum dose of 600 mg) twice, at 1 h and 4 h after the injection, to reduce the possibility of side effects (e.g., myalgia, fever, or flu-like symptoms), none of the subjects exhibited symptoms or took oral acetaminophen.

2.4. Skin sensitisation profiles

Three skin sensitisation profiles were used for the evaluation of the polysensitisation status and polydesensitisation effects of IFN-gamma. A positive item count refers to the number of items that yield positive SPT results. The mean skin reactivity is the average of the grade of the skin prick test for all positive allergens. The grade of the skin prick test was calculated by the ratio of the wheal size for allergens to the wheal size for histamine. The skin sensitisation index is the sum of the score of the skin prick test for all positive allergens.

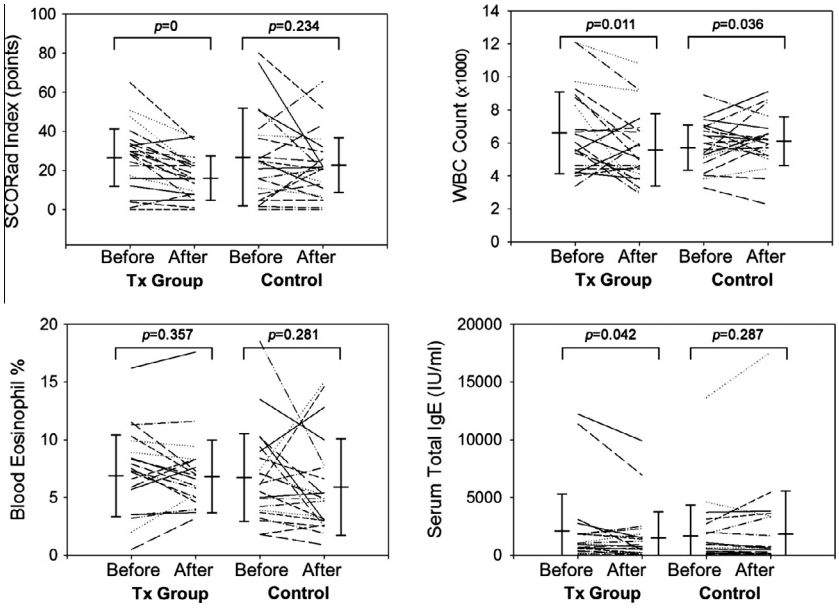

Fig. 2. Clinical and laboratory changes induced by IFN-gamma therapy. (a) Clinical severity scores, (b) WBC counts, (c) blood eosinophil percentages, and (d) serum total IgE levels.