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Original article

Oral challenge tests for soybean allergies in Japan: A summary of 142 cases

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Abbreviations:

AD	atopic dermatitis
FA	food allergy
SPT	skin prick test
BA	bronchial asthma

ABSTRACT

Background: Soybeans are one of causative foods for infantile onset allergies in Japan. This study aimed to analyze the results of soybean challenge tests that were conducted over approximately 7 years at our institution. Using the test data, we sought to identify the responses and clinical profiles of patients with soybean allergies, and to investigate the relationship between the responses and soybean sensitization status.

Methods: Between July 2004 and May 2010, 142 cases (125 patients) underwent food challenge tests (100 g of silken tofu) for the diagnosis of soybean allergy or confirmation of their tolerance. The patients' characteristics, soybean sensitization status, and responses to the challenge tests were retrospectively evaluated.

Results: Among the subjects who underwent the soybean challenge test, the male/female ratio was 1.6 (87/55), and the mean age at the test was 2.8 ± 1.7 years. The positive rate for the challenge test was 38.7%. Induced symptoms were observed in the skin (81.8%), respiratory system (50.9%), and gastrointestinal system/mucosal membrane/anaphylaxis (12.7%). Intramuscular epinephrine was administered to all 7 patients who experienced an anaphylactic reaction. The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic efficiency of soybean-specific IgE titers were low for predicting the responses to the challenge test.

Conclusions: Soybean allergies were diagnosed in only 18% of the subjects with positive sensitization to soybeans. Therefore, soybean-specific IgE titers are not an effective predictor of a positive response to the challenge test.

Introduction

In Japan, soybeans are often ingested in the form of tofu, and this food is used for weaning during early infancy. Therefore, soybean allergies often occur in the form of infant atopic dermatitis that is caused by food allergies or as immediate-type reactions and oral allergy symptoms after early childhood. Based on a report by Ito *et al.*,[1] soybeans are the fourth most common food in Japan that is responsible for infant atopic dermatitis (AD) due to food allergies (FA) (after eggs, milk, and wheat). Furthermore, according to a national Japanese survey, soybeans are the 11th most common food that is responsible for immediate-type food allergies.[2] Moreover, many children who are sensitized to soybeans can unintentionally ingest soybeans. Therefore, we retrospectively analyzed the responses to a soybean challenge test (that was performed using tofu) among patients who underwent the test at our institution.

Methods

Patients

This retrospective study evaluated children who presented to the Department of Pediatrics, Sagamihara National Hospital (Kanagawa, Japan), between July 2004 and May 2010, and were tested for food-specific IgE titers and/or underwent the skin prick test (SPT), due to suspicion of any food allergy. Among these patients, we found 1710 children who were positive for soybean sensitization (Fig. 1). Among these children, 1403 cases were

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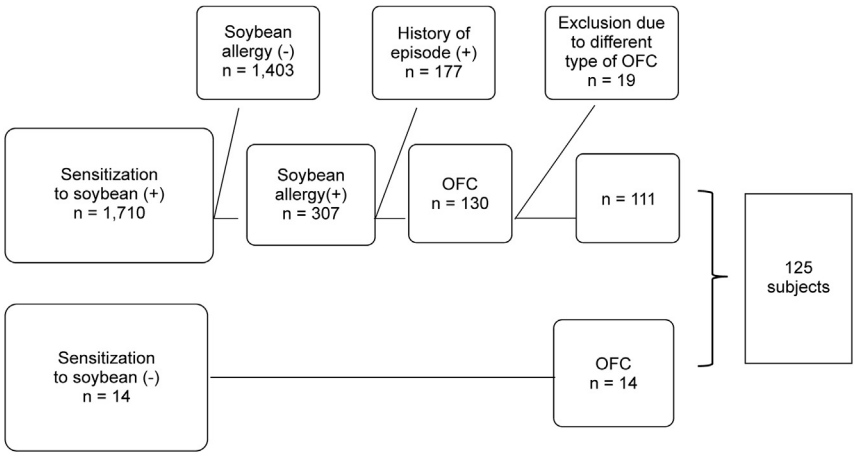

Fig. 1. Soybean allergy among sensitized participants at Sagamihara National Hospital between 2004 and 2010. *Sensitization to soybean* was defined as a titration result positive for soybean-specific IgE antibody or a skin prick test result positive for soybean. *Soybean allergy* was defined as a positive result in a soybean challenge test or convincing immediate reaction to soybean. OFC, Oral food challenge.

excluded from this study because they were asymptomatic after ingesting soybeans and were diagnosed as not having a soybean allergy. Among the remaining 307 children, 177 children exhibited clear immediate-type reactions after unknowingly ingesting soybeans, and were excluded. Therefore, a soybean challenge test was administered to the remaining 130 children. However, we subsequently excluded 19 children because they had undergone an oral food challenge test at another hospital or clinic. Furthermore, we included 14 children who were referred to our department from other hospitals and underwent the soybean challenge test with no history of sensitization. Therefore, this study included a total of 125 children (mean age at testing, 2.8 ± 2.7 years). Among these children, 13 children underwent the challenge test twice, 4 underwent the soybean challenge test 3 times, and no patients underwent the test ≥4 times. Therefore, the results of the soybean challenge test were investigated in 142 cases (87 boys, 55 girls).

All patients and/or their guardians provided their informed consent before the testing, and all tests were performed in the presence of the guardian and a physician. This study's design was reviewed and approved by the ethics committee of Sagamihara National Hospital.

Candidates for the food challenge test

The food challenge tests were conducted for two purposes: to definitively diagnose a soybean allergy (after food elimination testing, n = 82 cases) and to determine tolerance after food elimination had been initiated (based on a prior diagnosis, n = 60 cases). The challenge test to determine tolerance was conducted when >1 year had passed since the last symptom episode (due to accidental ingestion) or when a challenge test was requested by the guardian, due to an observed declining trend in the soybean-specific IgE levels during the elimination period.

Oral soybean challenge test

The challenge tests were conducted under the assumption that soybean ingestion was avoided for >2 weeks, that no anti-allergic drugs (e.g., antihistamines or other anti-allergic drugs) had been administered within the last 48 h, and that the patient's health status was suitable for determining symptoms. Candidates for the challenge test in the outpatient department were patients whose soybean-specific IgE antibody titers were was less than class 2 and who had no history of an immediate-type reaction. All other patients underwent the challenge test in the inpatient department.

Two different challenge test protocols were used during the study period (Fig. 2). For the first protocol, 100 g of silken tofu (4.9 g of soybean protein) was divided into 5 unequal pieces, which were given to children at 15-min intervals for 1 h. However, since January 2009, we have used a revised protocol whereby the tofu is divided into 3 unequal pieces, which are given to children at 0 min, 30 min, and 1 h. We have previously compared the results for these two tests, and found that no significant differences were observed in the test results (unpublished data). All symptoms were evaluated using a scoring sheet that was based on the Symptom Scoring System, which is a reorganized version of the American Academy of Allergy, Asthma, and Immunology's Challenge Test Manual.[3] Children were followed for 24 h after the challenge test in the inpatient department, and for 3 h after the challenge test in the outpatient department. Open challenges are routine at our clinic for very young children, and follow the practices that are recommended by the European Academy of Allergology and Clinical Immunology.[4]

Immunology testing

Hematological tests (total serum and soybean-specific antibody titers) were conducted within the 6 months before the challenge test. All patients' IgE antibody titers were measured using the CAP-FEIA immunoassay (Phadia, Uppsala, Sweden), and the SPT was administered alongside the challenge test in some cases, using drop-by-drop administration (2-cm intervals) of a soybean antigen solution (Torii scratch extract; Torii Pharmaceutical). Next, the drop sites were pressured using a bifurcated needle (Allergy Laboratories of Ohio; USA) that was oriented perpendicular to the skin, and the reaction was evaluated after approximately 15 min. Finally, a control solution (Torii Pharmaceutical) was used as a negative control. The criteria for a positive SPT result included a response that was >2-fold greater than the response for the negative control, with a wheal measuring >2 mm in diameter, or an erythema measuring >5 mm in diameter.[5]

In addition, the following parameters were extracted from the patients' medical records for analysis:

1. **Patient characteristics**

We investigated the male/female ratio of the patients, the age at which the challenge test was administered, the reason for