

Allergy to soy formula and to extensively hydrolyzed whey formula in infants with cow's milk allergy: A prospective, randomized study with a follow-up to the age of 2 years

Timo Klemola, MD, Timo Vanto, MD, Kaisu Juntunen-Backman, MD, Kirsti Kalimo, MD, Riitta Korpela, PhD, and Elina Varjonen, MD

Objectives: We conducted a prospective, randomized study to evaluate the cumulative incidence of allergy or other adverse reactions to soy formula and to extensively hydrolyzed formula up to the age of 2 years in infants with confirmed cow's milk allergy.

Study design: Infants (n = 170) with documented cow's milk allergy were randomly assigned to receive either a soy formula or an extensively hydrolyzed formula. If it was suspected that the formula caused symptoms, a double-blind, placebo-controlled challenge (DBPCFC) with the formula was performed. The children were followed to the age of 2 years, and soy-specific immunoglobulin E antibodies were measured at the time of diagnosis and at the ages of 1 and 2 years.

Results: An adverse reaction to the formula was confirmed by challenge in 8 patients (10%; 95% confidence interval, 4.4%-18.8%) randomly assigned to soy formula and in 2 patients (2.2%; 95% confidence interval, 0.3% to 7.8%) randomly assigned to extensively hydrolyzed formula. Adverse reactions to soy were similar in IgE-associated and non-IgE-associated cow's milk allergy (11% and 9%, respectively). IgE to soy was detected in only 2 infants with an adverse reaction to soy. Adverse reactions to soy formula were more common in younger (<6 months) than in older (6 to 12 months) infants (5 of 20 vs 3 of 60, respectively, $P = .01$).

Conclusions: Soy formula was well tolerated by most infants with IgE-associated and non-IgE-associated cow's milk allergy. Development of IgE-associated allergy to soy was rare. Soy formula can be recommended as a first-choice alternative for infants ≥ 6 months of age with cow's milk allergy. (J Pediatr 2002;140:219-24)

Cow's milk allergy affects 2% to 3% of infants in unselected cohorts.^{1,2} Possible alternatives are soy formulas, extensively hydrolyzed protein formulas, or in some cases, amino acid-based formulas. Soy formulas are cheaper and often more palatable than extensively hydrolyzed formulas or amino acid formulas. The energy content of soy formulas and extensively hydrolyzed formulas is similar, and both meet the nutritional requirements of infants. Healthy infants who are fed with a soy formula are reported to grow as well as infants who are fed a cow's milk-based formula.³

DBPCFC	Double-blind, placebo-controlled food challenge
IgE	Immunoglobulin E

Because of potential sensitization to soy proteins, extensively hydrolyzed formulas are often used instead of soy formulas. Intolerance to soy has been reported to occur in 10% to 35% of infants with cow's milk allergy.⁴⁻⁶ Recently, the prevalence of soy allergy in children with IgE-associated cow's milk allergy was shown to be 14%.⁷ However, in children with non-IgE-associated cow's milk allergy, the occurrence of intolerance to soy has been shown to be more common, and extensively hydrolyzed formulas have been recommended for these patients.⁸ However, no prospective, controlled trials have investigated the incidence of adverse reactions or allergy to soy formulas in infants with cow's milk allergy. We

From the Department of Pediatrics, Jorvi Hospital, Espoo; the Department of Allergy, Skin and Allergy Hospital, the Research and Development Center, Valio Ltd, Helsinki; and the Departments of Pediatrics and Dermatology, Turku University Hospital, Finland.

Supported by Turku University Hospital, the Social Insurance Institution, and Valio Ltd.

Submitted for publication Dec 12, 2000; revisions received May 3, 2001, and Oct 25, 2001; accepted Nov 28, 2001.

Reprint requests: Timo Klemola, MD, Jorvi Hospital, FIN-02740 Espoo, Finland.

Copyright © 2002, Mosby, Inc. All rights reserved.

0022-3476/2002/\$35.00 + 0 9/21/121935

doi:10.1067/mpd.2002.121935

Table I. Characteristics of infants randomly assigned to either soy formula or extensively hydrolyzed whey formula

	SF (n = 80)	EHF (n = 90)
Sex (m/f)	49/31	50/40
Age, mo (mean $\pm$ SD)	7.1 $\pm$ 2.4	6.9 $\pm$ 2.1
Immediate/delayed CMA	41/39	59/31
SPT with CM (≥ 3 mm; %)	38	37
IgE abs to CM (≥ 0.35 kU/L; %)	37	34
Atopic eczema (%)	52	64
Gastrointestinal symptoms (%)	19	28

SF, Soy formula; EHF, extensively hydrolyzed whey formula; SPT, skin prick test; CM, cow's milk; CMA, cow's milk allergy.

therefore conducted a prospective study in which infants with IgE-associated or non-IgE-associated cow's milk allergy were randomly assigned to either a soy formula or an extensively hydrolyzed cow's milk-based formula. We investigated the development of adverse reactions to soy or extensively hydrolyzed formula during the first 2 years of life and the emergence of IgE antibodies to soy after use of a soy formula in infants with cow's milk allergy.

MATERIAL AND METHODS

Patients

The study comprised 170 children with cow's milk allergy (99 boys and 71 girls); the mean age at the time of diagnosis was 7 months (range, 2-11 months).

Diagnosis of Cow's Milk Allergy

Cow's milk allergy was diagnosed by means of double-blind, placebo-controlled food challenge (DBPCFC) in all the patients except in 4 patients with a history of an anaphylactic reaction, who showed positive IgE antibodies to cow's milk. Details of study patients and the DBPCFC have been reported earlier.⁹ Briefly, the milk challenge was carried out with a mixture of cow's milk-based formula and extensively hydrolyzed formula (1:1). Extensively hydrolyzed formula was used as a placebo. Placebo and the milk formula

were given in randomized order in the hospital out-patient department in gradually increasing amounts, starting from a drop of the formula up to the normal daily dose or until an adverse reaction occurred. Positive reactions occurring within 2 hours of the last challenge dose in hospital were classified as immediate reactions. If no symptoms occurred, the cow's milk formula was continued at home ad libitum for 5 days, and the parents kept a diary of the symptoms. Later reactions within 5 days were classified as delayed reactions.

Random Assignment to Study Formulas

Infants were randomly assigned to receive either an extensively hydrolyzed formula (90 infants; Peptidi-Tutteli, Valio Ltd, Valio, Finland) or a soy protein-based formula (80 infants; SoijaTutteli, Valio Ltd) according to a computer-generated randomization list (Table I). The randomization was blocked in blocks of 4 and was stratified according to center (3 centers) and age (0-2 months, 3-5 months, 6-8 months, and 9-11 months) to obtain an even age distribution for both formula groups.

The infants were supplied free of charge with the randomized formula to be used ad libitum to the age of 2 years. During the first year, the use of soy protein (other than the study formula) and egg products, fish, citrus fruit, peanuts, peas, tomatoes, strawberries, and chocolate was avoided in the infants.

Challenge With the Study Formula

When it was suspected that the study formula caused symptoms, a DBPCFC was performed by using both the extensively hydrolyzed formula (PeptidiTutteli, Valio Ltd) and the soy protein-based formula (SoijaTutteli, Valio Ltd). The suspected formula was eliminated from the diet and replaced by the other study formula (extensively hydrolyzed formula or soy formula). The parents were not told which formula was used as a study formula and which formulas were used in the challenges. If both formulas were suspected of causing symptoms or if the child refused to drink them, the infant was switched to an amino acid formula (Neocate, SHS, Liverpool, United Kingdom).

Positive reactions occurring within 2 hours of the last challenge dose in the hospital were classified as immediate reactions and later reactions were classified as delayed reactions. Delayed challenge results were further classified into 3 categories: positive, doubtful, and negative. A challenge reaction was considered positive when symptoms occurred during the active challenge but not during the placebo challenge. A challenge reaction was considered doubtful when some symptoms also occurred during the placebo challenge and the difference between the challenges was not clear or symptoms were subjective (restlessness, crying, etc). The challenge was considered negative

Table II. Characteristics of the patients with a positive challenge with a study formula

Patient No.	Sex	Age* in months	Type of CMA†	Symptoms caused by study formula	Challenge reaction (type, symptoms)	Soy-specific IgE‡ (kU/L)
1	Male	5	IgE-	urt	Immediate, urt	≤0.35
2	Male	11	IgE+	urt, ery	Immediate, urt, ery	25.7
3	Female	8	IgE+	ae, gi	Immediate, ery	≤0.35
4	Male	5	IgE-	ae	Immediate, ery	≤0.35
5	Male	5	IgE+	urt	Immediate, urt	0.63
6	Male	6	IgE-	gi, restlessness	Delayed, gi, restlessness	≤0.35
7§	Female	6	IgE+	ae	Delayed, ae	≤0.35
8	Female	9	IgE-	gi	Delayed, gi	≤0.35
9	Female	7	IgE-	ery	Immediate, ery	≤0.35
10	Female	7	IgE+	urt	Immediate, urt	≤0.35

EHF, Extensively hydrolyzed whey formula; SF, soy protein-based formula; ae, atopic eczema; urt, urticaria; ery, erythema; gi, gastrointestinal symptoms.

Patients 1 through 8 received SF; patients 9 and 10 received EHF.

*Age at the time randomized formula started.

†CMA, cow's milk allergy; IgE+ = IgE = skin prick test ≥3 mm and/or IgE to cow's milk ≥0.35 kU/L; IgE- = skin prick test ≤3 mm and/or IgE to cow's milk ≤0.35 kU/L.

‡Soy-specific IgE measured at the age of 12 months.

§Only patient 7 had a formula prick test reaction (3 mm).

when there was no difference between the active and the placebo challenge periods. The results of the delayed challenges were classified independently by 5 pediatric allergists, and if the allergists disagreed, the classification shared by the majority was chosen.

When a positive challenge reaction was observed with one of the study formulas, the code of the challenge formula was broken. The formula was discontinued and the family was offered the alternative of continuing with the study to the age of 2 years, using a formula tolerated by the infant. If the challenge was negative, the randomized formula was continued as before.

Skin Prick Test

A skin prick test was carried out in all the children on the volar aspect of the forearms (duplicate tests) with cow's milk-based formula (milk powder diluted to normal feeding concentration), the extensively hydrolyzed formula (PeptidiTutteli), the soy protein-based formula (SoijaTutteli), a negative control, and 10 mg/mL histamine hydrochloride. The results are expressed as the mean wheal diameter in millime-

ters. The test was performed at the time of diagnosis of cow's milk allergy and at the ages of 12 and 24 months.

Specific Immunoglobulin E Antibodies

Immunoglobulin E (IgE) antibodies to cow's milk and soy protein were determined by means of the Pharmacia CAP System RAST RIA (Pharmacia, Uppsala, Sweden), according to the manufacturer's instructions. The cutoff level for the presence of IgE antibodies was 0.35 kU/L. The test was performed at the time of diagnosis of cow's milk allergy and at the ages of 12 and 24 months.

Statistical Analyses

The primary outcome was the incidence of adverse reactions to soy and extensively hydrolyzed formulas in patients with cow's milk allergy, as determined by DBPCFC. The 95% confidence intervals (CI) for incidences were calculated by using the exact binomial distribution. Risk ratios (RR) were calculated to compare soy formula with extensively hydrolyzed formula. A χ^2 test for categorical variables was used for statistical analyses.

Ethical Considerations

Written informed consent was obtained from all parents. The study was approved by the ethics committee of each of the participating hospitals.

RESULTS

The parents suspected adverse reactions to the study formula significantly more often in infants randomly assigned to the soy formula than in infants randomly assigned to the extensively hydrolyzed formula (28%; 95% CI, 18-39% vs 11%; 95% CI, 5-19%, respectively; RR, 2.48; $P = .006$).

In the soy formula group, an adverse reaction to soy formula was confirmed in the DBPCFC in 6 patients, 3 of whom had an immediate challenge reaction, whereas 3 had a delayed reaction (Table II). A further 2 infants reacted immediately at the first introduction of study formula, and the parents refused any further challenges. The code was broken, and the formula was proven to be soy in both cases; these were considered as probable adverse reactions to the soy

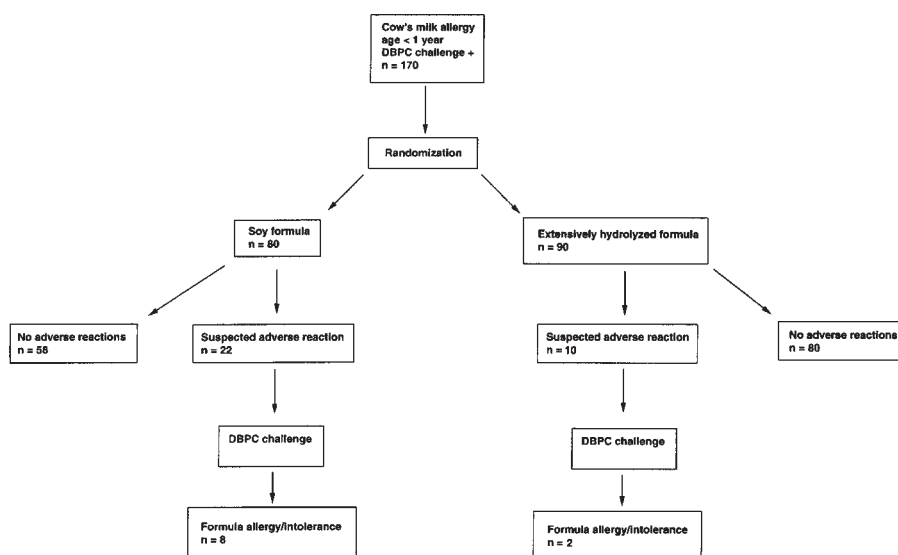


Figure. Flow chart of the study shows number of suspected and confirmed adverse reactions to soy and extensively hydrolyzed whey formulas in infants with cow's milk allergy.

formula, even though a DBPCFC was not performed.

In the group receiving the extensively hydrolyzed formula, an adverse reaction to the study formula was confirmed in 2 infants, both of whom had an immediate DBPCFC reaction.

However, the cumulative incidence of adverse reactions confirmed by DBPCFC was low both for the soy formula and for the extensively hydrolyzed formula. Adverse reactions were more often confirmed with soy than with the extensively hydrolyzed formula (10%; 95% CI, 4.4-18.8% vs 2.2%; 95% CI, 0.3-7.8%, respectively; RR, 4.50; $P = .031$; Figure).

In 18 cases, symptoms during the study formula challenges were subjective and not clearly different between the study and the control formulas, so that the challenge result remained doubtful (14 of these with soy and 4 with extensively hydrolyzed formula). None of these doubtful reactions included an immediate reaction or severe symptoms.

Of the 5 patients with an immediate reaction to soy formula, only 2 had detectable IgE antibodies to soy, and none had a positive skin prick test result with the soy formula. Of the 14 patients with

a doubtful challenge reaction to soy, IgE antibodies to soy were detected in one, and no positive skin prick test reactions to soy were observed (Table III).

Before random assignment, 19 of 155 (12%) patients from whom serum was available for analyses had IgE antibodies (≥ 0.35 kU/L) to soy (Table IV). Of those, 8 were randomly assigned to the soy formula and 11 to the extensively hydrolyzed formula. Four patients with IgE antibodies to soy who were randomly assigned to the soy formula were suspected of having symptoms from the soy formula. Soy allergy was confirmed by DBPCFC in two. Hence, adverse reactions to soy were confirmed in 2 of 8 patients who before random assignment had positive IgE antibodies to soy.

During the 2-year follow-up, infants randomly assigned to soy formula more frequently had IgE antibodies (≥ 0.35 kU/L) to soy than those randomly assigned to the extensively hydrolyzed formula (20% vs 16%, respectively), but the difference was not statistically significant (Table IV).

Of the 80 infants randomly assigned to the soy formula, 46 (58%) had IgE antibodies (≥ 0.35 kU/L) to cow's milk or a positive (≥ 3 mm) skin prick test re-

action with the cow's milk formula. The rest of the children had no signs of IgE-associated cow's milk allergy. Adverse reactions to soy were suspected in 12 of 46 (26%) of infants with IgE-associated cow's milk allergy and in 13 of 34 (38%) of non-IgE-associated cow's milk allergy ($P = .25$). Adverse reactions to soy were confirmed by challenge in 5 of 46 (11%) infants with IgE-associated cow's milk allergy and in 3 of 34 (9%) infants with non-IgE-associated cow's milk allergy ($P = .76$).

Twenty of 80 children randomly assigned to the soy formula were <6 months old at the time of random assignment. Adverse reactions to soy formula were suspected by parents in 8 of 20 (40%) of infants compared with 16 of 60 (27%) of infants who were randomly assigned at the age 6 months and older ($P = .26$). Adverse reactions were confirmed by challenge in 5 of 20 (25%) of the younger infants and in 3 of 60 (5%) of the older infants ($P = .01$).

DISCUSSION

This randomized, prospective study evaluated the usability of soy formula compared with extensively hydrolyzed formula in infants with cow's milk allergy. Most infants with cow's milk allergy tolerated soy formula, and IgE-associated allergy to soy rarely developed. Adverse reactions to soy were not more common in infants with non-IgE-associated cow's milk allergy compared with infants with IgE-associated cow's milk allergy. We did not, however, have infants in this study with severe gastrointestinal symptoms (enterocolitis or enteropathy), so the results cannot be applied to such patients with non-IgE-associated cow's milk allergy.

We found evidence for the hypothesis that adverse reactions to soy are more common in younger patients with cow's milk allergy. However, there were few patients <6 months of age, and conclusions for young infants with cow's milk

Table III. Skin prick test with soy and soy-specific IgE in infants randomly assigned to soy protein formula

Challenge reaction	n	Skin prick test >3 mm	Soy-specific IgE (>0.35 kU/L)
Immediate	5	0/5	2/5
Delayed	3	1/3	0/3
Doubtful	14	0/14	1/14
Tolerant	58	0/58	11/58
Total	80	1/80	14/80

Patients with suspected intolerance to soy formula were challenged with the formula in a double-blind test; challenge results were considered as immediate (<2 hours after the last challenge dose), delayed, or doubtful reactions.

Table IV. Number of infants with positive soy-specific IgE test result (≥ 0.35 kU/L) and positive soy skin prick test reaction (≥ 3 mm) in patients from different formula-feeding groups before random assignment and at the ages of 12 months and 24 months

		Soy formula, n (%)	EHF formula, n (%)
Positive soy skin prick test (>3 mm)	Before randomization	1/78 (1.3)	0/88 (0)
	12 mo	0/76 (0)	1/85 (1.2)
	24 mo	0/73 (0)	2/79 (2.5)
Positive soy specific IgE (>0.35 kU/L)	Before randomization	8/73 (11.0)	11/82 (13.4)
	12 mo	15/75 (20.0)	13/82 (15.9)
	24 mo	15/76 (19.7)	12/81 (14.8)

EHF, extensively hydrolyzed whey formula.

allergy should be approached with caution.

The drawback of our study is the great number of doubtful delayed reactions in DBPCFCs. In these cases, we could not totally exclude mild intolerance to the study formula. The parents were reluctant to repeat long drawn-out DBPCFCs, because their infants were usually doing well with the formula given instead of the study formula. To confirm or exclude formula intolerance, these patients would have needed 2 more sets of DBPCFCs,^{10,11} which would have been intolerable to the parents and time-consuming for the investigators. If all of the infants with doubtful DBPCFC reactions had true intolerance to soy, the cumulative incidence of adverse reactions to soy in infants with cow's milk allergy could be as high as 28%.

Documentation of slowly evolving reactions to food proteins is a major challenge to pediatric allergists both in clinical practice and in research when they conduct DBPCFCs over pro-

longed periods. It is proposed that patients should be followed for 48 hours for late-phase reactions such as atopic eczema.¹² Sampson suggests that non-IgE-associated gastrointestinal symptoms may require observation periods up to 3 or 4 days.¹³ There is no agreement as how to quantify symptoms such as distressed behavior and gastrointestinal symptoms such as vomiting and diarrhea.^{12,14} In our study, the long challenge period of 5 days and the recording of subjective symptoms as challenge end points have probably increased the number of doubtful challenge reactions.

During the first 2 years, the parents were not informed which formula was given to their child if adverse reactions to the formula were not suspected. In these cases, the basis of the formula was told to the parents after the challenges. However, parents might be familiar with the differences between soy formulas and extensively hydrolyzed formulas and might have guessed which formula the infant was given. Since the

aim of the study was to study the allergenicity of soy formulas in infants with cow's milk allergy, it might be possible that parents who thought that their child was receiving a soy formula would more often suspect symptoms. Parents of 46 infants were asked if they guessed which formula (soy or extensively hydrolyzed formula) was being given to the child. Only 62% of the parents guessed right. It is not likely, therefore, that this would have biased study results.

Most infants with immediate or delayed reactions to soy formula had negative skin prick test with the soy formula and also undetectable IgE antibodies to soy. Thus, negative allergy tests with soy do not reliably exclude true intolerance to soy. The discrepancy between the soy formula prick test and the IgE measurement in the 2 infants with immediate reactions was probably because of various antigen materials used in these tests. The amount of protein in the soy formula might be too low for diagnostic purposes. It also remains

uncertain whether enzymatic activity could somehow enhance the allergenic activity of soy proteins in the gastrointestinal tract.

Low levels (0.35 to 1.0 kU/L) of soy-specific IgE were frequently found both in children fed with the soy formula and those fed with the extensively hydrolyzed formula. As reported earlier,^{7,15,16} only a minority of patients with positive soy-specific IgE had any symptoms or a suspicion of soy allergy. In a prospective study in which healthy infants were receiving breast milk, cow's milk-based formula, or a soy-based formula, soy-specific IgE antibodies were found in only 0.5% of the infants, whereas IgE antibodies to cow's milk were found in 1.8%.¹⁷ In our study, most infants with low (<1 kU/L) soy-specific IgE tolerated soy formula without any symptoms. The nonspecific nature of low levels of IgE antibodies to soy is also shown in the relatively great number (13%) of children who already had IgE to soy before the randomization. Thus, in some cases, IgE to soy may also reflect only a cross-reaction with other legumes without indicating specific clinical symptoms to soy.

This study showed that >70% of infants with cow's milk allergy tolerate soy formula without any symptoms and that 10% of infants with cow's milk allergy have adverse reactions to soy formula. Severe allergic reactions or development of IgE-mediated allergy to soy are uncommon in infants with cow's milk allergy. This study, like that of Zeiger et al,⁷ shows that soy formula may be considered as a first-choice alternative formula in infants with cow's milk allergy, with the exception, per-

haps, of young infants (aged <6 months). The greater palatability and lower cost of soy formulas further increases their usefulness.

We thank Drs Antti Koivikko, Erkka Valovirta, and Pirkko Syvänen, and Marja Marja-aho and Janette Räikkönen, the two nurses who worked on the study, for assisting with DBPCFCs. Pellervo Marja-aho, PhD, helped greatly in the collection of data and Tuija Poussa, MSc, helped in the statistical analysis. Mimi Ponsonby edited the English manuscript.

REFERENCES

1. Høst A, Halken S. A prospective study of cow's milk allergy in Danish infants during the first 3 years of life. *Allergy* 1990;45:587-96.
2. Saarinen KM, Juntunen-Backman K, Järvenpää A-L, Kuitunen P, Lope L, Renlund M, et al. Supplementary feeding in maternity hospitals and the risk of cow's milk allergy: a prospective study of 6209 infants. *J Allergy Clin Immunol* 1999;104:457-61.
3. Köhler L, Meeuwisse G, Mortensson W. Food intake and growth of infants between six and twenty six weeks of age on breast milk cow milk formula or soy formula. *Acta Paediatr Scand* 1984; 73:40-8.
4. Jacobsson J, Lindberg T. A prospective study of cow's milk protein intolerance in Swedish infants. *Acta Paediatr Scand* 1979;68:853-9.
5. Verkasalo M, Kuitunen P, Savilahti E. Changing pattern of cow's milk protein intolerance. *Acta Paediatr Scand* 1981; 70:289-95.
6. Savilahti E, Kuitunen P, Visakorpi JK. Cow milk allergy. In: Textbook of gastroenterology and nutrition in infancy. New York: Raven Press Ltd; 1989. p. 473-89.
7. Zeiger RS, Sampson HA, Bock A, Burks AW, Harden K, Noone S, et al. Soy allergy in infants and children with IgE-associated cow's milk allergy. *J Pediatr* 1999;134:614-22.
8. American Academy of Pediatrics Committee on Nutrition. Soy protein-based formulas: recommendations for use in infant feeding. *Pediatrics* 1998;101:148-53.
9. Vanto T, Juntunen-Backman K, Kalimo K, Klemola T, Koivikko A, Koskinen P, et al. The patch test, skin prick test, and serum milk-specific IgE as diagnostic tools in cow's milk allergy in infants. *Allergy* 1999;54:1-6.
10. Bock S, Sampson H, Atkins F, Zeiger R, Lehrer S, Sachs M, et al. Double-blind placebo-controlled food challenge (DBPCFC) as an office procedure: a manual. *J Allergy Clin Immunol* 1988;82:986-97.
11. Goldman AS, Anderson DW, Sellers WA, Saperstein S, Kniker WT, Halpern SR. Milk allergy, I: oral challenge with milk and isolated milk proteins in allergic children. *Pediatrics* 1963;32:425-43.
12. Niggemann B, Wahn U, Sampson HA. Proposals for standardization of oral food challenge test in infants and children. *Pediatr Allergy Immunol* 1994; 5:11-3.
13. Sampson HA. Food allergy, II: diagnosis and management. *J Allergy Clin Immunol* 1999;103:981-9.
14. Hill DJ, Cameron DJS, Francis DEM, Gonzales-Andaya AM, Hosking CS. Challenge confirmation of late-onset reactions to extensively hydrolyzed formulas in infants with multiple food protein intolerance. *J Allergy Clin Immunol* 1995;96:386-94.
15. Cantani A, Lucenti P. Natural history of soy allergy and/or intolerance in children, and clinical use of soy-protein formulas. *Pediatr Allergy Immunol* 1997; 8:59-74.
16. Bruno G, Giampietro PG, Del Guercio MJ, Gallia P, Giovannini L, Lovati G, et al. Soy allergy is not common in atopic children: a multicenter study. *Pediatr Allergy Immunol* 1997;8:190-3.
17. Halpern SR, Sellers WA, Johnson RB, Anderson RB, Salperstein S, Reisch JS. Development of childhood allergy in infants fed breast, soy or cow milk. *J Allergy Clin Immunol* 1973;51:139-51.