

Soy protein sensitization in cow's milk allergy patients

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ABSTRACT

Background The management of cow's milk allergy (CMA) is avoidance of cow's milk as strictly as possible. Extensive hydrolyzed protein and amino acid based formulas are recommended dietary products for treatment of CMA. However, they have some disadvantages, such as bitter taste and high cost. Alternative protein sources from vegetable proteins, such as soy, can be used as milk-substitute. Previous studies showed the prevalence of soy allergy in CMA patients in Western countries ranged between 0 to 63%, but the prevalence in Asia was not greater than 20% and no data about this prevalence in Indonesia.

Objectives To determine the proportion of soy protein sensitization in CMA patients and characteristics of CMA patients who were sensitized to soy protein.

Methods Fifty seven CMA patients who consumed soy protein were taken their blood sample to examine the soy-specific IgE.

Results From 57 CMA patients, we found only 18% of patients who were sensitized to soy protein. Seven out of ten CMA patients who were sensitized to soy protein were under 12 months old. Atopic dermatitis was the most frequent clinical manifestation (8/10) and all of them had family history of atopic diseases. Soy sensitization in IgE-mediated and non-IgE mediated CMA were 6/10 and 4/10, respectively.

Conclusions Proportion of soy sensitization in CMA patients in this study was 18%. Soy protein can be used as an alternative for cow's milk substitute in CMA patients. [Paediatr Indones 2007;47:78-82]

Keywords: cow's milk allergy (CMA), soy protein sensitization, soy-specific IgE, food allergy, atopic diseases, extensive hydrolyzed formula.

Cow's milk allergy (CMA) is one of the most common food allergies in infancy and early childhood.¹⁻³ The management of cow's milk allergy is avoidance of cow's milk as strictly as possible. Extensive hydrolyzed protein and amino acid based formulas are the recommended dietary products for CMA's treatment. However, they have some disadvantages, such as bitter taste and high cost.⁴ Alternative protein sources from vegetable proteins, such as soy, could be used as milk-substitute.^{4,5}

Previous studies showed that the prevalence of soy allergy in CMA patients ranged between 0 to 63%.⁶ Therefore, CMA patients were given an extensive hydrolyzed formula to avoid the potential sensitization to soy protein. Most of the studies were conducted in Western countries where consumption of soy was not common. Soy protein has been consumed in Asia for a long time,⁷ but data about prevalence of soy sensitization or allergy in Asia is limited. Recent studies found soy protein sensitization

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in CMA patients in Western countries ranged between 20 to 59.4%, but after soy protein challenge they found soy allergy ranged between 10-14%.^{6,8,9} In Asia, several studies conducted in Korea, Japan, Thailand indicated that soy protein sensitization and allergy were not greater than 20% (Table 1).¹⁰⁻¹³ There is no reported data about soy protein sensitization or allergy in CMA patients in Indonesia.

The purpose of this study was to identify the proportion of soy protein sensitization in CMA patients and the characteristics of CMA patients with soy protein sensitization.

Methods

This descriptive, cross-sectional study was conducted in Department of Child Health, Cipto Mangunkusumo Hospital, Jakarta. We enrolled CMA patients who fulfilled the inclusion criteria to join this study. Estimation of the sample size was calculated using a sample size formula for single proportion. Cow's milk

allergy patients who had already diagnosed by the previous physician and consumed soy protein were included in this study. The diagnosis of CMA was based on history of allergic manifestations of CMA, elimination and provocation test, and data of IgE specific or skin prick test of cow's milk. Patients with exclusive breastfeeding or parents refused to join this study were excluded. After informed consent was signed, the parents were interviewed about clinical manifestations of CMA and family history of atopic disease. Blood specimens were taken for determination of soy-specific IgE by Pharmacia CAP system specific IgE fluoroenzymeimmunoassay (FEIA). Soy-specific IgE greater than or equal to 0.35 kUA/L were defined as positive and categorized as CMA patients with soy sensitization. Soy-specific IgE classes were divided into 6 classes (Table 2).¹⁴ All descriptive data were presented in text and tables.

Results

Fifty-seven CMA patients were enrolled in this study with mean age of 17 months and ranged between two to 60 months; boys outnumbered girls. Atopic dermatitis was the most common CMA's symptoms (60%), followed by diarrhea (42%), and chronic cough (33%). The majority of CMA patients had family history of atopic diseases (91%). IgE-mediated CMA and non-IgE mediated CMA were 74% and 26%, respectively (Table 3).

Ten out of 57 CMA patients were sensitized to soy protein (17.5%). Nine patients had low level of soy-specific IgE (0.36–0.69 kUA/L) and one patient had moderate level of soy-specific IgE (0.74 kUA/L). Mean soy-specific IgE was 0.48 kUA/L. Most of these patients were infants (7/10) and after three years of age there were no CMA patients who were sensitized to soy protein. Mean age of CMA patients who were sensitized to soy protein was 13 months. All of CMA patients who were sensitized to soy protein had family history of atopic diseases. Nearly all CMA patients who were sensitized to soy protein had atopic dermatitis (8/10), followed by diarrhea (3/10), chronic cough (2/10), and gastroesophageal reflux (1/10). Soy sensitization in IgE-mediated and non-IgE mediated CMA were 6/10 and 4/10, respectively (Table 4).

Table 1. Studies on soy protein sensitization and allergy

Study	Population	Prevalence (%)	
		Soy sensitization	Soy allergy
Western countries			
United States ⁶	CMA	59.4	14
Finland ⁸	CMA	20	10
Finland ⁹	CMA	31	0
Asian countries			
Japan ¹³	National survey	ND	1.4
	Food allergy	ND	11
Japan ¹¹	Food allergy	20	ND
Thailand ¹²	CMA	ND	17
Korea ¹⁰	CMA	18.3	ND

ND: no data

Table 2. Evaluation of soy-specific IgE classes¹⁴

Soy-specific IgE class	Soy-specific IgE (kUA/L)		Level
	Less than	Greater than or equal to	
0	0.35	-	Undetectable
1	0.7	0.35	Low
2	3.5	0.7	Moderate
3	17.5	3.5	High
4	50	17.5	Very high
5	100	50	Very high
6	-	100	Very high

Three of CMA patients who were sensitized to soy protein (patient number 16, 20, and 38) did not have any allergic symptoms when they have already eliminated cow's milk and substituted it with soy

protein. But the others (patient number 5, 6, 13, 18, 29, 44, and 45) still had allergic symptoms. We highly suspected that these seven patients had soy allergy.

Discussion

Table 3. Characteristics of CMA patients

Characteristics	Total (n=57)	Percentage (%)
Age groups		
0–12 months	32	56
13–24 months	13	23
25–36 months	5	9
37–48 months	4	7
>49 months	3	5
Gender		
Male	32	56
Female	25	44
Clinical manifestations *		
Atopic dermatitis	34	60
Urticaria	4	7
Rhinitis	5	9
Chronic cough	19	33
Asthma	1	2
Diarrhea	24	42
Constipation	1	2
Gastroesophageal reflux	2	4
Anaphylaxis	0	0
Family history of atopic disease		
Positive	52	91
Negative	5	9
Family member history of atopic disease		
Mother	17	30
Father	18	32
Mother and father	15	26
Siblings	17	30
CMA type#		
IgE-mediated	42	74
Non IgE-mediated	15	26

*: One patient can suffer one or more clinical manifestations
 #: IgE-mediated CMA: if skin prick test for cow's milk positive or cow's milk IgE > 0.35 kUA/L. Non IgE-mediated: if skin prick test for cow's milk negative or cow's milk IgE < 0.35 kUA/L.

Allergic reactions in food allergy can be divided into the sensitization phase, the effector phase and the chronic phase. In the sensitization phase, there were no allergic symptoms but the specific IgE could be already detected by skin prick test or specific IgE examination.¹⁵ This study only determined soy sensitization by soy-specific IgE examination without elimination and challenge test with soy protein to prove that the symptoms were still existed because of soy allergy. For that reason, this study could not describe proportion of soy allergy in CMA patients.

Cow's milk allergy is one of the most common food allergies in infancy and early childhood because generally cow's milk was the first foreign protein introduced to infants.^{1,2} Management of CMA is avoidance of cow's milk protein. It is recommended that dietary products for treatment of CMA should be tolerated by at least 90% patients with CMA. These criteria fulfilled by extensive hydrolyzed protein and amino acid based products.⁴ American Academy of Pediatrics (AAP) recommended that soy formula could be given in the IgE-mediated CMA patients above six months old.¹⁶

Soy formula was described as cow's milk substitute for CMA since 1929 with some advantages, i.e., free of cow-milk protein, lower immunogenicity and allergenicity than cow-milk formulas, nutritional

Table 4. Characteristics of CMA patients with soy protein sensitization

No	Age (months)	Family history of atopic disease	Clinical manifestation(s) of CMA	CMA type	Soy-specific IgE	IgE Class
5	7	+	AD, D	Non IgE-mediated	0.69	1
6	11	+	AD	IgE-mediated	0.74	2
13	2	+	AD	Non IgE-mediated	0.41	1
16	36	+	AD	IgE-mediated	0.46	1
18	19	+	D, CC	IgE-mediated	0.46	1
20	8	+	AD, CC	IgE-mediated	0.46	1
29	28	+	D, GER	IgE-mediated	0.48	1
38	5	+	AD	Non IgE-mediated	0.36	1
44	7	+	AD	Non IgE-mediated	0.36	1
45	8	+	AD	IgE-mediated	0.36	1

AD: atopic dermatitis; D: diarrhea; CC: chronic cough; GER: gastroesophageal reflux

adequacy similar to cow-milk formulas, better palatability and less expensive than extensive hydrolyzed formulas.⁵ Cross reaction between soy (11 S globulin) and cow's milk allergen (casein) was found in few cases.¹⁷ Most Asian children are exposed to soy-based food, such as formula, tofu or soy sauce, since a very young age. Many Asian mothers choose tofu for weaning because it is widely available at low cost. The soft consistency is also an important factor. Asian infants accept tofu because it is highly palatable.⁷

Unfortunately, previous studies showed that the prevalence of soy allergy in CMA patients was relatively high, and consequently, CMA patients were given an extensive hydrolyzed formula as milk substitute to avoid the potential sensitization to soy protein.⁶ Proportion of soy sensitization in CMA patients in this study was 17.5%, which was similar to that of other studies in Asia¹⁰⁻¹³ and lower than that of other studies in Western countries.^{6,8,9} Mean soy-specific IgE was 0.48 kUA/L which is categorized as low level of allergen. This result was lower than that of other studies. Other studies found the mean soy-specific IgE was moderate and very high levels of allergen.^{6,10}

Most of CMA patients who were sensitized to soy were under 12 months old and after three years of age there were no CMA patients who were sensitized to soy. It indicates that immaturity of the immune system and gastrointestinal tract predisposes young infants to food sensitization and allergy because gradual maturation of mucosal immune response and intestinal barrier occur in the first 2 years of life.¹⁸

Most of them also suffered from atopic dermatitis which is in accordance with other studies.^{10,19,20} Soy sensitization in IgE-mediated and non-IgE mediated CMA were similar. Klemola et al⁸ also reported that adverse reactions to soy were similar in IgE-mediated and non IgE-mediated CMA.

Seven out of ten CMA patients who were sensitized to soy protein had allergic symptoms. We highly suspected that these patients had soy allergy as well, although we had not performed elimination and provocation test yet. However, the test still needs to be done to make a definitive diagnosis. Previous studies showed that only a minority of patients with positive soy-specific IgE had any allergic symptoms or a suspicion of soy allergy.^{6,8,9,20-23} In some cases, IgE to soy could also reflect a cross-reaction with other

legumes without demonstrating specific clinical symptoms to soy.¹¹

In conclusion, proportion of soy sensitization in CMA patients in this study is 17.5%, which is similar to other studies in Asia, and low level of soy-specific IgE (0.48 kUA/L). For clinical practice, soy protein could be used as an alternative for cow's milk-substitute in CMA patients with caution of soy allergy. Further studies consist of larger sample size with elimination and challenge test are needed to determine proportion of soy allergy in CMA patients in Indonesia.

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