

A follow-up study of nutrient intake, nutritional status, and growth in infants with cow milk allergy fed either a soy formula or an extensively hydrolyzed whey formula^{1–3}

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ABSTRACT

Background: Infants with cow milk allergy (CMA) are reported to have reduced growth and special nutritional needs.

Objective: The aim of the present study was to compare nutrient intake, nutritional status, and growth in infants with CMA who were fed either a soy formula or an extensively hydrolyzed whey formula.

Design: The study group comprised 168 double-blind challenge-proven infants with CMA. Eighty-four of the infants were fed a soy formula (mean starting age: 7.8 mo), and the other 84 infants were fed an extensively hydrolyzed whey formula (mean starting age: 7.5 mo).

Results: The length (SD score) of the infants was close to the mean Finnish reference growth by age 2 y in both groups. Weight-for-length measurements continued to reach the 50th percentile by age 4 y in both study groups. The mean nutrient intake followed the recommended intake in both groups, although most of the infants were supplemented with calcium and vitamin D. The observed serum transferrin receptor concentrations indicated a greater iron inadequacy in the tissue of infants in the soy formula group than in the hydrolyzed whey formula group ($P = 0.08$). However, there were no significant differences between the groups either in the percentages of abnormally low laboratory values (mean cell volume, hemoglobin, zinc, and ferritin) or in the percentages of high alkaline phosphatase activity, which indicates the comparable safety and effectiveness of the formulas studied.

Conclusions: Both nutritional status and growth were well within reference values in the 2 groups, and the selection of a formula can largely be made on the basis of infant tolerance to the formulas. *Am J Clin Nutr* 2005;82:140–5.

KEY WORDS Infant nutrition, cow milk allergy, extensively hydrolyzed whey formula, soy formula

INTRODUCTION

Allergy to cow milk protein occurs in 2–3% of infants (1–4). Almost half of these infants begin to tolerate cow milk by the age of 2 y (5, 6).

After weaning from breast milk, infants with cow milk allergy (CMA) are usually given either an extensively hydrolyzed formula or a soy formula. Soy formulas have a long history as alternative formulas for infants who are allergic to cow milk. Eight to 14% of infants with symptoms of immunoglobulin E (IgE)-associated CMA also react adversely to soy (7), but reports

of anaphylaxis to soy are rare. Previously, we performed a randomized controlled study of infants with CMA in which 10% of the infants randomly assigned to a soy formula had adverse reactions from the formula compared with 2% of those randomly assigned to an extensively hydrolyzed formula (8). In some studies, growth was impaired in infants with CMA compared with healthy children (9–11), whereas in other studies growth reached the average rate after consumption of an elimination diet (12–14). The aim of the present study was to compare the effects of a soy formula or an extensively hydrolyzed whey formula on the nutritional status of infants until age 2 y and on their growth until age 4 y.

SUBJECTS AND METHODS

Subjects

The study involved 168 infants with CMA. The allergy was confirmed by a double-blind, placebo-controlled milk challenge, except in the case of 2 subjects who had a history of anaphylactic reaction to cow milk and who also had a positive skin-prick test and IgE antibodies to cow milk (15). Positive reactions that occurred within 2 h of the last challenge dose in the hospital were classified as immediate reactions; positive reactions that occurred later during the 5 d of challenge were classified as delayed reactions. At inclusion in the study, the symptoms that occurred most often in the infants because of CMA were atopic eczema

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TABLE 1

Baseline characteristics of the subjects in the soy formula group (SFG) and the hydrolyzed whey formula group (HWFG)¹

	SFG (n = 84)	HWFG (n = 84)
Sex (n)		
Male	51	47
Female	33	37
Age (mo)	7.8 ± 2.1	7.5 ± 2.2
Reaction during cow milk challenge (n)		
Immediate	47	55
Delayed	36	28
No challenge	1	1
Skin-prick test (n)		
0–2 mm	44	49
≥3 mm	40	35
IgE antibodies to cow milk		
<0.35 kU/L	36	39
≥0.35 kU/L	38	34

¹ In 2 subjects, cow milk allergy was confirmed on the basis of a history of anaphylactic reaction to cow milk, a positive result from a skin-prick test, and the presence of immunoglobulin E (IgE) antibodies to cow milk. There were no significant differences between groups (independent-samples *t* test for age and chi-square test for the other variables).

(59%) and gastrointestinal symptoms (22%). When CMA was confirmed, the infants were allocated to groups that received either a soy formula (SoijaTutteli; Valio Ltd, Helsinki, Finland) or an extensively hydrolyzed whey formula (PeptidiTutteli; Valio Ltd) according to a computer-generated block randomization list; a block size of 4 was used. The participating hospital (of 2 hospitals) and the age group (0–2, 3–5, 6–8, and 9–11 mo) were used as stratification variable factors in the randomization. The baseline characteristics of the infants are presented in **Table 1**.

The study protocol was approved by the Joint Commission on Ethics of Turku University and Turku University Central Hospital and by the Commission on Ethics of the Skin and Allergy Hospital, Helsinki University Central Hospital.

Study design

Twenty-one of 84 infants (25%) in the soy formula group (SFG) and 5 of 84 infants (6%) in the hydrolyzed whey formula group (HWFG) switched to another formula before the age of 2 y on the basis of suspected adverse reactions to the formula studied. An adverse reaction to the study formula was confirmed in 8 of 84 infants (9%) in the SFG and in 2 of 84 infants (2%) in the HWFG, as discussed in more detail in articles by Vanto et al (6) and Klemola et al (8).

Sex distribution did not differ significantly between the groups: there were 51 boys and 33 girls (61% and 39%, respectively) in the SFG and 47 boys and 37 girls (56% and 44%, respectively) in the HWFG. The mean (±SD) duration of breastfeeding (sum of total and partial breastfeeding) was 7.1 ± 4.0 mo in the SFG and 7.7 ± 4.7 mo in the HWFG. The infants began to receive the study formula at a mean age of 7.8 mo in the SFG and 7.5 mo in the HWFG. About one-half of the infants (45% in the SFG and 47% in the HWFG) were being partially breastfed when they began ingestion of the study formula. Common food allergens (egg, fish, strawberries, tomato, citrus fruit, peas, and chocolate) were excluded from the diet up to the age of 1 y. Other food products that caused any suspected hypersensitivity in the infants

TABLE 2

Composition of study formulas¹

	Soy formula	Hydrolyzed whey formula
Energy (kJ)	285	280
Protein (g)	1.9	1.6
Fat (g)	3.5	3.5
Carbohydrate (g)	7.0	7.3
Calcium (mg)	65	51
Phosphorus (mg)	42	30
Magnesium (mg)	5.9	5.2
Zinc (mg)	1.0	0.4
Copper (mg)	52	45
Iron (mg)	1.0	0.8
Vitamin E (mg)	1.3	1.0
Vitamin C (mg)	7.2	7.8
Riboflavin (μg)	78	130

¹ Mean analyzed concentration per 100 mL prepared product.

were also eliminated from the diet. Daily supplements of vitamin D (240–400 IU) were recommended for all of the infants up to the age of 2 y according to general health counseling in Finland. Calcium powder or tablets (250–500 mg) was recommended for all infants up to age 2 y, according to general health counseling in Finland for infants who are allergic to cow milk products. Otherwise, the Finnish well-baby clinics' guidelines for supplementary feeding were followed.

Both formulas complied with the nutrient recommendations of the European Union for infant formulas (16). The composition of the study formulas is presented in **Table 2**. In the extensively hydrolyzed whey formula, the size of all the peptides was <1600 Da. The phytate content of the soy-based formula was 4.1 μmol/100 g powder.

Calculation of nutrient intake

A 2-d dietary recall was completed by the infants' parents or by daycare personnel when the infants were 1 and 2 y old. The NUTRICA program with a Finnish database (17), which was compiled from the manufacturer's data and family recipes, was used for the calculation of energy and the contents of protein, fat, carbohydrate, calcium, riboflavin, iron, zinc, and vitamin E.

Laboratory analyses

Venous blood samples were obtained from the infants before the start of the study and at the ages of 1 and 2 y. The laboratory values of 6 infants who had received a formula for <1 mo by age 1 y were excluded from the analyses. The laboratory values for infants who discontinued using the study formula because of adverse reactions were included in the analyses at the age at which they were before the formula change. Serum alkaline phosphatase activity was determined by a kinetic method; hemoglobin concentrations, red blood cell indexes, and leukocyte concentrations were measured with the use of a Coulter Counter T-890 (Coulter Electronics, Tokyo, Japan); and serum calcium concentrations were measured with the use of a Hitachi 917 AutoAnalyzer (Hitachi Ltd, Tokyo, Japan). Serum ferritin concentrations were measured with a radioimmunoassay (Diagnostic Products, Los Angeles, CA), and serum transferrin receptor concentrations were measured with an enzyme-linked immunosorbent assay (Ramco, Houston, TX). After the dilution of blood samples with 10% nitric acid (1:5, by vol), serum zinc and

TABLE 3

Daily nutrient intakes of children with cow milk allergy in the soy formula group (SFG) and the hydrolyzed whey formula group (HWFG) at ages 1 and 2 y

	1 y		2 y		Mean difference (95% CI)	<i>P</i> ²
	SFG (<i>n</i> = 75–77)	HWFG (<i>n</i> = 69–71)	SFG (<i>n</i> = 70–73)	HWFG (<i>n</i> = 69–71)		
Energy (kJ/kg)	387 ± 76 ¹	384 ± 79	364 ± 87	372 ± 70	−3 (−25, 19)	0.77
Energy from the study formula (%)	45 ± 14	41 ± 19	22 ± 15	14 ± 15	6 (1, 11)	0.03
Protein (g/kg)	2.6 ± 0.6	2.6 ± 0.7	3.0 ± 0.9	3.1 ± 0.9	−0.1 (−0.3, 0.2)	0.55
Fat (g)	33 ± 9	32 ± 10	40 ± 12	39 ± 10	1 (−2, 3)	0.58
Carbohydrate (g)	125 ± 25	125 ± 26	139 ± 37	144 ± 28	−5 (−13, 3)	0.23
Calcium (mg) ³	518 ± 166	449 ± 176	506 ± 262	464 ± 338	49 (−18, 116)	0.15
Riboflavin (mg)	0.82 ± .22	0.98 ± .33	1.03 ± 0.43	1.11 ± 0.55	−0.14 (−0.26, −0.02)	0.02
Iron (mg)	9.7 ± 2.4	8.8 ± 2.2	9.1 ± 3.1	8.6 ± 2.3	0.6 (−0.05, 1.26)	0.07
Zinc (mg)	7.9 ± 2.7	5.9 ± 1.5	8.0 ± 2.6	6.7 ± 1.5	1.7 (1.10, 2.21)	<0.01
Vitamin E (mg)	9.9 ± 2.7	8.0 ± 2.7	8.2 ± 3.8	6.9 ± 2.6	1.6 (0.8, 2.4)	<0.01

¹ $\bar{x} \pm SD$ (all such values).² Repeated-measures ANOVA. The interaction between group and time was not significant for all variables.³ Values do not include intake from supplements.

copper concentrations were measured by atomic absorption spectrometry and with the use of National Institute of Standards and Technology (Gaithersburg, MD) standards.

Growth

The weight of the infants was measured with the use of electronic scales. The length of the infants who were up to age 2 y was measured by an experienced study nurse using a stadiometer while the infants were in a supine position. At the ages of 3 and 4 y, the standing height of each child was measured. The growth values of 6 infants who had received a formula for <1 mo by age 1 y were excluded from the analyses. Only growth values for those infants who did not change study formulas because of adverse reactions were included in the analyses. Length in SD score (SDS) and weight-for-length (% wt), which were expressed as the percentage deviation from the median weight for length and sex, were calculated with the use of the Finnish reference growth data (18). Length and weight were measured at the ages of 0, 6, 8, 10, 12, 18, 24, 36, and 48 mo.

Statistical analyses

For length (as SDS and in cm) and weight (percentage of weight-for-length and in kg), repeated laboratory measurements, and nutrient intake, the results are expressed as means ± SDs or means ± SEMs. Length as SDS and percentage of weight-for-length are the primary variables to indicate growth. Weight (in kg) and length (in cm) were considered secondary variables because the measurements of all the children were not taken at the exact predefined ages of 6, 8, 10, 12, 18, 24, 36, and 48 mo, and the actual length (in cm) and weight (in kg) may cause bias to the analysis. The differences in weight and length were not significant between the groups. For the length (SDS) and weight (percentage of weight-for-length) of infants aged 1–4 y, an analysis of variance (ANOVA) for repeated measures was performed as a primary analysis. The comparisons between the SFG and the HWFG are shown as mean differences with 95% CIs. The weight and length of infants aged <12 mo were not analyzed because consumption of the study formula began between the ages 2 and 11 mo.

Nutrient intake and laboratory results at ages 1 and 2 y were also analyzed with an ANOVA for repeated measures, and the corresponding baseline value was included as a covariate when appropriate. The differences between the groups (SFG compared with HWFG) are shown as means with 95% CIs. The association between laboratory measurements and nutrient intake was assessed with the use of Pearson's correlation coefficients. The data were analyzed by using SPSS (version 12.0; SPSS Inc, Chicago, IL).

The decision to analyze the iron, zinc, and copper status was made post hoc, ie, not until the clinical study had been finished. At this time all the samples had been collected, and specific informed consent could not be obtained. The samples were analyzed without any patient identifiers at the University of California, Davis. Written informed consent was obtained from the infants' parents for all the other parts of the present study.

RESULTS

At age 1 y, the mean (±SD) daily intake of the formula was 580 ± 194 mL in the SFG and 559 ± 267 mL in the HWFG. At age 2 y, 70% of the infants were still being fed the study formulas, and the mean (±SD) daily intake of formula was 420 ± 199 mL in the SFG and 369 ± 221 mL in the HWFG.

Nutrient intake

The infants in the SFG received significantly more percentage of energy from the study formula than did the infants in the HWFG (Table 3). Dietary intakes of zinc and vitamin E were significantly lower in the HWFG infants than in the SFG infants, and the intake of riboflavin was significantly higher in the HWFG than in the SFG.

Laboratory results

Laboratory results are presented in Table 4. The concentrations of transferrin receptors tended to indicate a greater tissue need for iron in the SFG than in the HWFG when analyzed by an ANOVA for repeated measures (*P* = 0.08).

TABLE 4

Laboratory results for infants with cow milk allergy in the soy formula group (SFG) and the hydrolyzed whey formula group (HWFG) at baseline and at ages 1 and 2 y¹

	Baseline		1 y		2 y		Mean difference (95% CI)	P ²
	SFG (n = 53)	HWFG (n = 63)	SFG (n = 51)	HWFG (n = 59)	SFG (n = 47)	HWFG (n = 53)		
Transferrin receptor (mg/L)	6.4 ± 2.1 ³	5.8 ± 1.8 ⁴	6.6 ± 1.4 ⁵	6.0 ± 1.3 ⁶	6.0 ± 1.0 ⁷	5.7 ± 1.2 ⁵	0.4 (−0.02, 0.8)	0.08
Ferritin (μg/L) ²	61 ± 50 ³	88 ± 95 ^{4,8}	30 ± 16 ⁵	44 ± 33 ⁶	27 ± 18 ⁷	29 ± 22 ⁵	−6.5 (−14.9, 1.9)	0.13
<12 μg/L (%)	11	4	7	12	22	24		
Zinc (mg/L)	0.71 ± 0.13 ³	0.69 ± 0.14 ⁴	0.67 ± 0.09 ⁵	0.66 ± 0.10 ⁶	0.72 ± 0.16 ⁷	0.74 ± 0.19 ⁵	−0.02 (−0.08, 0.03)	0.47
<0.70 mg/L (%)	15	21	60	72	47	52		
Hb (g/L)	115 ± 8	117 ± 8	117 ± 7	116 ± 8	121 ± 8	121 ± 7	0.9 (−1.4, 3.2)	0.45
<110 g/L (%)	21	16	16	19	6	6		
MCV (fL)	78 ± 4	80 ± 4	79 ± 4	80 ± 3	81 ± 4	81 ± 3	0.4 (−0.6, 1.4)	0.41
<75 fL (%)	17	8	10	2	6	4		
S-AFOS (U/L)	643 ± 284	834 ± 1297	635 ± 198	790 ± 1432	580 ± 140	637 ± 702	−127 (−372, 118)	0.31
>1000 U/L (%)	4	7	4	5	0	6		
Calcium (mmol/L)	2.61 ± 0.08	2.62 ± 0.07	2.56 ± 0.08	2.58 ± 0.09	2.50 ± 0.07	2.53 ± 0.08	−0.02 (−0.05, 0.002)	0.08
Copper (μg/L)	0.9 ± 0.2 ³	1.0 ± 0.2 ⁴	1.1 ± 0.2 ⁵	1.1 ± 0.2 ⁶	1.1 ± 0.2 ⁷	1.1 ± 0.2 ⁵	0.01 (−0.05, 0.07)	0.77

¹ Data for infants who did not change study formulas because they had no adverse reactions and those who did but who received the study formula for ≥1 mo by the age of 1 y are included. Hb, hemoglobin; MCV, mean cell volume; S-AFOS, serum alkaline phosphatase. The interaction between group and time was not significant for all variables.

² Repeated-measures ANOVA, with the baseline value included as a covariate.

³ n = 47.

⁴ n = 56.

⁵ n = 42.

⁶ n = 52.

⁷ n = 36.

⁸ Significantly different from baseline SFG, *P* < 0.05.

The percentages of low ferritin (<12 μg/L), hemoglobin (<110 g/L), mean cell volume (<75 fL), and zinc (<0.70 mg/L) concentrations and the percentage of high serum alkaline phosphatase (>1000 U/L) concentrations in the 2 groups are presented in Table 4. There were no significant differences between the groups, nor was there any relation between the concentrations of zinc and ferritin (κ coefficient = 0.02, *P* = 0.89). No correlation between dietary intake and the results of the biochemical analysis was found.

Growth

Length (SDS) and percentage of weight-for-length at 0, 6, 10, 12, 18, 24, 36, and 48 mo of age are shown in **Figure 1**. The growth data (length in SDS and in cm, and weight as a percentage of weight-for-length and in kg) were not significantly different between the groups at baseline. The growth data from 1 to 4 y were analyzed with an ANOVA for repeated measures. In all of the analyses, the interactions (group × time) were not significant (*P* = 0.723 for SDS, *P* = 0.260 for cm, *P* = 0.664 for percentage of weight-for-length, and *P* = 0.627 for kg).

The mean length as SDS during that period was 0.10 in the SFG and −0.03 in the HWFG. The mean length in cm was 89.6 in the SFG and 89.4 in the HWFG. The mean difference between the groups was 0.13 SDS (95% CI: −0.18, 0.44; *P* = 0.392) or 0.2 cm (95% CI: −0.9, 1.4; *P* = 0.682).

The mean weight as a percentage of weight-for-length during the period from 1 to 4 y was −1.8% in the SFG and −3.2% in the HWFG. The mean weight was 13.2 kg in the SFG and 13.0 kg in the HWFG. The mean difference between the groups was 1.4%

(95% CI: −0.7, 3.5; *P* = 0.191) or 0.3 kg (95% CI: −0.2, 0.7; *P* = 0.301).

Forty infants in the SFG and 48 infants in the HWFG had immediate, often IgE-mediated, reactions to cow milk; 25 infants in the SFG and 27 infants in the HWFG had delayed, often non-IgE-mediated, reactions. There were no significant differences in weight or length between the infants with immediate reactions to cow milk and those with delayed reactions in the SFG or in the HWFG.

A percentage of weight-for-length value of <−15% was found in 4 infants (6.1%) in the SFG and 5 infants (6.6%) in the HWFG who were between the ages of 1 and 4 y. The age when the infants began to ingest the study formula did not correlate with growth by ages 1 or 2 y.

DISCUSSION

As far as we know, no previous prospective randomized studies have compared the effects of the 2 types of formula used in the present study on the nutritional status and growth of infants. Nutritional status and growth were well within the reference values in the 2 groups, and the selection of a formula can largely be based on the infant's tolerance to the formulas. Adverse reactions to the soy formula occurred more often than did adverse reactions to the hydrolyzed formula (10% compared with 2%), but these reactions were seldom severe or IgE-mediated (8). On the other hand, soy formulas are cheaper and probably more palatable, which was indicated by the slightly higher intake of the soy formula than of the extensively hydrolyzed formula and by the good catch-up growth in the SFG.

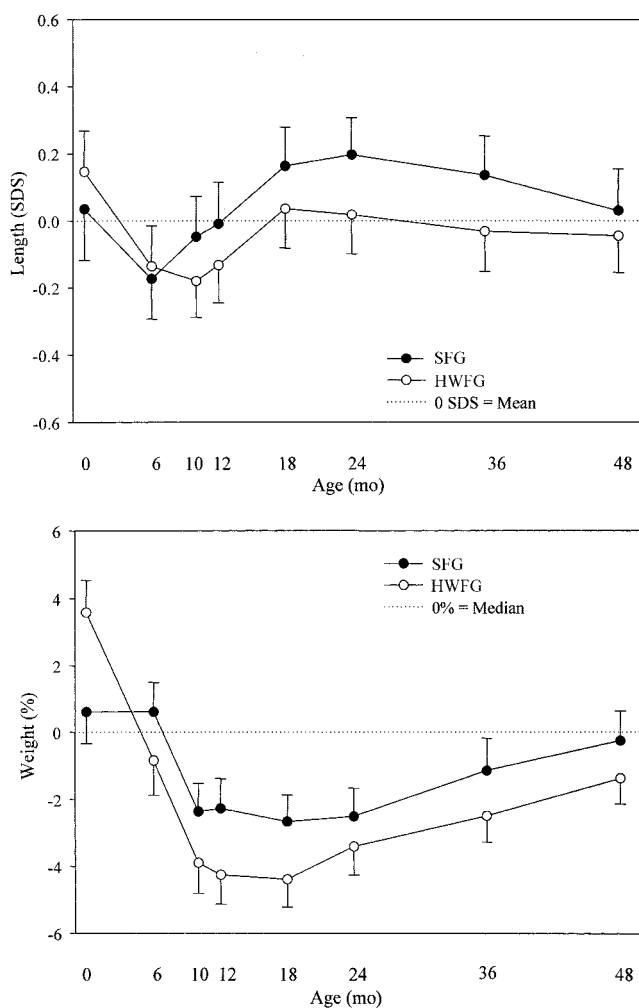


FIGURE 1. Mean ($\pm$ SEM) length SD score (SDS) and weight-for-length during the first 4 y in the soy formula group (SFG; $n = 66$) and in the extensively hydrolyzed whey formula group (HWFG; $n = 76$). Only infants who did not change study formulas because of adverse reactions and infants who had received the study formula for ≥ 1 mo by the age of 1 y were included. At baseline [ages 2–11 mo; mean ($\pm$ SD) age: 7.8 ± 2.1 mo in the SFG and 7.5 ± 2.2 mo in the HWFG], length was not significantly different between the groups (-0.04 in the SFG compared with -0.08 in the HWFG; $P = 0.85$). At birth, weight was lower in the SFG than in the HWFG ($P < 0.05$). At baseline, weight was no longer significantly different between the groups (-0.4 in the SFG compared with -0.2 in the HWFG; $P = 0.92$). There were no significant differences between the groups in growth from 1 to 4 y (ANOVA for repeated measures).

It has been suggested that infants with food allergies need more nutrients than do healthy infants because of their impaired ability to utilize nutrients, which may be caused by allergy-induced bowel inflammation (19). In the present study, the negative effects on growth in infants with CMA were seen before an appropriate diet was substituted; however, catch-up growth was good in the infants after the substitution of cow milk with either the soy formula or the hydrolyzed whey formula. In our study, the energy intake of the infants was ≈ 390 kJ/kg at age 1 y, which was slightly less or similar when compared with other studies in Finnish infants who were either allergic to cow milk (11) or healthy (20).

Protein intake at age 1 y in the 2 groups was twice the lowest amount of safe protein intake according to international dietary

recommendations (21). Infant formulas with protein contents of only 12–13 g/L, along with high-protein supplement foods, were shown to ensure normal infant growth (22, 23). The main effect of high protein intake is on weight and fat; differences in height gain are less marked (24). The soy formula studied contained more protein than did the whey hydrolyzed formula (1.9 compared with 1.6 mg/L), which may partly explain the good weight-for-length catch-up growth, especially in the SFG.

In the present study, the calculated mean intake of other nutrients exceeded the lowest recommended intake. Calcium intake in the infants met the recommended intake only because of supplementation with calcium powder or tablets. Seventy percent of the infants were still drinking a formula at age 2 y, which explains the significant differences still seen at that age in the intake of nutrients that occur in different concentrations in the soy formula and the extensively hydrolyzed formula (eg, zinc and vitamin E). Parents received the study formula free of charge and may have increased the duration of formula consumption and also the quantity of formula ingested, which in turn may have affected the nutritional status of the infants.

The measured concentrations of serum transferrin receptors tended to indicate greater tissue needs for iron in infants in the SFG than in the HWFG, although iron intake was higher in the SFG. Whether this modest difference between the groups is physiologically significant is uncertain; however, better iron status probably protects against iron deficiency in later life. Serum transferrin receptor concentrations indicate tissue needs for iron, whereas ferritin concentrations are a measure of stored tissue iron. Soy formulas contain phytates, which bind iron (25) and were shown to reduce iron absorption (26). Persson et al (27) studied healthy Swedish 1-y-old infants and found that as many as one-fourth had low serum ferritin concentrations ($< 12 \mu\text{g/L}$). In our study, only 7–12% of the infants with CMA had low serum ferritin values at age 1 y. However, formula intake was high in both groups, and both formulas were generously supplemented with iron. At age 2 y, however, 22–24% of the infants had low serum ferritin concentrations, which suggests that as the infants' consumption of the formula decreased, the prevalence of iron deficiency increased.

Phytate in a soy formula was also reported to influence zinc absorption (27, 28). In our study, serum zinc concentrations did not differ between the 2 groups; however, the soy formula contained 10 mg Zn/L and the whey hydrolyzed formula 4 mg Zn/L, which likely compensated for the differences in zinc bioavailability. In earlier studies with small study groups, it was found that 5–60% of the infants with CMA had low serum zinc concentrations (9, 29). We found that 60–72% had low serum zinc concentrations ($< 0.7 \mu\text{g/L}$). Both study groups had high protein intakes, which may also lead to low serum zinc values. However, serum zinc concentration is not considered a very good indicator of zinc nutritional status because it is affected by many factors particularly relevant in infants with CMA, eg, acute stress, infections, and growth rate (30).

There were no significant differences between the groups either in the percentages of abnormally low laboratory values (mean cell volume, hemoglobin, zinc, and ferritin) or in the percentage of high alkaline phosphatase, which indicates the comparable safety and effectiveness of the formulas studied. Furthermore, there were only a few infants (6–7%) in both formula groups who were underweight.

In conclusion, the length growth of infants with CMA reached the mean Finnish reference value by age 2 y in both groups. Weight-for-length measurements in the infants remained below the 50th percentile by age 2 y. However, the weight-for-length measurements in the infants continued to reach the 50th percentile by age 4 y in both study groups. The mean intake of nutrients and nutritional status followed recommendations; however, individual dietary counseling was needed in many cases. Even with such counseling, it appears that nutritional status and growth did not differ between the groups, and the selection of a formula can therefore largely be made on the basis of tolerability and, to some extent, on cost.



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TV, KJ-B, TK, and RK were the principal investigators of the study. BL analyzed serum zinc, copper, ferritin, and transferrin receptor concentrations. LS, RK, and TV prepared the manuscript. LS counted the intake of nutrients. LM and AP were the infant nutrition specialists for this study. KJ-B, TK, and BL contributed to the preparation of the manuscript. None of the authors reported any conflicts of interest.

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