Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
www.all-imm.com

ORIGINAL ARTICLE

OPEN ACCESS

Real-life data on the effectiveness of extensively hydrolyzed protein-based formula and amino acid-based formula in regaining weight and height in infants on a cow's milk protein elimination diet

Dayane Pêdra Batista de Faria[a], Marcela Duarte de Sillos[a], Patrícia da Graça Leite Speridião[b], Mauro Batista de Morais[c]*

[a,c]*Pediatric Gastroenterology Department, Federal University of Sao Paulo, Sao Paulo, Brazil*
[b]*Department of Health, Education and Society, Institute of Health and Society, Federal University of São Paulo - Baixada Santista Campus, Santos, Brazil*

Received 1 September 2022; Accepted 7 January 2023
Available online 1 March 2023

KEYWORDS
Hypersensitivity to Milk;
Food Hypersensitivity;
Nutritional Status;
Height

Abstract
Objective: To compare the effectiveness of extensively hydrolyzed protein-based formula (EHF) or amino acid-based formula (AAF) in reversing the weight and height deficit in infants on a cow's milk protein elimination diet.
Methods: Infants from a retrospective cohort who were fed EHF (n = 17) or AAF (n = 16) for at least 2 months on a cow's milk protein elimination diet were included. The weight and height values recorded in the infants' medical records were obtained.
Results: The mean age of the infants at the start of EHF and AAF were 5.8 ± 2.6 and 4.4 ± 2.5 months, respectively (P = 0.061). There was no difference between the groups in terms of the monthly weight gain (373.0 ± 212.2 and 453.1 ± 138.5 g, P = 0.223, respectively, for EHF and AAF), while the monthly increase in height was greater in the group fed with AAF (1.3 ± 0.5 and 1.8 ± 0.6, P = 0.030). A comparison between the difference in the initial z-score and in the oral challenge test of weight-for-age (+0.7 ± 1.2 and +1.3 ± 1.4, P = 0.262, respectively, for the EHF and AAF groups), height-for-age (+0.2 ± 1.1 and +1.2 ± 1.8, P = 0.090), and body mass index (BMI)-for-age (+0.7 ± 1.3 and +0.7 ± 1.5, P = 0.971) did not reveal a statistically significant difference between the groups. Correlation coefficients showed that the greater the initial nutritional deficit, the greater the positive variation between the beginning of each formula and the oral challenge test.
Conclusion: EHF and AAF provided similar increases in the weight-for-age, height-for-age, and BMI-for-age z-scores in both groups. The monthly increase in height was greater in infants who received AAF.

***Corresponding author:** Mauro Batista de Morais, Pediatric Gastroenterology Department, Federal University of Sao Paulo, Street Pedro de Toledo, 669 - 12th floor, Sao Paulo 04039-032, Brazil. *Email address*: maurobmorais@gmail.com

https://doi.org/10.15586/aei.v51i2.768

Introduction

The most common food allergy in the first 2 years of life is caused by cow's milk proteins.[1,2] Control of the clinical manifestations of cow's milk protein allergy (CMPA) is achieved by excluding allergenic proteins from the diet.[3-6] Considering the high rate of growth and development in the first 2 years of life, it is essential that the cow's milk protein elimination diet fully meets all the nutritional needs that are required at this stage of life.[3,6,7] According to several guidelines,[1,3-6] infants with CMPA and gastrointestinal tract involvement should receive replacement food formulas with extensively hydrolyzed proteins or exclusively with amino acids.

Formulas with extensively hydrolyzed protein-based formula (EHF) and amino acid–based formulas (AAF) meet the nutritional demands of this stage of life that are set out in the Codex Alimentarius. In practice, it is estimated that up to 10% of children with CMPA may persist with clinical manifestations while on an exclusion diet containing EHF. In turn, only AAF is considered fully hypoallergenic for all infants with CMPA.[3,6] If the clinical symptoms do not improve on a diagnostic elimination diet with AAF, then it is highly unlikely that the symptoms are due to cow's milk protein.[6] In this context, the guidelines recommend that EHF be used as a first option for infants with CMPA, taking into account their effectiveness, palatability, and lower cost.[1,3-6] For patients with CMPA who persist with symptoms in the presence of EHF or with severe clinical manifestations, such as intestinal malabsorption syndrome and/or impaired nutritional status, the use of AAF is recommended.[1,3-6] However, there are concerns not only about the higher cost of AAF but also about its possible association with a later occurrence of spontaneous development of oral tolerance.[8] Although there are no specific references, some experts believe that AAF may be associated with lower growth rates.

On the other hand, there is evidence showing that AAF is associated with a faster clinical response.[9-11] Some articles show that normal infants exhibit adequate growth when fed with EHF or AAF in the first months of life.[12,13] However, few studies have compared the growth of infants who were fed an elimination diet with EHF or AAF for suspected or diagnosed CMPA, which may even have nutritional impairment at the beginning of the cow's milk protein elimination diet.[7,14-19]

Thus, the objective of this study was to compare the effectiveness of EHF with that of AAF in the evolution of weight and height of infants on a cow's milk protein elimination diet by CMPA in real life.

Material and Methods

Study design and casuistry

A retrospective cohort study in which two groups of infants on a cow's milk protein elimination diet were compared, who had received EHF or AAF for at least 2 months as part of the cow's milk protein elimination diet. During the follow-up period, there was no exchange of formulas. The previous diagnosis and treatment of CMPA were defined by different physicians using their own usual diagnostic criteria and therapeutic options.

All infants who met the above criteria when undergoing the open oral food challenge test at Hospital São Paulo by the Discipline of Pediatric Gastroenterology at Federal University of São Paulo – Escola Paulista de Medicina between January 2015 and March 2019 were admitted.

Thus, infants who received only EHF with whey proteins (n = 17) or AAF (n = 16) between the start of administration of each of these formulas and the results of the open oral food challenge test were included in the study.

From 6 months of age, the patients received complementary food according to the recommendations by the professionals responsible for the follow-up.

Infants with serious diseases or congenital malformations that could interfere with the growth and nutritional status were excluded.

The research was approved by the Research Ethics Committee of the Federal University of São Paulo (Approval number: 0718/10), and the legal guardians signed the Free and Informed Consent Term.

Weight and height assessment

The weight and height at the initiation of formula use were obtained by secondary data collection from the infants' medical records. On the day of the open oral challenge test, weight and height were measured as part of the oral challenge test. Anthropometric data were classified based on standards provided by the World Health Organization.[20]

To assess the nutritional status and increment of weight and height, weight-for-age, height-for-age, and body mass index (BMI)-for-age, z-scores were calculated. The z-scores were calculated using Anthro Software, version 3.2.2.

The weight gain (g/month) and height increase (cm/month) were calculated based on the differences in weight or height between the onset of EHF or AAF and the oral food challenge test (value in the oral food challenge test – value at the beginning of the EHF or AAF) divided by the duration of use of each formula expressed in months.

Open oral food challenge test

The open oral food challenge test was performed in the morning when the infants were fasting, under medical and nutritionist supervision, staying for 2 h and 30 min in the health service. Infants who did not have clinical manifestations suggestive of CMPA during this initial period were instructed to continue observation at home. A diet with cow's milk and dairy products was allowed, with a recommendation of a minimum intake of 150 mL a day of cow's milk or infant formula with cow's milk proteins. After 30 days of reintroduction of cow's milk proteins, the infants were reassessed to investigate possible late positive reaction. The open food oral challenge test was defined as negative if the infant did not have any consistent symptoms of CMPA during this period of follow-up.[3,7,18]

Statistical analysis

A statistical analysis was performed using SigmaPlot 12.5 Software (Systat Software, San Jose, CA, USA). The quantitative variables were expressed as mean and standard deviation and qualitative variables as number and percentage. A comparison between groups was performed using the Student's t-test or Mann–Whitney test, respectively, for variables with or without normal distribution. An intragroup comparison between the values at the beginning of the formula and in the open oral food challenge test was performed with the paired t-test or Wilcoxon test for variables with or without normal distribution, respectively. The Pearson's correlation coefficient was used to relate the z-scores from the beginning of the use of each formula to the respective differences until the open oral food challenge test. P-values less than 0.05 were considered as statistically significant.

Results

Table 1 presents the characteristics of the two groups studied at the time of initiation of EHF or AAF. Similarities were observed between the groups with respect to the sex, history of prematurity, low birth weight, and previous duration of natural breastfeeding.

All patients included in this study had digestive symptoms. Some of them had skin and respiratory clinical manifestation associated with digestive symptoms. No patient had a history of anaphylaxis, angioedema, or a diagnosis of eosinophilic esophagitis. The diagnostic elimination diet (therapeutic test for CMPA) was used for all patients and had a positive effect in controlling the clinical manifestations of CMPA. In the group that were provided with EHF, a previous consumption of preparations with whole protein from cow's milk or soy formula predominated. The difference between the mean age of the two groups was 1.4 months (P = 0.061). At the beginning of each of the formulas, it was found that the weight-for-age and height-for-age z-scores were lower in the AAF group, and the differences were statistically significant. The proportion of positivity in the oral food challenge test was similar in both groups.

Table 2 shows that both groups showed an increase in values referring to anthropometric parameters between the beginning of each formula and the oral food challenge test. In the group that received EHF, the increases were statistically significant for weight-for-age and BMI-for-age. In the AAF group, the positive variation was statistically significant for the weight-for-age and height-for-age.

Table 3 presents the monthly averages of weight and height increase during the period of use of EHF or AAF. The monthly increase in weight was similar in both groups, while the monthly increase in height was greater in the AAF group. The comparison between the differences in the z-scores between the beginning of each formula and the value in the oral food challenge test did not reveal a statistically significant difference between the groups.

Figure 1 presents the correlations between the initial values of the z-scores and their corresponding differences over the period of use of each formula (z-score in the oral food challenge test – z-score at the beginning of each formula). All the correlation coefficients calculated showed that the greater the initial nutritional deficit, the greater the positive variation between the beginning of each formula and the oral food challenge test.

Discussion

This study evaluated the gain in body weight and growth of infants on a cow's milk protein elimination diet with clinical signs of CMPA fed with EHF or AAF, from the moment of introduction of the formula until the performance of the oral food challenge test. It was evidenced that both groups showed increases in the mean z-scores indicative of nutritional recovery. The AAF-fed group showed a greater monthly increase in the height, probably due to the greater height-for-age deficit at the time of initiation of formula. Thus, according to the correlation coefficients, the greater the recovery of weight-for-age, height-for-age, and BMI-for-age, the greater the initial anthropometric deficit was observed to be.

The treatment of CMPA is based on the exclusion of cow's milk proteins from the diet.[1,3,4,6] The elimination diet aims at the disappearance of clinical manifestations, maintenance of the integrity of the intestinal mucosa, prevention of absorption of food antigens, and prevention of triggering of new immunological or inflammatory reactions.[14] On the other hand, patients with CMPA may have an impaired nutritional status as well as reduced growth when compared to healthy children.[7,15,18,19,21-24] Thus, it is extremely important to provide periodic assistance to children with CMPA, by trained professionals, such that the correct indication of the formula is carried out, according to the needs of each child, as well as adequate dietary guidelines regarding the requirements for nutrient supplementation, in order to avoid nutritional deficiencies.[1,3,4-6]

It is important to highlight that nutritional catch-up can provide an equalization to the growth observed in healthy children; however, accelerated nutritional recovery can contribute to the development of chronic noncommunicable diseases in adult life.[15,25]

The performance of the oral food challenge test for the diagnosis of CMPA or to characterize the acquisition of tolerance to cow's milk proteins is essential to define the end of the elimination diet. Although the EHF and AAF meet the requirements required by the Codex Alimentarius, there is evidence of lower growth during the cow's milk protein elimination diet,[23] as well as higher growth when the diet is restarted without restriction.[18,19]

In this study, the EHF group received a cow's milk protein elimination diet for a mean period of 9.5 months, while in the AAF group, the mean time on the elimination diet was 8.7 months. It is important to highlight that half of the number of infants (50.0%) fed with AAF previously received EHF as a first option. Despite the fact that only 5–10% of children fed with EHF showed persistence of signs and symptoms, in the composition of our series, a similar number of patients receiving AAF and EHF[16,26] was observed, similar to the proportion found in a study carried out in another Brazilian city.[15] It is noteworthy that

Table 1 General characteristics of the groups studied at the beginning of the use of the formula with extensively hydrolyzed protein-based formula (EHF) or amino acid–based formula (AAF).

	Type of formula		P
	Extensively hydrolyzed protein-based formula (n = 17)	Amino acid–based formula (n = 16)	
Sex			
Male	11 (64.7%)	9 (56.3%)	0.888[a]
Female	6 (35.3%)	7 (43.7%)	
History of prematurity (N and %)	2 (11.8%)	4 (25.0%)	0.398[b]
Low birth weight, less than 2500 g (N and %)	2 (11.8%)	5 (31.3%)	0.225[b]
Previous duration of breastfeeding (months)	2.2 ± 1.9	1.7 ± 1.9	0.444[c]
Clinical manifestations before initiation of EHF or AAF[d]	-	-	-
Digestive	-	-	-
Infant colic	4 (23.5%)	2 (12.5%)	0.358[a]
Constipation	5 (29.4%)	3 (18.8%)	0.380[a]
Diarrhea	5 (29.4%)	6 (37.5%)	0.450[a]
Abdominal distension	4 (23.5%)	3 (18.8%)	0.536[a]
Bloody stool	5 (29.4%)	8 (50.0%)	0.197[a]
Nausea	1 (5.9%)	1 (6.3%)	0.742[a]
Food refusal	1 (5.9%)	3 (18.8%)	0.277[a]
Regurgitation	6 (35.3%)	8 (50.0%)	0.308[a]
Vomiting	3 (17.6%)	2 (12.5%)	0.530[a]
Cutaneous	-	-	-
Urticaria	1 (5.9%)	3 (18.8%)	0.277[a]
Skin rash	3 (17.6%)	2 (12.5%)	0.530[a]
Respiratory	-	-	-
Bronchospasm	2 (11.8%)	3 (18.8%)	0.469[a]
Dairy used for feeding before initiation of EHF or AAF	-	-	-
Breast milk	2 (11.8%)	2 (12.5%)	0.004[a]
Formula with cow's milk proteins	11 (64.7%)	6 (37.5%)	-
Soy formula	4 (23.5%)	0 (0.0%)	-
Extensively hydrolyzed formula	0 (0.0%)	8 (50.0%)	-
Age at initiation of EHF or AAF (months)	5.8 ± 2.6	4.4 ± 2.5	0.061[e]
Anthropometric indicators at the beginning of EHF or AAF	-	-	-
Weight-for-age z-score	−0.9 ± 1.1	−2.0 ± 1.4	0.026[c]
Height-for-age z-score	−0.6 ± 1.3	−2.4 ± 1.9	0.006[c]
BMI-for-age z-score	−0.7 ± 1.4	−0.8 ± 1.5	0.787[c]
Duration of cow's milk protein elimination diet (months)	9.9 ± 5.0	9.6 ± 8.5	0.280[e]
Duration of EHF or AAF use until oral challenge test (months)	9.5 ± 5.0	8.7 ± 8.7	0.130[e]
Oral food challenge test	-	-	-
Positive	4 (23.5%)	3 (18.8%)	1.000[b]
Negative	13 (76.5%)	13 (81.2%)	-

[a]Chi-squared test; [b]Fisher's exact test; [c]Student's t-test; [d]Each patient could have more than one type of clinical manifestation before admission; [e]Mann–Whitney test.

Table 2 Z-scores for weight, height, and BMI (body mass index) for age at the time of initiation and on the day of the oral food challenge test for groups receiving extensively hydrolyzed protein-based formula (EHF) or amino acid-based formula (AAF).

	Extensively hydrolyzed protein-based formula (n=17)		P	Amino acid-based formula (n=16)		P
	Initiation of EHF	Oral challenge test		Initiation of AAF	Oral challenge test	
Weight-for-age z-score	−0.9 ± 1.1	−0.2 ± 1.1	0.030[a]	−2.0 ± 1.4	−0.7 ± 1.1	0.003[a]
Height-for-age z-score	−0.6 ± 1.4	−0.4 ± 1.1	0.306[b]	−2.4 ± 1.9	−1.1 ± 1.4	0.014[a]
BMI-for-age z-score	−0.7 ± 1.3	0.0 ± 1.1	0.031[a]	−0.8 ± 1.5	−0.1 ± 1.2	0.064[a]

[a]Paired t-test; [b]Wilcoxon test.

Table 3 Monthly increase in the weight and height, and differences in z-scores between the initiation of extensively hydrolyzed protein-based formula (EHF) or amino acid-based formula (AAF) and the oral food challenge test (value in the oral food challenge test – value at the initiation of formula).

	Extensively hydrolyzed protein-based formula (n=17)	Amino acid-based formula (n=16)	P
Weight (g/month)	373.0 ± 212.2	453.1 ± 138.5	0.223[a]
Height (cm/month)	1.3 ± 0.5	1.8 ± 0.6	0.030[a]
Difference in the z-scores between EHF or AAF initiation and oral food challenge test	-	-	-
Weight-for-age	+0.7 ± 1.2	+1.3 ± 1.4	0.262[a]
Height-for-age	+0.2 ± 1.1	+1.2 ± 1.8	0.090[b]
BMI-for-age	+0.7 ± 1.3	+0.7 ± 1.5	0.971[b]

[a]Student's t test; [b]Mann–Whitney test.

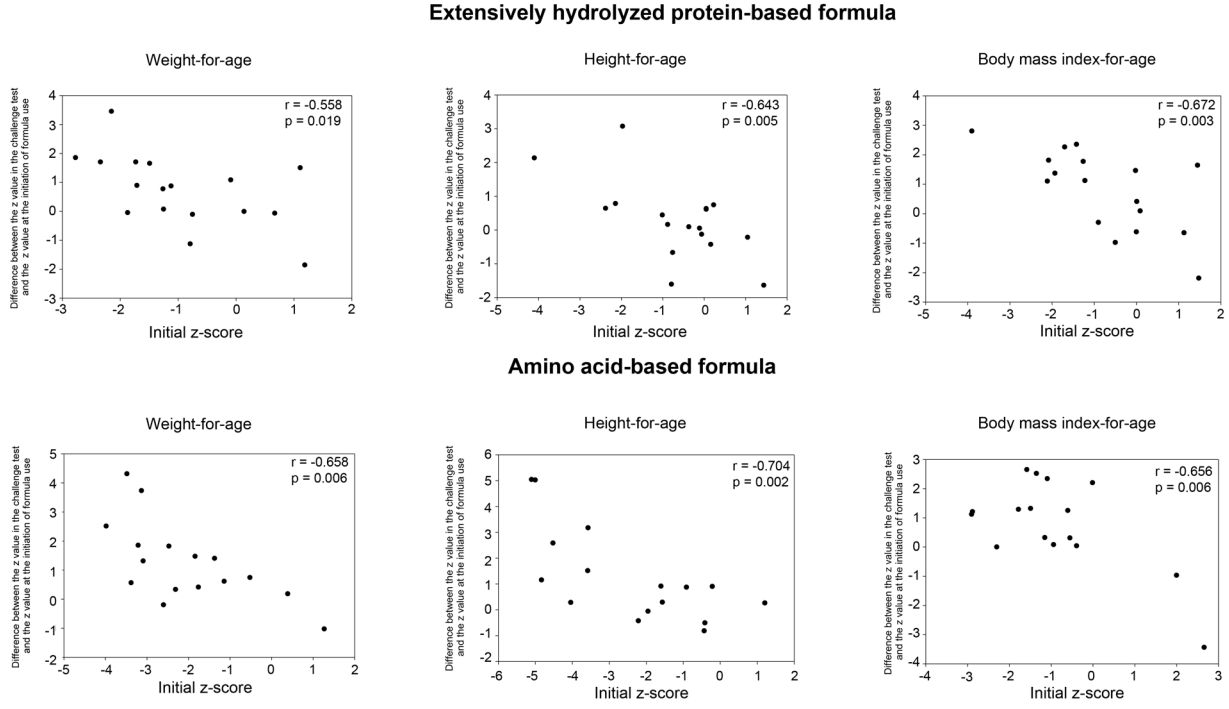

Figure 1 Pearson's correlation coefficient between the initial z-scores and their variations until the oral challenge test (z-score value in the oral food challenge test – value at baseline) in the groups that were fed extensively hydrolyzed protein-based formula or amino acid-based formula.

both studies were carried out in specialized outpatient clinics that potentially treat more severe cases.

In this context, national and international scientific societies[1,3-6] recommend that for children with persistent symptoms to protein hydrolysate and, in cases of severe intestinal malabsorption syndrome and/or with severe impairment of nutritional status (z-scores of weight-for-height less than 2 SD), one should use AAF. In our findings, a considerable portion of infants used AAF, and it is possible to suggest that this fact occurred because they had a more severe form of CMPA and/or more severe impairment of nutritional status, because at the beginning of the AAF, several infants had average z-scores ≤ −2 SD for weight-for-age and height-for-age.

Another study[27] evaluated the efficacy of AAF in 30 infants with a history of weight loss and persistent allergic symptoms using EHF. Prior to the introduction of AAF, infants were below the 50th percentile of the WHO reference population for weight and had watery stools or vomiting among other symptoms. After a 12-week period of being fed with AAF, there was an increase in the weight gain and a decrease in allergic symptoms and a significant reduction in the severity of food allergy (P = 0.020). It is likely that children with non-IgE-mediated allergies, such as those included in the present study, may be more susceptible to persistent allergic manifestations in the presence of formulas with extensively hydrolyzed proteins.

In the present study, after nutritional intervention with EHF or AAF, the oral food challenge test demonstrated that both formulas provided improvement in all anthropometric parameters. As for the nutritional status of the groups at the time of initiating the formulas and in the oral food challenge test, it was possible to observe an improvement in the nutritional status in both groups, with a statistically significant increase in the anthropometric indices of weight-for-age and BMI-for-age in the EHF group, and weight-for-age and height-for-age in the AAF group, demonstrating that both formulas increased the weight and height in infants on a cow's milk protein elimination diet. In addition, the correlation coefficients of all anthropometric indices evaluated showed that the greater the initial nutritional deficit, the greater the positive variation between the beginning of each formula and the oral food challenge test.

There are few studies on the use of hypoallergenic formulas and their relationship with the growth and development of children on a cow's milk protein restriction diet. Studies[12,13] carried out with healthy infants fed with EHF or AAF showed adequate growth during the evaluation period. Another study[14] followed the nutritional status of infants with CMPA fed with EHF or AAF for 9 months. The authors observed that the relative weight increased similarly in both groups during the first few months of follow-up; however, there was a gradual decrease in the EHF-fed group. Contrastingly, the relative weight continued to increase in the AAF group. Compared with the measurement at baseline, the relative length increased in the AAF group but not in the EHF group.

In our study, the assessment of monthly weight gain and the difference in z-scores for weight-for-age, height-for-age, BMI-for-age, at the time of initiation of formulas and in the oral food challenge test, were similar in both groups, indicating that the formulas improved the children's nutritional status. However, the group with AAF showed a greater monthly increase in height, which may suggest that this group of infants had more severe CMPA, requiring replacement of the EHF, introduced at the beginning of the follow-up. With the introduction of AAF and the remission of symptoms, it is possible that the children benefited from accelerated growth recovery. A previous study[10] carried out in children with CMPA and persistence of symptoms also highlighted the replacement of EHF by AAF. The authors observed that there was an increase in height-for-age z-scores after the introduction of AAF. These findings suggest that both formulas, despite substantial differences regarding protein components, were able to promote progressive improvement in anthropometric parameters. In turn, it has been suggested that the reintroduction of whole cow's milk protein may be one of the factors involved in the acceleration of growth after the oral challenge test.[19]

Another aspect that should be mentioned is the similar rate of oral tolerance development with the previous use of EHF and AAF, which disagrees with a previous study that showed a lower rate of oral development with the previous use of AAF.[8] A direct comparison between the results is difficult due to the differences in the criteria used to compose the sample of the two studies. In this context, the present data point to the need for this aspect to be evaluated in future studies.

It is important to emphasize that the major limitation of this study is that the groups are not constituted by randomization. However, the studied sample allowed us to conclude that both formulas improved the weight-for-age, height-for-age, and BMI-for-age z-scores. It is worth noting that the group fed with AAF showed a greater monthly increase in height, possibly because they had a greater nutritional deficit at the time of initiation of AAF use.

Conclusion

EHF and AAF provided similar increases in the weight-for-age, height-for-age, and BMI-for-age z-scores in both groups. The monthly increase in height was greater in infants who received AAF.

Acknowledgments

This study was supported by National Council for Scientific and Technological Development (Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPq).

Conflict of Interest

The authors declare no potential conflicts of interest with respect to research, authorship, and/or publication of this article.

References

1. Boyce JA, Assa'a A, Burks AW, Jones SM, Sampson HA, Wood RA, et al. Guidelines for the diagnosis and management of food allergy in the United States: Summary of the NIAID-Sponsored expert panel report. J Allergy Clin Immunol. 2010;126(6):1105–18.
2. Savage J, Johns CB. Food allergy: Epidemiology and natural history. Immunol Allergy Clin North Am. 2015;35(1):45–59. https://doi.org/10.1016/j.iac.2014.09.004
3. Solé D, Silva L, Rodrigues Cocco R, Targa Ferreira C, Oselka Sarni R, Camargo Oliveira L, et al. Sociedade Brasileira de Pediatria e Associação Brasileira de Alergia e Imunologia. Consenso Brasileiro sobre Alergia Alimentar: 2018 – Parte 2: diagnóstico, tratamento e prevenção. Arq Asma Alerg Imunol. 2018;2(1):7-38. https://doi.org/10.5935/2526-5393.20180005
4. Luyt D, Ball H, Makwana N, Green MR, Bravin K, Nasser SM, et al. Standards of Care Committee (SOCC) of the British Society for Allergy and Clinical Immunology. BSACI guideline for the diagnosis and management of cow's milk allergy. Clin Exp Allergy. 2014;44(5):642-72. https://doi.org/10.1111/cea.12302
5. Muraro A, Werfel T, Hoffmann-Sommergruber K, Roberts G, Beyer K, Bindslev-Jensen C, et al. EAACI food allergy and anaphylaxis guidelines: Diagnosis and management of food allergy. Allergy. 2014;69(8):1008-25. https://doi.org/10.1111/all.12429
6. Koletzko S, Niggemann B, Arato A, Dias JA, Heuschkel R, Husby S, et al. Diagnostic approach and management of cow's-milk protein allergy in infants and children: ESPGHAN GI Committee practical guidelines. J Pediatr Gastroenterol Nutr. 2012;55(2):221-9. https://doi.org/10.1097/MPG.0b013e31825c9482
7. Medeiros LCS, Speridião PGL, Sdepanian VL, Fagundes-Neto U, Morais MB. Nutrient intake and nutritional status of children following a diet free from cow's milk and cow's milk by-products. J Pediatr. 2004;80(5):363-70. https://doi.org/10.2223/1220
8. Berni Canani R, Nocerino R, Terrin G, Frediani T, Lucarelli S, Cosenza L, et al. Formula selection for management of children with cow's milk allergy influences the rate of acquisition of tolerance: A prospective multicenter study. J Pediatr. 2013;163(3):771-7.e1. https://doi.org/10.1016/j.jpeds.2013.03.008
9. Sicherer SH, Noone SA, Koerner CB, Christie L, Burks AW, Sampson HA. Hypoallergenicity and efficacy of an amino acid-based formula in children with cow's milk and multiple food hypersensitivities. J Pediatr. 2001;138(5):688-93. https://doi.org/10.1067/mpd.2001.113007
10. De Boissieu D, Dupont C. Allergy to extensively hydrolyzed cow's milk proteins in infants: Safety and duration of amino acid-based formula. J Pediatr. 2002;141(2):271-3. https://doi.org/10.1067/mpd.2002.126299
11. Niggemann B, Binder C, Dupont C, Hadji S, Arvola T, Isolauri E. Prospective, controlled, multicenter study on the effect of an amino-acid-based formula in infants with cow's milk allergy/intolerance and atopic dermatitis. Pediatr Allergy Immunol. 2001;12(2):78-82. https://doi.org/10.1034/j.1399-3038.2001.012002078.x
12. Adams CB, Johnston WH, Deulofeut H, Leader J, Rhodes R, Yeiser M. Growth and tolerance of healthy, term infants fed lower protein extensively hydrolyzed or amino acid-based formula: Double-blind, randomized, controlled trial. BMC Pediatr. 2021;21(1):323. https://doi.org/10.1186/s12887-021-02617-z
13. Borschel MW, Ziegler EE, Wedig RT, Oliver JS. Growth of healthy term infants fed an extensively hydrolyzed casein-based or free amino acid-based infant formula: A randomized, double-blind, controlled trial. Clin. Pediatr. 2013;52(10):910-7. https://doi.org/10.1177/0009922813492883
14. Isolauri E, Sütas Y, Mäkinen-Kiljunen S, Oja SS, Isosomppi R, Turjanmaa K. Efficacy and safety of hydrolyzed cow milk and amino acid-derived formulas in infants with cow milk allergy. J Pediatr. 1995;127(4):550-7. https://doi.org/10.1016/S0022-3476(95)70111-7
15. Assis PP, Menezes JSS, Diniz AS, Antunes MMC, Cabral PC. Growth of infants with gastrointestinal manifestations of cow's milk protein allergy. Rev Nutr. 2022;35:e210075. https://doi.org/10.1590/1678-9865202235e210075
16. Sampson HA, James JM, Bernhisel-Broadbent J. Safety of an amino acid-derived infant formula in children allergic to cow milk. Pediatrics. 1992;90(3):463-5.
17. Dupont C, Bradatan E, Soulaines P, Nocerino R, Berni-Canani R. Tolerance and growth in children with cow's milk allergy fed a thickened extensively hydrolyzed casein-based formula. BMC Pediatr. 2016l;18;16:96. https://doi.org/10.1186/s12887-016-0637-3
18. Faria DPB, Sillos MD, Speridião PGL, Morais MB. Outcome of food intake and nutritional status after discontinuation of a cow's-milk-free diet post negative oral food challenge in infants and children. Allergol Immunopathol (Madr). 2022;50(1):1-8. https://doi.org/10.15586/aei.v50i1.471
19. Yanagida N, Minoura T, Kitaoka S. Does terminating the avoidance of cow's milk lead to growth in height. Int Arch Allergy Immunol. 2015;168(1):56-60. https://doi.org/10.1159/000441499
20. Organización Mundial de la Salud. Interpretando los Indicadores de Crecimiento Interpretando los Indicadores. Curso Capacit sobre la Evaluación del Crecim del Nino. Ginebra: OMS; 2008.
21. Tiainen JM, Nuutinen OM, Kalavainen MP. Diet and nutritional diet and nutritional status in children with cow's milk allergy. Eur J Clin Nutr. 1995;49(8):605-12.
22. Boaventura RM, Mendonça RB, Fonseca RA, Mallozi M, Souza FS, Sarni ROS. Nutritional status and food intake of children with cow's milk allergy. Allergol Immunopathol (Madr). 2019;47(6):544-50. https://doi.org/10.1016/j.aller.2019.03.003
23. Isolauri E, Sütas Y, Salo MK, Isosomppi R, Kaila M. Elimination diet in cow's milk allergy: Risk for impaired growth in young children. J Pediatr. 1998;132(6):1004-9. https://doi.org/10.1016/S0022-3476(98)70399-3
24. Robbins KA, Wood RA, Keet CA. Milk allergy is associated with decreased growth in US children. J Allergy Clin Immunol. 2014;134(6):1466-1468.e6. https://doi.org/10.1016/j.jaci.2014.08.037
25. Ong KKL, Ahmed ML, Emmett PM, Preece MA, Dunger DB. Association between postnatal catch-up growth and obesity in childhood: Prospective cohort study. BMJ. 2000;320(7240):967-71. https://doi.org/10.1136/bmj.320.7240.967
26. Sampson HA. Anaphylaxis and emergency treatment. Pediatrics. 2003;111(6 Pt 3):1601-8. https://doi.org/10.1542/peds.111.S3.1601
27. Vanderhoof J, Moore N, Boissieu D. Evaluation of an amino acid-based formula in infants not responding to extensively hydrolyzed protein formula. J Pediatr Gastroenterol Nutr. 2016;63(5):531-33. https://doi.org/10.1097/MPG.0000000000001374