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Research Article

Infants on Cow's Milk Protein Elimination Diet are Shorter and Have a Lower Calcium and Vitamin D Intake

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Keywords

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- Hypersensitivity to milk
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Abstract

Objective: To evaluate the dietary intake and the anthropometric profile of infants on a diet eliminating cow's milk proteins (CMP), compared to infants on a free diet.

Method: Prospective cross-sectional study carried out with infants aged 6-24 months, in the gastroenterology and childcare/pediatric outpatient clinics of a children's hospital. The anthropometric evaluation included weight, height, head and arm circumferences, tricipital and subscapular skinfolds, ranked by z-score according to the World Health Organization. Dietary intake was assessed by two 24-hour food recalls, expressed in energy, carbohydrates, proteins, lipids, vitamins and minerals and was compared with the dietary reference intakes (DRIs).

Results: 43 infants on a CMP-elimination diet and 47 infants on a free diet (12.66 ± 4.97 months) were evaluated. When compared to the group on a free diet, the group on an elimination diet showed shorter height (p=0.026) and lower intake of vitamins B1 (p=0.020), B2 (p=0.000), B5 (p=0.007), B12 (p=0.025), D (p=0.006), except for vitamin K (p=0.009), and minerals calcium (p=0.000), phosphorus (p=0.000) and zinc (p=0.030). The intake of most nutrients with significant differences was in accordance with or greater than the recommendations of the DRIs in the exclusion diet group, with the exception of calcium and vitamin D, which was lower in at least one of the daily intake recommendations.

Conclusions: Infants on a CMP-elimination diet were shorter and showed lower intake of some vitamins and minerals compared to the group on a free diet, although within the normal range according to the DRIs, except for calcium and vitamin D.

ABBREVIATIONS

AI: Adequate Intakes; CMPA: Allergy to cow's milk proteins; AC: Arm circumference; CCEB: Brazil Economic Classification Criterion; BF: Breastfeeding; CMP: Cow's milk protein; DRIs: Dietary Reference Intakes; EAR: Estimated Average Requirements; EBF: Exclusive breastfeeding; UFCSPA: Federal University of Health Sciences of Porto Alegre; GA: Gestational age; g/kg: Grams of nutrient per kilogram of current weight; HC: Head circumference; H/A: Height for age; kcal: Kilocalories; kcal/kg: Kilocalories per kilogram of current weight; mcg: Micrograms; mg: Milligrams; NA: Not available; RDA: Recommended Dietary Allowances; SD: Standard deviation; SSSF: Subscapular skinfold; UL: Tolerable Upper Intake Level; EER: Total mean Estimated Energy Requirement; TSF: Tricipital skinfold; W/A: Weight for age; W/H: Weight for height; WHO: World Health Organization.

INTRODUCTION

Food allergy is considered a public health problem [1,2], and "a disease resulting from an anomalous immune response, which occurs after intake of and/or contact with certain food(s)" [1]. Cow's milk is one of the commonest foods to cause allergies in infants and young children [3]. According to the World Allergy Organization [4], the prevalence of allergy to cow's milk proteins (CMPA) in childhood ranges from 1.9% to 4.9%.

The treatment is basically of dietary nature [5], and involves the total elimination of cow milk and dairy products, with nutritionally adequate substitution [6]. The cow's milk protein (CMP), elimination diet usually occurs in the first year of life [7]. In breastfed children, it is recommended that this is continued [5,8,9], and that the mother follows a diet that eliminates cow's milk and dairy products [5,8,10]. For non-breastfed children, a substitute infant formula [8-10], without intact cow's milk proteins is recommended; this includes extensively hydrolyzed protein formulas, free amino acids formulas, or isolated soy protein formulas [5].

Nutritional deficiencies can occur when a food group is avoided during childhood, especially when involving cow's milk and dairy products [7].Therefore, elimination diets can impair nutrient intake [9], and the consequences can have a lasting impact on young children [11]. CMPA is a condition that requires attention for potential growth disorders [11].

There are few studies which, in addition to nutritional status, aimed at assessing nutrient intake in infants and children on a CMP-elimination diet, without eliminating other allergens from their diet [12-16]. Many studies include the elimination of other foods besides CMP from the diet, thus making reliable conclusions difficult. Furthermore, in Brazil, only the study by Medeiros et al. [17], and Boaventura et al. [18], that were designed for this purpose. Medeiros et al. [17], concluded that further studies are needed "in order to provide more information, which would allow greater reliability in the dietary orientation of CMPA-patients on an elimination diet". Therefore, the objective of the present study is to evaluate the dietary intake and the anthropometric profile of infants on a CMP-elimination diet compared to infants on a free diet.

MATERIALS AND METHODS

Prospective cross-sectional study, carried out between May 2018 and January 2019 in the pediatric gastroenterology and childcare/pediatric outpatient clinics of a pediatric hospital, which compared two groups of infants: one on a diet eliminating cow's milk proteins (CMP), and the other on a free diet.

Children aged 6 to 24 months were included. The infants in the CMP-elimination diet group were selected consecutively by referral after medical attendance at the pediatric gastroenterology outpatient clinics. During the follow-up consultation, they had been on an elimination diet for at least one month and their diet did not eliminate any other allergens. Elimination occurred after medical diagnosis of CMPA based on clinical history and symptoms remission after the elimination diet. The group on a free diet was composed of infants who did not restrict any kind of food. The inclusion in the study was by medical referral after consultation at the pediatric/childcare outpatient clinics.

Data collection was performed by a nutritionist (LDN), only. The anthropometric assessment included weight, length, head circumference (HC), arm circumference (AC), tricipital skinfold (TSF), and subscapular skinfold (SSSF). The measurements were taken according to the technical measurement recommendations. The indices assessed were weight for age (W/A), height for age (H/A), and weight for height (W/H). The infants were ranked by using the growth curves of the World Health Organization (WHO) 2006, according to the cutoff points for z-score proposed by WHO 2006 [19], using the WHO Anthro software version 3.2.2 for children up to five years of age. The ranking of HC, AC, TSF and SSSF measurements was performed using curves proposed by WHO 2007 [20]. Children born preterm (<37 weeks of birth), were classified according to the corrected age.

The dietary intake was assessed by two 24-hour food recalls, the first of which in a face-to-face interview and the other by telephone call the following day. The calculation of food surveys was performed using the Dietwin® software, version 30.90, and the results were expressed in energy, carbohydrates, proteins, lipids, fibers, vitamins and minerals, with the average of the two recalls having been considered in the analysis. The analysis was performed only on the diet, not including nutrient supplementation. Nutrient intake was compared between the groups and with the daily intake recommendations proposed by the Dietary Reference Intakes (DRIs) [21]. The values of Adequate Intakes (AI) – and of the Recommended Dietary Allowances (RDA) when the former are unavailable – were used, since the values of Estimated Average Requirements (EAR) are unavailable for most nutrients in the age group of 6-12 months. It was also compared with Tolerable Upper Intake Level (UL).

A general questionnaire was applied, addressing issues such as gender, age, skin color/race, education, socioeconomic conditions as classified by the Brazil Economic Classification Criterion - CCEB (ABEP) [22], first signs and symptoms presented (group on a CMP-elimination diet), nutritional formula and/or milk being currently used, occurrence of breastfeeding, weight, length and gestational age at birth.

Infants who were suspected or diagnosed with other acute or chronic diseases that led or not to nutritional treatment which eliminated some types of foods from the diet, breastfeeding infants, infants submitted to feeding routes other than oral feeding, and infants whose parents/guardians refused to participate or who were unable to complete the entire study protocol, were excluded. A pilot project with nine patients was carried out to test the proposed methodology and these infants were not included in the final sample.

The sample size was calculated based on the study by Medeiros et al. [17], including 54% of patients on a diet free from cow's milk and dairy products and with an energy intake lower than the DRIs and 17% in the control group. The G. Power version 3.1.9.2 software was used, with an alpha of 0.05 and a power of 80%, which resulted in a total of 38 patients in each group.

Statistical analyses were performed using IBM's SPSS version 22.0 software. Quantitative variables were described by means and standard deviations. Median and interquartile range were used for violating the Gaussian assumptions. Categorical variables were described by counts and percentages. The comparison of means was performed by Student's t-test and, in the asymmetry situation, the Mann-Whitney U test was used. Fisher's exact test was used for proportions. When comparing the components of the dietary analysis between the groups, an adjustment for age was performed in an analysis of covariance model (ANCOVA). For asymmetric variables, a logarithmic transformation was performed before ANCOVA. The level of significance was 5% ($p<0.05$).

Parents and/or guardians agreed to participate in the study by signing a term of free and informed consent. The study was approved by the Ethics and Research Committee under number 2.620.592.

RESULTS

Ninety infants were included in the study, of which 43 were in the CMP-elimination diet group and 47 in the free diet group. The sample's characteristics are shown in Table 1.

The average onset of signs and symptoms that led to the medical consultation and the indication by the attending physician to go on a CMP-elimination diet was 1.7 ± 1.98 months (Table 2).

Table 1: Characterization of infants of the cow's milk protein elimination diet and free diet groups.			
Variables	**Total (n=90)**	**Group on free diet (n=47)**	**Group on CMP-elimination diet (n=43)**
Age (months) – mean and ± SD	12.66 ± 4.97	13.87 ± 5.14*	11.33 ± 4.47*
Gender – n(%)			
Male	43 (47.8)	21 (44.7)	22 (51.2)
Female	47 (52.2)	26 (55.3)	21 (48.8)
Skin color/race - n (%)			
Black	5 (5.6)	4 (8.5)	1 (2.3)
Caucasian	77 (85.6)	38 (80.9)	39 (90.7)
Mixed race	8 (8.9)	5 (10.6)	3 (7.0)
Education of parents/guardians - n (%)			
Up to junior high	1 (1.1)	0 (0.0)	1 (2.3)
Up to high school	37 (41.1)	21 (44.7)	16 (37.2)
College or above	52 (57.8)	26 (55.3)	26 (60.5)
Economic Ranking (CCEB) – n (%)			
A, B1, B2	63 (70)	31 (66.0)	32 (74.4)
C1, C2, D, and E	27 (30)	16 (34.0)	11 (25.6)
GA at birth – mean and ± SD	38.58 ± 1.67	38.79 ± 1.57	38.35 ± 1.76
Birth weight – mean and ± SD	3188.69 ± 607.32	3222.15 ± 592.12	3152.12 ± 628.45
Birth length – mean and ± SD	48.04 ± 2.83	48.00 ± 2.66	48.09 ± 3.05
Breast feeding – n (%)	87 (96.7)	45 (95.7)	42 (97.7)
EBF time (days) - median and interquartile range	60 (0-150)	90 (7.5-150)	30 (0-135)
BF time (days) - median and interquartile range	157.5 (52.5-240)	150 (60-270)	180 (30-210)

SD: standard deviation; CMP: cow's milk proteins; GA: gestational age; CCEB: Brazilian Criteria of Economic Classification; EBF: exclusive breastfeeding; BF: breastfeeding
*Statistically significant difference between groups (p=0.014)

Table 2: Signs and symptoms reported by parents leading to cow's milk protein elimination diet.	
Signs and symptoms - n (%)	**n=43**
Vomiting, regurgitation and/or reflux	31 (72.1)
Excessive crying, irritability and/or agitation	25 (58.1)
Blood and/or mucous in stool	20 (46.5)
Abdominal pain and/or cramps	17 (39.5)
Liquid stools/diarrhea	16 (37.2)
Abdominal distension and/or flatulence	11 (25.6)
Dermatitis and/or eczema	9 (20.9)
Restless sleep and/or insomnia	4 (9.3)
Diaper rash	4 (9.3)
Food aversion and/or lack of appetite	3 (7.0)
Low weight gain	3 (7.0)
Choking, difficult swallowing and/or coughing	2 (4.7)
Hives	1 (2.3)
Blood vomiting	1 (2.3)
Number of associated signs and symptoms - n (%)	n=43
Four	13 (30.2)
Three	12 (27.9)
Five	7 (16.3)
Two	7 (16.3)
One	3 (7.0)
Seven	1 (2.3)

A statistically significant difference was found in the H/A index between the two groups. No differences were found for the W/H and W/A indices, as well as in the z scores for HC, AC, TSF, and SSSF (Table 3).

The CMP-elimination diet group had been on a treatment formula for 7.1 ± 4.6 months (n=41). 55.81% (n=24), of the infants used an extensively hydrolyzed formula, 32.56% (n=14), an amino acid formula, and 11.63% (n=5), a soy-based formula. The average amount of formula consumed by each infant was 600.87 ± 291.25 mL/day (n=41). In the free diet group, 36.17% (n=17), consumed cow's milk, 31.91% (n=15), starting and/or follow-up formula, 25.53% growing-up milk (n=12), 4.25% (n=2), cow's milk and growing-up milk, and 2.12% (n=1), lactose-free formula, with an average intake of 629.35 ± 325.86 mL/day (n=47). There were no differences regarding the average milk and/or formula intake between groups.

In view of the age difference between the groups, the analyses of dietary intake were adjusted for age in order to age not to influence the results. No differences were found between groups in terms of mean energy intake and mean macronutrient intake. Regarding micronutrients, differences were found in the mean intake of vitamins B1, B2, B5, B12, D, and K and of minerals calcium, phosphorus, and zinc (Table 4).

DISCUSSION

In this study, a significant difference was found in the H/A index, showing that the group on CMP-elimination diet had shorter height compared to the group on free diet. This result is similar to those reported in the literature. According to Meyer [11], food allergy seems to have a negative impact on H/A. Boaventura et al. [18], found lower parameters for H/A in children with IgE-mediated CMPA compared to controls. Tuokkola et al. [15], found a lower SD (0.2 and 0.3), in children's height during their first year on a CM-elimination diet, suggesting that they "grew slightly slower than the controls". Meyer et al. [23], found a higher rate of short height to age (11.5%), compared to tall height to age (5.5%), in children with food allergies (IgE-mediated and/or non-IgE mediated), with CM being the most common allergen. Canani et al. [16], concluded that CMPA "is an atrisk condition for body growth", as they found differences in z scores for height and weight at different times of follow-up among infants on hypoallergenic formulas and on a non-restricted diet. Despite the difference found in this study, most individuals are ranked as having an appropriate height for their age.

Studies carried out with children with suspected CMPA already showed nutritional deficits before starting treatment.

Table 3: Anthropometric assessment of infants of the cow's milk protein elimination diet and free diet groups.

Variables	Total (n=90)	Group on free diet (n=47)	Group on CMP-elimination diet (n=43)	p
Current weight (kg) - mean and ± SD	9.77 ± 1.83	10.21 ± 1.76	9.29 ± 1.79	
Length (cm) - mean and ± SD	75.50 ± 6.57	77.57 ± 6.94	73.23 ± 5.35	
HC (cm) - mean and ± SD	46.67 ±3.30	46.97 ± 1.86	46.33 ± 4.38	
AC (cm) - mean and ± SD	15.94 ±1.64	16.00 ±1.63	15.87 ±1.67	
TSF (mm) - mean and ± SD	9.52 ± 2.02	9.65 ± 2.12	9.38 ± 1.92	
SSSF (mm) - mean and ± SD	6.71 ± 1.44	6.55 ± 1.53	6.88 ± 1.34	
W/H (z score) - mean and ± SD	0.34 ± 1.14	0.37 ±1.14	0.31 ±1.17	0.805
Eutrophy (-2 ≥ z score ≤ +1)	68 (75.6)	36 (76.6)	32 (74.4)	
Risk for overweight (+1> z score <+2)	16 (17.8)	8 (17.0)	8 (18.6)	
Overweight (+2> z score ≤ +3)	5 (5.6)	2 (4.3)	3 (7.0)	
Obesity (z score > +3)	1 (1.1)	1 (2.1)	0 (0)	
W/A (z score) - mean and ± SD	0.20 ±1.19	0.36 ± 1.10	0.03 ±1.26	0.179
Low weight (-3 ≥ z score <-2)	4 (4.4)	2 (4.3)	2 (4.7)	
Adequate weight (-2 ≥ z score ≤ +2)	81 (90.0)	42 (89.4)	39 (90.7)	
Increased weight (z score> +2)	5 (5.6)	3 (6.4)	2 (4.7)	
H/A (z score) – mean and ± SD	-0.05 ± 1.22	0.22 ± 1.24	-0.35 ± 1.12	0.026
Very short height (z score < -3)	1 (1.1)	1 (2.1)	0 (0)	
Short height (-3 ≥ z score < -2)	6 (6.7)	3 (6.4)	3 (7.0)	
Adequate height (z score ≥ -2)	83 (92.2)	43 (91.5)	40 (93.0)	
HC (z score) – mean and ± SD		0.95 ± 1.11	0.55 ± 1.38	0.131
AC (z score) – mean and ± SD	1.16 ±1.29	1.14 ± 1.33	1.17 ± 1.25	0.906
TSF (z score) – mean and ± SD	0.63 ± 1.08	0.74 ± 1.14	0.51 ± 1.01	0.318
SSSF (z score) – mean and ± SD	-0.01 ± 1.13	-0.11 ±1.24	0.10 ± 1.00	0.380

SD: standard deviation; HC: head circumference; AC: arm circumference; TSF: tricipital skin fold; SSSF: subscapular skinfold; W/H: weight for height; W/A: weight for age; H/A: height for age

Table 4: Evaluation of dietary energy, macro and micronutrient intake of infants of the cow's milk protein elimination diet and free diet groups.

Energy, macro and micronutrients - mean (95% CI)	Group on free diet (n=47)	Group on CMP-elimination diet (n=41)[1]	p	DRIs[2]
Energy				
kcal	1027.96[a] (944.21-1109.71)	1047.65[a] (958.73-1136.56)	0.742	794.11[3]
kcal/kg	104.91[a] (95.19-114.63)	107.422[a] (97.11-117.73)	0.731	81.10[4]
Carbohydrates				
grams	129.87[a] (118.46-141.29)	134.82[a] (122.55-147.09)	0.569	95 and 130
%	50.91[a] (48.94-52.88)	51.632[a] (49.52-53.75)	0.630	NA and 45-65
g/kg	13.27[a] (11.93-14.61)	13.83[a] (12.42-15.25)	0.575	-
Proteins				
grams	44.48[a] (39.73-49.23)	41.51[a] (36.41-46.62)	0.411	11 and 13
%	16.84[a] (15.53-18.14)	15.61[a] (14.21-17.01)	0.217	NA and 5-20
g/kg	4.46[a] (3.93-4.99)	4.24[a] (3.68-4.80)	0.580	-
Lipids				
grams	36.70[a] (32.81-40.58)	38.09[a] (33.92-42.27)	0.637	30 and ND
%	32.30[a] (30.59-34.02)	32.77[a] (30.93-34.61)	0.721	NA and 30-40
g/kg	3.79[a] (3.36-4.21)	3.91[a] (3.46-4.36)	0.697	-
Fiber (g)	10.98[ab] (9.24 – 13.05)	9.40[ab] (7.81-11,31)	0.236	NA and 19
Vitamin B1 (mg)[5]	0.99[a] (0.86-1.13)	0.75[a] (0.60-0.89)	0.020	0.3 and 0.5
Vitamin B2 (mg)[5]	1.45[a] (1.31-1.60)	0.94[a] (0.79-1.10)	0.000	0.4 and 0.5
Vitamin B3 (mg)[5]	12.41[a] (10.82-14.01)	10.10[a] (8.39-11.82)	0.059	4 and 6
Vitamin B5 (mg)[5]	4.58[a] (3.97-5.19)	3.32[a] (2.66-3.97)	0.007	1.8 and 2
Vitamin B6 (mg)[5]	0.77[ab] (0.68-0.87)	0.75[ab] (0.66-0.86)	0.814	0.3 and 0.5
Vitamin B8 (mcg)[5]	49.65[ab] (39.53-62.36)	41.02[ab] (32.10-52.40)	0.271	6 and 8
Vitamin B9 (mcg)[5]	157.91[ab] (131.50-189.61)	139.35[ab] (114.43-169.52)	0.370	80 and 150
Vitamin B12 (mcg)[5]	3.29[a] (2.80-3.79)	2.44[a] (1.91-2.97)	0.025	0.5 and 0.9
Vitamin A, retinol (mcg)[5]	565.10[ab] (478.19-668.47)	465.22[ab] (413.64-592.88)	0.299	500 and 300
Vitamin C (mg)[5]	110.61[ab] (93.13-131.37)	105.42[ab] (87.71-126.85)	0.715	50 and 15
Vitamin D, calciferol (mcg)[5]	11.32[a] (9.86-12.79)	8.22[a] (6.64-9.79)	0.006	10 and 15
Vitamin E, alpha-tocopherol (mg)[5]	10.83[a] (8.90-12.75)	12.25[a] (10.18-14.32)	0.331	5 and 6
Vitamin K (mcg)[5]	15.33[ab] (9.99-23.52)	36.45[ab] (23.03-57.74)	0.009	2.5 and 30
Calcium (mg)[5]	857.67[a] (763.51-951.83)	470.97[a] (369.80-572.15)	0.000	260 and 700
Iron (mg)[5]	10.94[a] (9.52-12.37)	8.88[a] (7.35-10.42)	0.060	11 and 7
Phosphorus (mg)[5]	712.49[a] (648.93-776.06)	528.15[a] (459.85-596.45)	0.000	275 and 460
Selenium (mcg)[5]	14.67[ab] (11.08-19.43)	13.89[ab] (10.38-18.58)	0.790	20 and 20
Zinc (mg)[5]	9.76[a] (8.56-10.95)	7.75[a] (6.47-9.04)	0.030	3 and 3

a.Values adjusted for age; covariables are evaluated at the age=12.455
b. Asymmetric variables: logarithmic transformation performed prior to ANCOVA
1.2 incomplete recalls excluded
2. Dietary reference intakes(DRIs): according to Adequate Intakes(AI), and Recommended Dietary Allowances(RDA) when not available, for the age groups of 6-12 months and 1-3 years
3. Total mean Estimated Energy Requirement(EER) -reference values for energy intake- calculated for each infant
4. Total mean EER for kg of weight calculated for each infant
5. Not include supplementation
Kcal: kilocalories, energy measuring unit; kcal/kg: kilocalories per kilogram of weight; %: percentage each macronutrient in total energy; g/kg:grams of nutrient per kilogram of weight; mg: milligrams; mcg: micrograms; NA: not available

Vieira et al. [24], emphasize that "height-for-age deficit was the most predominant indicator of nutritional impairment in contrast with the expected predominance of weight-for-age deficit". They found high percentages of deficits in W/A, W/H and H/A (15.1%, 11.3% and 23.9%, respectively), and concluded that "failure to thrive or malnutrition may occur as a consequence of cow's milk allergy". Vera & Ramírez [25], observed that 15% of infants during their first medical consultation showed nutritional deficit (z score <2 SD), while 32.2% were at nutritional risk (z score between -1 and -2 SD), in W/A.

One study found that the majority of children with CMPA (67.8%), were eutrophic, but 12.9% were thin/markedly thin [26]. Medeiros et al. [17], found significantly lower rates (H/A, W/A and W/H), in Brazilian children on a diet free of CM and dairy products compared to the control group. Furthermore, they observed deficits of 11.5% for H/A, 7.7% for W/H and 23% for W/A (z score <-2.0), the latter being significant between groups. Dong et al. [12], when comparing with the control group, found significantly lower z scores in W/A and W/H and a lower percentage of body fat and fat mass in babies on CM-elimination diet at different times of follow-up, mainly in their first year of life. In contrast, in the present study, no differences were found in the z-score means in the other anthropometric parameters (W/H, W/A, HC, AC, TSF, and SSSF) between children on CMP-elimination diet and on free diet. Other studies have also found no differences between children on an CM-elimination diet and on an unrestricted diet [13,27].

In this study, no infant was classified as thin by the W/H index. However, 23.4% of infants on a free diet and 25.6% on a CMP-elimination diet were at risk for overweight, overweight and obesity. Studies are finding overweight in children with food allergies, showing a new look beyond malnutrition. According to Meyer et al. [23], "dietary interventions should aim to address both under and overnutrition", due to the finding of overweight (W/A), in 8.5% of children, where the majority restricted CM intake. A Brazilian study [26], found 15.2% and 4.1% of children with CMPA at risk for overweight and obesity (BMI/I), respectively.

The results of the studies are heterogeneous and many include children eliminating more than one type of food from their diet. In this study, we included children on a CMP-elimination diet only so as to keep the sample as uniform as possible. Moreover, this study used those reference standards considered the most appropriate for assessing nutritional status [11].

A significant difference was found in the intake of vitamins B1, B2, B5, B12, D, and K and minerals calcium, phosphorus and zinc between the groups. Despite the differences found, showing that the intake of these nutrients is higher in the group on a free diet, except for vitamin K, the average intake of most of these nutrients equaled or was higher than the daily intake recommendations defined in the DRIs. However, vitamin D intake is below recommended levels, and the group on CMP-elimination diet had a lower average intake in both recommendations according to age group. Regarding minerals, there is an adequate or higher average intake of phosphorus and zinc in both groups. The intake of zinc even exceeded the upper allowable intake level. However, the average calcium intake was lower than recommended only in the CMP elimination group in one of the recommendations. Thus, calcium and vitamin D intake, a frequent concern in children who follow a CMP-elimination diet, deserves greater attention and corroborates the findings of other studies.

The discussion on the nutritional intake of children on a CMP-elimination diet started from such studies as Paganus et al. [28], who found low dietary intake of calcium, zinc and vitamin B2, comparable energy intake, and high protein intake among children (2 years old), on CMP-elimination diet compared to unrestricted diet. According to Tuokkola et al. [15], "children on elimination diets received enough energy and protein, but their intake of calcium and vitamins D and B2, together with other micronutrients, need to be monitored". Another study [29], found a lower calcium intake and a tendency to lower vitamin D and energy intake in children undergoing CMPA treatment, concluding with "The need for nutritional supervision, calcium and vitamin D supplementation (where appropriate), and close monitoring of growth for milk-allergic children".

The higher calcium intake in babies on a free diet can be explained by the prevalence of CM intake (36.17%), because in addition to the intake of CM and/or infant formulas, children also consume dairy products (yogurt, cheese, cookies, etc.), since there were no differences in the average amount of milk/formula intake between the groups. Moreover, most industrialized CM-based foods are fortified with vitamins and minerals.

The Brazilian study that investigated nutrients intake in children on a CM and dairy products elimination diet [17], found a lower intake of calcium and phosphorus. Another Brazilian study also found a lower calcium intake in children with IgE-mediated CMPA [18]. Medeiros et al. [17], emphasize "the need to monitor the food intake and nutritional status of children on a diet free of CM and dairy products to avoid nutrients deficiency during the elimination diet". Unlike Medeiros et al. [17], who found a lower intake of energy, proteins and lipids, in the present study we identified an energy and macronutrient intake comparable between the groups and above recommendations (DRIs). It is important to highlight the high protein intake observed, which was also reported by Tuokkola et al. [15], in children on an CM-free diet.

Regarding dietary treatment, infants on an elimination diet had consumed a hypoallergenic formula for an average of 7.1 ± 4.6 months, which means an adequate time to assess nutritional status. Most infants were consuming an extensively hydrolyzed formula (55.81%), meeting the recommendation to use these formulas as first option for non-breastfed infants [5,8,10].

The most reported signs and symptoms were vomiting, regurgitation and/or reflux (72.1%), corroborating the study by Vieira et al. [24], who also found vomiting/regurgitation (53.5%), as the main symptom in children under 24 months with suspected CMPA who consulted with pediatric gastroenterologists across Brazil. Another study in a gastroenterology clinic also found vomiting/regurgitation (50%), as the main symptom (3.0 ± 0.4 months [25]. In studies conducted in clinics of pediatric medicine, 98% [30], and 81.8% [26], of babies around nine months showed gastrointestinal symptoms. As reported [6,8], gastrointestinal symptoms of CMPA are mostly variable and nonspecific.

It should be emphasized that, in order to minimize potential differences between the groups dietary intake analyses were adjusted for age. Furthermore, we included children in a limited age group, prioritizing infants in a similar period of development and who had not been breastfeed so as to make the sample as uniform as possible. As a limitation, in studies involving food intake, the methods of assessing intake may present information and memory bias, since they are intake estimating methods.

CONCLUSION

In conclusion, infants on a CMP-elimination diet were shorter compared to infants on a free diet. However, the mean values are within the normal range. A lower mean intake of vitamins B1, B2, B5, B12, and D and of minerals calcium, phosphorus, and zinc was observed in the CMP-elimination group. In spite of this, most of these nutrients equaled or were higher than the daily intake recommendations stipulated by the DRIs, except for calcium and vitamin D, which were below in at least one of the recommendations. Therefore, greater attention should be paid to these two nutrients. This study signalizes the need for nutritional monitoring of these children, emphasizing the importance of the nutritionist [6,11,23], together with the physician, in nutritional management.

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