Measuring and Evaluating the Adherence to and Effectiveness of Formula Milk Use in Healthy Infants in Türkiye

Türkiye'deki Sağlıklı Bebeklerde Formül Süt Kullanımına Uyum ve Etkinliğin Ölçülmesi ve Değerlendirilmesi

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ABSTRACT

Objective: Formula milk aims to mimic breast milk or can serve as a complementary diet, thus reducing the risk of developing nutritional deficiencies. In this study, we evaluated the factors affecting compliance with the use of prebiotic formula milk with a galacto-oligosaccharides/fructo-oligosaccharides ratio of 9:1.

Methods: The study included 63 healthy girls and 58 healthy boys who consumed formula milk for 4-12 months. A brief survey was conducted among the parents of these children at the end of the first and third months. Height, weight for age, and weight for height z-scores were compared between the first and follow-up visits. Perceived symptoms, frequency of infections, complementary food intake, and frequency of stool movements were also discussed.

Results: The anthropometrics significantly increased over the three months. Intolerability negatively affected compliance with formula use (p<0.001). The infection rate decreased in 13.3% of the infants, and 65.3% experienced no change in complementary food intake. The parent's opinion about the benefits of formula milk, the parent's forgetfulness, and the thought that formula milk reduces the intake of complementary foods were the factors that negatively affected compliance with formula milk use. The mothers of infants who were introduced to a complementary diet <17 weeks were 2.4 years younger (p=0.006).

Conclusion: Parents should be educated regarding the benefits of formula milk. Formula milk used led to an anthropometrical z-score increase and a significant decrease in the rate of infection, which should be emphasized to the parents to maximize compliance.

Keywords: Formula milk, adherence, nutritional deficiency, growth

ÖZ

Amaç: Formül süt, anne sütünü taklit etmeyi amaçlar veya tamamlayıcı bir diyet olarak hizmet edebilir, bu nedenle beslenme bozukluğunun gelişme riskini azaltır. Bu çalışmada, galakto-oligosakkaritler/frukto-oligosakkaritler oranı 9:1 olan prebiyotik formül süt kullanımıyla ilgili uyumu etkileyen faktörleri değerlendirmeyi amaçladık.

Yöntem: Çalışma, 4-12 ay boyunca formül süt tüketen 63 sağlıklı kız ve 58 sağlıklı erkek çocuğu içeriyordu. Bu çocukların ebeveynleri arasında ilk ve üçüncü ayın sonunda kısa bir anket yapıldı. İlk ve takip ziyaretleri arasında boy, kilo yaşa göre ve boy kilo için z puanları karşılaştırıldı. Semptomlar, enfeksiyon sıklığı, tamamlayıcı gıda alımı ve dışkılama sıklığı da tartışıldı.

Bulgular: Antropometrik ölçümler üç ay boyunca önemli ölçüde arttı. Tahammülsüzlük, formül kullanımına uyumu olumsuz etkiledi (p<0,001). Bebeklerin %13,3'ünde enfeksiyon oranı azaldı ve %65,3'ünde tamamlayıcı gıda alımında değişiklik olmadı. Ebeveynlerin formül sütün faydaları hakkındaki düşünceleri, ebeveynlerin unutkanlığı ve formül sütün tamamlayıcı gıda alımını azalttığı düşüncesi, formül süt kullanımına uyumu olumsuz etkileyen faktörlerdi. Tamamlayıcı bir diyete <17 hafta içinde başlatılan bebeklerin anneleri 2,4 yaş daha gençti (p=0,006).

Sonuç: Ebeveynler, formül sütün faydaları hakkında eğitilmelidir. Formül süt kullanımı, antropometrik z puanlarında bir artışa ve enfeksiyon oranında önemli bir azalmaya yol açmıştır, bu nedenle ebeveynlere uyumu maksimuma çıkarmak için bu durum vurgulanmalıdır.

Anahtar Kelimeler: Formül süt, bağlılık, beslenme yetersizliği, büyüme

INTRODUCTION

Nutritional deficiency and growth retardation at an early age increase the risk of cardiovascular disease, obesity, insulin resistance, and metabolic syndrome later in life.[1] In addition, mortality due to any cause is higher than normal in those who experienced growth retardation in infancy.[2] Therefore, regular follow-ups of infants, close monitoring of their nutritional status, and full compliance with the treatments are important factors for life-long health.[3,4]

Formula milk is designed to mimic the nutritional content of breastmilk to provide an effective alternative.[5] Additionally, first infant formula (growing formula) milk provides the energy and proteins that infants aged between 0 and 1 years of age need for healthy growth and development. It also contains some vitamins and minerals that breastfed infants should take as supplements. Along with the required micronutrients, formula milk contains prebiotics, galacto-oligosaccharides (GOS), and fructo-oligosaccharides (FOS). These oligosaccharides enhance the microbiota of infants (*Bifidobacterium*).[6] Moreover, a GOS/FOS ratio 9:1 is the conventionally accepted ratio in breastmilk.[7] Standard formula is suitable for healthy infants and an appropriate alternative to breastmilk for infants who cannot be breastfed or for whom breastmilk alone is not sufficient for optimal growth. Determining the degree of compliance with formula milk use and the factors associated with this compliance are important for the development of a successful feeding strategy.[8]

Several studies have underlined the importance of pediatric malnutrition, but fewer studies have focused on the nutrition of healthy children. Thus, the objective of this study was to evaluate compliance with the use of prebiotic grow-up formula milk with a GOS/FOS ratio of 9:1 to investigate the relationship between factors related to the infant, the product, and the family that may influence compliance with formula use and to compare anthropometric measurements with or without compliance with formula use. In addition, the frequencies of bowel movements, infections, and complementary food consumption were assessed.

METHODS

The primary endpoint of the study was the percentage of adherence to the use of formula milk. In most studies in the literature, researchers accepted 0.05 as the threshold of significance, which converts to a standard value of 1.96. However, studies focusing on the use of growing-up formula milk are limited, with none covering İstanbul. The standard deviation of formula milk use adherence was calculated as 10% based on retrospective eligibility information and approved by each physician. Aiming at a 2% precision, the sample size was calculated as requiring at least 96 patients to cover the mean adherence rate. This was a multicenter, prospective, observational study involving nine different Pediatric Clinics in Bahçeşehir University.

A total of 121 infants (63 girls and 58 boys) aged between 0 and 1 years and partially or exclusively using growing-up formula milk for 4-12 months were included in the study. The vast majority of the included participants were enrolled during summer (June 2021-September 2021). The other inclusion criteria were that the infants' legal guardians provided informed consent for the study, and the participants continued to be cared for as healthy infants by the center where they participated in the study. Dropouts were excluded, and data analysis was performed on participants who were fully compliant with the protocol. Infants who had lactose intolerance and/or cow-milk protein allergy, who did not attend the study visits, whose parents did not complete the study questionnaires, and who were diagnosed with a medical condition requiring special formula feeding and/or treatment were excluded from the study.

Our study participants excluded any mother who was contradicted for breastfeeding due to infection or a disease. However, in others, breastfeeding was partially

or fully limited because of previous breast surgery, insufficient glandular tissue, insufficient feeding, or endocrine problems, which were the reasons why formula was chosen as a substitute for breastmilk. Demographic data of the infant and mother were collected. At the end of the first and third months of using prebiotic formula milk with a GOS/FOS ratio of 9:1, a brief survey, specifically developed for this study, was administered to the parents regarding compliance with the recommended dosage of formula milk. We chose our study formula, and our protocol did not specify a transition period from the previously used formula. Additionally, we chose prebiotic formula milk with a GOS/FOS ratio of 9:1 because this specific ratio is conventionally used for healthy infants, when necessary, in Bahçeşehir University. The switch or start of the study formula was performed according to our discretion. The recommended daily amount of milk (milliliters) was calculated by the physician according to the amount of non-adherence to breastfeeding in infants between 0 and 6 months of age exclusively consuming breastmilk in compliance with UNICEF and World Health Organization recommendations. For those who were consuming a complementary diet along with breastmilk, the physician considered the amounts consumed via the complementary diet and breastfeeding. Only two patients started exclusively on formula milk because they lacked both breast milk and a complementary diet in their feeding regime. However, this number was too small to separately analyze the exclusive formula milk users using statistical methods. The percentage difference between the recommended daily dose of formula milk (milliliters) and the amount consumed by the infant was recorded after each visit as the rate of compliance with the formula milk used. At the first visit, when the infants started on formula milk and in the first and third months of formula milk use, their weight (grams) and height (centimeters) were measured, and their height z-score, weight for age z-score, and weight for height z-score values were calculated using Pediatric Endocrinology and the Diabetes Association's Cedd solution auxology calculation system.[9] In addition to the anthropometric data collected at all subsequent visits, the frequencies of infection, off-formula food intake, and defecation were recorded, and the changes in these data were as-sessed. The anthropometric z-score change was also evaluated for infants with <80% formula milk use adherence. The presence of perceived symptoms caused by formula milk, their relationship with anthropometric data, and compatibility were analyzed. Finally, a questionnaire on the suspected factors affecting compliance with formula milk use was administered to the parents, and the responses were compared with the rates of compliance with formula milk use recommendations. The factors affecting formula milk adherence were relatively free from the covariant effects of breast milk and com-plementary diet as the dose was measured by eliminating formula milk diets by a physician.

This study was approved by the Bahçeşehir University of Local Ethics Committee on October 14, 2020 with session number 2020-13/04.

Statistical Analysis

Data were analyzed using IBM Statistical Package for the Social Sciences statistics for Windows v.20.0 (IBM Corp. USA). The Shapiro-Wilk test and histogram analysis were used to evaluate the normality of the data distribution. Data with $p \geq 0.05$ results in the normality test were accepted as having a parametric distribution after visual histogram analysis, and data with $p < 0.05$ results were accepted as having a non-parametric distribution after histogram analysis. No sample group had a histogram that was incompatible with the Shapiro-Wilk test. Chi-square and Fisher's exact tests were used to analyze binary categorical variables in groups with sample numbers ≥ 5 and < 5, respectively. Continuous variable data with no-parametric distribution were compared with data with two categorical variables using the Mann-Whitney U test, and data with more than two categorical variables were compared using the Kruskal-Wallis test. Pearson correlation (r) and Spearman's correlation (rs) were used to compare two continuous variables with parametric and non-parametric distribution. The significance of the correlation coefficient for both correlation tools was grouped as "zero" for 0-0.1, "weak" for 0.1-0.4, "moderate" for 0.4-0.7, and "strong" for 0.7-1.0. The statistical significance threshold was $p < 0.05$. The threshold of significance was $p < 0.05$ for Spearman and Pearson correlations.

RESULTS

Demographic and Anthropometric Data

The demographic and anthropometric data of the infants and parents who participated in the study are shown in Table 1. Of the participants, 63 (52.1%) were girls and 58 (47.9%) were boys. The mean rate of adherence to the recommended nutrition therapy at the end of the first and third months was calculated as 95.2±12.60 and 97.3±8.48, respectively. No effect of infant sex, age, mother's education, or family income on compliance with nutritional therapy was observed (p=0.312, p=0.840, p=0.974, and p=0.308, respectively). Mothers of infants who were introduced to a complementary diet <17 weeks (n=26, 35.1% of infants <17 week of age) were 2.4 years younger (p=0.006). No difference in an early start on the complementary diet was found between mothers with or below high school

education versus mothers with university and above education (0.896).

The descriptive statistics and statistical analysis of the anthropometric growth of the infants for three months after starting nutritional support are listed in Table 2a, and a growth graph is depicted in Figure 1. The anthropometrical development data of infants with <80% adherence for 3 months are provided in Table 2b.

The weight-for-age and height-for-age z-scores of the infants participating in the study significantly increased, and the weight-for-height z-score improved from near zero on the date they started formula milk to a healthy level at the third month (p<0.001 for all). In addition, the same anthropometric measurements significantly increased between admission and the first month and between each visit (p<0.05 for all), except for the height z-score at admission versus the first month visit (p=0.099). Figure 1 shows the significant anthropometric changes between the first and second visits. We found a weak correlation between weight for height z-score at the third month and formula milk compliance (r=0.190, p=0.038). No correlations were found between height and age and weight and age (p=0.065 and p=0.287, respectively). No difference in any anthropometric z-score was observed in infants with <80% formula milk adherence (p>0.122 for all).

Perceived Symptoms

The distribution of perceived symptoms that appeared after the initiation of formula milk consumption is given in Table 3. Infants with tolerability exhibited significantly higher compliance than infants with intolerability (p=0.001).

Table 4 compares the frequency of bowel movements, infections, and the use of additional food before and after the initiation of formula milk. Of the infants with constipation, 75% had a decreased frequency of defecation, and 100% of infants with diarrhea had an increased frequency of defecation. No perceived symptoms were associated with formula milk use in 84.2%, 50.0%, and 32.4% of infants who showed a decrease, increase, and no change in infection

Table 1. Patient demographics and anthropometrics	
Sex, n (%)	
Boys	58 (47.9)
Girls	63 (52.1)
Mother's employment status, n (%)	
Employed	58 (47.9)
Unemployed	62 (51.2)
Dead	1 (0.8)
Family income status, n (%)	
High or middle	119 (98.4)
Low	2 (1.7)
Age, mean±SD (IQR), mo	4.0±2.37 (4.0)
Maternal age, mean±SD (IQR), y	31.9±4.12 (6.0)
CD starting age, mean±SD (IQR), mo	4.3±2.15 (4.0)
Maternal age of mothers introduced CD <17 weeks, mean±SD (IQR), y	30.4±4.27 (5.0)
Maternal age of mothers introduced CD 17≥ weeks, mean±SD (IQR), y	32.8±3.72 (5.0)
Amount of reported daily formula intake at the end of 1st month, mean±SD (IQR), mL	619.9±263.00 (400.0)
Formula-based treatment adherence rate at the end of 1st month, mean±SD (IQR), %	95.2±12.60 (0.0)
Amount of reported daily formula intake at the end of 3rd month, mean±SD (IQR), mL	687.7±292.89 (420.0)
Formula-based treatment adherence rate at the end of 3rd month, mean±SD (IQR), %	97.3±8.48 (0.0)
Height at first admission, mean±SD (IQR), cm	62.6±6.70 (11.0)
Weight at first admission, mean±SD (IQR), g	6291.5±1964.01 (2915.0)
Height at the end of 1st month, mean±SD (IQR), cm	65.1±6.19 (9.0)
Weight at the end of 1st month, mean±SD (IQR), g	7086.4±1753.72 (2417.5)
Height at the end of 3rd month, mean±SD (IQR), cm	69.4±5.54 (7.0)
Weight at the end of 3rd month, mean±SD (IQR), g	8251.9±1620.93 (1996.3)
SD: Standard deviation, IQR: Interquartile range, CD: Complementary diet, mo: Month, y: Year	

frequency, respectively. However, the subgroups were not too small for statistical analysis. Among the 27.3% of infants whose frequency of complementary food intake decreased, the most common perceived symptoms were constipation (50.0%) and bloating (66.7%).

Although no significant relationship was found between the number of complementary meals and formula milk use compliance (p=0.409), only 78.6% of infants taking four or more complementary meals showed a compliance

Figure 1. Mean anthropometrical scores of all infants over 3 months after starting nutritional support. A) Mean height for age z-score difference. B) Mean weight for age z-score. C) Mean weight for height z-score

of >90% with formula milk use recommendations. Additionally, >90% formula milk compliance was observed in 91.2%, 96.0%, and 100% infants having three, two, and zero complementary meals, respectively.

Questionnaire on Factors Affecting Compliance with Formula Milk Recommendations

Factors affecting formula milk compliance, questionnaire questions, and the distribution of responses are shown in Table 5.

The majority of the mothers of the infants (83.4%) reported that their infants liked the taste of formula milk, 14.0% were neutral, and 2.5% disliked it. The compliance of these subgroups with formula milk was calculated as 97.3%, 96.6%, and 79.3%, respectively. We found a significant positive correlation between compliance with formula milk use and the infant's liking of the taste of the formula (p=0.012). In addition, the rate of compliance observed in infants of parents who thought that formula milk was healthy was significantly higher than that in those who thought otherwise (p=0.003). The results for forgetfulness were the same, strongly correlating with non-adherence to formula use recommendations (p<0.001). The level of compliance of the parents who reported that the use of formula milk reduced the intake of complementary foods or mother milk was significantly lower than that of those who reported the opposite (p<0.001). Finally, compliance of parents who reported that the formula had a negative impact was significantly lower than that of parents who reported that they did not (p=0.005).

DISCUSSION

Insufficient nutrition in healthy infants may cause malnutrition. Starting a complementary diet earlier and the lack of consumption of breastmilk are the main causes of malnutrition and obesity in children.[10,11] Our results showed that younger mothers tended to start eating complementary food earlier than the suggested age. This demonstrates the indirect relationship between maternal age and responsibility, knowledge, and seriousness toward raising children, as found in several other studies.[12-14] However, no correlation was observed in the case of education, which was probably caused by the small number of participants in the current study, as the uneducated category (16 of 18 mothers) included mothers who were high school graduates, which prevented us from analyzing less-educated participants. The mean value of adherence to recommended nutritional support at both the first and third months in the healthy infants was significantly higher than the cutoff value of 70%[4,15] for non-adherence to nutritional support (95.2±12.60 and 97.3±8.48, respectively). We found that the anthropometric
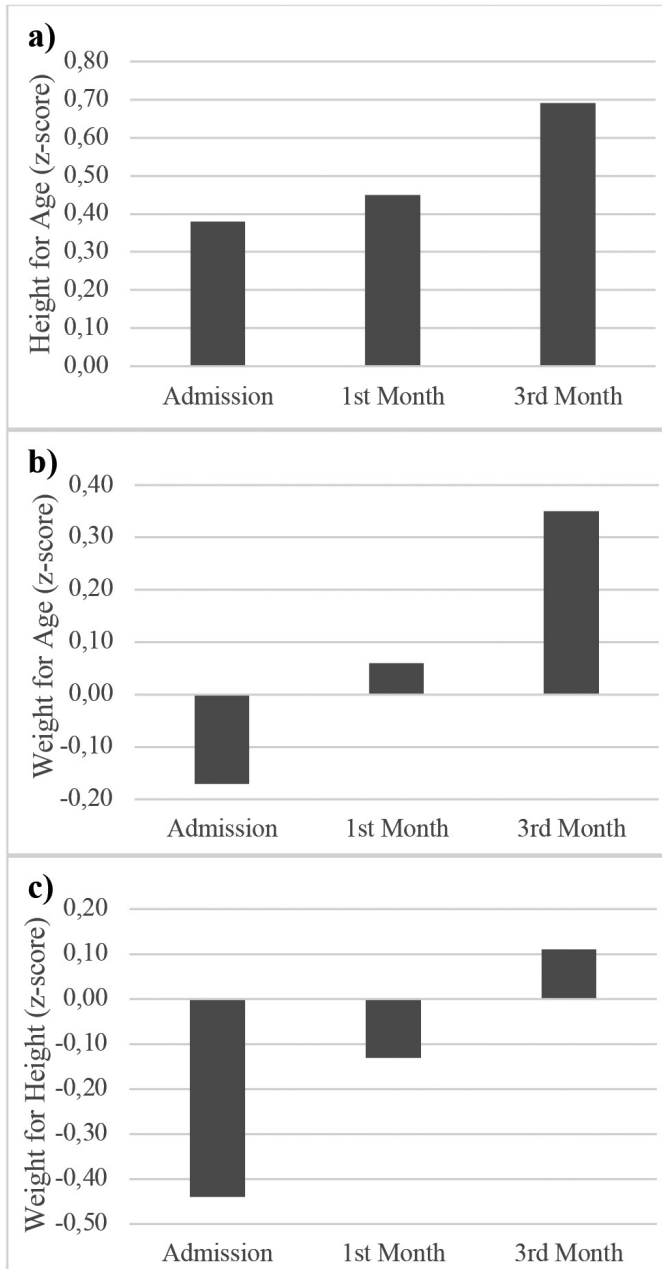
Table 2. Descriptive statistics and statistical analysis of the anthropometrical development of infants for 3 months after starting nutritional support

a. Anthropometrical development of infants for 3 months

	Mean±SD (IQR)	p value[†]	p value[††]
Height for age at admission	0.38±1.30 (1.54)		0.099*
Height for age at 1 month	0.45±1.25 (1.38)	<0.001	<0.001**
Height for age at 3 months	0.69±1.30 (1.50)		<0.001***
Weight for age at admission	-0.17±1.08 (1.10)		<0.001*
Weight for age at 1 month	0.06±1.03 (1.03)	<0.001	<0.001**
Weight for age at 3 months	0.35±1.02 (1.02)		<0.001***
Weight for height at admission	-0.44±1.20 (1.22)		<0.001*
Weight for height at 1 month	-0.13±1.07 (1.07)	<0.001	<0.001**
Weight for height at 3 months	0.11±1.06 (1.09)		<0.001***

[†]Friedman's test, [††]Wilcoxon test, *admission versus 1st month, **1st month versus 3rd month, ***admission versus 3rd month.
SD: Standard deviation, IQR: Interquartile range

b. Anthropometrical development of infants with <80% adherence for 3 months

	Mean±SD (IQR)	p value[†]
Height for age at admission	-0.28±1.09 (1.35)	
Height for age at 1 month	-0.11±1.07 (1.59)	0.122
Height for age at 3 months	0.02±0.88 (1.30)	
Weight for age at admission	-0.61±1.04 (1.71)	
Weight for age at 1 month	-0.43±1.06 (1.59)	0.150
Weight for age at 3 months	-0.22±0.95 (0.95)	
Weight for height at admission	-0.46±0.96 (1.33)	
Weight for height at 1 month	-0.56±1.06 (1.18)	0.497
Weight for height at 3 months	-0.42±1.02 (1.13)	

[†]Friedman's test.
SD: Standard deviation, IQR: Interquartile range

Table 3. Distribution of perceived symptoms that appeared after the initiation of formula milk consumption and their relationship with adherence rate

Perceived symptoms[†]	n (%)	Adherence %	p value*
None	85 (70.2)	99.1	0.001
Total number of patients with perceived symptoms	36 (29.8)	93.1	
Constipation	21 (17.4)	95.4	
Bloating	15 (12.3)	90.4	
Abdominal pain	8 (7.5)	88.1	
Diarrhea	4 (1.7)	82.5	
Vomiting	2 (1.6)	100.0	
Fatigue	0	0	

*Mann-Whitney U test, [†]some patients have more than one perceived symptom

Table 4. Comparison of defecation, infection, and additional food usage frequencies before and after formula milk use

Frequency	Defecation, n (%)	Infection, n (%)	Additional food, n (%)
Decreased	46 (38.0)	16 (13.3)	22 (18.2)
Has not changed	45 (37.2)	92 (76.0)	79 (65.3)
Increased	30 (24.8)	13 (10.7)	20 (16.5)

Table 5. Questionnaire on factors affecting compliance with formula milk, distribution, and statistical analysis of the answer-based adherence rates at the third month

My infant loves the taste of formula milk	n (%)	Mean adherence rate, %±SD	p value*
1) I totally disagree	0 (0)	0	
2) I partially disagree	3 (2.5)	79.3±17.06	
3) Neutral	17 (14.0)	96.6±7.84	0.031
4) I partially agree	28 (23.1)	95.6±11.31	
5) I totally agree	73 (60.3)	98.9±3.11	
The formula is beneficial for my infant's health			
1) I totally disagree	1 (0.8)	100	
2) I partially disagree	7 (5.8)	90.0±8.97	
3) Neutral	17 (14.0)	90.0±13.21	0.015
4) I partially agree	51 (42.1)	99.3±3.66	
5) I totally agree	45 (37.2)	98.7±2.85	
I should persuade my infant to drink formula milk			
1) I totally disagree	26 (21.5)	98.6±3.29	
2) I partially disagree	31 (25.6)	93.6±13.66	
3) Neutral	19 (15.7)	97.1±7.59	0.081
4) I partially agree	31 (25.6)	98.8±3.42	
5) Totally agree	14 (11.6)	100	
I often forget to give my infant formula milk			
1) I totally disagree	103 (85.1)	98.9±3.60	
2) I partially disagree	15 (12.4)	89.4±18.25	
3) Neutral	2 (1.7)	78.3±16.55	< 0.001
4) I partially agree	1 (0.8)	100	
5) I totally agree	0 (0)	0	
The formula keeps the stomach full			
1) I totally disagree	1 (0.8)	98.9±3.67	
2) I partially disagree	0 (0)	100	
3) Neutral	8 (6.6)	100	0.577
4) I partially agree	62 (51.2)	98.0±5.90	
5) Totally agree	50 (41.3)	95.9±4.91	
The formula improves my infant's sleep patterns			
1) I totally disagree	2 (1.7)	100	
2) I partially disagree	4 (3.3)	90.4±8.22	
3) Neutral	19 (15.7)	98.2±6.07	0.899
4) I partially agree	55 (45.5)	98.0±5.14	
5) I totally agree	41 (33.9)	96.5±9.57	
The formula makes my infant tranquil			
1) I totally disagree	1 (0.8)	100	
2) I partially disagree	8 (6.6)	95.2±7.29	
3) Neutral	22 (18.2)	96.4±8.89	0.361
4) I partially agree	47 (38.8)	98.9±4.00	
5) I totally agree	43 (35.5)	96.8±10.09	

Table 5. Continued			
My infant loves the taste of formula milk	**n (%)**	**Mean adherence rate, %±SD**	**p value***
The formula reduces my infant's intake of complementary foods or breastmilk			
1) I totally disagree	26 (21.5)	99.8±1.11	
2) I partially disagree	15 (12.4)	100	
3) Neutral	36 (29.8)	99.0±3.53	< 0.001
4) I partially agree	34 (28.1)	92.5±12.71	
5) I totally agree	10 (8.3)	97.1±5.39	
The formula often has side effects in my infant			
1) I totally disagree	67 (55.4)	99.2±2.54	
2) I partially disagree	22 (18.2)	96.1±7.03	
3) Neutral	6 (5.0)	100	0.010
4) I partially agree	20 (16.5)	90.1±12.78	
5) I totally agree	6 (5.0)	98.8±3.20	
*Kruskal-Wallis test. SD: Standard deviation			

z-score values of the infants who received formula milk to compensate for breastmilk diet non-adherence were significantly higher. However, the weight-for-height z-score approached the ideal z-score value after three months. The anthropometric z-score changes were insignificant in the case of <80% adherence, probably due to low sample number (n=10). However, the weight-for-height z-score means stabilized compared with those of the whole group, which seems to have resulted from the lower overall formula milk adherence. We could not analyze infants with <70% adherence due to the small sample number (n=4). A parallel study of anthropometric z-score changes in a separate cohort of healthy infants who did not use formula milk in addition to nutrients during the same follow-up period may further support the findings of our study.

As expected, the increase in the frequency of defecation was directly proportional to complaints of diarrhea; its decrease was directly proportional to complaints of constipation. Only 18.8% of parents of infants with decreased frequency of infection reported any perceived symptoms associated with formula milk use, whereas this rate was two-fold higher in infants with unchanged or increased frequency of infection (30.4% and 38.4%, respectively). This result could be explained by the increase in direct or indirect reactions to formula milk, which are directly related to increases in allergies and infections in infants with developing immune systems.[16-18] The decrease in supplementary food intake in infants with no perceived symptoms could be explained by 100% of the parents of infants belonging to this subgroup stating that formula milk kept them satiated.

The formula milk use adherence of infants who showed or showed any perceived symptoms was lower than that of infants without perceived symptoms. Similar to the findings of another study, in which constipation was the most frequent adverse effect, symptoms were eliminated by administering a magnesium-rich formula to the appropriate patients.[19] In addition, increased fluid intake and the inclusion of fiber-rich foods in the diet help reduce these effects.[19,20] The reason why the mean formula milk compliance of infants consuming four or more complementary meals per day was relatively low may have been due to satiety and the feeling of meal sufficiency, which reduce the perception of the need to use formula milk compared with infants consuming three, two, and zero complementary meals per day. However, a statistical analysis should be conducted with a larger cohort to determine the specific correlation.

The reason why compliance was higher in infants of parents who considered the product as healthy than in infants with parents who did not was possibly because parents who considered formula milk healthy were more careful about compliance. The significant positive difference in the compliance of infants whose formula milk consumption was not forgotten by their parents was an expected result. Negative responses to the questionnaire on the use and effects of the product were directly related to low compliance. Similarly, parents indicating that formula milk reduced the intake of ancillary nutrients may have led them to reduce formula milk use to below the required amount.

Despite the formula milk dose being determined according to the breastmilk and complementary diets, we lacked information about adherence to the reported complementary and breastmilk diets, which could

have affected the formula milk dosage, thus influencing the adherence to formula milk recommendations. We lacked the exact frequencies of the types of breastmilk insufficiency. Thus, we could not add that question to the survey, and we could not perform any related statistical analysis. Moreover, because this study focused on compliance with the recommended amount of formula milk and the factors affecting compliance, all infants participating in the study consumed formula milk. Therefore, the differences between the growth rates of infants who did not use formula milk as a control group and those who did were not considered in our study.

Study Limitations

Because this study focused on the amount of formula milk compliance and the factors affecting compliance, all infants participating in the study used formula milk. Therefore, the difference between the growth rates of babies who do not use formula milk and those who do is not considered in our study. Furthermore, because the foods that babies consume other than formula milk vary, it was not possible to perform a definitive analysis based only on formula milk or to create a control group that did not use formula milk but consumed the same byproducts.

CONCLUSION

After three months of formula milk use, a significant improvement was observed in the weight-for-height z-score and significant increases were observed in the height and weight-for-age z-scores of the infants. The weight-for-height z-score did not change for infants with <80% formula milk adherence. The percentage of perceived symptoms due to formula milk use was 29.8%, which negatively affected compliance with formula milk recommendations (p<0.001). The percentage of patients whose defecation frequency increased after formula milk use was 38.0%. The frequency of infection decreased in 13.3% of infants. Most infants (65.3%) experienced no change in supplementary food intake. Among the questions on the questionnaire about the factors affecting compliance with formula milk recommendations, the parent's opinion about the benefits of formula milk, the parent's forgetfulness, and the thought that formula milk reduces the intake of supplementary foods were the factors that negatively affected compliance with formula milk use. Although the most reliable and best known method is breast milk, the use of formulas in which breast milk is insufficient is helpful.

Ethics

Ethics Committee Approval: This study was approved by the Bahçeşehir University of Local Ethics Committee on October 14, 2020 with session number 2020-13/04.

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: İ.K., C.S., T.D.B., D.Ç., N.U., D.G., G.D., V.E., Concept: F.Ö., A.S., M.A.S., Design: F.Ö., A.S., M.A.S., Data Collection or Processing: İ.K., C.S., T.D.B., D.Ç., N.U., D.G., G.D., H.T., A.S., V.E., Analysis or Interpretation: F.Ö., H.T., D.Ç., A.S., M.A.S., Literature Search: F.Ö., A.S., M.A.S., Writing: F.Ö., A.S., M.A.S.

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