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ARTICLE

Maternal and pediatric nutrition

Relationship between age at giving fortified powdered cow's milk and cessation of breastfeeding on the nutritional status of a Chilean child cohort followed from birth to 3 years of age

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Abstract

Background/objectives To examine how much of the variation in weight-for-height (WHZ) *z*-scores were associated with age at which breastfeeding ceased and provision of fortified cow's milk (Leche Purita Fortificada, LPF) commenced in a cohort of children studied from birth to 3 years of age.

Subjects/methods Longitudinal data were obtained from routine medical check-ups on 8373 children from nine Chilean counties through convenience sampling. WHZ *z*-scores were generated at six-monthly intervals using WHO 2006 standards from birth to 3 years old (seven measurements). Age of cessation of breastfeeding and age of commencement of LPF were the independent variables. Repeated-measures ANOVA were used to analyse the changes in WHZ over the seven measurements. Binomial generalised estimating equations (GEE) were used to analyse the effect of each independent variable on the change from normal to overweight, and normal to obese over the seven measurements.

Results ANOVA indicated that children given LPF milk before 3 months of age had, on average, higher mean WHZ of about 0.11 SD from 18 months of age onwards ($p < 0.001$). GEE analyses showed that children given LPF before 3 months of age were significantly more likely to be overweight or obese (OR = 1) compared with children given LPF later (overweight OR: 0.809–0.970, $p = 0.009$, obese (OR: 0.666–0.901, $p = 0.001$).

Conclusions Early intake of LPF increases WHZ and is a risk factor for overweight and obesity in young children, while prolonged breastfeeding acts as protective factor against obesity.

Introduction

Childhood obesity has become increasingly common in developed and some developing countries [1]. Chile is not exempt from this and the prevalence of obesity below five years of age of 9.3% is one of the highest in The Americas [2]. One of the most important determinants of childhood obesity is the quality and quantity of food. During the weaning process breast milk is gradually substituted with other types of food, including alternative milk sources. This is a culturally mediated phenomenon and varies both spatially and temporally.

Breastfeeding has been associated with a reduction in risk of obesity, Type-I and -II diabetes in children, and a reduction of Type-II diabetes, breast and ovarian cancers in mothers [3, 4]. The WHO commission on Ending Childhood Obesity recommends exclusive breastfeeding for the first 6 months of age [5]. However the protective effect of breastfeeding on body mass and overnutrition is still controversial and some researchers have found that breastfeeding has a protective effect [6–9], while other studies have shown no clear associations [10–12]. Owen et al. [13] found that children who ceased breastfeeding earlier had higher WHZ and so were at greater risk of overweight or obesity before 16 years of age compared with later breast feeders of the same age. A systematic review by Prell et al. [14] suggested that infants should be exclusively breastfed

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up to 4 months of age and thereafter be fed with low-protein and long-chain polyunsaturated fatty acids infant formula.

Formula-based milk also has been subject of controversy due to its role in overnutrition. For example, Cu et al. [15] found that both the absence of breastfeeding and exclusive formula feeding were significantly associated with an increased risk of developing obesity in 1-year-old Mexican children. In the presence of maternal pre-pregnancy obesity and exclusive formula feeding, there was a 64.4% greater risk of being overweight or obese at 12 months old. A prospective randomised control trial found that infants fed a nutrient-enriched infant diet (28% more protein which promoted faster weight gain) had 30% greater body fat up to 8 years later [16]. Formula-based milk contains, on average, about 15% more energy than breast milk [17], which could lead to faster growth and weight gain. Faster weight gain is associated with greater adiposity even in those who were breastfed, and programming effects on infant growth are independent of protein intake and method of infant feeding [18–20].

In Chile, all children younger than 18 months of age have the right to receive complementary feeding through the National Program of Complementary Feeding (Plan Nacional de Alimentación Complementaria or PNAC). The product, named Leche Purita Fortificada (LPF), is a powdered whole cow's milk gluten-free fortified with vitamin C, iron, zinc and copper. However, this product is not adapted to be an infant formula. Little research has been undertaken on the dual effects of age of cessation of breastfeeding and age of giving LPF on the nutritional status of young Chilean children. Therefore, the objective of this study was to determine how much of the variation in child nutritional status was associated with the age of breastfeeding cessation and the age of commencing LPF in a cohort of Chilean children studied from birth to 3 years of age. The hypothesis being that children giving LPF at an earlier age will have a higher WHZ and be at greater risk of being overweight and/or obese at 3 years old, compared with children given this milk at an older age.

Material and methods

This was a retrospective longitudinal study of a cohort of Chilean infants examined regularly between birth and 3 years of age and born between January 2007 and January 2011 in nine urban counties across the country (Easter Island, Alto Hospicio, Coquimbo, Lo Prado, Quinta Normal, Talcahuano, Puerto Montt and Punta Arenas). Sampling methods and data have been described in detail elsewhere [21]. Briefly, data on 8373 children (4080 females, 4293 males) were obtained from routine medical check-ups undertaken approximately every 6 months. In order to generate the exact heights and weights every 6 months, third order polynomial regressions were generated for each child which provided excellent curve fits ($R^2 = 99\%$). These weights and heights were used to calculate weight-for-height z-scores (WHZ) utilising WHO Anthro, and children were also categorised as normal (WHZ > −1 and <1 SD), overweight (WHZ ≥ 1 and <2 SD) and obese (WHZ ≥ 2 SD) following the Chilean current recommendations [22]. WHZ were analysed both as a continuous as well as a categorical variable.

During each routine medical check-up, the feeding habits and types of food consumed were recorded. The age of breastfeeding cessation was calculated as the age in days between birth and the date of the last report of giving breast milk. The age of LPF commencement was calculated as the age in days between birth and the date of the first reported use of LFP. Both variables were categorised into three age intervals of <3 months of age, between 3 and 6 months of age and >6 months of age. County of birth, household occupation, birth order, sex of the child, year of birth, age of giving other types of food and the age of the mother at birth of the child were controlled before testing for the impact of age of breastfeeding cessation of LPF commencement. In the continuous analyses, sequential repeated-measures ANOVA were used to examine the changes in WHZ from birth to 36 months of age as well as between birth to 12 months and 18–36 months of age. For the categorical analyses binomial generalised estimating equations (GEEs) were used to analyse the effect of having (1) normal or overweight and (2) having normal or obese WHZ from birth to 36 months of age as well as from birth to 12 months and 18 to 36 months of age. Odds ratios were calculated in order to determine the likelihood of changing from normal to overweight/obese type in relation breastfeeding cessation or LFP commencement. Eta square (η^2) statistic was used to calculate the effect size [23].

Ethical clearance

Study protocols were approved by ethical committees from each health service and county where the data were collected.

Results

Figure 1 shows the WHZ means at six-monthly intervals in relation to the age of LPF commencement based on the sequential repeated-measures ANOVA. Overall mean WHZ increased up to 18 months with an oscillating pattern thereafter. Children giving LPF > 6 months of age had higher WHZ means between birth and 12 months of age compared with those given LPF < 3 months of age.

However, from 18 months onwards children receiving LPF < 3 months of age had higher mean WHZ than the other two LPF groups.

Table 1 shows the results of repeated-measures ANOVA in relation to breastfeeding and LPF age groups. When the age at breastfeeding cessation was analysed, the >6 months of age group showed significantly higher WHZ means from birth to 12 months of age and significantly lower WHZ means from 18 to 36 months of age. However, there was no overall heterogeneity in age of cessation of breast milk from birth to 36 months of age. The effect size was small in all analyses.

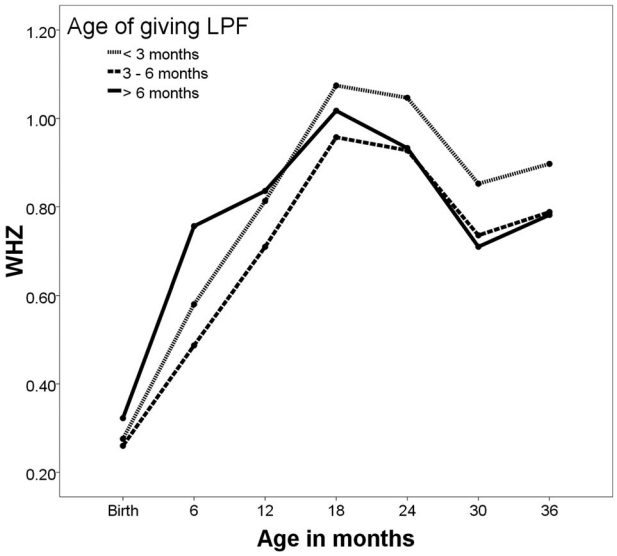

Fig. 1 WHZ means by 6-month intervals by age of commencing LPF (obtained after sequential repeated-measures ANOVA).

When the age groups of LPF commencement were analysed, sequential repeated-measures ANOVA showed a significant interaction effect indicating that the lines were not parallel, which was mainly due to >6 months of age group which had a sharper rise in WHZ mean between birth and 6 months of age, followed by plateauing until 18 months of age. When the average *z*-score from birth to 36 months of age was calculated, there was significant heterogeneity in means with a lower mean in the 3–6 months age group (0.695 SD) and a higher mean in the <3 months (0.791 SD). Similar results were found when the average *z*-score was calculated from birth to 12 months of age and from 18 to 36 months of age.

Table 2 shows the results of the GEE comparing normal and overweight WHZ. The main finding was that over the period 18–36 months children who were given LPF at <3 months of age were significantly more likely to be overweight (OR = 1.0) than those given LPF between 3 and 6 months (OR = 0.851) or at >6 months of age (OR = 0.843). Over the period birth to 36 months, the same general pattern was found. When the analyses were repeated for obese children (Table 3) the same pattern emerged with children given LPF at <3 months of age being more likely to be obese that if given LPF at a later age. In addition, between birth to 12 months, children who ceased breastfeeding at >6 months

Table 1 Results of sequential repeated-measures ANOVA for WHZ.

Variable	Age (months)	Overall mean	*F*	*p* value	η^2
Birth to 36 months					
Cessation breast milk	<3	0.764	0.785	n.s.	<0.001
	3–6	0.730			
	>6	0.758			
Commencing LPF	<3	0.791	8.074	<0.001	0.002
	3–6	0.695			
	>6	0.765			
Birth to 12 months					
Cessation breast milk	<3	0.517	22.380	<0.001	0.012
	3–6	0.517			
	>6	0.646			
Commencing LPF	<3	0.556	23.460	<0.001	0.006
	3–6	0.486			
	>6	0.638			
18–36 months					
Cessation breast milk	<3	0.949	10.630	<0.001	0.003
	3–6	0.890			
	>6	0.841			
Commencing LPF	<3	0.968	10.630	<0.001	0.003
	3–6	0.852			
	>6	0.860			

Table 2 Results of GEE utilising normal (>−1 and <1 SD) and overweight (>1 and <2 SD) WHZ.

Variable	Age (months)	OR	RSE	*z*	*p* value	95% Confidence interval		η^2
						Lower limit	Upper limit	
Birth to 36 months								
Commencing breast milk	<3	1.000	–	–	–	–	–	0.007
	3–6	0.931	0.053	−1.250	n.s.	0.834	1.041	
	>6	0.964	0.046	−0.770	n.s.	0.877	1.058	
Giving LPF	<3	1.000	–	–	–	–	–	
	3–6	0.886	0.041	−2.620	0.009	0.809	0.970	
	>6	0.947	0.039	−1.320	n.s.	0.873	1.027	
Birth to 12 months								
Commencing breast milk	<3	1.000	–	–	–	–	–	0.008
	3–6	1.000	0.063	0.000	n.s.	0.883	1.132	
	>6	1.195	0.064	3.320	0.001	1.076	1.327	
Giving LPF	<3	1.000	–	–	–	–	–	
	3–6	0.919	0.047	−1.660	n.s.	0.830	1.016	
	>6	1.104	0.049	2.220	0.027	1.011	1.206	
18–36 months								
Commencing breast milk	<3	1.000	–	–	–	–	–	0.013
	3–6	0.893	0.064	−1.570	n.s.	0.776	1.029	
	>6	0.823	0.050	−3.190	0.001	0.729	0.928	
Giving LPF	<3	1.000	–	–	–	–	–	
	3–6	0.851	0.049	−2.780	0.005	0.759	0.954	
	>6	0.843	0.044	−3.250	0.001	0.761	0.935	

OR odds ratio, *RSE* robust standard error, *n.s.* not significant.

Table 3 Results of GEE utilising normal (>−1 and <1 SD) and obese (>2 SD) WHZ.

Variable	Age (months)	OR	RSE	*z*	*p* value	95% Confidence interval		η^2
						Lower limit	Upper limit	
Birth to 36 months								
Cessation breast milk	<3	1.000	–	–	–	–	–	0.010
	3–6	0.965	0.091	−0.380	n.s.	0.802	1.160	
	>6	1.064	0.083	0.790	n.s.	0.913	1.239	
Commencing LPF	<3	1.000	–	–	–	–	–	
	3–6	0.775	0.060	−3.310	0.001	0.666	0.901	
	>6	0.962	0.063	−0.600	n.s.	0.847	1.093	
Birth to 12 months								
Cessation breast milk	<3	1.000	–	–	–	–	–	0.017
	3–6	1.014	0.119	0.120	n.s.	0.805	1.276	
	>6	1.591	0.151	4.880	<0.001	1.320	1.917	
Commencing LPF	<3	1.000	–	–	–	–	–	
	3–6	0.759	0.071	−2.960	0.003	0.633	0.911	
	>6	1.267	0.096	3.120	0.002	1.092	1.470	
18–36 months								
Cessation breast milk	<3	1.000	–	–	–	–	–	0.019
	3–6	0.930	0.097	−0.690	n.s.	0.758	1.141	
	>6	0.865	0.076	−1.650	n.s.	0.727	1.028	
Commencing LPF	<3	1.000	–	–	–	–	–	
	3–6	0.749	0.065	−3.350	0.001	0.633	0.887	
	>6	0.823	0.063	−2.560	0.011	0.710	0.956	

OR odds ratio, *RSE* robust standard error, *n.s.* not significant.

showed a higher mean WHZ and were more likely to be overweight and obese compared with those who ceased breastfeeding at <3 months. When the age of ceasing breastfeeding was analysed from birth to 36 months, no significant differences were observed between the age groups. The effect size was small in all analyses.

Discussion

The results of repeated-measures ANOVA showed that the changes in WHZ between birth and 3 years of age were not significant in relation to the age of breastfeeding cessation. Similar results were observed in the GEE analyses. However, between birth and 12 months, children who ceased breastfeeding at >6 months had a higher mean WHZ and were more likely to be overweight compared with children who ceased breastfeeding at <3 months. These findings are in accordance with previous studies indicating that exclusive breastfed infants gained weight more rapidly during the first 2 months, but grew less rapidly from 3–12 months [24]. Exclusively breastfed infants under 6 months have been shown to gain more weight (WHZ) between birth and 4–6 months [17] or earlier [25, 26]. After 6 months of age, breastfed infants experience a physiological drag in growth velocity [13, 27, 28]. Consequently, longer duration of breastfeeding was associated with lower prevalence of obesity at age 3 [29], and breastfed babies have a lower rate of weight gain over the 1st year. In addition, the patterns of WHZ of the 6-month-breastfed infants and the infants who received LPF later than age 3 months, closely resemble each other after 24 months of age. These findings suggest that there is a window of sensitivity to LPF before the age of 3 months, leading to obesity developmental programming associated with high intake of protein provided by cow's milk [30, 31]. LPF does not appear to inhibit growth in length as height (or length)-for-age *z*-scores were within the normal ranges.

Children given LPF before 3 months of age had higher WHZ means between birth to 12 months of age, as well as between 18 and 36 months of age. GEE analyses showed that children giving LPF before 3 months of age had a greater likelihood of being obese compared with those given LPF after 3 months of age. These results are in accord with previous studies showing different growth patterns between early and later formula-fed infants. Early formula-fed children grow faster and gain more weight, which has been associated with cardiovascular risk in adulthood [17], and greater propensity to obesity, dyslipidemia, raised blood pressure and insulin resistance [32]. In contrast, persistent exclusive breastfed children have less insulin response [33], explaining their lower nutrient intake compared with formula-fed children. Over 30% of children in the current study started consuming LPF before 3 months of age, and over 20% of children started consuming LPF between 3 and 6 months of age, which would imply a risk of overnutrition. In addition, 40.4% (3379) of children were exclusive breastfed until 6 months of age. This figure contrasts with that shown in the National Survey of Breastfeeding (Encuesta Nacional de Lactancia Materna) [34] ($n = 9604$), where exclusive breastfeeding until 6 months of age was 56.3% ($n = 5407$). It is possible that these contrasting figures are due to different methodologies in data acquisition and sampling between the studies.

The rapid weight gain observed after 18 months of age in children consuming LPF is of concern. Lucas et al. [33] showed that formula-based milk has, on average, 15% more energy than breast milk, while other studies have shown that the introduction of formula-based milk with high protein content increases weight gain and growth rate, which would trigger obesity and metabolic syndrome in late infancy [18, 35–39]. In Chile, Castillo et al. [40] reported that LPF has double the amount of protein content than infant formulas used in other countries. It also has a casein to serum protein ratio equal to 20/80, while other formula milks have a casein to serum protein ratio equal to 60/40, which is easier to digest and have similar protein and amino acid content compared with breast milk. Energy, carbohydrates and fat in LPF are at normal recommended levels [40].

There is still controversy concerning the effect of high protein levels in formula-based milk on weight gain. Totzauer et al. [41] show that infant formula with high protein levels induces greater fat mass in children between 2 and 6 years of age. Prell and Koletzko [14] recommend children should be fed with low-protein food after 4 months of age. However, Patro-Golab et al. [42] conducted a systematic review based on 12 studies and did not find evidence that low-protein content in formula milk reduces later risk of obesity. However, the same authors observed that data from large randomised controlled trials show that consumption of a lower-protein infant formula may reduce body mass index at 12 months of age, and the risk of obesity at 6 years of age. Therefore, it is important to evaluate more critically the milk product (LPF) distributed freely in Chile by the Public Health System, in order to know whether it is giving the appropriate nutrients to children for their optimal development. Also, it is important to know the reasons associated with this milk being given before 6 months of age. It would be necessary to compare the effect of LPF with other infant formulas on the nutritional status in Chilean children.

Conclusions

The intake of LPF before 6 months of age was associated with higher WHZ after 18 months of age and an increased

likelihood of overweight and obesity. For decades the PNAC has contributed to improving the access of healthy foods to the most vulnerable people in Chile. However, there is an urgent need to evaluate the protein content of LPF given to children <12 months of age since this study has shown that LPF contributes to excessive weight gain and obesity. In addition, there is a need to reinforce public policies to promote exclusive breastfeeding for the first 6 months of life.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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