COMPARISON OF GROWTH, INFECTIONS AND FEEDING HABITS AMONG FORMULA-FED INFANTS STARTING COMPLEMENTARY FEEDING AT 4 TO 6 MONTHS OLD WITH THOSE STARTING AT 6 MONTHS OLD

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Abstract. The World Health Organization recommends starting complementary feeding among infants beginning at 6 months old, as opposed to 4 to 6 months old. We prospectively studied 21 formula-fed infants beginning complementary feeding at 4 to 6 months old and compared them with 20 formula-fed infants starting feeding at 6 months old to determine difference in growth, number of infections and feeding habits. The studied infants were each enrolled at age 4 months. The decision as to which group the infants were classified into was based on the parental decision as to when to start complementary feeding. Initial demographic data were obtained for each subject. Growth, infections, and feeding habit data were recorded. No significant differences in growth were detected between the 2 groups. Respiratory infections at age 10 to 12 months were more common among children who began complementary feeding later. By age 12 months, the percentages of subjects who were bottle feeding and night feeding, and new food acceptance were not different from each other, but those who began complementary feeding at age 6 months were less picky eaters. By 15 months old, those who began complementary feeding at age 6 months had less bottle feeding and better food acceptance. In conclusion, for formula-fed infants, age of onset of complementary feeding was not associated with infant growth or infection rates. However, some feeding habits differed between the two groups. It is unclear if the age of introducing complementary feeding caused these differences or was merely associated with these differences.

Keywords: infant nutrition, infant feeding, complementary feeding, feeding habits, formula-fed infants

INTRODUCTION

Breastfeeding is the best source of nutrition for healthy term infants. It has many nutritional, neurodevelopmental, immunological, metabolic, and socioeconomic advantages. Several health agencies, including the World Health Organization (WHO), recommend exclusive breastfeeding until six months of

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age (American Academy of Pediatrics, 2012; Kramer and Kakuma, 2012). This recommendation has been accepted as public health policy in many countries, including Thailand.

The WHO defines complementary feeding as "the process starting when breast milk alone is no longer sufficient to meet the nutritional requirements of infants, and therefore other foods and liquids are needed, along with breast milk" (Dewey, 2002). This definition is different from those of other credible health organizations and leads to confusion (Agostoni *et al*, 2008; American Academy of Pediatrics - Committee on Nutrition, 2014). It attaches complementary feeding to breastfeeding and does not address formula-fed infants. Regardless of breast- or formula feeding, complementary feeding has a unique role. It ensures proper nutrition for infants after six months old when human milk alone may not be adequate (American Academy of Pediatrics - Committee on Nutrition, 2014). It prepares the infant for solid foods, which will become the main source of nutrition after their first birthday and stimulates the infant's socio-psycho-motor development (Agostoni *et al*, 2008). The latter two roles are unique to complementary feeding and breastfeeding cannot replace them. The appropriate age to introduce complementary feeding has been a topic of discussion for over a decade (Qasem *et al*, 2015). The WHO encourages starting complementary foods at age 6 months (Dewey, 2002), but some studies have recommended otherwise (Agostoni *et al*, 2008; Greer *et al*, 2008; Jonsdottir *et al*, 2012; Qasem *et al*, 2015). Many authorities recommend starting complementary feeding between 4 and 6 months of age, when most healthy term infants are physiologically and developmentally ready for food other than milk (Agostoni *et al*, 2008). The basis for this discrepancy may be the WHO assumes most infants ingest only human milk. With this assumption, infants have the advantages of breastfeeding longer, such as infection reduction. In less-than-ideal situations, rates of exclusive breastfeeding for 6 months are unsatisfactory despite vigorous campaigns (Soni *et al*, 2011; Brown *et al*, 2013; van Beusekom *et al*, 2013; Puapompong *et al*, 2014). In Thailand, the Ministry of Public Health has recommended the same as the WHO but more than half of infants have changed to mainly formula feeding by 6 months of age (Puapompong *et al*, 2014). These formula-fed infants are not protected from infections by delaying complementary feeding to 6 months; on the contrary, there may be downsides to such a practice, such as growth and micronutrient deficiencies, and improper feeding habits. There is little data to form evidence-based recommendations about the best time to initiate complementary feeding among formula-fed infants (Fewtrell *et al*, 2007). There are no recommendations for this group.

This poses the question as to when is the best time to introduce complementary feeding among formula-fed infants. We explored this question by studying two groups of infants to determine when is the best time to begin complementary feeding.

MATERIALS AND METHODS

Subjects

This study was conducted at the Department of Pediatrics, Phramongkutklao Hospital, Thailand from March 2014 to September 2015. Inclusion criteria were: being a healthy 16- to 20-week-old infant born at 37 to 41 weeks gestation with a birth weight of 2,500 - 4,000 grams who had exclusively formula-fed for at least 2

weeks prior to the entrance in the study. Exclusion criteria were: apparent physical disease, doubtful medical history, abnormal growth and development, needing a special diet, breastfeeding at the time of screening, and those who had already begun complementary feeding prior to entrance in the study. The two study groups were those starting complementary feeding between 4 and 6 months old (4-to-6-months group) and those starting complementary feeding at age 6 months (at-6-months group).

Study design

This study was conducted prospectively. Parents were informed about the objectives of the study and written consent was obtained prior to being included in the study. Demographic data (date of birth, birth weight, sex, caregivers, and amount of formula intake per day) were recorded and initial anthropometric measurements (body weight, length, and head circumference) were taken and recorded. Infants were allocated into either the 4-to-6-months group or the at-6-months group based on the parental decision about when to begin complementary feeding. Parents were encouraged to follow their choice for when to begin complementary feeding but were told they were free to change their minds, in which case the infant's information was not included in the analysis. Parents were advised about age-appropriate complementary foods as recommended in a guidebook published by the Thai Ministry of Public Health and other local health organizations. Appointments with investigators were made at 6, 9, and 12 months of age. Interviews regarding the amount of formula consumed, amount and type of complementary food consumed, illness, feeding habits, anthropometric measurements, general physical examination, well-baby care and routine vaccinations were conducted when appropriate at each visit. Investigators also called the parents monthly, when the child was aged 5 to 15 months to obtain data regarding feeding, illness, and feeding habits.

Growth was determined by the weight increase (in gram), length increase (in centimeter), and head circumference increase (in centimeter) from enrollment to 12 months old. Episodes of infection, such as respiratory, gastrointestinal, and other infections were recorded from enrollment to age 15 months and feeding habits, such as bottle feeding, nighttime feeding, new food acceptance, and picky eating were recorded during ages 12 to 15 months.

This study protocol was approved by the Royal Thai Army Medical Department Institutional Review Board before being conducted. The study was conducted in accordance with the Helsinki Declaration. Funding was provided by Research Support Committee, Department of Pediatrics, Phramongkutklao Hospital, Bangkok, Thailand.

Statistical analysis

The sample size was calculated using G*power software, version 3.0.5 (by Franz Faul, University Kiel, Germany). In order to detect a 20% difference between groups for weight gain from enrollment to 12 months old, a p-value of ≤ 0.05 and a power of 0.85 with a sample size of 40 infants (20 in each group) was required.

Descriptive data were presented as means (with standard deviations), medians (with inter-quartile ranges) and percentages. The Fisher's exact test was used to compare categorical parameters and either the Student's t-test or the Mann-Whitney U test was used where appropriate to compare numerical parameters.

Table 1
Demographic data.

Characteristics	4-to-6-months[a] (n=21)	At-6-months[b] (n=20)	p-value
Male: female ratio	8:13	8:12	1.000[c]
Birthweight in gram[d]	3,211.0±405.6	3,108.1±381.2	0.408[e]
Age at enrollment in days[d]	131.6±6.4	128.6±5.7	0.117[e]
Weight at enrollment in gram[d]	7,014.3±870.2	6,990.0±839.1	0.928[e]
Length at enrollment in centimeter[d]	62.2±2.3	62.3±2.3	0.969[e]
Head circumference at enrollment in centimeter[d]	41.3±1.0	41.0±1.3	0.473[e]
Amount of formula intake at enrollment in oz per day[d]	27.7±5.7	28.3±4.6	0.721[e]
Amount of formula intake at age nine months of age in oz per day[d]	28.1±3.8	29.7±4.9	0.245[e]
Amount of formula intake at age 12 months of age in oz per day[d]	27.0±5.8	28.7±4.3	0.294[e]
Percent of subjects with parents as their primary caregivers	52.4	60.0	0.612[c]

[a]4-to-6-months, infants starting complementary feeding during ages 4 to 6 months. [b]At-6-months, infants starting complementary feeding at age 6 months. [c]Fisher's exact test. [d]In means ± SD. [e]Student's t-test.

RESULTS

Forty-one infants were enrolled in the study: 21 in the 4-to-6-months group and 20 in the at-6-months group. A summary of the demographic data is shown in Table 1. Both groups were comparable. Infants in both groups had about the same growth and ingested about the same amounts of formula on enrollment and at 9 and 12 months of age. All infants in the 4-to-6-months group reportedly started complementary feeding at around 4 months old (after enrollment). Infants in the at-6-months group started complementary feeding at about 6 months old. Most infants in both groups had the same number of complementary food meals per day (2 meals at 9 months old and 3 meals at 12 months old, without a statistically significant difference). Parents reportedly followed investigator's advice about healthy complementary feeding.

There were no statistically significant differences in growth between the groups (Table 2). A number of reported infections did not significantly differ between the 2 groups, except for respiratory tract infections during ages 10 to 12 months, which were more common in the at-6-months group (median of 1 episode compared to 0 episodes for the 4-to-6-months group, $p = 0.035$). Some feeding habits differed significantly between the groups, such as picky eating at 12 months old, which was significantly more common in the 4-to-6-months group, but by 15 months old the difference was no longer present. Bottle feeding at 15 months old was also more common among the 4-to-6-months group infants but all the infants in both groups were bottle-fed by 12 months old. Infants in the at-6-months group accepted new foods better than in the 4-to-6-months group by age 15 months.

Table 2
Outcome comparisons.

Outcomes	4-to-6-months[a] (*n*=21)	At-6-months[b] (*n*=20)	*p*-value
Weight at age 12 months in gram[c]	9,990.5±1,199.5	9,775.0±1,621.8	0.630[d]
Weight increase from enrollment to age 12 months in gram[c]	2,976.2±1,086.2	2,785.0±1,156.8	0.588[d]
Length at age 12 months in centimeter[c]	74.1±2.9	74.4±3.1	0.741[d]
Length increase from enrollment to age 12 months in centimeter[c]	11.9±2.1	12.2±2.2	0.674[d]
Head circumference at age 12 months in centimeter[c]	45.7±1.1	45.2±1.4	0.186[d]
Head circumference increase from enrollment to age 12 months in centimeter[c]	4.4±1.1	4.2±0.6	0.305[d]
Number of infections from enrollment to age 15 months[e]	3.0 (1.0-4.0)	2.5 (0.5-4.5)	0.731[f]
Respiratory tract infections[e]	2.0 (1.0-3.0)	2.0 (0.5-3.0)	0.968[f]
Gastrointestinal infections[e]	0 (0-1.0)	0 (0-1.0)	0.909[f]
Other infections[e]	0 (0-1.0)	0 (0-1.0)	0.922[f]
Feeding habits			
Bottle feeding at age 12 months in %	100.0	100.0	n/a
Night time feeding at age 12 months in %	76.2	70	0.734[g]
New food acceptance at age 12 months in %	71.4	95	0.093[g]
Picky eating at age 12 months in %	57.1	15	0.009[g]
Bottle feeding at age 15 months in %	100	80	0.048[g]
Nighttime feeding at age 15 months in %	42.9	40	1.000[g]
New food acceptance at age 15 months in %	71.4	100	0.021[g]
Picky eating at age 15 months in %	38.1	30	0.744[g]

[a]4-to-6-months, infants starting complementary feeding during 4 to 6 months. [b]At-6-months, infants starting complementary feeding at age 6 months. [c]In means±SD. [d]Student's *t*-test. [e]In medians (interquartile range). [f]Mann-Whitney *U* test. [g]Fisher's exact test.

DISCUSSION

In this study, formula-fed infants who started complementary feeding at 4 months old had the same growth as those who started complementary feeding at 6 months old as measured by weight, length, and head circumference at 12 months old and the increase in these measurements from enrollment to age 12 months. These results are in accordance with a study among breastfed infants (Kramer and Kakuma, 2012). We were not able to find this type of study among formula-fed infants in the literature. We had assumed that if no growth deficits were seen in breastfed infants, the same would be true among formula-fed infants, and our findings confirmed this assumption. Poorer growth was not among the disadvantages of formula feeding in our study. Formula-fed infants are known to be larger than their breastfed counterparts and may even be at risk for overweight during infancy (Mandic *et al*, 2011). We conclude growth should not be a decisive

factor in the decision as to when formula-fed infants should start complementary feeding.

According to the WHO, one of the most important benefits of exclusive breastfeeding for 6 months is the reduction of infection risk (Dewey, 2002; Kramer and Kakuma, 2012). An association between exclusive-breastfeeding duration and reduced infection and mortality rates has been observed in both developing and developed countries (WHO Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality, 2000; American Academy of Pediatrics, 2012), although reverse causality cannot be ruled out (Kramer and Kakuma, 2012). One explanation, apart from the immunologic properties of human milk, may be the longer an infant is exclusively breastfed, the less likely they will be exposed to external sources of water, which may be contaminated and can cause infections. If this is the case, our formula-fed subjects should not have benefitted from delaying complementary feeding to 6 months old, since they were exposed to water used to prepare the formula. This means the infection rates among formula-fed infants would not be affected by when they start complementary feeding. In our study, we found no difference in the number of infections between the groups, as expected. The only exception was a slightly higher number of respiratory tract infections from 10 to 12 months old in the at-6-months group (median of 1 episode, compared to 0 episodes in the 4-to-6-months group). No other types of infections were found to be differed between the 2 groups. The reason for this lack of difference is unclear. The data regarding infections was reported by the parents only and could be subject to bias. We cannot discuss severity of infections either since this was not recorded. Our data suggest no benefit of delaying complementary feeding to 6 months old in terms of infection prevention for children until 15 months old.

An important role of complementary feeding is to prepare the infant for solid foods (Agostoni *et al*, 2008). Neurodevelopmentally, most healthy term infants are ready for semi-solid foods beginning at age 4 months. One study found it was important to introduce semi-solid foods prior to age 10 months (Northstone *et al*, 2001) to reduce the risk for unfavorable feeding habits later on. We explored feeding habits in this study. Differences in feeding habits were found between the two groups but they were random and no clear explanation could be found for them (Table 2). A reason to this could be flaws in our study methodology. The specific habits we studied were not defined, leaving them open to variable interpretations; the feeding habits were self-reported, not explored in detail and subject to bias; potential confounding factors (family socioeconomic status, parental education level, attitudes and experiences about infant feeding) were not recorded. The sample size was not calculated based on feeding habits which could cause it to be too small to obtain significant conclusion. A small sample size can also increase the risk for both α-errors (*eg*, the at-6-months group had less picky eaters and better new food acceptance by chance) and β-errors (*eg*, both groups had equal numbers of nighttime feeders by chance). Further studies are needed to evaluate these factors.

Our findings suggest for formula-fed infants, unlike breastfed infants, there is no advantage to starting complementary feeding at 6 months over 4 months old. Feeding habits were somewhat different but did not favor one group over the other.

Neurological, gastrointestinal and renal development is sufficient to introduce complementary feeding at age 4 months (Ziegler and Fomon, 1971). Exposure to solid foods stimulates hormonal responses resulting in more rapid maturation of digestive function (Girard *et al*, 1993). It is therefore logical to conclude formula-fed infants are ready for complementary feeding by 4 months old and there are no clear drawbacks to this.

This study had a number of limitations. It was only observational; therefore, causality cannot be determined. The primary outcomes were only anthropometric; no other clinical or subclinical findings were assessed. Blood tests could have allowed us to evaluate micronutrient status and biochemical changes. Infections and feeding habits were self-reported and subject to bias, as discussed earlier. Tools other than phone calls, such as diaries or medical records, should have been utilized to more accurately collect data. Potential confounding factors should have been recorded so other explanations could be considered, such as details of vaccination, severity of infection and medical attention, and details about each feeding habit. The negative finding in our study could be due to the study being underpowered. The 20% difference in weight gain used to calculate sample size could be an overestimation. Although we think the number is clinically reasonable, it could have resulted in an inadequate sample size. Further studies with improved methodology, with a larger sample size, are needed to clarify these issues.

In conclusion, the age of complementary feeding introduction had no association with growth or infection rates in our study. Some feeding habits were different but whether these are actually due to the age of onset of complementary feedings or not is unclear and further studies are needed to clarify this.

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