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Risk of Bottle-feeding for Rapid Weight Gain During the First Year of Life

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Objective: To better understand the mechanisms behind breastfeeding and childhood obesity, we assessed the association of weight gain with the mode of milk delivery aside from the type of milk given to infants.

Design: A longitudinal study of infants followed up from birth to age 1 year. Multilevel analyses were conducted to estimate infant weight gain by type of milk and feeding mode.

Setting: Pregnant women were recruited from a consumer mail panel throughout the United States between May 2005 and June 2007.

Participants: One thousand eight hundred ninety nine infants with at least 3 weight measurements reported during the first year.

Main Exposures: Six mutually exclusive feeding categories and proportions of milk feedings given as breastmilk or by bottle.

Main Outcome Measures: Weight measurements reported on 3-, 5-, 7-, and 12-month surveys.

Results: Compared with infants fed at the breast, infants fed only by bottle gained 71 or 89 g more per month when fed nonhuman milk only ($P < .001$) or human milk only ($P = .02$), respectively. Weight gain was negatively associated with proportion of breastmilk feedings, but it was positively associated with proportion of bottle-feedings among those who received mostly breastmilk. Among infants fed only breastmilk, monthly weight gain increased from 729 g when few feedings were by bottle to 780 g when most feedings were by bottle.

Conclusions: Infant weight gain might be associated not only with type of milk consumed but also with mode of milk delivery. Regardless of milk type in the bottle, bottle-feeding might be distinct from feeding at the breast in its effect on infants' weight gain.

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THE ESTIMATED PERCENTAGE of US children aged 2 to 5 years and 6 to 11 years classified as overweight increased from 5.0% and 6.5% in 1980 to 10.4% and 19.6%, respectively, in 2007-2008.¹⁻³ The increase in childhood obesity was also observed among those aged 6 to 23 months, from

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7.2% in 1980 to 11.6% in 2000.¹ Given the numerous health risks related to childhood obesity,⁴⁻⁷ its prevention is becoming a public health priority.⁸ It has been reported that feeding practices affect growth and body composition in the first year of life, with breastfed infants gaining less rapidly than formula-fed infants.⁹⁻¹⁴ There is also evidence that breastfed infants continue to have a low risk for later childhood obesity.¹⁵⁻¹⁸

There are multiple hypotheses for the mechanisms behind breastfeeding and childhood obesity and one of them pertains to the poor self-regulation of energy intake among formula-fed infants.¹⁹ In contrast to infants fed at the breast who may need to actively suckle, formula-fed infants are more likely to be passive in the feeding process, and caregivers' control might undermine infants' capability for self-regulation to balance energy intake against internal cues of hunger and satiety. Theoretically, feeding babies with expressed breastmilk could increase infant weight gain because it is fed by bottle. So far, only one pilot study has examined early growth patterns of babies fed breastmilk by breast vs by bottle.²⁰ The purpose of this study was to compare infant weight gain by both milk type (human vs nonhuman milk) and feeding mode (breast vs bottle) and examine whether bottle-fed infants gain weight more rapidly than those fed at the breast during the first year. The study had 2 specific hypothesis: (1) Infant weight

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gain is not only affected by type of milk but also by mode of milk delivery and (2) Regardless of the type of milk in the bottle, bottle-feeding might put infants on a faster track of weight gain.

METHODS

SAMPLE

The Infant Feeding Practices Study II is a longitudinal study of new mothers and their infants conducted by the Food and Drug Administration and the Centers for Disease Control and Prevention from May 2005 to June 2007. Women were recruited in their third trimester of pregnancy from a consumer opinion panel of approximately 500 000 households throughout the United States. Eligibility criteria included mothers aged 18 years or older and infants born after 35 weeks' gestation with a birth weight of at least 2.25 kg. About 3000 infants were followed up from birth for 1 year, with 10 postnatal questionnaires mailed at approximately monthly intervals. The response rates for each postpartum survey varied from 63% to 83%. All data collection procedures were approved by the Food and Drug Administration institutional review board. The details of overall Infant Feeding Practices Study II design and response rates were presented elsewhere.²¹

OUTCOME MEASURES

The outcome measures were 4 weight measurements reported on the 3-, 5-, 7-, and 12-month surveys. Mothers were asked at each of these surveys what was their infant's weight measured at the most recent doctor's visit and visit date. Because weights reported on each survey were measured at different times across infants, age at weight measurement varied from infant to infant. To limit reporting errors, we calculated the *z* score of weight for age using the Centers for Disease Control and Prevention's reference and considered *z* scores of 5 or greater or -5 or less as biologically implausible.²²

MAIN EXPOSURES

Because infant weight is a cumulative function of previous feedings over time, we first identified the time interval between 2 consecutive weight measurements and then aggregated all the feeding data available within each interval to tie each weight outcome to its corresponding feeding exposures. The 3 main exposure variables from each interval were milk feeding category, percentage of milk feedings given as breastmilk, and percentage of milk feedings given by bottle.

At each postpartum survey (about 1, 2, 3, 4, 5, 6, 7, 9, 10, and 12 months of age), mothers were asked how often they breastfed or fed pumped breastmilk as well as how often they fed formula and other types of milk in the past 7 days, which was used to categorize infants by whether they were fed at the breast, by expressed milk, or by formula and other types of milk. Aggregating all the feeding data within the same weight measurement interval, each infant was classified into 1 of the 6 mutually exclusive overall milk feeding categories: (1) Breastfed only; (2) Breastfed and human milk by bottle; (3) Breastfed and nonhuman milk by bottle; (4) Human milk by bottle only; (5) Human and nonhuman milk by bottle; and (6) Nonhuman milk by bottle only.

For the percentage of milk feedings given as breastmilk or by bottle, we first calculated the percentage of total milk feedings that were of the breast (BF%); expressed breastmilk (EBM%); or nonhuman milk (NHM%) including formula, cow's, or other milk at each survey (BF% + EBM% + NHM% = 100%).

We then calculated the mean proportion of milk feedings as breastmilk (BF% + EBM%) or by bottle (EBM% + NHM%) during each interval. Both breastmilk and bottle-feeding proportions were further classified as less than 33%, 33% to 66%, and greater than 66% to represent low, medium, or high frequency of milk feedings as breastmilk or given by bottle.

OTHER MEASURES

To control for potentially confounding effects, we adjusted for the following factors in our multilevel analysis: maternal age; race/ethnicity; maternal education; percentage of poverty; marital status; parity; postpartum participation in the Special Supplemental Nutrition Program for Women, Infants, and Children program; prepregnancy body mass index (calculated as weight in kilograms divided by height in meters squared); infant sex; gestational age; age at solid food introduction; average number of sweet drinks consumed per day during the first half year (including juice drinks, soft drinks, soda, sweet tea, Kool-Aid, etc); and birth weight. Percentage of poverty was defined as a ratio of household income to the poverty threshold by household size. Prepregnancy body mass index was based on maternal recall during the prenatal survey. Age at solid food introduction was defined as the infant's age when any solid food was first reported on any of the monthly surveys. Birth weight was obtained from a short telephone interview with prenatal respondents within a week after birth. Except for gestational age, age at solid food introduction, sweet drinks consumption, and birth weight, all other confounding factors were adjusted using categorical variables as shown in **Table 1**.

STATISTICAL ANALYSIS

Neonatal questionnaires were available from 3033 mothers. Of these, 13% (n=392) did not complete the 3-, 5-, 7-, and 12-month surveys; 6% (n=184) reported fewer than 3 out of 5 possible weight measurements; 1% (n=41) reported biologically implausible weight; 2% (n=75) had an invalid visit date for the weight measurement; 4% (n=126) reported smaller weight in the subsequent survey; 1% (n=38) had missing data on feeding exposures; and 9% (n=278) had missing data on covariates. This yielded a final sample of 1899 mother-infant pairs with a total of 5719 observations from 4 weight measurement intervals.

Individual growth curve models were developed for multilevel analysis and specifically designed for exploring longitudinal data on individual changes over time.²³ Using this approach, we applied the MIXED procedure in SAS (SAS Institute) to account for the random effects of repeated measurements.²⁴ To specify the correct model for our individual growth curves, we compared a series of MIXED models by evaluating the difference in deviance between nested models.²³ Both fixed quadratic and cubic MIXED models fit our data well, but we selected the fixed quadratic MIXED model because the addition of a cubic time term was not statistically significant based on a log-likelihood ratio test. We first modeled infant weight as a function of corresponding milk feeding categories. This model estimated linear slopes of weight gain for each feeding category with final estimates adjusted for the potential confounding factors listed previously. Infant age at weight measurement was the time variable, and age squared was the quadratic term included in the model. Because milk feeding categories varied from time to time, we entered them into the model as a time-varying covariate to allow the linear effect of milk feedings to vary with age. As such, the model accommodates infants who were fed in one category for one period but another category for a different period.

We then modeled infant weight as a function of proportions of milk feedings given as breastmilk or by bottle with both terms entered simultaneously into the model as continuous variables. Because the association of weight gain with proportion of bottle-feedings might vary by proportion of breastmilk feedings, we added a product term between these 2 continuous variables in the model to test the significance of its interaction. We also categorized these 2 proportions into 3 groups (<33%, 33%-66%, and >66%) and conducted a log-likelihood ratio test for the nested models with and without all 2-way interactions between them. Because both interaction tests suggested a significant interaction between type of milk and feeding mode ($P < .001$), we conducted stratified analysis to examine the association of weight gain with proportion of milk feedings either as breastmilk or by bottle separately. Specifically, for each level of bottle-feedings proportion, we examined monthly weight gain by 10% increments in breastmilk-feedings proportion; for each level of breastmilk feedings proportion, we examined monthly weight gain by 10% increments in bottle-feedings proportion. To further separate the effects of bottle use from type of milk, we also estimated the monthly weight gain by proportion of bottle-feedings among infants fed only breastmilk as well as monthly weight gain by proportion of breastmilk feedings among infants fed only by bottle. All the data analyses for this study were conducted using SAS software version 9.2 (SAS Institute Inc).

RESULTS

Most of the study sample was aged 25 to 34 years, white, married, and had education beyond high school (Table 1). Approximately half were overweight or obese prior to pregnancy and one-third was participating in the Special Supplemental Nutrition Program for Women, Infants, and Children program. Although infant weight was reported at 3, 5, 7, and 12 months, it was measured at an average of 10, 18, 28, and 52 weeks, respectively.

Table 2 shows weight gain by corresponding feeding categories from the same interval. Not counting groups 4 and 5, which had very small sample sizes, infants fed with nonhuman milk by bottle only (group 6) had the largest weight gains at 3 to 5 months, >5 to 7 months, and >7 to 12 months. Infants who were breastfed and fed nonhuman milk (group 3) had rates of weight gain intermediate between those who were breastfed only (group 1) and those who were only fed nonhuman milk (group 6) in each of these age ranges.

To summarize the estimates for fixed-effect parameters from the MIXED modeling in an easy way to interpret, we present linear monthly weight gain for each feeding category compared with infants fed at the breast only (**Table 3**). Compared with infants fed at the breast only, infants fed only by bottle gained 71 or 89 g more per month when fed nonhuman milk only ($P < .001$) or expressed human milk only ($P = .02$), but they gained only 37 g more per month when fed both expressed human milk and nonhuman milk ($P = .08$). Infants fed both at the breast and by bottles of expressed human milk gained similar to infants fed at the breast only, whereas infants fed both at the breast and by bottles of nonhuman milk gained 45 g more per month ($P < .001$).

The results from a main-effects model with both breastmilk-feedings proportion and bottle-feedings proportion

Table 1. Characteristics of Analytical Sample of 1899 Mother-infant Pairs

Characteristic	%
Maternal age, y	
18-24	16.01
25-29	33.65
30-34	31.60
≥ 35	18.75
Race/ethnicity	
White	86.99
Black	3.32
Hispanic	5.21
Other	4.48
Education level	
≤High school	18.11
Some college	36.23
College graduate	45.66
Household income as percentage of poverty level	
<185%	36.55
185%-350%	37.02
>350%	26.43
Married	
No	15.90
Yes	84.10
Parity	
Primiparous	28.33
Multiparous	71.67
Postpartum WIC participation	
Yes	33.18
No	66.82
Prepregnancy body mass index, kg/m ²	
Underweight (<18.5)	3.95
Normal (18.5-24.9)	45.97
Overweight (>25.0-29.9)	25.07
Obese (≥30.0)	25.01
Infant's sex	
Male	48.18
Female	51.82
Gestational age, mean (SD), wk	39.31 (1.25)
Infant age at first introduction of solid food, mean (SD), wk	22.95 (8.91)
Sweet drinks consumed per day during the first half year, No.	0.02 (0.11)
Infant weight reported from each survey, mean (SD), kg	
At birth	3.48 (0.46)
3 mo (actual measurement age=10.01±2.28 wk)	5.55 (0.81)
6 mo (actual measurement age=18.29±2.40 wk)	6.81 (0.93)
9 mo (actual measurement age=27.65±2.70 wk)	7.88 (1.05)
12 mo (actual measurement age=52.01±3.62 wk)	9.59 (1.22)

Abbreviation: WIC, Special Supplemental Nutrition Program for Women, Infants, and Children.

considered as primary exposure variables indicated that a 10% increase in the proportion of breastmilk feedings was associated with a 3.6-g decrease in weight gain per month ($P = .07$), whereas a 10% increase in proportion of bottle-feedings was associated with a 4.1-g increase in weight gain per month ($P = .05$). Because of the significant interactions between feeding mode and type of milk, we stratified the analysis by examining their effects separately (**Table 4**). Among those with more than 66% of feedings by bottle, a 10% increment in the proportion that were of breastmilk was associated with a 5.9-g decrease in monthly weight gain. In contrast, infants gained 8 g more per month for each 10% increment in the proportion of

Table 2. Crude Gain in Weight (g/mo) by Corresponding Feeding Categories at Each Weight Measurement Interval for 1899 Infants

Group No./Feeding Category	Birth to 3 mo		>3 to 5 mo		>5 to 7 mo		>7 to 12 mo	
	No.	Mean (SD)	No.	Mean (SD)	No.	Mean (SD)	No.	Mean (SD)
1/Breastfed only	333	937 (299)	211	640 (282)	191	433 (177)	128	275 (167)
2/Breastfed and human milk by bottle	369	916 (286)	326	614 (366)	214	452 (172)	102	280 (114)
3/Breastfed and nonhuman milk by bottle	442	896 (287)	311	686 (348)	244	496 (258)	288	319 (124)
4/Human milk by bottle only	13	1024 (263)	9	634 (147)	6	561 (156)	3	438 (92)
5/Human and nonhuman milk by bottle	39	953 (273)	26	678 (588)	19	590 (245)	9	304 (71)
6/Nonhuman milk by bottle only	377	913 (270)	459	742 (348)	467	576 (298)	468	346 (170)

Table 3. Multilevel Analyses of Linear Monthly Weight Gain for Each Feeding Category Compared With Infants Fed at Breast Only for 1899 Infants^a

Group No./Feeding Category	No.	Weight Gain, g/mo	95% CI
1/Breastfed only (reference)	936	0	
2/Breastfed and human milk by bottle	1108	10.11	-8.72 to 26.88
3/Breastfed and nonhuman milk by bottle	1518	45.15	30.00 to 60.30
4/Human milk by bottle only	34	88.83	13.19 to 164.47
5/Human and nonhuman milk by bottle	107	37.18	-5.06 to 79.42
6/Nonhuman milk by bottle only	2016	71.25	56.03 to 86.47

^aThe estimates were obtained after adjusting for maternal age; race/ethnicity; education; household income; marital status; parity; postpartum Special Supplemental Nutrition Program for Women, Infants, and Children program participation; prepregnancy body mass index; infant sex; gestational age; birth weight; age at solid food introduction; and sweet drinks consumption.

Table 4. Multilevel Analyses of Associations of Weight Gain With Increment in Proportion of Milk Feedings Either as Breastmilk or by Bottle for 1899 Infants^a

	No.	Mean	95% CI
Proportion of Bottle Feedings			
Weight Gain by Every 10% Change in Proportion of Breastmilk Feedings, g/mo			
Low (<33%)	2730	-15.36	-26.95 to -3.77
Medium (33%-66%)	495	0.75	-9.59 to 11.09
High (>66%)	2494	-5.89	-10.42 to -1.36
Proportion of Breastmilk Feedings			
Weight Gain by Every 10% Change in Proportion of Bottle-feedings, g/mo			
Low (<33%)	2287	-0.19	-17.78 to 17.38
Medium (33%-66%)	398	-8.13	-22.69 to 6.43
High (>66%)	3034	8.08	4.45 to 11.71

^aThe estimates were obtained after adjusting for maternal age; race/ethnicity; education; household income; marital status; parity; postpartum Special Supplemental Nutrition Program for Women, Infants, and Children program participation; prepregnancy body mass index; infant sex; gestational age; birth weight; age at solid food introduction; and sweet drinks consumption.

bottle-feedings among those who received at least two-thirds of their feedings with breastmilk.

Because type of milk and feeding mode were confounded by each other, examining bottle effects among infants fed by breastmilk only and examining breastmilk ef-

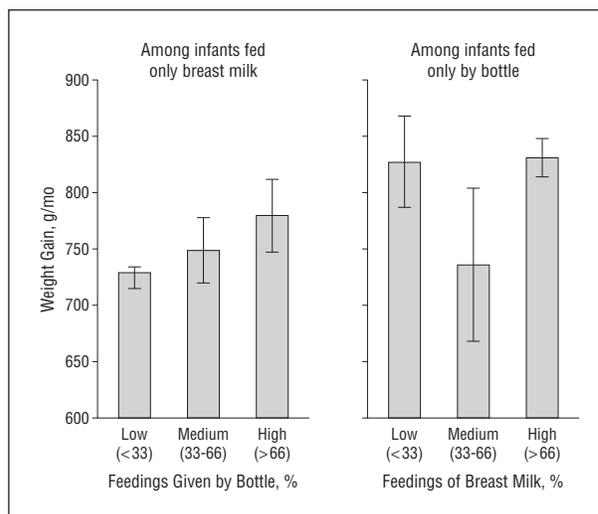


Figure. Mean and standard errors of monthly weight gain after adjusting for maternal age; race/ethnicity; education; household income; marital status; parity; postpartum Special Supplemental Nutrition Program for Women, Infants, and Children program participation; prepregnancy body mass index (calculated as weight in kilograms divided by height in meters squared); infant sex; gestational age; birth weight; age at solid food introduction; and sweet drinks consumption.

fects among infants fed by bottle only would be useful to tease out this confounding effect (**Figure**). Among infants fed by breastmilk only, weight gain increased from 729 g per month at low bottle-feedings to 780 g per month at high bottle-feedings. However, the relationship between weight gain and percentage of breastmilk feedings among infants fed by bottle only was U-shaped.

COMMENT

Our study suggests that bottle-feeding, aside from the type of milk used, might be an independent factor associated with infant weight gain. Regardless of milk type in the bottle, bottle-feeding might be distinct from feeding at the breast in its effect on infants' weight gain.

The mechanisms behind breastfeeding and childhood obesity are unclear. In addition to the biological mechanism of unique properties of breastmilk, such as leptin and adiponectin found in human milk,²⁵⁻²⁷ the ability of breastfed infants to self-regulate their energy intake might be another possibility. Infants might play a more active role in determining their intake when feeding at the breast. Mothers who breastfeed might also develop a feeding style that is less controlling.²⁸ On the con-

trary, the duration and amount of bottle-feeding more likely depend on the caregivers' decisions, which are often based on visual observations of the remaining milk in the bottle with encouragement to finish the bottle.^{29,30} In addition, the variations in the taste and nutrient content within each breastfeeding episode (much higher fat content toward the end) might also serve as a physiological signal for babies to stop suckling. This variation does not occur with bottle-feeding. Thus, infants frequently fed by bottles may gradually lose their ability to self-regulate and ultimately gain weight more rapidly than those fed at the breast.

Giving expressed breastmilk provides benefits when direct breastfeeding is impossible, but breastfeeding and breastmilk feeding might be fundamentally different. In addition to caregivers' control of feeding expressed breastmilk, some of the immune components, vitamins, and fat might be lost during the storage and handling.³¹ Nevertheless, feeding expressed breastmilk is certainly as close to breastfeeding as one can get when breastfeeding is infeasible. We found that infants categorized as "breastfed and human milk by bottle" grew similarly to those fed only at the breast, but infants categorized as "breastfed and nonhuman milk by bottle" grew more rapidly (Table 3). This suggests that supplementing breastfeeding with expressed breastmilk would be preferable to supplementing breastfeeding with nonhuman milk. Thus, breastfeeding mothers who need to feed their infant by bottle should be supported for expressing breastmilk.

Infants categorized as consuming "human milk by bottle only" and "nonhuman milk by bottle only" gained more weight than infants fed at the breast only, but there was no such bottle effect observed among infants categorized as consuming "human and nonhuman milk by bottle." This might be owing to the fact that infants in this mixed feeding category were more likely fed at the breast previously than the other 2 groups (data not shown). Our previous study suggests that infants fed at the breast develop a better self-regulation of milk intake, which may be carried over even after feeding is transitioned from breast to bottle.³² Similarly, mothers who previously breastfed might better recognize infants' cues of hunger and satiety, which may last even after they stop breastfeeding.²⁸

Stratified analysis allowed us to examine the effects of bottle use and breastmilk feeding separately. While weight gain was negatively associated with breastmilk feeding, it was positively associated with bottle-feeding when the proportion of breastmilk feedings was high (Table 4). The dose-response relations between weight gain and bottle use among infants fed only breastmilk further implies a potential risk of bottle-feeding for rapid weight gain during infancy (Figure).

There are several limitations of this study. First, because black and Hispanic mothers were underrepresented in the study population, our results may not be applicable to the entire US population. Second, because both weight measurement and feeding practice were reported by mothers, reporting errors may have occurred. However, the recall period was relatively short and it is unlikely that the misclassification of feeding exposures depended on weight outcomes given the longitudinal de-

sign of this study. For nondifferential misclassification, the reporting errors would bias the results toward the null value.³³ Third, the final analytical sample excluded 278 cases owing to missing data on covariates. However, our sensitivity analysis based on the full sample without controlling for these covariates in the models indicated similar results. Fourth, despite our statistical efforts to minimize the confounding effects, we may not have completely separated out the effects of bottle use from the type of milk because of the complexity of infant feeding and observational nature of this study. Lastly, a large number of infants were fed completely at the breast or completely with nonhuman milk, so the continuous results presented in Table 4 could be driven by patterns in these extreme groups. However, we eliminated these infants to limit the contribution of extreme values to the estimates but observed similar findings.

The strengths of this study include that the Infant Feeding Practices Study II was the largest longitudinal study on infant feeding practices in the United States, the reporting bias for the feeding variables was minimized by a short 7-day retrospective recall at a monthly interval, and the residual effects of other variables were limited by controlling a wide range of potentially confounding variables in the multilevel analysis. Of the many advantages of multilevel analyses, individual growth modeling accounts for correlated data from repeated weight measurements as well as the changes in feeding categories from time to time on an individual basis.^{34,35}

In conclusion, regardless of milk type in the bottle, bottle-feeding might be distinct from breastfeeding in its effect on infant weight gain. Feeding at the breast needs to be the first feeding choice for babies. When feeding at the breast is not always feasible, supplementing breastfeeding with expressed breastmilk is a good alternative, but special attention is needed for infants' internal feeding cues while bottle-feeding.

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