Do Infants Fed From Bottles Lack Self-regulation of Milk Intake Compared With Directly Breastfed Infants?

WHAT'S KNOWN ON THIS SUBJECT: Breastfeeding reduces the risk of developing childhood obesity.

WHAT THIS STUDY ADDS: How breastfeeding reduces the risk of childhood obesity is unclear; in our study we tested the potential mechanism pertaining to the ability of breastfed infants to self-regulate their energy intake.

abstract

OBJECTIVE: How breastfeeding reduces the risk of childhood obesity is unclear, and 1 hypothesis pertains to the ability of breastfed infants to self-regulate. We studied whether infants' self-regulation of milk intake is affected by feeding mode (bottle versus breast) and the type of milk in the bottle (formula versus expressed breast milk).

PATIENTS AND METHODS: Participants in the 2005–2007 Infant Feeding Practices Study II received monthly questionnaires during their infant's first year, and compete data were available for 1250 infants. We tested the impact of feeding mode and type of milk during early infancy on self-regulation during late infancy.

RESULTS: Although only 27% of infants fed exclusively at the breast in early infancy emptied the bottle or cup in late infancy, 54% of infants who were fed both at the breast and by bottle did so, and 68% of those who were fed only by bottle did so. Multivariate regression analysis indicated that infants who were bottle-fed more intensively early in life were ~71% or 2 times more likely to empty the bottle or cup later in life than those who were bottle-fed less intensively (⅓–⅔ or ⅔ of milk feeds given by bottle versus <⅓ of milk feeds). When feeding formula and expressed milk were considered separately, similar dose-response relationships were observed.

CONCLUSIONS: Infants who are bottle-fed in early infancy are more likely to empty the bottle or cup in late infancy than those who are fed directly at the breast. Bottle-feeding, regardless of the type of milk, is distinct from feeding at the breast in its effect on infants' self-regulation of milk intake. *Pediatrics* 2010;125:e1386–e1393

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KEY WORDS

self-regulation, bottle-feeding, direct breastfeeding, childhood obesity

ABBREVIATIONS

IFPS—Infant Feeding Practices Study
NNS—nonnutritive sucking
NS—nutritive sucking

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The estimated percentage of children aged 2 to 5 and 6 to 11 years in the United States classified as overweight increased from 5.0% and 6.5%, respectively, in 1980 to 12.4% and 17.0%, respectively, in 2005–2006.[1–3] The increase in childhood obesity was also observed among children aged 6 to 23 months, from 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 major public health challenge.[8]

Feeding practices affect growth and body composition in infancy,[9–14] and many studies have shown that breastfed infants have a continued lower risk for later childhood obesity.[15–18] The mechanisms for the association between breastfeeding and obesity are unclear. One hypothesis pertains to the ability of breastfed infants to self-regulate their energy intake to match their energy needs.[19] Infants fed directly at the breast must actively suckle to draw milk out, whereas infants are passive when being fed from a bottle. The control of caregivers in bottle-feeding could lead to infants' poor self-regulation on the basis of internal cues of hunger and satiety. Theoretically, feeding infants human milk in a bottle would have a similar negative effect on self-regulation as feeding formula in a bottle. There have been few systematic efforts to explore the mechanisms underlying the association between breastfeeding and obesity, and to our knowledge, no available studies have examined whether infants' self-regulation may be affected by how the milk is delivered (bottle versus breast) and whether these effects differ according to type of milk in the bottle (formula versus human milk).

Our purpose was to explore whether infants' self-regulation of milk intake is a possible mechanism behind the relationship between breastfeeding and childhood obesity. Specifically, we tested 2 hypotheses: (1) compared with infants fed directly at the breast in early infancy, infants who are bottle-fed are more likely to empty the bottle or cup offered to them in late infancy; and (2) the use of a bottle, not the type of the milk in the bottle, is more important in limiting infants' ability to self-regulate milk intake.

PATIENTS AND METHODS

Sample

The sample was taken from the Infant Feeding Practices Study (IFPS) II, a US population-based longitudinal study (2005–2007) conducted collaboratively by the US Food and Drug Administration and the Centers for Disease Control and Prevention. The IFPS II sample was drawn from a US national consumer-opinion panel and consisted of mothers 18 years or older with healthy newborns whose gestational age at birth was ≥35 weeks and whose birth weight was ≥5 lb. Infants were followed longitudinally with questionnaires mailed almost monthly until 12 months of age. We included 1597 infants for whom there were data on how often the infant emptied the milk in the bottle or cup offered to them during the second half-year of infancy; of these infants, there were complete data for 1250 infants for the regression analysis. Infants who never received milk from a bottle or cup in the second half-year of infancy were excluded. The details of the overall IFPS II design and response rates are available elsewhere.[20]

Outcome Measures

We divided the IFPS II data into the first and second half-years of infancy. Whether infants completely emptied the milk in the bottle or cup offered to them in late infancy was used to indicate infants' self-regulation of milk intake.

Because energy intake is difficult to measure in most settings, other measures such as emptiness of bottles, bowels, and plates have been used to indicate food regulation.[21–23] For this study, bottle-emptying initiated by infants was used as an indicator for self-regulation of milk intake and measured by asking 2 survey questions at 7, 9, 10.5, and 12 months and using a 5-point Likert scale: (1) "How often does your infant drink all of his or her cup or bottle of formula?" and (2) "How often does your infant drink all of his or her cup or bottle of pumped milk?"

We estimated the average Likert score of these questions for infants with at least 2 responses during the second half-year. We then categorized this average score into a binary outcome: "yes" represented infants who "most of time" or "always" emptied the bottle, and "no" represented infants who "never," "rarely," or "sometimes" emptied the bottle.

Main Exposures

To examine whether infants' self-regulation in the second half-year of infancy was affected by how milk was delivered in the first half-year, feeding mode (breast only, bottle and breast, or bottle only) and bottle-feeding intensity (the percentage of milk feeds given by bottle) were used as main exposure variables in this study.

There are 4 types of milk-feeding categories: (1) breast milk fed directly at mother's breast (breastfed milk); (2) expressed human milk fed by bottle (expressed milk); (3) formula milk fed by bottle (formula); and (4) other milks fed by bottles (such as cow's milk or soy milk). Because feeding infants 1 type of milk more frequently implies less frequency of other types, percentages of milk feeds from a particular milk type among total milk feeds (intensity measures) were used rather than the absolute frequency of feeding

each type of milk to show the shifting across different milk feedings. At each survey, mothers were asked to indicate how often their infants were fed breast milk, formula, other milks, and various types of other foods and drinks in the previous 7 days. In addition, mothers were asked, "How many times in the past 7 days was your infant fed pumped breast milk to drink, including breast milk expressed in any way as pumped milk?" From these responses, we estimated the intensity of feeding each type of milk. With expressed-milk–feeding intensity as an illustration, its calculation can be described in a simple way as (expressed milk/[breastfed milk + expressed milk + formula milk + other milks]) × 100%.

Although each survey targeted a particular infant age, some mothers did not complete the survey on time, and their infants' ages were out of the targeted age range. To match the age at which feeding data were collected with the infants' actual age, we used the procedure described by Grummer-Strawn et al[24] to regroup the feeding data during the first half-year into the following age categories: 3 to 6 weeks (~1 month), 7 to 10 weeks (~2 months), 11 to 14 weeks (~3 months), 15 to 18 weeks (~4 months), 19 to 23 weeks (~5 months), and 24 to 28 weeks (~6 months). The mean intensity of feeding each type of milk over the first half-year was then calculated for infants who had at least 3 of 6 possible intensity measures during this period. On the basis of the mean intensity measures for feeding breastfed milk, expressed milk, and formula, a total of 7 mutually exclusive milk feeding practices were identified: breastfed milk; expressed milk; formula; breastfed milk and expressed milk; breastfed milk and formula; expressed milk and formula; and breastfed milk, expressed milk, and formula. These practices were further grouped according to 3 different feeding modes: (1) fed only at the breast; (2) fed at the breast and by bottle; and (3) fed only by bottle.

To examine the dose-response effect of bottle-feeding regardless of the type of milk, bottle-feeding intensity was calculated as the sum of formula- and expressed-milk–feeding intensities and considered to be "low" if less than one-third of total milk feeds were given by bottle, "medium" if one-third to two-thirds were given by bottle, and "high" if more than two-thirds were given by bottle.

Other Measures

To control for potentially confounding effects in our multivariate analyses, we adjusted for sociodemographic characteristics, maternal prepregnancy BMI, maternal smoking status 3 months after delivery, infant age at first introduction of solid food, infant age at which a bottle of formula or expressed milk was first introduced, average frequency of bottle-feeding other than formula or expressed milk during the first half-year, and infants' *z* score of weight-for-age at the last clinic visit (Table 1).

Mothers' BMI was computed as weight/height^2 (kg/m^2). An infant's age at which solid food was first introduced was derived from the mother's first positive response to the questions about feeding solid foods. Because bottle-fed infants may learn to finish a bottle by being introduced to bottles earlier regardless of type of milk, we created a covariate for the earliest age at which a bottle of formula or expressed milk was introduced. We also created a covariate for frequency of bottle-feeding of liquids other than milk during the first half-year. Because of the confounding effect of infants' weight on the relationship between bottle-feeding and self-regulation of milk intake, we controlled the *z* score of weight-for-age for the weight measured at the last clinic visit by using the Centers for Disease Control and Prevention growth charts.[25] In addition, we adjusted for the age at which the question for the outcome variable was answered during the second half-year to eliminate the confounding effects of age at the measurement of outcome.

Statistical Analysis

We first calculated the percentage of infants who completely emptied the milk in the bottle or cup in late infancy according to each early-infancy feeding category and then compared the differences according to feeding mode (only fed at the breast, fed at the breast and by bottle, or only fed by bottle) by using χ^2 tests. To examine the dose-response relationship between bottle-feeding and self-regulation, we applied multiple logistic regressions to model the probability of emptying the bottle or cup in late infancy as a function of bottle-feeding intensity in early infancy. We controlled for all the covariates listed in Table 1, plus the age at which the outcome variable was measured. Bottle-feeding intensity was entered into the model as either a continuous variable or a categorical variable with 3 levels (less than one-third, one-third to two-thirds, or more than two-thirds of milk feeds by bottle).

To test the hypothesis that bottle-feeding is more important than the type of the milk in the bottle in limiting infants' ability to self-regulate milk intake, we analyzed bottle-feeding intensity separately for formula and expressed milk. Because both the type of milk and the mode of delivering milk to infants might play roles in self-regulation, we entered the formula and expressed-milk–feeding intensities in the multivariate model simultaneously to control for the effect of one on the other. Formula- and expressed-milk–feeding intensities were entered

TABLE 1 Characteristics of the Study Sample ($N = 1597$), IFPS II: United States, May 2005 to June 2007

Maternal age, *n* (%)	
18–24 y	303 (18.98)
25–29 y	497 (31.14)
30–34 y	497 (31.14)
≥35 y	299 (18.73)
Parity, *n* (%)	
Primiparous	494 (31.59)
Multiparous	1070 (68.41)
Maternal education, *n* (%)	
High school or less	291 (19.32)
Some college	539 (35.79)
College graduate	676 (44.89)
Household income, % of federal poverty index, *n* (%)	
<185	588 (36.82)
185 to <350	563 (35.25)
≥350	446 (27.93)
Participation in the Supplemental Nutrition Program for Women, Infants, and Children, *n* (%)	
Yes	571 (35.75)
No	1026 (64.25)
Race/ethnicity, *n* (%)	
Non-Hispanic white	1336 (85.86)
Non-Hispanic black	63 (4.05)
Hispanic	92 (5.91)
Other	65 (4.18)
Prepregnancy BMI, kg/m^2, *n* (%)	
Underweight (<19.8)	153 (9.71)
Normal (19.8–26.0)	711 (45.11)
Overweight (>26.0 to 29.0)	254 (16.12)
Obese (>29.0)	458 (29.06)
Maternal smoking 3 mo after delivery, *n* (%)	
Yes	212 (14.65)
No	1235 (85.35)
Infant gender	
Boy	794 (49.75)
Girl	802 (50.25)
Gestational age, *n*; mean (SD), wk	1597; 39.31 (1.27)
Birth weight, *n*; mean (SD), kg	1597; 3.45 (0.45)
Age at which solid food was first given, *n*; mean (SD), wk	1597; 19.59 (6.85)
Age at which bottle of formula or expressed milk was first introduced, *n*; mean (SD), wk	1597; 2.78 (5.43)
Mean bottle feeds other than formula or expressed milk in early infancy, *n*; mean (SD), times per day	1597; 0.20 (0.62)
z score of weight-for-age at the last measurement, *n*; mean (SD)	1554; −0.14 (1.17)

into the models as either continuous or dummy variables. The fitness of multiple logistic regression models was assessed by using the Hosmer-Lemeshow goodness-of-fit statistic,[26] and all the analyses were conducted by using SAS 9.2 (SAS Institute, Inc, Cary, NC).

RESULTS

We excluded 280 infants whose mothers reported that they did not feed either formula or expressed milk in the second half of infancy, and we excluded 4 infants for whom there were feeding data from early infancy but no answers to the outcome questions on bottle-emptying in late infancy. Of the 1597 infants for whom there were data on the outcome variables, data for 52 infants were not provided on formula-feeding intensity; data for 14 infants were not provided on expressed-milk–feeding intensity; 24 infants were fed from cups only during the first half-year, which may have different effects than feeding from a bottle; and data for 257 infants were not provided on other covariates. These eliminations left us with 1250 infants whose data could be used in the multivariate analyses.

Characteristics of the 1597 mothers whose infants had data on emptying milk in the bottle or cup during the second half-year are listed in Table 1, along with selected feeding characteristics and the average *z* score of weight-for-age for the weight measured at the last clinic visit.

Figure 1 shows the mean percentage of milk feeds that were directly from the breast, expressed milk, formula, or other milks at each month of age until 6 months. Although mean direct breastfeeding intensity decreased from 52% at 1 month to 27% at 6 months, mean formula-feeding intensity increased from 41% to 66%. Expressed-milk–feeding intensity re-

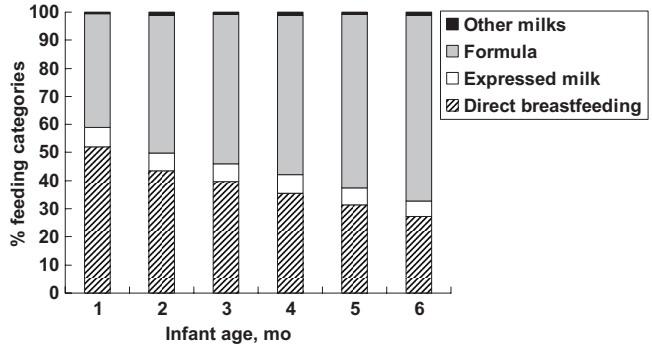

FIGURE 1
Mean percentage of milk feeds that were directly from the breast, expressed milk, formula, and other milks at each month of age. $n = 998$, 1238, 1380, 1305, 1392, and 1378, respectively, for 1, 2, 3, 4, 5, and 6 months of age.

mained constant over the first half-year, and few infants were fed with milk other than formula or breast milk.

Table 2 summarizes the distribution of bottle-, formula-, and expressed-milk–feeding intensity over the first half-year of infancy. Although only a small number of infants were fed with medium or high expressed-milk intensity, ~50% of the infants were fed with high formula intensity during this period.

Table 3 compares the percentage of infants who completely emptied the bottle or cup during the second half-year among different modes of milk delivery during the first half-year. Although only 27% of the infants who were fed exclusively at the breast in early infancy emptied the milk in the bottle or cup given to them in late infancy, 54% of the infants who were fed both at the breast and by bottle did so, and 68% of the infants who were fed only by bottle did so. Figure 2 shows the percentage of infants who finished the bottle during the second half-year according to intensity of bottle use during the first half-year. Results were considered separately for any type of milk in the bottle, formula only in the bottle, and expressed milk only in the bottle during the first half year. Regardless of the type of milk in the bottle, a similar trend was observed for more bottle-feeding early in life and more infant-led emptying of milk bottles or cups later in life.

Results of our multiple logistic regression analyses indicated dose-response relationships between bottle-feeding and self-regulation of milk intake. Specifically, a 10% increase in bottle-feeding intensity during the first half-year increased the rates of infant-led emptying of milk from bottles or cups by 9%, and infants who were given bottles more intensively early in life were ~71% or 2 times more likely to empty the bottle or cup later in life than those bottle-fed less intensively (one-third to

TABLE 2 Distribution of Bottle-Feeding of Formula and Expressed Milk During the First Half-Year of Infancy, IFPS II: United States, May 2005 to June 2007

	Bottle-Feeding Intensity	Formula-Feeding Intensity	Expressed-Milk–Feeding Intensity
Sample size, *n*	1531	1545	1531
Mean (SD)	62.5 (39.2)	55.7 (42.4)	6.3 (13.4)
Intensities of milk feeding in early infancy, %[a]			
Low	32.7	38.6	95.6
Medium	12.3	10.9	3.3
High	55.0	50.5	1.1
Total	100	100	100

[a] $P < .01$, measured by using a χ^2 test for equal proportions for each milk-feeding column. We considered bottle-fed formula or expressed-milk–feeding intensity to be "low" if less than one-third of milk feeds were formula or expressed-milk fed by bottle, "medium" if one-third to two-thirds were formula or expressed-milk fed by bottle, and "high" if more than two-thirds were formula or expressed-milk fed by bottle.

Bottle-feeding intensity is percentage of milk feeds that were a bottle of either formula or expressed milk. Formula-feeding intensity is percentage of milk-feeds that were formula, and expressed-milk–feeding intensity is percentage of milk feeds that were expressed milk.

TABLE 3 Percentage of Infants Completely Emptying Their Bottle or Cup of Formula or Expressed Milk During the Second Half-Year of Infancy According to Feeding Mode During the First Half-Year of Infancy, IFPS II: United States, May 2005 to June 2007

Feeding Mode in Early Infancy	Infants Finishing the Bottle in Late Infancy	
	n	% Yes (95% Confidence Interval)
Only fed at the breast (exclusive direct breastfeeding)	22	27.3 (8.7–45.9)
Fed at the breast and bottle	920	53.8 (50.6–57.0)
Direct breastfeeding + expressed milk	226	46.9 (40.4–53.4)
Direct breastfeeding + formula	179	55.3 (48.0–62.6)
Direct breastfeeding + expressed milk + formula	515	56.3 (52.0–60.6)
Fed only by bottle	542	67.9 (64.0–71.8)
Only fed expressed milk	3	66.7 (13.3–120.0)
Only fed formula	513	68.0 (64.0–72.1)
Fed both expressed milk and formula	26	65.4 (47.1–83.7)
All infants	1484	58.6 (56.1–61.1)

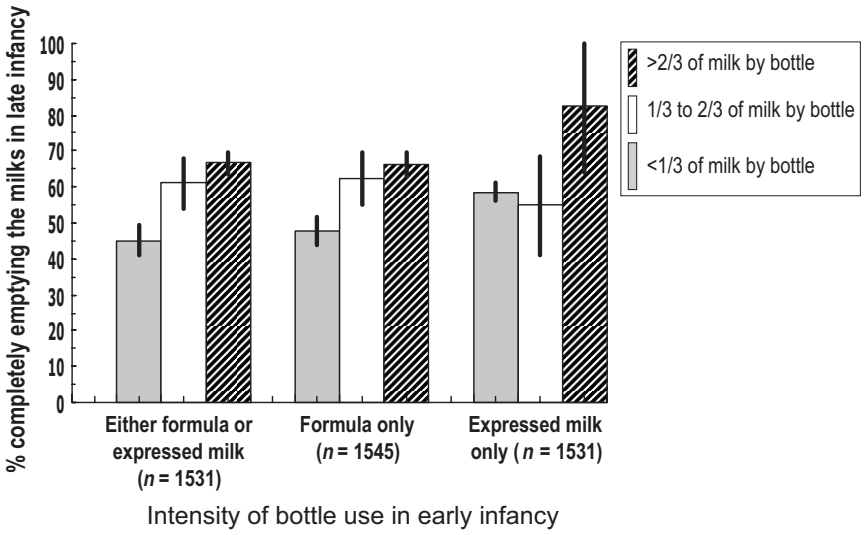

FIGURE 2
Percentage of infants completely emptying the milk in the bottle or cup in late infancy according to intensity of bottle use in early infancy. A confidence interval of 95% is indicated by the line on each bar.

TABLE 4 Estimated Adjusted Odds Ratio and 95% Confidence Interval for Infants Who Completely Emptied Their Bottle or Cup of Formula or Expressed Milk During the Second Half-Year of Infancy ($N = 1250$), IFPS II: United States, May 2005 to June 2007

	Adjusted Odds Ratio	95% Confidence Interval
Overall bottle-feeding intensities during the first half-year of infancy[a]		
I. Bottle-feeding intensity was treated as a continuous variable with a metric in 10%	1.09	1.05–1.13
II. Bottle-feeding intensities were treated as dummy variables		
Low (less than one-third of milk feeds by a bottle)	Reference	
Medium (one-third to two-thirds of milk feeds by a bottle)	1.71	1.16–2.52
High (more than two-thirds of milk feeds by a bottle)	2.03	1.50–2.74
Formula- or expressed-milk–feeding intensities during the first half-year of infancy[b]		
III. Formula-feeding intensity was treated as a continuous variable with a metric in 10%	1.09	1.05–1.13
Expressed-milk–feeding intensity was treated as a continuous variable with a metric in 10%	1.15	1.04–1.27
IV. Formula-feeding intensities were treated as dummy variables		
Low (less than one-third of milk feeds were formula)	Reference	
Medium (one-third to two-thirds of milk feeds were formula)	1.81	1.21–2.72
High (more than two-thirds of milk feeds were formula)	1.80	1.33–2.43
Expressed-milk–feeding intensities were treated as dummy variables		
Low (less than one-third of milk feeds were expressed milk)	Reference	
Medium (one-third to two-thirds of milk feeds were expressed milk)	0.81	0.41–1.62
High (more than two-thirds of milk feeds were expressed milk)	5.71	1.57–20.68

[a] The multivariate models listed were controlled for all variables listed in Table 1 and for the age at which the outcome variable was measured.

[b] In models III and IV, formula- and expressed-milk–feeding intensity were entered into each multivariate model simultaneously to control for each other's effect.

two-thirds or more than two-thirds of milk feeds given by bottle versus less than one-third) (Table 4). When formula- and expressed-milk feedings were considered separately, similar dose-response relationships were observed.

DISCUSSION

We confirmed our hypothesis that infants who are bottle-fed in early infancy are more likely than those who are fed directly at the breast to empty the milk in the bottle or cup offered to them in late infancy. The more frequently the infant was fed by bottle early in life, the more likely the infant was to empty the bottle or cup later in life. Bottle-feeding, regardless of type of milk in the bottle, is distinct from feeding at the breast in its effect on infants' self-regulation of milk intake.

The association between breastfeeding and reduced childhood obesity has been well established.[15–17] However, the mechanism that explains this association has yet to be clarified. Authors of previous studies have suggested that unique properties of human milk, such as leptin and adiponectin, might be biological mechanisms in reducing the risk of obesity.[27–29] Another possible mechanism is the ability of breastfed infants to self-regulate their energy intake to balance their energy needs. It has been proposed that infants are born with some ability to regulate their energy intake in response to internal appetite cues.[30,31] However, this innate ability might be disrupted by the type of milk (human versus nonhuman) and by the feeding mode (breast versus bottle).[32]

Dewey and Lönnerdal[19] found that infants who were breastfed exclusively could self-regulate their energy intake and were able to continue to consume only what they needed even after their mother's milk supply was stimulated and increased. Heinig et al[33] found that when solid foods were introduced, breastfed infants consumed less breast milk, whereas formula-fed infants consumed the same amount of formula as before. The negative correlation between the amount consumed and the fat content of breast milk among breastfed infants and the more consistent milk consumption among formula-fed infants suggest that breastfed infants may have better self-regulation than formula-fed infants.[32–35]

The results of our study reveal that infants' self-regulation of milk intake can be affected by how the milk is delivered to them and that it is bottle-feeding, not the type of the milk in the bottle, that may be more important in self-regulation. The effect of bottle-feeding on infants' self-regulation might be explained by the following factors.

First, infants who are fed from the breast can control milk intake, because they are the ones who decide when to start and when to stop sucking. Mothers who breastfeed might develop a feeding style that is less controlling, thereby allowing their infants to maintain their natural ability to regulate their energy intake.[36] Infants who are bottle-fed are less likely to control their milk intake. The duration and amount of bottle-feeding might depend on caregivers' decisions on the basis of visual cues regarding the amount of milk remaining in the bottle. Mothers who lack confidence in their ability to produce sufficient milk find that formula-feeding enables them to quantify and visualize their infants' milk intake.[37,38] Therefore, bottle-feeding mothers may tend to routinely control the volume of milk consumed by bottle. When infants are frequently encouraged to finish a bottle even if they are full, they may not learn how to regulate their milk intake.

Second, infants fed at the breast need to suck nonnutritively until the milk-ejection reflex occurs, and it is known

that as sucking pressure decreases, the duration of each suck lengthens, and suckling frequency decreases from nonnutritive sucking (NNS) to nutritive sucking (NS).[39] This transition from NNS to NS may play an important role in establishing infants' self-regulation of milk intake. When an infant has repeated opportunities to initiate and terminate their mother's milk flow by adjusting their sucking behaviors, they may establish a greater level of responsiveness to internal cues of hunger and satiety. A study revealed that infants' sucking pressure changed from NNS to NS in the opposite direction between infants fed directly at the breast and those fed expressed milk by bottle when a 1-way valve was affixed to imitate the transition from NNS to NS. This result demonstrated that bottle-feeding is a completely different feeding mode regardless of attempts to make it more closely resemble breastfeeding.[40]

Third, milk composition and taste vary within each breastfeeding, as well as between feeds and over time, whereas they remain constant during bottle-feeding. For example, breast milk fat content toward the end of the feeding episode is much higher than that at the start of the episode, which might signal to the infant that the feeding episode is coming to an end. In contrast, bottle-fed infants are not exposed to such "physiologic signaling" during the feeding episode. Research on regulation of food intake by chemosensory receptors suggests that bottle-fed infants who had no exposure to the varied flavors of breast milk may miss the important oropharyngeal sensory experience that is needed for the development of physiologic regulation of food intake later in life.[41]

There are several limitations to this study. First, because the panel sample underrepresents black and Hispanic mothers, our results may not be applicable to the entire US population. Second, because both feeding practices and bottle-emptying behaviors were reported by mothers, reporting errors may have occurred. However, because there was no time overlap between feeding practices during the first 6 months (exposures) and infant-led bottle-emptying after 6 months (outcome), it is unlikely that the misclassification of exposure and outcome data were dependent on one another. For nondifferential misclassification such as this, reporting errors would bias the results toward the null value.[42] Third, we did not address whether self-regulation of milk intake during the infancy period relates to self-regulation of other foods and drinks later in life.

The strengths of the study include minimizing the reporting bias for both exposure and outcome measures by requesting only a short retrospective recall of the previous 7 days for each questionnaire. The residual effects of other variables were limited by controlling a wide range of confounding variables in the multivariate analysis, including sociodemographic characteristics, anthropometrics of mothers and infants, and other feeding practices that may be associated with bottle-feeding and self-regulation. Also, the study sample is national, longitudinal, and relatively large.

CONCLUSIONS

To our knowledge, this is the first study to examines infants' self-regulation in association with both feeding mode (bottle versus breast) and type of milk in the bottle (formula versus human milk). Infants fed at the breast learn and develop better control of their milk intake, whereas bottle-feeding may decrease infants' abilities to self-regulate milk intake. On the basis of our findings and the association we observed previously in the IFPS II between poor self-regulation and infants' overweight,[12] infants fed directly at the breast have better self-regulation, which in turn could mediate the relationship between breastfeeding and childhood obesity. Our results also indicate that bottle-feeding may be more important than the type of the milk in the bottle in limiting infants' ability to self-regulate milk intake.

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REFERENCES

1. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999–2000. *JAMA*. 2002;288(14):1728–1732
2. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999–2004. *JAMA*. 2006;295(13):1549–1555
3. Ogden CL, Carroll MD, Flegal KM. High body mass index for age among US children and adolescents, 2003–2006. *JAMA*. 2008;299(20):2401–2405
4. Dietz WH. Health consequences of obesity in youth: childhood predictors of adult disease. *Pediatrics*. 1998;101(3 pt 2):518–525
5. Freedman DS, Dietz WH, Srinivasan SR, Berenson GS. The relation of overweight to cardiovascular risk factors among children and adolescents: the Bogalusa Heart Study. *Pediatrics*. 1999;103(6 pt 1):1175–1182
6. Deckelbaum RJ, Williams CL. Childhood obesity: the health issue. *Obes Res*. 2001;9(suppl 4):239S–243S
7. Gortmaker SL, Must A, Perrin JM, et al. Social and economic consequences of overweight in adolescence and young adulthood. *N Engl J Med*. 1993;329(14):1008–1012
8. US Department of Health and Human Services. *The Surgeon General's Call to Action to Prevent and Decrease Overweight and Obesity*. Rockville, MD: US Department of

Health and Human Services, Office of the Surgeon General; 2001. Available at: www.surgeongeneral.gov/topics/obesity. Accessed March 16, 2010

9. Yeung DL, Pennell MD, Leung M, Hall J. Infant fatness and feeding practices: a longitudinal assessment. *J Am Diet Assoc.* 1981; 79(5):531–535
10. Baker JL, Michaelsen KF, Rasmussen KM, Sorensen TI. Maternal prepregnant body mass index, duration of breastfeeding, and timing of complementary food introduction are associated with infant weight gain. *Am J Clin Nutr.* 2004;80(6):1579–1588
11. Butte NF, Wong WW, Hopkinson JM, Smith EO, Ellis KJ. Infant feeding mode affects early growth and body composition. *Pediatrics.* 2000;106(6):1355–1366
12. Li R, Fein S, Grummer-Strawn L. Association of breastfeeding and bottle-emptying behaviors with excess weight at late infancy. *Pediatrics.* 2008;122 (suppl 2):S77–S84
13. WHO Multicentre Growth Reference Study Group. *WHO Child Growth Standards: Length/Height-for-Age, Weight-for-Age, Weight-for-Length, Weight-for-Height and Body Mass Index-for-Age: Methods and Development.* Geneva, Switzerland: World Health Organization; 2006
14. Dewey KG, Heinig MJ, Nommsen LA, Peerson JM, Lonnerdal B. Breastfed infants are leaner than formula-fed infants at 1 y of age: the DARLING study. *Am J Clin Nutr.* 1993; 57(2):140–145
15. Singhal A, Lanigan J. Breastfeeding, early growth, and later obesity. *Obes Rev.* 2007; 8(suppl 1):51–54
16. Arenz A, Rückerl R, Koletzko B, von Kries R. Breastfeeding and childhood obesity: a systematic review. *Int J Obes Relat Metab Disord.* 2004;28(10):1247–1256
17. Harder T, Bergmann R, Kallischnigg G, Plagemann A. Duration of breastfeeding and risk of overweight: a meta-analysis. *Am J Epidemiol.* 2005;162(5):397–403
18. Owen CG, Martin RM, Wincup PH, et al. Effect of infant feeding on the risk of obesity across the life course: a quantitative review of published evidence. *Pediatrics.* 2005; 115(5):1367–1377
19. Dewey KG, Lonnerdal B. Infant self-regulation of breast milk intake. *Acta Paediatr Scand.* 1986;75(6):893–898
20. Fein SB, Labiner-Wolfe J, Shealy K, Li R, Chen J, Grummer-Strawn LM. Infant Feeding Practices Study II: study methods. *Pediatrics.* 2008;122(suppl 2):S28–S35
21. Johnson SL. Improving preschoolers' self-regulation of energy intake. *Pediatrics.* 2000;106(6):1429–1435
22. Fisher JO, Birch LL, Smiciklas-Wright H, Picciano MF. Breast-feeding through the first year predicts maternal control in feeding and subsequent toddler energy intakes. *J Am Diet Assoc.* 2000;100(6):641–646
23. Kavanagh K, Cohen R, Heinig M, Dewey K. Educational intervention to modify bottle-feeding behaviors among formula-feeding mothers in the WIC program: impact on infant formula intake and weight gain. *J Nutr Educ Behav.* 2008;40(4):244–250
24. Grummer-Strawn LM, Scanlon KS, Fein SB. Infant feeding and feeding transitions during the first year of life. *Pediatrics.* 2008; 122(suppl 2):S36–S43
25. Ogden CL, Kuczmarski RJ, Flegal KM, et al. Centers for Disease Control 2000 growth charts for the United States: improvements to the 1977 National Center for Health Statistics version. *Pediatrics.* 2002;109(1): 45–60
26. Hosmer DW, Lemeshow S. *Applied Logistic Regression.* New York, NY: Wiley-Interscience; 1989
27. Houseknecht KL, McGuire MK, Portocarrero CP, McGuire MA, Beerman K. Leptin is present in human milk and is related to maternal plasma leptin concentration and adiposity. *Biochem Biophys Res Commun.* 1997;240(3):742–747
28. Qi Y, Takahashi N, Hileman SM, et al. Adiponectin acts in the brain to decrease body weight [published correction appears in *Nat Med.* 2004;10(6):649]. *Nat Med.* 2004; 10(5):524–529
29. Singhal A, Farooqi IS, O'Rahilly S, et al. Early nutrition and leptin concentrations in later life. *Am J Clin Nutr.* 2002;75(6):993–999
30. Fox MK, Devaney B, Reidy K, Razafindrakoto C, Ziegler P. Relationship between portion size and energy intake among infants and toddlers: evidence of self-regulation. *J Am Dent Assoc.* 2006;106(1 suppl 1):S77–S83
31. Birch LL, Fisher JO. Development of eating behaviors among children and adolescents. *Pediatrics.* 1998;101(3 pt 2):539–549
32. Bartok CJ, Ventura AK. Mechanism underlying the association between breastfeeding and obesity. *Int J Pediatr Obes.* 2009;4(4): 196–204
33. Heinig MJ, Nommsen LA, Peerson JM, Lönnerdal B, Dewey KG. Intake and growth of breast-fed and formula-fed infants in relation to the timing of introduction of complementary foods: the DARLING study. *Acta Paediatr.* 1993;82(12):999–1006
34. Nommsen LA, Lovelady CA, Heinig MJ, Lonnerdal B, Dewey KG. Determinants of energy, protein, lipid, and lactose concentrations in human milk during the first 12 months of lactation: the DARLING study. *Am J Clin Nutr.* 1991;53(2):457–465
35. Pérez-Escamilla R, Cohen RJ, Brown KH, Rivera LL, Canahuati J, Dewey KG. Maternal anthropometric status and lactation performance in a low-income Honduran population: evidence for the role of infants. *Am J Clin Nutr.* 1995;61(3):528–534
36. Taveras EM, Rifas-Shiman SL, Scanlon KS, Grummer-Strawn LM, Sherry B, Gillman MW. To what extent is the protective effect of breastfeeding on future overweight explained by decreased maternal feeding restriction? *Pediatrics.* 2006;118(6): 2341–2348
37. Dykes F, Williams C. Falling by the wayside: a phenomenological exploration of perceived breast-milk inadequacy in lactating women. *Midwifery.* 1999;15(4):232–246
38. Nelson AM. A metasynthesis of qualitative breastfeeding studies. *J Midwifery Womens Health.* 2006;51(2):e13–e20
39. Righard L, Alade MO. Sucking technique and its effect on success of breastfeeding. *Birth.* 1992;19(4):185–189
40. Mizuno K, Ueda A. Changes in sucking performance from non-nutritive sucking to nutritive sucking during breast- and bottle-feeding. *Pediatr Res.* 2006;59(5): 728–731
41. Poothullil JM. Regulation of nutrient intake in humans: a theory based on taste and smell. *Neurosci Biobehav Rev.* 1995;19(3): 407–412
42. Rothman KJ, Greenlan S. *Modern Epidemiology.* 2nd ed. Philadelphia, PA: Lippincott-Raven; 1998