Are the stool characteristics of preterm infants affected by infant formulas?

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SUMMARY: Duman N, Utkutan S, Özkan H, Özdoğan Ş. Are the stool characteristics of preterm infants affected by infant formulas? Turk J Pediatr 2000; 42: 138-144.

The aim of this study was to investigate the relationship between the type of formula consumed and the stool characteristics and gastrointestinal symptoms of preterm infants prospectively. Seventy-five preterm infants weighing < 2000 g in our neonatal intensive care unit (NICU) were investigated. Four groups of 15 each were fed one of four commercial formula preparations (Prematil, Nenatal, Humana-0 and S-26) and the fifth group was breast-fed in a prospective, randomized, double-blind study. The stool characteristics and gastrointestinal problems were recorded daily from the first day till the time they were discharged by the nurses of NICU. No significant differences of daily weight gain was observed between the groups. No significant difference was observed in daily frequency of stool, distention, vomiting and gas passage between the groups during the enteral+parenteral and full-enteral nutrition periods. The infants fed by Prematil during the enteral+parenteral nutrition period had a higher percentage of hard stool occurrence than infants receiving Humana-0 and breast milk. In the full-enteral nutrition period, infants receiving Prematil had a higher percentage of hard stool occurrence than all the other groups, whereas breast-fed infants had a lower percentage of hard stool than all the other groups. While the group fed with Humana-0 had a higher percentage of green stool occurrence in the enteral+parenteral nutrition period, no significant difference was observed in the full-enteral nutrition period. In the enteral+parenteral nutrition period no additional therapy affected stool characteristics or the gastrointestinal system except in the case of the infant receiving phototherapy for whom the daily number of detections was significantly high. In this study, it was shown that the color and consistency of stool in preterm infant differs according to the preterm infant formulas, but no differences were observed in the frequency of defecation or in gastrointestinal system problems. When the infant formulas were compared with breast milk, it was shown that they cause a higher percentage of hard stool occurrence. An increased number of formula feedings are necessary to obtain a similar daily weight gain, but the color and the frequency of the stool and the gastrointestinal system problems were similar for breast-fed and formula-fed infants.

Key words: breast feeding, infant formulas, stool characteristics.

While the effects of breast-feeding on stool characteristics are well known, few studies have been published about the effects of different formulas[1-3]. Preterm infants, although in need of more, have a lower ratio of breast-feeding due to their prematurity and maternal health problems. However, knowledge about the effects of premature formulas on the stool characteristics in insufficient. What we know is mostly about the effects of enteral nourishment on the first stool passage[4-10]. Many premature infants are switched between multiple formula preparations either in the neonatal intensive care unit (NICU) or after discharge from the hospital because of perceived abnormalities in the stooling pattern as well as gastrointestinal symptoms.

This stuy has been designed prospectively to reveal the effects of breast-milk and four different formulas on stool characteristics and gastrointestinal symptoms of premature infants.

Material and Methods

Infants born in Dokuz Eylül University Hospital or transferred from another hospital on their first day to the NICU between January 1996 and November 1997 with a birth weight less than 2000 g were enrolled in the study. The infants were fed with breast milk or one of four different formulas (Prematil, Nenatal, Humana 0, and S-26) prepared for low birth weight infants in a randomized, double-blind prospective study. Composition of the study formulas is shown in Table I. The formulas were used only in the absence of breast milk. Infants with feeding alterations were excluded from the study (e.g. Infants fed by formulas at the beginning but changed to breast-milk in the following days or those first fed by breast-milk but needing additional nutrients).

Table I. Composition of Study Milk

	Breast	Prematil	Nenatal	Humana 0	S-26
Carbohydrate g/100 ml	6.8 (lactose)	7.7 (lactose, maltodextrine)	8 (lactose, corn syrup solids)	8.2 (lactose, maltodextrine)	8.4 (lactose, maltodextrine)
Protein g/100 ml	0.9 40% casein 60% whey	2 40% casein 60% whey	2.2 40% casein 60% whey	2 50% casein 50% whey	1.6 40% casein 60% whey
Fat g/100 ml	3.8	3.5 (milk, vegetable and animal fats)	4.4 (vegetable and milk fats)	3.8 (vegetable fat)	4.3 (vegetable and animal fats)
Iron mg/100 ml	0.3	0.07	0.9	1.1	0.38
Energy kcal/100 ml	71	70	80	75	79

Infants with anatomic, metabolic or neurological pathologies which could effect gastrointestinal system function were also excluded from the study.

The nurses of the NICU recorded the following daily: the time of passage of first stool and beginning of enteral and full-enteral feeding; the volumes of enteral feeding; changes in body weight; treatments which may affect the stool characteristics (antibiotics, aminophylline, calcium, indomethacin, furosemide, steroid, iron, phototherapy); stool frequency, color and consistency; and gastrointestinal problems (gas, vomiting, distention). The nurses referred to a special card[11] to evaluate the consistency and color of the stool objectively. A scoring system was used for evaluating gas and vomiting characteristics. According to this system no gas was defined as absent or minimal gas (0 point), "mild" connoted gas passed several times during the day (1 point), and "severe" referred to very frequent gas passage (2 points). Vomiting was described as none (0 point), "few" if it occurred no more than twice daily and involved only a mouthful of milk (1 point), and "many" if there were three or more episodes of effortless emesis or forceful vomiting (2 points). All the parameters were evaluated in two different categories, the parenteral+enteral feeding period and the full-enteral feeding period.

Statistical Analysis: Information form the daily logs of stool characteristics was summarized as follows. Totals for the parenteral+enteral and full-enteral feeding periods were obtained by adding daily totals for number of stools, and the number each of yellow, brown, or green stools, and of hard, firm, or watery stools. An average daily stool number was calculated. Stool color and consistency totals were expressed as the percentage of all stools for each feeding period.

The scores of gas and vomiting characteristics and distention occurrence were calculated for each day and expressed as the percentage of the total day per each period. The average of these values for each infant were calculated. Group means for each feeding type were calculated for all these values per each period. Group means for each feeding type were also calculated for the following: birth weight, gestational age, body weight at the time of discharge, time of passage of first stool, time birth weight was

regained and the time enteral and full-enteral feeding were begun. Group means of the daily weight gain and volume of milk ingested were calculated only during the full-enteral feeding period for each feeding type. If the group mean differences were statistically significant with Kruskal-Wallis one-way analysis of variance test ($p < 0.05$), Mann-Whitney U test was used for multiple group comparisons. The effects of additional therapies on stool frequency, color, consistency and gas, distention, and vomiting characteristics during the parenteral+enteral feeding period were evaluated. An error of < 5% was accepted as evidence of statistical significance.

Results

A total of 75 infants, 15 infants from each group, completed the study. Eighteen infants with a deviation from feeding protocol and two infants who were operated because of perforated necrotizing enterocolitis during the parenteral+enteral feeding period (in Humana 0 group) were excluded from the study. No infant was dropped from the study because of milk related problems. The results of the study were derived from the observation of 4,835 stools passed by 75 preterm infants during 2,097 infants days.

The characteristics of the study infants are shown in Table II. Sex, the time of passage of first stool, beginning of enteral feeding, regaining of the birth weight and body weight at the time of discharge were not statistically different for all feeding groups.

However, breast-fed infants had a lower birth weight ($p = 0.485$, $p = 0.0061$, $p = 0.0368$, respectively) and gestational age ($p = 0.0171$, $p = 0.0044$, $p = 0.0172$, respectively) than infants fed by Prematil, Humana 0 or S-26. Full-enteral feeding was started earlier in the Humana 0 group tahn in the breast-fed or Nenatal groups ($p = 0.0021$, $p = 0.0053$, respectively). In the full-enteral feeding period, the volume of milk ingested was less in breast-fed infants than in infants fed Prematil, Nenatal or Humana 0, whereas no significant difference in daily weight gain ($p = 0.0009$, $p = 0.0179$, $p = 0.0051$, respectively) was observed during the same period. But breast-fed infants with a lower birth weight were discharged from the hospital with a lower body weight than infants in the Prematil, Nenatal, and Humana 0 groups ($p = 0.0066$, $p = 0.0249$, $p = 0.0084$, respectiely).

Stool Frequency: The relationship of milk type to stooling frequency is shown in Tables III and IV. No significant difference was observed in the full-enteral feeding period ($p = 0.1224$). Stool numbers were similar in all feeding groups in the same period ($p = 0.1173$). Only stooling frequency was compared in the parenteral+enteral feeding period because it differs from infant to infant, but no significant difference was observed ($p = 0.2569$). Although not statistically significant, stooling frequency was observed to be higher in those infants receiving breast milk compared with the other four formulas in both periods.

Table II. Characteristics of the Study Groups

	Breast	Prematil	Nenatal	Humana 0	S-26
Number completing study	15	15	15	15	15
Birth weight (g)	1340 ± 363* (750-2000)	1642 ± 350 (1030-2000)	1577 ± 288 (995-2000)	1751 ± 283 (1185-2000)	1676 ± 308 (1000-2000)
Gestational age (wk)	29.7 ± 2.4*	31.7 ± 1.8 (28-34)	31.3 ± 2.3 (28-35)	32.3 ± 1.9 (27-35)	32.1 ± 1.9 (28.34)
Male-Female (no)	8/7	7/8	9/6	6/9	5/10
First stool passage time (d)	2 ± 0.9 (1-3)	1.4 ± 0.5 (1.-2)	1.5 ± 0.7 (1-3)	1.6 ± 0.7 (1-3)	1.7 ± 0.9 (1-3)
Length of hospital stay (d)	46.2 ± 30.4 (13-111)	25.2 ± 14.7 (11-64)	29.7 ± 15.7 (13-58)	20.7 ± 11.2 (9-48)	28.6 ± 22.0 (10-59)
Beginning of enteral feeding (d)	4.3 ± 2.6 (2-10)	5.1 ± 4.6 (2-15)	5.0 ± 4.0 (1-16)	3.7 ± 1.8 (2-7)	5.0 ± 6.3 (1-20)
Switch to full-enteral feeding (d)	22.9 ± 14.1 (7-55)	13.5 ± 8.1 (4-30)	19.7 ± 12.8 (7.49)	9.7 ± 4.6* (3.21)	18.4 ± 20.1 (3-53)
Volume of milk ingested in full-enteral feeding (ml)	34 ± 3* (30-41)	36 ± 2 (32-39)	36 ± 2 (34-39)	36 ± 2 (34-38)	35 ± 3 (30-39)
Daily weight gain in full-enteral feeding period (g)	28 ± 8 (10-41)	25 ± 11 (9-46)	28 ± 10 (8-51)	25 ± 10 (9-41)	23 ± 9 (10-37)
Body weight at the time of discharge (g)	1800 ± 154* (1550-2000)	1919 ± 102 (1690-2105)	1909 ± 107 (1745-2055)	1929 ± 101 (1790-2065)	1864 ± 134 (1670-2150)

Data expressed as mean ± standard deviation (min-max) *$p < 0.05$.

Table III. Stooling Frequency in the Full-enteral Feeding Period

Milk type	Total stools/7 days* Mean ± SEM (min-max)	Daily stools* Mean ± SEM (min-max)
Breast	25.07 ± 3.32 (7-41)	3.58 ± 0.47 (1-5.86)
Prematil	18.34 ± 2.4 (7-34)	2.62 ± 0.31 (1-4.86)
Nenatal	17.7 ± 2.1 (8-35)	2.52 ± 0.30 (1.14-5.0)
Humana 0	18.1 ± 1.4 (11-26)	2.63 ± 0.20 (1.57-3.71)
S-26	13.1 ± 2.7 (4-26)	1.87 ± 0.38 (0.57-3.71)

* $p > 0.05$, SEM: Standard error of mean.

Table IV. Stooling Frequency in the Parenteral+Enteral Feeding Period

Milk type	Daily stools* Mean ± SEM (min-max)
Breast	2.79 ± 0.38 (1.24-7.16)
Prematil	2.29 ± 0.23 (1-4)
Nenatal	1.89 ± 0.30 (0.5-4.5)
Humana 0	2.03 ± 0.20 (1.2-4)
S-26	1.98 ± 0.35 (0.67-3.75)

* $p > 0.05$, SEM: Standard error of mean.

Stool color: The relationship of stool color to type of infant feeding is shown in Figs. 1 and 2. In the parenteral+enteral feeding period no significant difference was observed in brown stool where as green stool was more common in the infants fed Humana 0 than in the other groups. However, no significant difference was observed between the groups in stool color during the full-enteral feeding period.

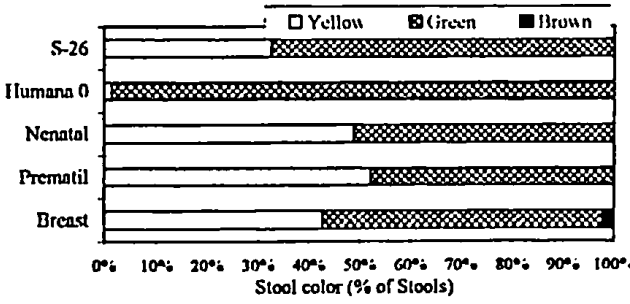

Fig. 1. Relationship of infant formula to stool color in the parenteral+enteral feeding period.

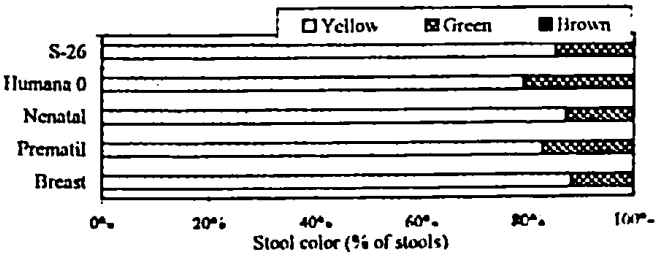

Fig. 2. Relationship of infant formula to stool color in the full-enteral feeding period.

Stool Consistency: In the parenteral+enteral feeding period, hard stools were significantly more frequent in those infants fed Prematil than in the breast-milk or Humana 0 groups ($p = 0.0228$, $p = 0.0033$, respectively) and similarly in infants fed Nenatal than in the Humana 0 group ($p = 0.0352$). No significant difference was observed between the groups in terms of watery stool (Fig. 3). In the full-enteral feeding period, hard stools were significantly more frequent in the Prematil group compared with all the others. In the same period no significant difference was observed in terms of watery stool. However, firm stool was more common in those infants fed Nenatal, Humana 0, S-26 or breast-milk than in the infants fed Prematil ($p = 0.0080$, $p = 0.0036$, $p = 0.0249$, $p = 0.0104$, respectively) (Fig. 4).

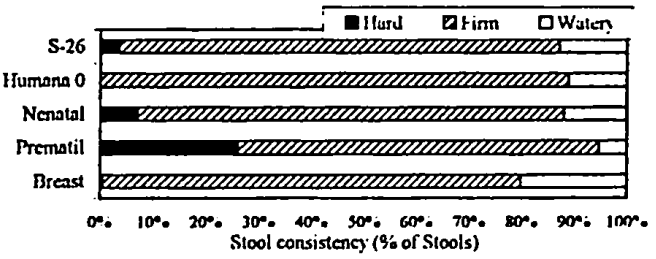

Fig. 3. Relationship of infant formula to stool consistency in the parenteral+enteral feeding period.

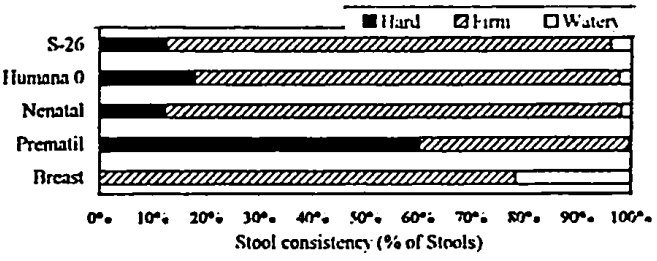

Fig. 4. Relationship of infant formula to stool consistency in the full-enteral feeding period.

Distention, Vomiting and Gas: The relationship of type of milk ingested to gas, distention and vomiting is shown in Figs. 5, 6, 7, 8, 9 and 10, for both feeding periods. No significant difference was observed between the groups.

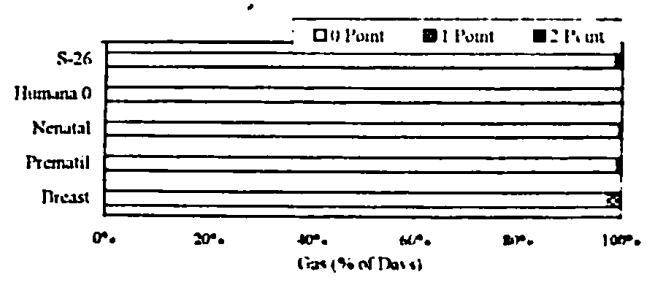

Fig. 5. Relationship of infant formula to gas in the parenteral+enteral feeding period.

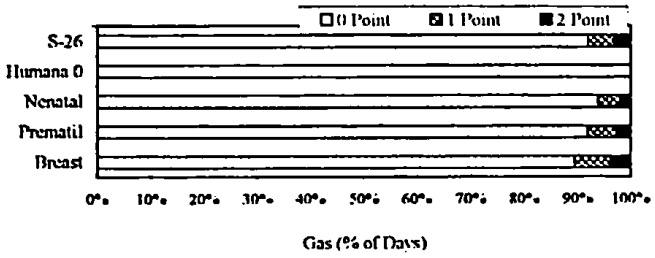

Fig. 6. Relationship of infant formula to gas in the full-enteral feeding period.

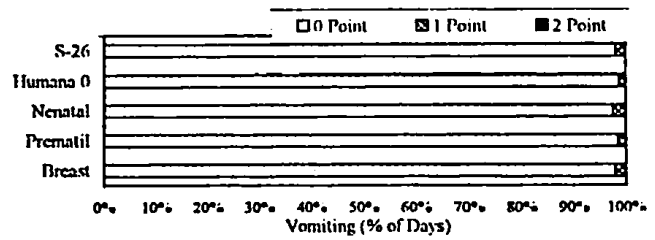

Fig. 7. Relationship of infant formula to vomiting in the parenteral+enteral feeding period.

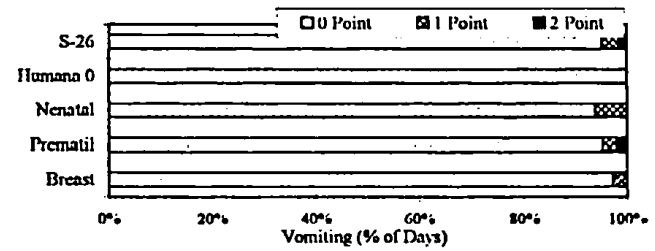

Fig. 8. Relationship of infant formula to vomiting in the full-enteral feeding period.

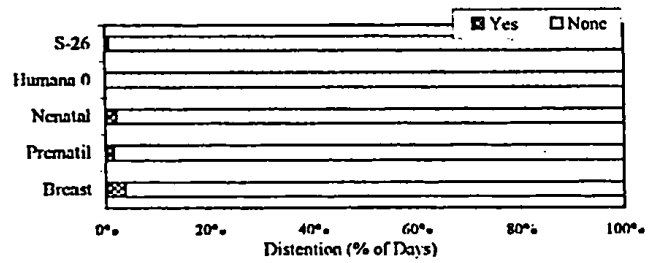

Fig. 9. Relationship of infant formula to distention in the parenteral+enteral feeding period.

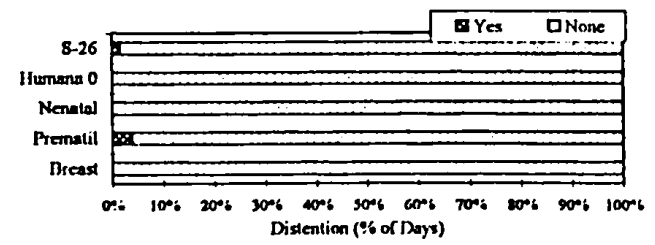

Fig. 10. Relationship of infant formula to distention in the full-enteral feeding period.

Effects of Additional Therapies: In the parenteral+enteral feeding period, additional therapies (antibiotics, aminophylline, calcium, indomethacin, furosemide, corticosteroid, iron) with the exception of phototherapy, had no effect on stool characteristics or gastrointestinal system problems. However, stool frequency of the infants receiving phototherapy was significantly high ($p = 0.0273$).

Discussion

In this prospective study, we investigated the stool characteristics and gastrointestinal system problems of infants with a birth weight less than 2000 g fed by a variety of commercial infant formulas as well as breast-milk in two periods, the parenteral+enteral feeding period and the full-enteral feeding period. Our data show that feeding with breast-milk or the other commercial infant formulas has no effect on the time of passage of the first stool. The inverse relation between gestational age and the time of the passage of first stool has been shown in previous studies. It has been well documented in earlier studies that over 95 percent of healthy full term infants pass their first stool within 24 hours of birth[12]. It has also been recognized that neonates of low birth weight (LBW) may have a delayed passage of meconium; only 80 percent of 500 infants of less than 2500 g passed meconium by 24 hours after birth[4-6]. Delayed passage (more than 48 hours) was also noted in 20.4 percent of 171 very LBW infants[7]. In a recent study including 611 infants with a birth weight less than 1850 g, 57 percent of infants born before 29 weeks' gestation, 66% of infants of 29-32 weeks, and 80 percent of preterm infants of greater than 32 weeks' gestation passed their first stool by the end of the second calendar day[8]. Our data confirm these findings. Delayed passage in infants small for gestational age can be explained by the physiological immaturity of the motor mechanisms of the gut and by the lack of triggering effect of enteral feeds on the gut hormones[9]. Another study, confirming our data, demonstrated that the type of feeding had no effect on the timing of the first stool in very LBW infants who were fed breast-milk or infant formula or on total parenteral nutrition during the first 14 days of life[10].

Stooling frequency, independent from gestational age, was found to be related with the volume of milk ingested. This relation was

found highly significant during the first week, and until the sixth week[8]. In the same study infants with a birth weight less than 1850 g passed one more stool each day for each 50 ml/kg increase in volume of milk ingested during the second to fourth weeks of life. Those infants who received human milk had a greater defecation rate than those receiving cows' milk formula throughout the first eight weeks after birth. The last finding was also shown in term infants[1-3]. We did not observe a direct relation between the volume of milk ingested and the number of stools passed each day in either study period. Although not statistically significant, stooling frequency was observed to be higher in the breast-fed group during the parenteral+enteral and full-enteral feeding periods.

Another effective factor on stooling frequency was phototherapy. In the parenteral+enteral feeding period, infants receiving phototherapy had an increase in stooling frequency, similar to previous studies[13,14], in all feeding groups.

In a study comparing two different fat containing commercial formulas, mean stool frequency was observed to be higher in the infants fed the formulas containing a higher fat ratio, but the mean weight gain was not significantly different[15]. Although all formulas in our study had a similar composition, mean weight gain was also not different between all groups during the full-enteral feeding period. However, it was significant that the mean weight gain of the infants fed by breast-milk was similar with the infants fed by formulas, although the volume of milk ingested is less because of the lower birth weight.

Previous studies demonstrated that green stool was more common with formulas containing more iron and yellow stool was more common with formulas containing less iron[16-18]. In a study designed to compare breast-milk and four different commercial formulas, one month old, healthy, term infants were fed two different iron-containing formulas for one week. Green stools predominated in infants fed by formulas containing more iron[1]. In the same study, it was also demonstrated that formulas containing 60 percent whey, 40 percent casein protein content, soy protein isolate or casein hydrolysate preparation were associated with primarily green stools. In our study no difference in stool color was observed in all groups during the full-enteral feeding period. While we did not observe any brown stool, the percentage of yellow stool was high in all groups. Although the amonut and bioavailability of the iron contents of the formulas were different, similarity to breast-milk explains the higher percentage rate of yellow stool. Stool color was not affected by the formulas containing different amounts of protein. Rates of yellow and green stools were similar during the parenteral+enteral feeding periods in all groups except for infants fed Humana 0. The higher rate of green stool in the full-enteral feeding period could be explained by the occurrence of green stooling after the meconium passage in this period. Also, the high percentage (98.6%) of green stool observed in infants fed Humana 0 could be explained by an earlier onset of the full-enteral feeding period. Because of this, more stool was passed in this period after the meconium passage. Brown stools were observed only in the breast-fed infants, in an insignificant ratio, during the parenteral+enteral feeding period. In a study in which term infants fed either breast-milk or formulas between 2-20 weeks were enrolled, stool color was observed uniformly yellow until the introduction of weaning feeds, when it changed to brown[3].

It was determined that infants fed breast-milk had more firm stool consistency than infants fed by commercial formulas in both term[1-3] and preterm[8] infants. Formulas containing soy protein isolate make the stool consistency firmer because of fiber they contain[1,19]. In a study designed to compare breast-milk and four different commercial formulas in term infants, it was determined that iron amount in formulas did not increase the stool consistency. Additionally, in infants fed breast-milk and lower fat and higher carbohydrate-containing formulas, watery stool was more common because of fast stool passage and looser stool structure[1]. In our study group, infants fed breast-milk had a significantly low percentage of hard stool compared to other groups in the full-enteral feeding period. But we could not explain the higher percentage of hard stool observed in infants fed Prematil than in infants fed other similar formulas in both feeding periods.

In our study group, similar to previous studies[1], no difference was found in the relationship between the feeding type and gas, distention and vomiting in both feeding periods. For this reason, the tendency to switch between multiple

formula preparations because of perceived abnormalities in the stooling pattern and gastrointestinal symptoms, without defined therapeutic goals, should be avoided. Also, additional treatments with the exception of phototherapy had no significant effect on stool characteristics and gastrointestinal system functions.

In this prospective study, the effects of different commercial formulas and breast-milk on stool characteristics were investigated by experienced NICU nurses rather than by parents in a wide perspective and for a long time. When the results were compared with the "gold standard" breast-milk, premature infant formulas caused more frequent hard stools, but in terms of stool color, frequency and gastrointestinal problems, they were similar with breast-milk. Further studies are needed to evaluate the effects of different commercial formulas on preterm infants' feeding. However, it must always be kept in mind that the best nutrient for all infants, especially for premature infants, is breast-milk.

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