of persistent neonatal hypoglycemia.[13, 14] Persistent hypoglycemia is not usually associated with congenital syphilis,[3] and hypopituitarism should be suspected in any infant with congenital syphilis and persistent hypoglycemia. Infants with these conditions should undergo a prompt and thorough evaluation of pituitary function, including tests of thyroid function and documentation of GH and cortisol reserve in hypoglycemia or during provocative testing. Early recognition and aggressive treatment of hypopituitarism could improve the poor outcome often seen in infants with this complication.

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Feeding premature infants banked human milk homogenized by ultrasonic treatment

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Premature neonates fed ultrasonically homogenized human milk had better weight gain and triceps skin-fold thickness than did a control group given untreated human milk ($p < 0.01$) and also had lower fat loss during tube feeding ($p < 0.01$). Ultrasonic homogenization of human milk appears to minimize loss of fat and thus allows better growth of premature infants. (J PEDIATR 1993;123:985-8)

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Feeding preterm neonates by tube with human milk is associated with significant nutrient losses.[1, 2] The slower the rate of infusion, the greater the loss of fat and fat-soluble nutrients in the infusion system.[3] These losses could compromise infant growth. To prevent fat losses, we developed a method of ultrasonic homogenization of human milk before feeding[3, 4]; fat losses were reduced from 47.5% to 16.8% during a 4-hour infusion period. Homogenization of human milk also may increase its digestibility by breaking up fat

Table I. Anthropometic measurements of 15 preterm infants fed homogenized human milk (experimental) and 15 preterm infants fed nonhomogenized human milk (control) for 20 days

	Initial		Final		Gain		
	Experimental	Control	Experimental	Control	Experimental	Control	p
Weight (gm)	1406 ± 140	1476 ± 142	1830 ± 167	1826 ± 179	424.6 ± 59.8	349.3 ± 74.9	<0.010
Length (cm)	40.0 ± 1.60	40.9 ± 1.30	42.2 ± 1.20	42.6 ± 1.40	2.2 ± 0.80	1.6 ± 0.70	0.057
Triceps skin-fold thickness (mm)	2.02 ± 0.37	2.10 ± 0.43	2.70 ± 0.32	2.41 ± 0.48	0.68 ± 0.44	0.31 ± 0.29	<0.010
Subscapular skin-fold thickness (mm)	2.20 ± 0.48	2.28 ± 0.36	2.80 ± 0.67	2.58 ± 0.47	0.60 ± 0.40	0.31 ± 0.42	0.061
Head circumference (cm)	28.90 ± 1.10	29.10 ± 1.10	31.40 ± 1.20	31.3 ± 1.10	2.5 ± 0.60	2.2 ± 0.50	0.139
Thorax circumference (cm)	23.5 ± 1.10	23.7 ± 1.30	25.9 ± 1.20	25.8 ± 1.30	2.5 ± 0.80	2.2 ± 0.80	0.340

Values (except *p* values) are expressed as mean ± SD.

Table II. Three-day fat balance of preterm infants tube-fed homogenized human milk (experimental) and nonhomogenized human milk (control) by mechanical infusion

	Group		
	Experimental (n = 13)	Control (n = 10)	p
Total milk infused (gm)	907.8 ± 84.9	1028.7 ± 188.7	NS
Total fat infused (gm)	30.1 ± 7.4	35.7 ± 12.1	NS
Fat loss during tube feeding (gm)	5.6 ± 2.4	11.3 ± 4.4	<0.01
Fat loss in feces (gm)	2.7 ± 1.7	2.7 ± 1.0	NS

Values (except *p* values) are expressed as mean ± SD.
NS, Not significant.

particles.[3, 4] The logical outcome of these effects should be better growth in infants fed homogenized human milk.

We compared somatic growth and fat balance in preterm neonates fed ultrasonically homogenized or nonhomogenized banked human milk.

METHODS

Thirty preterm infants were selected consecutively from patients admitted to the nursery of Hospital das Clínicas de Ribeirão Preto, São Paulo, Brazil. To be included in the study, infants had to meet the following criteria: (1) gestational age between 28 and 34 weeks, as determined from the date of the last menstrual period and substantiated by clinical examination of the infant, (2) birth weight <1600 gm and appropriate for gestational age, (3) absence of congenital anomalies, (4) absence of any conditions or clinical events needing special care, such as sepsis, hyaline membrane disease, patent ductus arteriosus, or use of ventilators or oxygen, and (5) ability to begin enteral feeding by the eighth day of life and to be on full enteral feeding 2 days before the beginning of the study. Informed consent was obtained from mothers of all infants enrolled in the study.

Thirty infants were assigned randomly to one of two groups receiving tube feeding: one group received homogenized human milk (experimental group) and the other nonhomogenized human milk (control group).

Human bank milk from human immunodeficiency virus–free donors was homogenized by ultrasonic vibration for 15 minutes during a maximum of 24 hours before being offered to the infants. The sonication intensity was set at 8, on a scale from 0 to 10 (Tekmar Sonic Disrupter TSD-P 250; Tekmar Co., Cincinnati, Ohio). Sonication disrupts the fat globules into fine particles of less than 2 μm in diameter, causing the fat to stabilize in milk and preventing its separation. The quality control of homogenization was carried out by microscopic examination of the fat particles.[3] Before homogenization, milk was submitted to pasteurization at 62.5° C for 30 minutes and was then used only after examination for bacteriologic acceptability based on the bacterial count per milliliter of milk.

At the end of the twentieth day of study, a 72-hour fat balance was determined in all infants. Feedings were offered every 3 hours, and the quantity of milk consumed by each preterm neonate during 30-minute periods was estimated by weighing the bottle before and after each feeding. A sample of each lot of milk was taken and stored at −20° C for fat determination. After each feeding, the milk remaining in the infusion system was taken out and the system was washed with 33% potassium hydroxide solution to remove the residual milk for analysis. Fecal samples were collected by placing the infants in metabolic cradles at-

tached to stainless steel receptacles. The collected feces were frozen in plastic containers for later fat analysis. The beginning and the end of the collection were marked by adding carmine to the first and last feedings. Milk fat was analyzed according to the method of Nakai and Le,[5] and fecal fat was estimated by the method of Van de Kamer et al.[6]

Infants were weighed daily. The other anthropometric measurements were taken at the beginning and at the end of a 20-day study period by a single observer. Crown-to-heel length was measured by using a measuring board with fixed head and side pieces and containing a built-in millimeter ruler. Skin-fold thickness was measured at the left side of the upper arm with Holtein skin-fold calipers (0.2 mm sensitivity), and 10 gm pressure per square millimeter was applied for 60 seconds.[7]

Statistical analysis of the data was carried out by using the nonparametric Mann-Whitney test.

RESULTS

No differences between groups were found at the beginning of the study regarding gender, gestational age, birth weight, and chronologic age. Mean gestational age was 31.9 ± 2.5 weeks for the experimental group and 32.6 ± 1.6 weeks for the control group. Mean birth weight was 1251 ± 180 gm for the experimental group and 1352 ± 151 gm for the control group.

Anthropometric measurements at the beginning of the study were similar between groups, whereas after the twentieth day of observation the group fed homogenized human milk had a significantly higher ($p < 0.01$) weight gain and triceps skin-fold thickness gain (Table I).

Total milk and fat infused during the study were similar in both groups. Fat loss during tube feeding was significantly greater in the control group ($p < 0.01$) than in the experimental group. No difference was found between groups regarding fat loss in feces (Table II). Only the results for 13 patients from the experimental group and 10 from the control group are reported because of problems with the material during and after collection. During collection, feces from two control infants were partially lost, and during one weekend, after an energy failure, samples from five other infants were thawed. None of those samples was used for the study.

The amount of fat lost in the infusion system during tube feeding was significantly lower in the group that received homogenized human milk than in the group that received nonhomogenized human milk (5.6 ± 2.4 gm vs 11.3 ± 4.4 gm; $p < 0.01$). This loss represents the fat that was left in the tubes and some residual fat remaining in the bottle. The amount left behind in the infusion tube was 3.4 ± 1.8 gm in the experimental group and 7.5 ± 3.7 gm in the control group.

During the 20-day trial, none of the infants who received ultrasonically homogenized human milk had any unusual clinical symptoms. No infant was withdrawn from the study. All infants from both groups remained well during the entire study, without any minor feeding intolerance.

DISCUSSION

Ultrasonic homogenization of human milk has been proposed to prevent fat losses during tube feeding.[3] Our results tend to confirm this hypothesis.

The daily weight gain and length gain of the control group during the study period were similar to those previously reported for preterm infants fed banked human milk.[8] Therefore the differences between the two groups were due to better growth of the infants fed homogenized milk rather than to inadequate growth of the control group. The better anthropometric measurements in the former infants could be due to better availability of nutrients, including fat, better digestibility of fat in the homogenized milk, or both. A 3-day fat balance trial was therefore carried out to clarify this point.

Although breaking up fat globules of human milk by homogenization may improve fat digestibility by facilitating the action of lipase, our results show no improvement in fat digestibility. The milk used for this study was a pool of banked pasteurized human milk. Pasteurization destroys enzymes present in milk, including human milk lipases, which play an important role in the digestion of milk fat.[9] The younger the gestational age, the more dependent the infant is on human milk enzymes.[10] Preterm infants should be able to digest and absorb fat in the same way that term infants do by the postconceptional age of the infants studied. In fact, the fecal fat loss in this trial was similar for both groups, suggesting no difference in fat digestion between groups; these values were comparable to those reported for term infants fed human milk.[11]

Infants fed homogenized milk received less fat but gained more weight. The possibility that this better weight gain was due to fluid retention is remote because skin-fold thickness was greater in the group given homogenized milk and was measured by applying the pressure for 60 seconds, time enough to avoid measuring edema.[7]

We conclude that ultrasonic homogenization of human milk or human milk formulas is an easy technique that can be used to help minimize loss of fat during tube feeding of premature infants. Although no adverse effect of sonication has been detected thus far,[4] the safety of the process needs to be better studied before routine use.[12]

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