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Absorption of carbon 13–labeled rice in milk by infants during acute gastroenteritis

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To determine whether rice cereal could be used to complement a cow milk–based diet in the nutritional management of infants with acute diarrhea, we assessed its digestion and absorption in eight affected male infants, 69 to 131 days of age. They received cow milk formula with 5.4% lactose (diluted 1:1 with water and precooked rice cereal) 5 to 22 hours after admission and rehydration. The first feeding consisted of milk diluted with carbon 13–enriched rice cereal. A 48-hour fecal collection and balance study was performed. Rice cereal was reasonably well absorbed (84.0% to 95.8%) by seven of the eight infants. The study was repeated in seven of the infants after they had recovered. Our results indicate that rice cereal is well absorbed by young infants with acute diarrhea and that it is an adequate nutrient supplement for this patient population. (J Pediatr 1991;118:526-30)

Several studies indicate that infants with acute diarrhea who are older than 6 months of age absorb the nutrients of various staple foods reasonably well.[1-4] This absorptive ability has not, however, been tested in younger infants. Rice is a staple for most of the world's population, and it is widely accepted in most cultures as an adequate food for infants with diarrhea. Furthermore, it seems to be relatively well digested and absorbed by healthy infants as young as 1 month of age.[5] Moreover, recent data demonstrated that the feeding of rice compared with that of formula had a positive effect on reducing stool output in infants with diarrhea.[6] Our study examined the digestion and absorption of the nutrients in a rice-milk formula in infants 2 to 4 months of age, both during acute diarrhea and 2 weeks after recovery. The rice was intended to supplement the energy intake of the infants, who were fed cow milk diluted with water, a routine practice in the hospital to which they were admitted.

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METHODS

Subjects. Eight infants less than 5 months of age who had watery diarrhea were admitted to the metabolic unit of the Instituto de Nutricion de Centro America y Panama (INCAP). The number of subjects was based on the amount of carbon 13–enriched rice available. Before becoming ill, all had been fed a cow milk formula and a cereal, the latter at least once daily. To facilitate collection of feces without urine, we selected boys for the study. The protocol was approved by the Baylor College of Medicine Institutional Review Board and the INCAP Human Rights Committee. Informed parental consent was obtained in writing.

Procedure. Mild or moderate dehydration in the infants was corrected with World Health Organization/UNICEF oral rehydration solution. All infants except one, whose parents did not agree to return, were admitted to repeat the study 14 to 17 days after diarrhea had stopped. After rehydration, infants began receiving a milk formula every 3 to 4 hours as desired. The formula (13.5% dry milk, wt/wt, with 19% fat) was diluted 1:1 with water to which isoenergetic amounts of precooked rice cereal (Gerber Products, Costa Rica) were added (7.7 gm rice cereal added to 1 dl of dilute milk). One deciliter of this milk-rice formula provided 2.4 gm protein, 3.1 gm lactose, 6.7 gm starch, 1.4 gm fat, and 61 kcal. The preparation contained approximately the same amount of energy, 40% less lactose, and 20% less protein than full-fat cow milk. Rice provided 27% of the protein, 68% of the carbohydrate, 5% of the fat, and 49% of the energy. The first feeding on the morning after admission consisted of 48 to 60 ml of dilute milk formula that contained 3.5 to 5 gm of ^{13}C-enriched rice cereal to provide approximately 1 gm ^{13}C-enriched rice per kilogram of body weight. It also contained 200 mg carmine red as a fecal marker. Additional small amounts of unlabeled milk formula were offered. Feeding with unlabeled rice-milk formula resumed 4 hours later. All stools were collected after the initial appearance of the carmine marker in feces, and we followed routine INCAP procedures for balance-study stool collection. A second carmine fecal marker was given with formula 48 hours after the first marker was fed. Fecal collections continued until the second marker appeared in the feces. Baseline feces and those collected during the balance were homogenized and aliquots were frozen at −20° C until analyzed.

Breath samples were collected immediately before ingestion of the labeled rice cereal, and then afterward at 15-minute intervals for 1 hour and at 30-minute intervals for the next 5 hours. An aliquot of the sample was analyzed immediately for breath hydrogen concentration; the remainder of the sample was stored in 30 ml evacuated test tubes (Vacutainer; Becton-Dickinson) for transport to the mass spectrometry laboratory in Houston, Tex.

Preparation of ^{13}C rice cereal. Rice plants grown under normal field conditions were enclosed in a large acrylic plastic chamber provided with pulses of $^{13}CO_2$.[7] The ^{13}C-labeled rice was processed into standard infant cereal through the courtesy of the Gerber Products Co., Fremont, Mich.[5]

Breath samples. A portion of each breath sample was analyzed immediately for breath hydrogen content by means of a CM2 MicroLyzer (Quintron, Milwaukee, Wis.). The portion of the breath sample stored in the Vacutainer tube was analyzed in the United States. The $^{13}C/^{12}C$ abundance of carbon dioxide was measured by automated gas isotope ratio mass spectrometry and results calculated as described previously.[8]

Stool samples. Frozen fecal samples were analyzed in the United States. Stool ^{13}C abundance was determined in the carbon dioxide formed by the combustion of a lyophilized aliquot of stool.[9] Osmolality was analyzed by freezing point. Nitrogen and energy were determined in both Houston and Guatemala City by a semiautomated Kjeldahl method (Tecator Inc., Herndon, Va.) and by bomb adiabatic calorimetry (Parr Instrument Co., Moline, Ill.), respectively.

Data analyses. Differences were analyzed for statistical significance with a paired Student *t* test. Correlation analysis was performed between fecal output and the coefficients of nitrogen, energy, and ^{13}C absorption.

RESULTS

The mean (±SD) age, weight, length, and weight-for-age z score of the infants with diarrhea were 95 ± 23 days (range 69 to 131 days), 4.92 ± 0.91 kg, 58 ± 3.6 cm, and −1.1 ± 1, respectively. Watery diarrhea had lasted for 2.6 ± 1.8 days. The study began 5 to 22 hours after admission, corresponding to 3.2 ± 1.8 days after diarrhea had begun, according to the mothers' reports. All infants gained weight between the first and second study (mean rate: 10.8 ± 4.6 gm/kg · day).

Four infants had purging rates of 39 to 101 gm feces/kg · day and 10 to 32 stools in 48 hours, most of which were liquid or semiliquid, during the 2 days of the first study; three infants had purging rates of 23 to 24 gm/kg · day during that interval, and one did not pass abnormal stools after ingesting the ^{13}C-enriched rice-milk dose. In the recovery phase of the study, one infant had a fecal output of 32 gm/kg · day.

Several infants had relatively low food intakes, especially on day 1 of the first admission (Table I). There was a greater formula intake during the recovery phase ($p = 0.0002$).

The mean coefficients of macronutrient absorption are shown in Table II. Intakes differed widely among infants, and even more so between the illness and recovery phases. All sick infants, including those with more severe diarrhea, absorbed at least 67% of the dietary energy and more than 50% of the nitrogen provided by the milk-rice formula. Those with milder diarrhea absorbed 84% to 87% of the dietary energy and 76% to 86% of the protein. On the first admission, the four infants with the lower purging rates had better fractional absorptions of dietary energy (86.0 ± 1.4% vs 71.0 ± 5.2%; $p < 0.01$) and nitrogen (78.2 ± 4.1% vs 60.2 ± 9.0%; $p < 0.02$) than those with higher purging rates. The apparent nitrogen absorption was significantly higher during the recovery phase ($p = 0.04$), but the difference in energy absorption did not reach statistical significance ($p = 0.057$).

Table I. Formula intake and fecal output during 48 hours of balance

	Formula intake			Fecal output			
	0-24 hr (ml)	24-48 hr (ml)	0-48 hr (ml/kg)	No. of stools (0-48 hr)	Purging rate (gm/kg · day)	Nitrogen (mg/48 hr)	Energy (kcal/48 hr)
Diarrhea							
Mean	539	680	249	12/16*	47	1432	180
SD	152	162	43	11/9	33	393	67
Recovery							
Mean	747	828	285	2/8	21	1261	152
SD	235	229	56	4/3	8	526	67

*Liquid or semiliquid stools/total number of stools.

Table II. Intake and absorption of nutrients during balance

	Nutrient intake			Apparent absorption		
	Protein (gm)	Energy (kcal/kg · day)	Lactose (gm)	N (%)	Energy (%)	^{13}C (%)
Diarrhea						
Mean	3.2	82	4.1	69	79	86.6
SD	0.5	14	0.7	12	9	12.8
Recovery						
Mean	3.6	93	4.8	81	87	94.0
SD	0.7	16	0.8	5	3	3.9

The severity of diarrhea, assessed in terms of purging rate, was inversely correlated with the absorption of dietary energy and nitrogen but not with that of ^{13}C (data not shown). The negative association between fecal output and energy or nitrogen absorption was sustained even after diarrhea ceased.

With the exception of one of the subjects in the first study (57%), absorption of the ^{13}C-labeled rice was high (84.0% to 99.5%), even when the infants were ill with diarrhea. Although the differences in ^{13}C rice absorption between infants in the illness phase and those in the recovery phase of the study were not statistically significant, there was a trend for absorption to be higher in the latter phase. During both phases, there was a very high correlation between energy absorption and apparent or true nitrogen absorptions (r = 0.923 and 0.921, respectively, with n = 15). Correlations with ^{13}C absorption were lower for energy (r = 0.636; p = 0.01) and nitrogen (r = 0.565; p = 0.03) and became weaker when the ^{13}C absorption results of the subject whose cereal absorption was only 57% were excluded from analysis (r = 0.404 for energy and r = 0.485 for nitrogen; p >0.05). The cumulative percentage of the ^{13}C dose recovered in exhaled carbon dioxide for 6 hours did not differ significantly between the illness and recovery phases (35.8 ± 8.4% and 33.9 ± 5.2%, respectively).

During the illness phase, breath hydrogen concentration in four of the eight infants increased by more than 20 ppm after the rice-milk formula was given. The highest elevations, 232 and 59 ppm above the baseline, were seen in infants with a high purging rate and low energy and nitrogen absorption. Another infant had a transient increase of 22 ppm, and yet another had a delayed peak of 25 ppm; each had a low purging rate and relatively good absorption of nutrients. During the recovery phase of the study, no infant had excess breath hydrogen after the dietary challenge.

DISCUSSION

An undetermined number of infants in developing countries are presumed to have transient lactose intolerance during acute gastroenteritis. For prevention of lactose intolerance, which is usually not documented adequately, many infants are fed diluted cow milk routinely for the first 48 to 72 hours after rehydration. The ingestion of diluted milk results in a decrease in the energy supplied to the infant, a decrease that can be deleterious to those with malnutrition or a marginally adequate nutritional status. The use of a lactose-free formula for infants who are intolerant to usual dietary amounts of lactose may offer a good alternative, but this type of formula is not always available or may be too expensive in developing countries. The substitution of a lactose-free nutrient (for example, rice) for part of the milk should circumvent the problem of reduced energy intake.

In most cultures, cereals are the first semisolid foods in the diets of infants. Staple foods, which in developing countries are mostly cereals, are frequently used as food supplements for both healthy infants and those recovering from malnutrition. In a study by Uriburu et al.,[10] the diets of infants and children aged 6 to 24 months were supplemented with (1) rice, either as rice cereal enriched with oil or as rice and beans, or (2) banana, in the form of cereal. A third, control group received no supplement. After 2 months of the dietary intervention, the catch-up growth in weight and length of the infants whose diets were supplemented with rice was greater than that in both the banana-cereal and the control groups. In addition, recent data demonstrated that the feeding of rice compared with that of formula alone had a positive effect on reducing stool output in infants with diarrhea.[6]

Compared with wheat, corn, sorghum, or barley, rice has relatively more lysine, and it is not limited in threonine or tryptophan.[11] Its low protein content and its lysine deficiency can be improved by adding protein-rich supplements or by combining it with other protein sources.[12] Protein availability can be augmented by the use of genetically improved varieties of rice with a higher protein content or by an increase in digestibility through processing.[13]

In this study, we combined a processed rice cereal with milk. The infants would otherwise have received diluted cow milk formula, which is customary in the hospital to which they were admitted; we do not know whether they were lactose intolerant. In the study, the same amount of energy supplied by a full-strength milk formula for infants would have provided about 8.6 gm lactose/kg · day or 6.2 gm if regular cow milk had been used. The addition of the rice cereal to the diluted milk formula allowed an average energy intake of 82 ± 14 kcal/kg · day during acute diarrhea in which only 4.1 ± 0.7 gm lactose/kg · day was administered in six to nine daily doses. The protein/energy ratio of the milk preparation we used in this study (0.04) was somewhat lower than that found in cow milk (0.05), which these infants usually ingest. Both values, however, are far from the value of 0.02 recommended by the National Research Council.[14]

The use of ^{13}C-labeled rice enabled us to calculate the amount of labeled cereal that was absorbed. During the illness phase of the study, seven of the eight infants absorbed between 84% and 96% of the labeled ^{13}C. We do not have an explanation for the unusually low (57%) absorption observed in one of the subjects. A more thorough characterization of the diarrheal syndrome might have provided an explanation.

Because no information about obligatory fecal nitrogen losses in infants is available, we adopted the figure of 20 mg/kg · day, which is the amount lost by children 1½ to 3½ years old who do not have diarrhea.[15] This figure, however, may be larger because obligatory losses probably are greater during diarrhea. Greater obligatory nitrogen losses may be the reason that "true" nitrogen absorption is very similar to the apparent absorption (79 ± 9% vs 69 ± 12% during illness and 84 ± 5% vs 81 ± 5% during recovery).

The cumulative recovery of $^{13}CO_2$ in breath was similar during both study periods. Breath $^{13}CO_2$ can result from the systemic oxidation of ^{13}C substrates after absorption, from bacterial activity in the lumen of the colon if the substrate was not absorbed completely in the small bowel, or from a combination of the two. Although in certain situations the shape and other characteristics of the breath test curve may help to differentiate $^{13}CO_2$ originated by systemic oxidation from that produced in the lumen of the colon,[8] in our study the breath carbon dioxide curves obtained for each patient during diarrhea and recovery did not differ from each other. The breath hydrogen data support the impression of good carbohydrate absorption, although breath hydrogen may be falsely normal in infants with diarrhea.[16]

The mean daily fecal energy output of the infants studied in the recovery phase (76 ± 34 kcal/day) was almost identical to that determined by Shulman et al.[5] (74 ± 43 kcal/day) in a group of healthy, formula-fed infants in the United States who were given supplements of 15 ± 8 kcal/day of rice cereal. Shulman et al. observed a significant increase in the dry stool weight and a decrease in the coefficients of energy and nitrogen absorption after the addition of rice cereal to the diet of healthy 1-month-old infants. These responses have been shown to be a consequence of an increase in bacterial mass in response to a larger amount of unabsorbed energy substrates in the colon.

Our study design did not allow us to determine whether the addition of rice had an adverse effect on milk digestion and absorption compared with the traditional dilution of milk. To answer that question, a similar study using ^{13}C-labeled lactose should be performed.

We conclude that the macronutrients in rice cereal and in its combination with cow milk are reasonably well absorbed by young infants with acute gastroenteritis. Rice seems to be an adequate alternative source of dietary energy when milk intake must be reduced, either because of cost, insufficient availability, or suspected lactose intolerance. A larger study is needed to confirm the practical advantages and applicability of the rice-supplemented diet for young infants with acute diarrhea, especially those whose illness is more severe than that of the infants in our study.

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