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Intact and Lactose-Hydrolyzed Milk to Treat Malnutrition in Guatemala[1]

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Introduction

Milk is the natural food for the young of all mammalian species. It is widely used to treat children with protein-energy malnutrition (PEM) and in feeding programs among populations with a high incidence of malnutrition. However, it has been suggested that its use can retard recovery of children with PEM due to the reduction in intestinal lactase activity commonly observed in malnourished children [2, 4]. The arguments in favor and against such a suggestion were recently reviewed [8]. The objections to milk feeding in PEM are usually based on two theoretical considerations: (1) that its carbohydrate, lactose, will be poorly absorbed with consequent decreased effective utilization of dietary energy; and (2) that the osmotic and fermentative effects of non-absorbed carbohydrates in the intestine will produce or exacerbate diarrhea that will result in the loss of much-needed nutrients.

Advancements in food technology now permit the reduction or elimination of lactose in milk by enzymatic hydrolysis [5]. This allowed the evaluation of the clinical and metabolic effects of milk lactose in the treatment of PEM, using therapeutic diets based on intact whole cow's milk or on the same milk after enzymatic lactose hydrolysis. 20 Guatemalan

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children with severe PEM of the edematous type were studied during the first 7 weeks of nutritional treatment. At the time of this symposium, complete clinical and most metabolic data were available from 18 children. The results are presented and discussed below.

Material and Methods

Patients. 18 boys of Mayan or mixed Mayan and Caucasian origin ('latinos'), 15–36 months old, were admitted to INCAP's Clinical Center with severe marasmic-kwashiorkor, characterized by anorexia, apathy, edema, skin lesions, hair loss and depigmentation, decrease in subcutaneous fat, enlarged fatty liver and decreased total plasma proteins. They were divided into two treatment groups with either intact (IM) or lactose-hydrolyzed milk (HM), by a process of stratified randomization in order to match both groups of patients with respect to age, severity and chronicity of malnutrition, history of diarrhea, estimated weight-for-height after loss of edema, degree of stunting, clinical features and plasma protein concentration. Their main characteristics are shown in table I.

Diets. All children ate on the day of admission 0.7 g casein and 70 kcal/kg/day. Casein was substituted by whole fat-dried milk on day 2 and the protein and energy intakes were increased on days 2, 4, 6 and 8, respectively, to 1 g and 100 kcal, 2 g and 120 kcal, 3 g and 150 kcal, and 4 g and 150 kcal/kg/day. Vegetable oil increased dietary fat to 40% of total energy and the remainder of the dietary energy was provided by refined cane sugar. The diets were divided into 5 identical meals and they were supplemented with vitamins, minerals, water and electrolytes to satisfy the children's requirements.

A commercial food-grade β-galactosidase (LactAid®, SugarLo Company, N.J., USA) was added according to the manufacturer's instructions to the milk formulas for the HM group. Lactose content was reduced by more than 90%. Children in this group were fed HM until day 45, after which they were fed the IM formula for 5 more days. Children in the IM group were fed intact milk formula throughout the study. All children remained at INCAP until fully recovered or until transferred to a nutritional recovery center.

Measurements and Laboratory Determinations. Clinical data and body weight were recorded daily. Other anthropometric measurements were taken every 7 days. 'Dry' weight was calculated after disappearance of edema, taking into account the rates of weight loss during the first days of treatment and the subsequent rate of weight gain. Total weight gain was calculated from the 'dry' weight and the average weight of days 43–47. The rates of weight gain during the rapid catch-up phase of initial nutritional recovery were calculated by regression analysis of weight over time.

Food intake was measured weighing the food containers immediately before and after every meal and making corrections for spillage and vomiting. Complete urinary and fecal collections were made on days 2–5, 12–14, 22–24, 32–34, 42–44 and, when a child was switched from HM to IM, on days 46–48. Food, urine and fecal aliquots were analyzed for total nitrogen (micro-Kjeldahl). Analyses are under way for total energy and calcium. Creatinine was also measured in urine.

Table I. Comparative data on admission and at the end of the study (mean ± standard deviation; 9 children in each group)

	Admission to INCAP		End of the study	
	intact milk	hydrolyzed milk	intact milk	hydrolyzed milk
Age, months	23 ±6	20 ±6	24 ±6	22 ±6
Height, cm	74.6±3.4	75.8±3.7	76.3±3.2	77.4±3.6
Height-age, months	12 ±2	13 ±3	13 ±2	14 ±3
Weight, kg	6.88±0.97[1]	7.22±1.04[1]	9.24±1.20	9.62±1.34
Weight-for-height[2], %	71 ±8[1]	72 ±7[1]	90 ±8	92 ±9
Lean arm diameter[3], mm	28 ±3	29 ±3	32 ±2	35 ±3
Calf circumference, cm	13.7±1.4	14.0±1.6	15.7±1.4	16.1±1.6
Skinfold thickness[4], mm	3.4±1.8	3.1±1.2	6.5±2.3	6.0±1.7
Creatinine-height index[5]	0.62±0.17	0.65±0.14	1.10±0.09	1.10±0.11
Severity of edema[6]	2.1±0.9	2.2±0.8	–	–
Plasma proteins, g/dl	4.2±0.6	4.4±0.6	7.1±0.3	7.1±0.5
Serum albumin, g/dl	2.3±0.8	2.2±0.4	5.4±0.3	5.2±0.3
Hemoglobin, g/dl	9.8±0.7	9.6±2.0	10.8±1.0	10.5±1.1
Serum iron, μg/dl	55±19	58±21	54±33	57±28
Iron-binding capacity, μg/dl	128±42	126±32	347±21	349±44

[1] Corrected for weight of edema.
[2] Relative to Boston standards, where 100% = 50th percentile.
[3] Corrected for skinfold thickness.
[4] Average of 3 sites: tricipital, subscapular and paraumbilical.
[5] Normal: ≥0.90 [9].
[6] 1 = Edema below knees; 2 = edema involving thighs; 3 = edema involving arms.

Hydrogen breath-analysis tests were performed in exhaled air collected hourly, as described by *Solomons* et al. [7], for 3 h after breakfast or 4 h after an oral dose of 6.7 g lactulose (Cephulac®, Merrell-National Lab., Ohio, USA). Breakfast contained 1.20 g of lactose (IM) or of milk galactose and glucose (HM) plus 2.6 g of sucrose per kg body weight. Hydrogen concentration was determined with a thermal conductivity chromatograph (MicroLyzer®, Quintron Instruments, Wisc., USA). A positive response was an increase in exhaled hydrogen concentration of 20 ppm or more after ingesting breakfast or lactulose.

Each stool was assessed for its volume, consistency and other physical characteristics. Diarrhea was defined as daily stools with 2 or 3 of the following: (a) three or more stools/day, (b) 50% or more abnormal stools (mucus, blood or liquid stools), and (c) 150 g or more feces/day. A semiquantitative measurement of reducing substances was done in each stool using Clinitest® tablets (Ames Laboratories, Ind., USA) and fecal pH was measured.

Hemoglobin (cyanmethemoglobin), total plasma protein (refractometry) and albumin (bromcresol purple) concentrations were determined weekly in blood samples obtained by finger-prick.

Table II. Intestinal, absorptive and metabolic functions

	Early admission (days 1–3)		First week of therapy (days 8–14)		Last week of therapy (days 39–45)		Whole period of therapy (days 6–45)	
	IM	HM	IM	HM	IM	HM	IM	HM
Children with diarrhea	8 of 9*	4 of 9*	7 of 9	4 of 9	2 of 9	1 of 9	2 of 9[1]	2 of 9[1]
Stools								
Number of evacuations, stools/day	4.1±0.8[2]**	2.8±1.2**	3.8±0.6**	3.1±0.7**	1.8±0.6	2.2±0.8	2.5±0.4	2.3±0.5
% with abnormal characteristics	85±20*	68±32*	51±20	40±27	26±22	24±28	37±8*	30±18*
Average daily weight, g/day	263±173	172±108	168±92	177±226	105±71	102±92	127±74	113±52
Children with acid stools (pH ≤ 5)[3]	5 of 9	4 of 9	4 of 9*	9 of 9*	4 of 9	4 of 9	0[1]	0[1]
Children with fecal reducing substances[3]								
Only traces	1 of 9	4 of 9	4 of 9	3 of 9	3 of 9	3 of 9	0[1]	0[1]
Clearly positive (+ to ++++)	7 of 9*	4 of 9*	4 of 9	5 of 9	1 of 9	1 of 9	0[1]	0[1]
Children with high exhaled hydrogen[4]								
After ingestion of lactulose	4 of 7	3 of 8	4 of 7	3 of 8	5 of 8	5 of 8	8 of 8[5]	5 of 8[5]
After breakfast	0	0	1 of 8	0	0	0	3 of 9[6]	1 of 8[7]
'True' nitrogen absorption[8], %	85±10	91±5	90±7	92±4	92±7	91±8	91±6	91±5
Nitrogen balance[9], mg/kg/day	120±41	141±37	328±45	353±59	255±99	263±52[10]	273±72	290±69
Nitrogen balance after switch from HM to IM[9] (days 46–48)	–	–	–	–	302±48[10]	–	–	–

* IM and HM groups differ, χ^2, $p < 0.05$.
** Mean values of IM and HM groups differ, Student's t-test, $p < 0.05$.
[1] Children who had diarrheal or abnormal stools frequently, but not always.
[2] Mean ± standard deviation.
[3] Positive result in one or more stools passed during the indicated period of time.
[4] Increase of 20 ppm or more after ingestion of carbohydrates. Instrumentation was not available for use with some children.
[5] Children with at least one positive (increased breath hydrogen) response after lactulose ingestion.
[6] 1 child with 1 positive response in 4 trials; 1 with 2 positive responses in 6 trials; 1 child with a positive response in the only trial performed.
[7] 1 child with 1 positive response in 7 trials.
[8] 'True' N absorption = ([ingested N – (fecal N – 20 mg N/kg/day obligatory fecal losses)] + fecal N) × 100.
[9] 'True' N balance = ingested N – urinary N – fecal N – 14 mg/kg/day integumentary and miscellaneous losses.
[10] Nitrogen retention increased after switch from HM to IM, Student's paired t, $p < 0.05$.

Results

Clinical Recovery and Growth. All children recovered satisfactorily. The signs of acute, severe PEM disappeared by days 15 and 18 of therapy in groups IM and HM, respectively. Table I shows the anthropometric and blood chemistry data. The average rates of weight gain in 45 days were 52±10 and 54±11 g/day. The period of fastest catch-up lasted 25±7 and 26±8 days in groups IM and HM, respectively, with growth rates of 8.5±0.9 and 8.7±1.5 g/kg/day (the normal growth rate at this age is 0.6–0.7 g/kg/day). Catch-up in height, lean tissues and subcutaneous adipose tissues was satisfactory and similar in both groups. A weight-for-height of 92%, which is one of the criteria used at INCAP to assess satisfactory recovery, was reached by 5 and 6 children in each group in 37±11 and 33±9 days.

All children reached a normal creatinine-height index (0.90 or more) [9] by the end of the study. Plasma proteins and albumin became normal and stable on the fourth week of treatment in both groups.

Intestinal Functions. Table II shows that the children assigned to IM had a higher prevalence of diarrhea when admitted. This might explain the greater number of stools passed during the first week with the full dose of dietary treatment. Diarrhea improved or disappeared without specific treatment as nutritional recovery progressed and there were no differences with either treatment. 2 children in each group frequently had abnormal or large stools but their growth and nutritional recovery were satisfactory and they were always well hydrated.

1 HM and 2 IM children had one positive breath hydrogen test after breakfast and 1 IM child had a positive result twice. This last child and the HM child with the positive response were 2 of the 4 patients with frequent large or abnormal stools. Only 1 child had a positive test after being switched from HM to IM on day 46.

Nitrogen Digestibility and Balance. Nitrogen absorption was similar in both groups and did not change throughout the study. Nitrogen balance was higher at the beginning of therapy. It remained stable and similar in both groups between days 22 and 45. Nitrogen retention improved in 6 children and did not change in 3 immediately after switching from HM to IM ($p<0.05$).

Discussion

The results support our contention from previous observations [8] that cow's milk is an excellent food for the treatment of severely malnourished Guatemalan children from Mayan, Caucasian and mixed ethnical origins and that it rarely produces persistent diarrhea that might impair their nutritional rehabilitation. Previous enzymatic hydrolysis of lactose did not reduce nor improve the effects of intact milk. The better results reported with lactose-hydrolyzed milk in Australia [1, 6] and with a milk-casein-sucrose-oil mixture in Nigeria [3] could be due to comparisons of patients with different severities of malnutrition and other diseases, to short-term evaluations that do not permit precise assessments of growth and recovery rates, and to the use of therapeutic diets with different energy densities.

The persistence of frequent abnormal stools in 4 children could have been due to the milk protein or to alterations in the digestion of sucrose or of monosaccharides. Only in 2 of those children it might have been related to the milk lactose. The children, however, recovered, grew well and had good nitrogen retentions. This indicates that when the nutritional quality of a food or diet is assessed, more attention should be paid to the amounts of nutrients that are absorbed and utilized than to those that are incompletely absorbed. Similarly, the overall therapeutic effects are more important than the occurrence of minor symptoms that will not impair health nor produce major discomfort.

When cow's milk is available for the treatment of malnutrition, there is no need to alter the lactose content routinely: HM is a good alternative for the treatment of those occasional patients who may not tolerate physiological amounts of dietary lactose or who will not grow adequately due to lactose malabsorption.

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