Randomized, Double-Blind Clinical Trial of a Lactose-Free and a Lactose-Containing Formula in Dietary Management of Acute Childhood Diarrhea

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Background : *Refeeding of artificially fed infants with lactose-containing formula after oral rehydration therapy in the treatment of acute diarrhea was concluded to be indifferent to non-lactose formula by a meta-analysis. In Thai as well as Asian infants and children with low lactase level from genetically determinant and with rotavirus infection, lactose malabsorption is most likely to occur and cause delayed recovery. The aim of this study was to compare the effect of a lactose-free and a lactose-containing formula in dietary management of acute childhood diarrhea.*

Patients and Method : *A randomized, double-blind clinical trial of 80 male children, formula-fed, aged 3 to 24 months, admitted with acute watery diarrhea and mild or moderate dehydration, was carried out. All children received oral rehydration therapy for the first 4 hours. After appropriate rehydration, they were fed either a lactose-free formula (Dumex® Lactose-Free Formula; treatment group, n = 40) or a lactose-containing formula (Dumex® Infant Formula; control group, n = 40) in adjunction with oral rehydration solution. In addition, the infants were fed rice gruel as tolerated. Comparisons of duration of diarrhea, weight gain, vomiting, biochemical changes, stool frequency and weight and unscheduled intravenous fluid were made.*

Results : *Three children (2 treatment, and 1 control) dropped out from the study. The total number of unscheduled intravenous infusions were 6 of 80 children (7.5%), including 2 (5.0%) in the treatment group and 4 (10.0%) in the control group. Three children in the control group did not resolve from diarrhea within 7 days of treatment. Rotavirus was identified in approximately 50% of the children in each group. Using survival analysis, the median duration of diarrhea was significantly shortened by 20.5 hours in the treatment group compared to the control group (77.0 hours in the treatment group vs 97.5 hours in the control group; P = 0.002). Significantly decrease in stool frequency and increase in percent weight gain were seen in the treatment group at 24 hours. Moderate acidosis cleared up to near normal at 24 hours in the treatment group but acidosis persisted in the control group. In the rotavirus diarrhea subgroup, moderate acidosis turned to be mild in treatment group, but acidosis was unchanged with increased plasma chloride level in the control at 24 hours thus suggesting that the children in the control group might have lactose malabsorption and osmotic diarrhea. Duration of rotavirus diarrhea was shortened 23.6 hours in treatment group compared to the control (P = 0.0034).*

Conclusions : *In this study, lactose-free formula was shown to be effective in the dietary management of acute childhood diarrhea. Duration of diarrhea was shortened, weight gain was better, and stool frequency was less when compared to lactose-containing formula. Moderate acidosis cleared up spontaneously at 24 hours. Unscheduled IV could be decreased by 50%. Children receiving lactose-free formula tolerated it well. Data of subgroup analysis of rotavirus diarrhea revealed lactose-free formula scored higher than the control group for all parameters studied.*

Keywords : *Acute diarrhea, Lactose-free formula, Oral rehydration therapy*

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Acute diarrhea is still an important cause of morbidity and mortality in developing countries. A report from the Bureau of Epidemiolgy, Department of Diseases Control, Thai Ministry of Public Health revealed the case fatality rate was 0.015 percent in 1999 and the reported cases of acute diarrhea in 2002 was 85,000/100,000 population in children under five years of age[1].

Management of acute diarrhea in children consists of oral rehydration therapy and early feeding. In case of shigellosis, severe cholera, and extra intestinal salmonella infection in small infants and immunocompromised hosts, antibiotics may also be used. Various auxiliary treatments aimed at shortening the diarrheal episodes are optional.

In the milk formula-fed infants, small frequent feeding is the recommendation. Lactose intolerance was once thought to be a major problem in children with diarrhea and being the reason to delay refeeding milk-based formula. When feeding was reintroduced often began with diluted milk or lactose-free formula. In a meta-analysis of the use of non-human milk in the dietary management of young children with acute diarrhea, it was concluded that the vast majority of cases could be successfully managed with continued feeding of undiluted human milk. It was also concluded that the routine dilution of milk formula and routine use of lactose-free milk formula were not necessary[2]. Furthermore, in the ESPGHAN study, only 3 percent of the children at admission had signs of lactose malabsorption, and none at day 5 post enrollment, after receiving a normal, lactose-containing formula[3].

However, the occurrence of lactose intolerance must not be completely disregarded. Physiologic low lactase level contributes to lactose non-digester and/or malabsorption in more than one-third of Thai infants after birth and the percentage of lactose malabsorption increase with age[4,5]. Chinese children also have been demonstrated to have low lactase level and commonly have lactose intolerance[6]. Moreover, rotavirus infection is the most common cause of diarrhea in children under five in which disaccharidases deficiency has long been recognized[7]. Thus, genetically determinant plays a role in lactose non-digester in normal Thai infants and children. When these children get rotavirus infection then overt lactose malabsorption is most likely to have occurred. Those who are fed exclusively with non-human milk, especially in very young infants and malnourished infants with severe diarrhea should be closely observed because diarrhea may be worsened on reintroduction of normal formula[8]. There is also a suggestion that if fecal pH decreases and more than 0.5 to 1 percent reducing substances are found in the stools, lactose intolerance should be assumed and a lactose-free formula employed at least temporarily to prevent persistent post enteritis diarrhea (PPD)[9].

The objective of the present study was to assess the clinical efficacy of a lactose-free formula compared with a lactose-containing formula in dietary management of acute childhood diarrhea.

Patients and Method

This randomized double-blind controlled clinical trial was conducted during 2 years (from December 2000 through January 2003) in the Department of Pediatrics, Maharat Nakhon Ratchasima Hospital, School of Medicine, Nakhon Ratchasima, Thailand.

Patients

Eighty male children, formula-fed, aged 3-24 months, with acute watery diarrhea present for no more than 7 days and had mild or moderate dehydration, were enrolled. Informed consent was obtained from the parents. Children with mucous bloody stools, major systemic illness, or third degree malnutrition were not enrolled.

Clinical characteristics

Medical history was recorded on admission. Nude weight was measured with scale with an accuracy of 10 g. Physical examination was performed to assess clinical status and degree of dehydration.

Rehydration and dietary treatment

According to WHO guidelines[10,11] children were rehydrated with 50 ml/kg of oral rehydration solution (standard WHO-ORS) in the case of mild dehydration and 100 ml/kg in the case of moderate dehydration during the first 4 hours. After the initial rehydration phase, children were randomly allocated to receive 90 ml/kg/day of either a lactose-free formula (treatment group, n = 40) or a lactose-containing formula (control group, n = 40) alternated with 90 ml/kg/day of standard WHO-ORS as maintenance treatment, the total fluid volume consumption was aimed at 180 ml/kg/day, for the 4- to 24-hours and 24- to 48-hours period. Children were fed rice gruel as tolerated and appropriate to age after 4 hours of initial rehydration.

The treatment was randomized in blocks of four (two lactose-free and two lactose-containing formula) and numerically coded to ensure a sequential distribution. The lactose-free formula (Dumex® Lactose Free Formula, International Nutrition Research Institute, Denmark), supplied in 450-g cans could not be distinguished from the lactose-containing formula (Dumex® Infant Formula, Dumex Ltd, Thailand). Each child was assigned a numerically coded package containing 3 cans.

Study parameters

Children were kept in hospital for at least 48 hours. Data were recorded on admission, at 4-, 24- and each following 24-hour period. Data included body weight, stool frequency and consistency. Stool weight was measured to the nearest gram (expressed as grams per kilogram of body weight), using the difference between dry and wet diapers. Urine and vomitus were recorded. Urine was separated from stool with a urine collector. The volume of ORS, milk formula and rice gruel consumed by each child were also recorded.

After 48 hours, the parents were asked to record in the record form the timing, frequency and consistency of stools at home for another 3 consecutive days, and showed the record to the examiner on the day of follow up. If children still presented with diarrhea symptoms, they were asked to come back with recorded data for another 2 consecutive days. Severity of dehydration and body weight were assessed at each visit. The total duration of children's participation in the study was 7 days.

Duration of diarrhea corresponded to the time from enrollment to the cessation of diarrhea, which was defined as the passage of the last watery or loose stool before passage of two consecutive formed stools or no stool in a 24-hour period.

Unscheduled intravenous infusion was defined as clinical requirement for intravenous infusion after oral rehydration had been started. The clinical requirement included aggravation of diarrhea, vomiting or dehydration.

Laboratory studies included gross stool examination, stool reducing substance (Clinitest®, Bayer Corp., USA), latex agglutination test for rotavirus (Virotect-Rota®, Omega Diagnostics, UK) and rectal swab specimen was taken for bacterial culture and sensitivity test. Blood samples were collected on admission for determination of complete blood count, blood urea nitrogen, creatinine and electrolytes and at 24 hours for electrolytes.

The primary outcome measure of this intervention was duration of diarrhea. The secondary outcome measures included biochemical changes, stool frequency and stool weight, body weight change (expressed as percentage of the weight of children compared with baseline) and unscheduled intravenous infusion.

Statistical analysis

The treatments were compared with regard to duration of diarrhea (primary outcome) using the log-rank test and Kaplan-Meier survival curve was presented. Continuous variables were compared using unpaired Student's *t*-test. Dichotomous variables were compared by X^2 test, and Fisher's exact test was used when appropriate. Data were analyzed by Stata release 6.0 (Stata Corp., College Station, TX, USA). $P < 0.05$ was considered statistically significant.

Ethical consideration

The study protocol was approved by the Committee on Human Rights Related to Research Involving Human Subjects, Maharat Nakhon Ratchasima Hospital, School of Medicine.

Results

Of the 80 enrolled children, three children (2 treatment, and 1 control) dropped out from the study but were still included in the analysis. The causes for dropout in the treatment group were; one comorbidity (pneumonia), and one antibiotic therapy (rectal swab culture: *Salmonella* group B; in addition, the child had extra intestinal symptoms). The cause in the control group was one antibiotic therapy (rectal swab culture: *V. cholerae* O139).

The total numbers of unscheduled intravenous infusions were 6 of 80 children (7.5%), including 2 (5.0%) in treatment group and 4 (10.0%) in control group ($P = 0.675$). Two children in the treatment group required intravenous infusions at the end of 48 hours. Compared to the control, one child and three children required intravenous infusions at the end of 24, and 48 hours, respectively. Three children in the control group did not resolve from diarrhea within 7 days of treatment.

No child was lost to follow-up review. The time-sequence clinical outcome of the enrolled children is shown in Fig. 1.

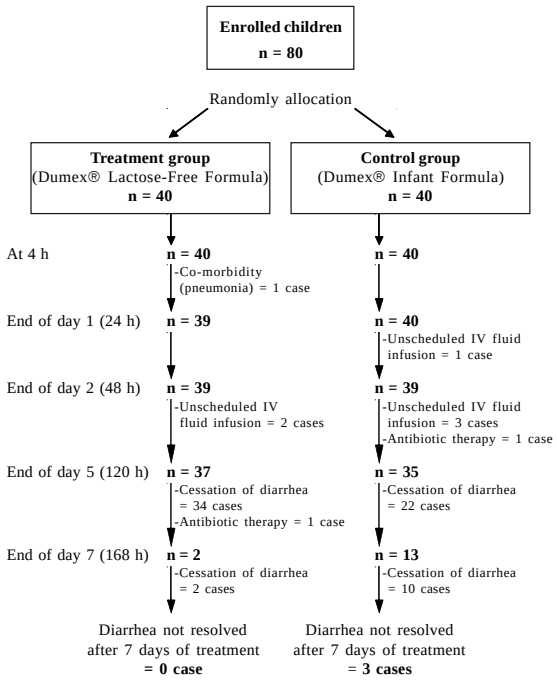

Fig. 1 Flow diagram of the time-sequence clinical outcomes of the enrolled children

Baseline characteristics

The demographic and clinical characteristics of the studied children in the two groups were comparable at the enrollment (Table 1). The mean age of the treatment group was slightly lower than that of the control group, but had no statistical significance, $P = 0.055$ (11.1 ± 4.2 vs 13.2 ± 5.1 months). This difference caused a slightly lower mean weight of the treatment group than the control group, $P = 0.125$ (8,861.7 ± 1,493.6 vs 9,234.7 ± 1,801.4 g). Eight children (2 treatment group, and 6 control) had received antimotility agents and adsorbents before inclusion (Table 2). Fifteen children (6 treatment, and 9 control) were rectal swab culture-positive for enteropathogens ($P = 0.567$) (Table 3). Rotavirus was identified in approximately 50% of the children in each group.

Clinical results

The survival analysis of duration of diarrhea showed a significant reduction in the lactose-free formula group compared with the control group $P = 0.002$ (log rank test) (Fig. 2). By this analysis, the median duration of diarrhea was 77.0 and 97.5 hours in the treatment and control groups, respectively.

Table 1. Baseline characteristics of children at the enrollment

Characteristics	Lactose-free formula *(n = 40)*	Control *(n = 40)*	*P*
Age (mo)	11.15 ± 4.21	13.18 ± 5.06	0.055
Previous antibiotic therapy	17 (42.5)	11 (27.5)	0.159
Previous antidiarrheal therapy	2 (5.0)	6 (15.0)	0.263
Duration of diarrhea (h)	62.1 ± 30.8	52.6 ± 38.2	0.225
Stool frequency (no./day)	7.7 ± 3.0	7.8 ± 3.3	0.861
Body weight (g)	8661.7 ± 1493.6	9234.7 ± 1801.4	0.125
Weight for age			
Normal	35 (87.5)	32 (80.0)	
First degree	5 (12.5)	8 (20.0)	0.544
Temperature (C)	37.1 ± 0.8	37.1 ± 0.9	0.989
Degree of dehydration			
Mild	31 (77.5)	35 (87.5)	
Moderate	9 (22.5)	5 (12.5)	0.377
Hemoglobin (g/dL)	11.9 ± 1.0	11.7 ± 1.0	0.357
Serum electrolytes (mmol/L)			
Na^+	138.2 ± 2.4	137.5 ± 2.8	0.224
K^-	4.7 ± 0.4	4.6 ± 0.5	0.256
Cl^-	113.2 ± 4.2	112.4 ± 4.5	0.439
CO_2 content	13.6 ± 3.6	14.1 ± 3.8	0.550
Stool culture: positive-enteropathogens	6 (15.0)	9 (22.5)	0.567
Stool rotavirus: positive	19 (50.0)*	23 (57.5)	0.662
Stool reducing substances			
Abnormal	11 (28.9)*	15 (37.5)	0.217

Data are expressed as mean ± SD or numbers with % in brackets, * n = 38

Table 2. Antidiarrheal drugs (antimotility agents and adsorbents) given to the children prior to enrollment

Drugs	Lactose-free formula (n = 40)	Control (n = 40)
Dioctahedral smectite (Smecta®)	1	2
Kaolin-pectin	1	2
Cholestyramine	0	1
Diphenoxylate HCl (Lomotil®)	0	1
Total	2	6

Table 3. Enteropathogens isolated from rectal swab cultures of children at the enrollment

Pathogens	Lactose-free formula (n = 40)	Control (n = 40)
Salmonella spp.	3	3
S. aureus	1	2
EPEC polyvalent 2	1	1
V. cholerae non O1, non O139	1	1
V. cholerae O139	0	1
V. parahemolyticus	0	1
Aeromonas carviae	0	1
Total	6	10*

* One case had 2 pathogens

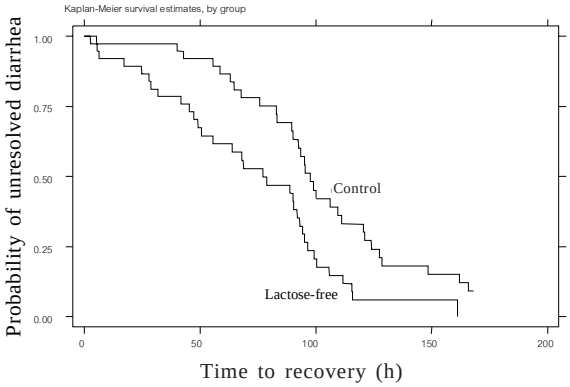

Fig. 2 Kaplan Meier survival curve, by group of duration of diarrhea in 80 patients treated with Dumex® Lactose-Free Formula (treatment group) and Dumex® Infant Formula (control group)

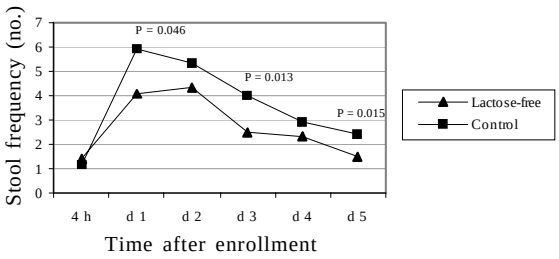

Fig. 3 Frequency of stools in children receiving lactose-free or lactose-containing formula. Feeding with lactose-free formula was associated with significant reduction of the number of stools on day 1, 3 and 5

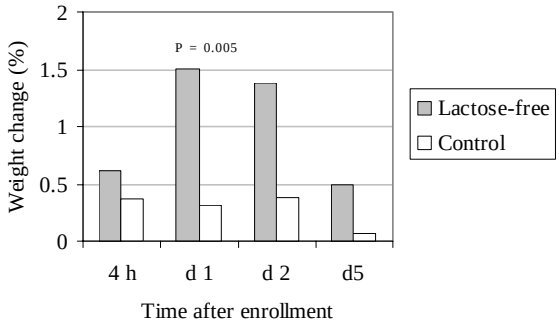

Fig. 4 Weight change (%) of children in lactose-free formula group compared with control group. There was a significant increment in weight of children in treatment group on day 1 (P = 0.005)

Even though the duration of diarrhea was analyzed by Student's *t*-test, children receiving lactose-free formula had a significantly reduced mean duration of diarrhea compared with the control group, (64.2 ± 39.9 vs 92.0 ± 43.3 hours, P = 0.003).

The variable outcomes (weight change, intake and output) of the studied children in each period of time are shown in Table 4. The stool frequency was significantly decreased in the treatment group on day 1, 3, and 5, P = 0.046, 0.013, and 0.015, respectively (Fig. 3). The significant increase in weight change of children in the treatment group at 24 hours was also observed in the present study, (1.51 ± 1.71 vs 0.31 ± 1.98 percent, P = 0.005) (Fig. 4). Patients in both groups had vomiting after refeeding but more frequent in the control group, P = 0.006 (20.5% in the treatment, and 50% in the control).

Moderate acidosis was presented initially in both groups. The acidosis cleared up spontaneously to near normal in the treatment group at 24 hours (total CO_2 content increased from13.6 ± 3.6 to 17.3 ± 4.2 mmol/L) but moderate acidosis persisted in the control group, (total CO_2 content 14.1 ± 3.8 initially and 14.4 ± 3.7 mmol/L, P = 0.0015).

Data of subgroup analysis of children with rotavirus infection are shown in Table 5. Significant difference in weight change was seen in the treatment

Table 4. Clinical outcomes of children after enrollment

Variables	Lactose-free formula	Control	*P*
0-4 hours	*(n = 40)*	*(n = 40)*	
Weight change (%)	0.62 ± 1.49	0.37 ± 1.24	0.431
Intake			
ORS (ml/kg BW)	51.58 ± 19.86	44.33 ± 20.45	0.112
Output			
Urine (ml/kg BW)	11.76 ± 10.60	10.03 ± 9.27	0.440
Stool frequency (no.)	1.4 ± 1.2	1.2 ± 1.1	0.391
Stool weight (g/kg BW)	11.36 ± 13.31	10.98 ± 14.46	0.902
Vomiting cases	5 (12.5)	4 (10.0)	1.000
4-24 hours	*(n = 39)*	*(n = 40)*	
Weight change (%)	1.51 ± 1.71	0.31 ± 1.98	0.005*
Intake			
ORS (ml/kg BW)	51.80 ± 19.82	52.99 ± 15.29	0.765
Milk formula (ml/kg BW)	78.81 ± 17.11	78.76 ± 12.87	0.988
Rice gruel (g/kg BW)	16.05 ± 11.53	15.63 ± 11.12	0.869
Output			
Urine (ml/kg BW)	41.95 ± 25.38	38.78 ± 27.45	0.597
Stool frequency (no.)	4.1 ± 3.8	5.9 ± 4.2	0.046*
Stool weight (g/kg BW)	38.87 ± 38.51	56.70 ± 50.49	0.082
Vomiting cases	8 (20.5)	20 (50.0)	0.006*
Serum electrolytes (mmol/L)			
Na^+	139.1 ± 2.2	139.3 ± 2.6	0.664
K^-	4.6 ± 0.5	4.5 ± 0.4	0.662
Cl^-	112.6 ± 2.7	115.2 ± 4.6	0.0028*
CO_2 content	17.3 ± 4.2	14.4 ± 3.7	0.0015*
Day 2 (24-48 h)	*(n = 39)*	*(n = 39)*	
Weight change (%)	1.38 ± 2.57	0.39 ± 2.25	0.073
Intake			
ORS (ml/kg BW)	73.89 ± 26.04	61.68 ± 23.48	0.033*
Milk formula (ml/kg BW)	77.54 ± 16.54	75.54 ± 17.12	0.601
Rice gruel (g/kg BW)	24.33 ± 16.84	26.65 ± 20.84	0.591
Output			
Urine (ml/kg BW)	68.06 ± 43.46	48.86 ± 34.19	0.033*
Stool frequency (no.)	4.3 ± 3.4	5.3 ± 4.3	0.258
Stool weight (g/kg BW)	41.85 ± 45.12	49.24 ± 44.96	0.470
Vomiting cases	11 (28.2)	15 (38.5)	0.337
Day 3 (48-72 h)	*(n = 37)*	*(n = 37)*	
Output			
Stool frequency (no.)	2.5 ± 2.2	4.0 ± 2.8	0.013*
Day 4 (72-96 h)	*(n = 37)*	*(n = 35)*	
Output			
Stool frequency (no.)	2.3 ± 1.8	2.9 ± 2.0	0.204
Day 5 (96-120 h)	*(n = 37)*	*(n = 35)*	
Weight change (%)	0.50 ± 2.10	0.07 ± 2.34	0.249
Output			
Stool frequency (no.)	1.5 ± 1.3	2.4 ± 1.9	0.015*
Day 6 (120-144 h)	*(n = 2)*	*(n = 13)*	
Output			
Stool frequency (no.)	2.0 ± 2.8	2.6 ± 1.9	0.695
Day 7 (144-168 h)	*(n = 2)*	*(n = 13)*	
Output			
Stool frequency (no.)	2.5 ± 0.7	3.0 ± 1.8	0.715

Data are expressed as mean ± SD or numbers with % in brackets
* Statistically significant

Table 5. Clinical outcomes of rotavirus-positive subgroup after enrollment (n = 42)

Variables	Lactose-free formula (n = 19)	Control (n = 23)	*P*
Weight change (%)			
4 h	0.97 ± 1.72	0.14 ± 1.22	0.076
4-24 h	1.40 ± 1.74	-0.42 ± 1.84	0.002*
Day 2	1.22 ± 2.25	-0.19 ± 2.41	0.062
Day 5	0.87 ± 2.11	-0.67 ± 3.09	0.083
Vomiting symptoms			
4 h	3/19 (15.8)	4/23 (17.4)	0.612
4-24 h	3/19 (15.8)	14/23 (60.9)	0.004*
Day 2	4/19 (21.0)	11/22 (50.0)	0.139
Stool frequency (no.)			
4 h	1.8 ± 1.4	1.1 ± 1.2	0.115
4-24 h	5.7 ± 4.8	7.3 ± 4.7	0.290
Day 2	6.1 ± 3.4	6.3 ± 4.9	0.875
Day 3	3.0 ± 2.7	4.3 ± 2.6	0.146
Day 4	2.7 ± 2.2	3.3 ± 2.2	0.397
Day 5	1.6 ± 1.2	2.4 ± 2.0	0.133
Serum electrolytes (mmol/L)			
On admission			
Na^+	137.9 ± 2.2	137.1 ± 3.0	0.299
K^+	4.6 ± 0.4	4.5 ± 0.5	0.273
Cl^-	114.2 ± 4.4	112.6 ± 5.7	0.304
CO_2 content	11.6 ± 2.7	13.5 ± 3.8	0.080
End of day 1			
Na^+	138.5 ± 2.1	138.9 ± 2.8	0.613
K^+	4.4 ± 0.5	4.4 ± 0.4	0.759
Cl^-	113.4 ± 2.7	116.4 ± 5.9	0.027*
CO_2 content	14.8 ± 4.0	12.5 ± 3.1	0.036*
Duration of diarrhea (h)	76.6 ± 32.7	100.2 ± 36.2	0.0034*

Data are expressed as mean ± SD or numbers with % in brackets
*Statistically significant

group which was 1.40 ± 1.74 percent compared to -0.42 ± 1.84 percent in the control group (*P* = 0.002). The stool frequency was less in the treatment group during the study period but was not statistically different (*P* = 0.290). Duration of diarrhea among rotavirus diarrhea was longer than the whole group (76.6 ± 32.7 hours in the treatment group, and 100.2 ± 36.2 hours in the control). The duration of rotavirus diarrhea was shortened by 23.6 hours in the treatment group compared to the control with rotavirus diarrhea (*P* = 0.0034). Moderate acidosis was seen more in rotavirus diarrhea initially and after refeeding, the total CO_2 content was 11.6 ± 2.7 initially and increased to 14.8 ± 4.0 mmol/L in the treatment group, and 13.5 ± 3.8 mmol/L initially and 12.5 ± 3.1 mmol/L at 24 hours in the control group. Persistent moderate acidosis at 24 hours was significantly different in the control group, *P* = 0.036. Serum chloride was also increased from 112.6 ± 5.7 to 116.4 ± 5.9 mmol/L in the control group. Stool output was greater in the control group (74.4 ± 55.2 g/kg) compared to the lactose-free formula group (58.06 ± 44.20 g/kg) but there was no statistical difference. Significant symptoms of vomiting were noted in the control group during the first day of refeeding (20.5 % in the treatment group vs 50.0% in the control group, *P* = 0.006) and in the rotavirus subgroup (15.8% vs 60.9%, *P* = 0.004).

Discussion

The results of the present study show that during the rehydration period at 4 hours, both groups had increased body weight 0.37-0.62%. After completion of 24 hours ORS replacement, serum sodium increased 1-2 mmol/L from the baseline and no case had serum sodium > 150 mmol/L. This indicates the efficacy of standard WHO-ORS for rehydration.

Moderate acidosis in the control group may be explained from lactose malabsorption. Unabsorbed lactose was fermented then liberated lactic acid in the intestinal lumen causing osmotic diarrhea as evident from reduction in total CO_2 content and rising of serum chloride level especially in the control group with rotavirus diarrhea. Lactose intolerance and moderate acidosis were probably the two factors which contributed to significant symptoms of vomiting observed in the control group and more so in the rotavirus control subgroup (*P* = 0.006, and *P* = 0.004). Stool frequency was significantly less than in the control group, *P* = 0.046 (4.1 ± 3.8 vs 5.9 ± 4.2 bowel movement). The increment of percent body weight changes was greater in the treatment group than in the control group (1.51 ± 1.71 vs 0.31 ± 1.98%, *P* =0.005). Duration of diarrhea was shortened by 20.5 hours in the overall children and 23.6 hours in the rotavirus diarrhea receiving lactose-free formula compared to lactose-containing formula. Other adjunct therapy had been reported to shorten the duration of diarrhea such as mucoprotective drugs[12] and probiotics[13-15] which shorten the duration of diarrhea by 17[12,13] to 20[14,15] hours or approximately one day. Unscheduled IV infusion was less by 50% (2 treatment, and 4 control). Milk is the main diet for infants and the lactose-free formula was shown in the present study to have efficacy for dietary management in non-breast fed children during acute diarrhea comparable to other adjunct therapy. Other advantages include providing nutrients for feeding enterocytes, supplying energy for body needs and

preventing additional acidosis from lactose malabsorption especially in infants with rotavirus diarrhea.

In conclusion, in the present study lactose-free formula was shown to be effective in dietary management of acute diarrhea. Duration of diarrhea was shortened when compared to lactose-containing formula. Stool frequency was less. Moderate acidosis cleared up spontaneously at 24 hours. Children tolerated it well and had better weight gain. Data of subgroup analysis of rotavirus diarrhea was shown to be more effective in all parameters studied.

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ประสิทธิผลของการให้นมผสมที่ไม่มีแลคโทสเปรียบเทียบกับนมผสมปกติในเด็กที่ป่วยด้วยโรคอุจจาระร่วงเฉียบพลัน

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การให้อาหารแก่เด็กที่เลี้ยงด้วยนมผสม ตามหลังการให้สารละลายน้ำตาลเกลือแร่ทางปากเพื่อรักษาภาวะขาดน้ำในเด็กที่เกิดจากโรคอุจจาระร่วงเฉียบพลันได้มีการทำ meta-analysis แล้วสรุปว่ามีผลไม่แตกต่างกัน แต่เนื่องจากเด็กไทยอาจมีผลให้หายช้าเพราะคนเอเชียมีน้ำย่อยแลคแทสต่ำกว่าคนตะวันตกอยู่แล้วโดยพันธุกรรม ยิ่งติดเชื้อโรตาไวรัสย่อมทำให้ขาดน้ำย่อยแลคแทสมากขึ้น ภาวะการดูดซึมแลคโทสบกพร่องอาจเป็นปัญหาที่สำคัญที่ทำให้หายช้าเมื่อเริ่มให้นมเป็นอาหารภายหลังแก้ไขภาวะขาดน้ำแล้ว

วัตถุประสงค์ *: เพื่อเปรียบเทียบประสิทธิผลของการให้นมผสมที่ไม่มีแลคโทสกับนมผสมปกติในเด็กที่ป่วยด้วยโรคอุจจาระร่วงเฉียบพลันภายหลังแก้ไขภาวะขาดน้ำแล้ว โดยเปรียบเทียบระยะเวลาของการหาย สารเคมีในเลือด อาเจียน น้ำหนักตัวที่เพิ่ม ความถี่ของการถ่ายและน้ำหนักอุจจาระ*

วิธีการศึกษา *: Randomized, double-blind clinical trial*

ผู้ป่วย *: ทำการศึกษาในเด็กเพศชายจำนวน 80 ราย ที่เลี้ยงด้วยนมผสม อายุระหว่าง 3 ถึง 24 เดือน และเข้ารับการรักษาในโรงพยาบาลด้วยโรคอุจจาระร่วงเฉียบพลัน และมีภาวะขาดน้ำน้อยถึงปานกลาง เด็กทุกรายได้รับสารละลายน้ำตาลเกลือแร่ทางปากเพื่อรักษาภาวะขาดน้ำใน 4 ชั่วโมงแรก หลังจากนั้นเด็กจะได้รับนมผสมโดยการสุ่มตัวอย่าง โดยกลุ่มแรกได้รับนมผสมที่ไม่มีแลคโทส (Dumex® Lactose-Free Formula) เป็นกลุ่มรักษาจำนวน 40 ราย และกลุ่มที่สองได้รับนมผสมปกติ (Dumex® Infant Formula) เป็นกลุ่มควบคุมจำนวน 40 ราย สลับกับการให้สารละลายน้ำตาลเกลือแร่ทางปาก และให้ข้าวบดในปริมาณเท่าที่จะสามารถรับได้*

ผลการศึกษา *: เด็ก 3 ราย (กลุ่มรักษา 2 ราย และกลุ่มควบคุม 1 ราย) ถูกคัดออกจากการศึกษา เด็กที่ได้รับสารน้ำทางหลอดเลือดดำมีจำนวน 6 ราย จากจำนวนทั้งหมด 80 ราย (ร้อยละ 7.5) โดยเป็นเด็กในกลุ่มรักษา 2 ราย (ร้อยละ 5.0) และกลุ่มควบคุม 4 ราย (ร้อยละ 10.0) และเด็ก 3 รายในกลุ่มควบคุมไม่หายจากโรคอุจจาระร่วงภายในระยะเวลา 7 วัน ผลการตรวจอุจจาระพบโรตาไวรัส ประมาณร้อยละ 50 ในแต่ละกลุ่ม จากการวิเคราะห์ระยะปลอดเหตุการณ์ (survival analysis) พบค่า median ของระยะเวลาหายจากอุจจาระร่วงในกลุ่มรักษาลดลง 20.5 ชั่วโมง อย่างมีนัยสำคัญทางสถิติเมื่อเทียบกับกลุ่มควบคุม (P = 0.002) โดยมีค่าเท่ากับ 77.0 และ 97.5 ชั่วโมง ในกลุ่มรักษาและกลุ่มควบคุมตามลำดับ จำนวนครั้งของการถ่ายอุจจาระลดลง และร้อยละของน้ำหนักตัวเพิ่มขึ้นอย่างมีนัยสำคัญในกลุ่มรักษาเมื่อครบ 24 ชั่วโมง ภาวะเลือดเป็นกรดปานกลางหายไปเกือบเป็นปกติเมื่อครบ 24 ชั่วโมง ในขณะที่ยังคงพบภาวะเลือดเป็นกรดในกลุ่มควบคุม ในกลุ่มอุจจาระร่วงที่เกิดจากโรตาไวรัส ภาวะเลือดเป็นกรดปานกลางลดลงเป็นระดับเล็กน้อยในกลุ่มรักษาเปรียบเทียบกับระดับเลือดเป็นกรดที่ไม่เปลี่ยนแปลงร่วมกับมีคลอไรด์ในเลือดสูงขึ้นในกลุ่มควบคุม เมื่อครบ 24 ชั่วโมง แสดงถึงการเกิดภาวะการดูดซึมแลคโทสบกพร่องและ osmotic diarrhea ระยะเวลาหายจากอุจจาระร่วงจากโรตาไวรัสในกลุ่มรักษาลดลง 23.6 ชั่วโมง เมื่อเทียบกับกลุ่มควบคุม (P = 0.0034)*

สรุป *: การใช้นมผสมที่ไม่มีแลคโทสในการให้อาหารเด็กที่ป่วยด้วยโรคอุจจาระร่วงเฉียบพลัน มีประสิทธิผลในการรักษาโรคโดยทำให้ระยะเวลาหายจากโรคสั้นเข้า น้ำหนักตัวขึ้นดี และจำนวนครั้งของการถ่ายอุจจาระลดลงเมื่อเปรียบเทียบกับนมผสมปกติ ภาวะเลือดเป็นกรดหายไปเมื่อครบ 24 ชั่วโมง และเด็กสามารถรับนมผสมที่ไม่มีแลคโทสนี้ได้ดี ข้อมูลจากการวิเคราะห์ในกลุ่มอุจจาระร่วงจากโรตาไวรัสก็แสดงถึงผลการรักษาที่ดีกว่าในทุกด้านของนมผสมที่ไม่มีแลคโทส*