Role of a Soy-Based Lactose-Free Formula in the Outpatient Management of Diarrhea

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ABSTRACT. The introduction of a soy-based, lactose-free formula during the acute phase of diarrheal illness in infants has been shown to reduce stool output and duration of diarrhea in hospitalized patients. In the United States, most infants with acute diarrhea are treated as outpatients. In the present study, infants with diarrhea who were treated as outpatients were randomly assigned to receive either a soy-based, lactose-free formula alternating with oral rehydration solution from the beginning of therapy ("early feeding") or oral rehydration solution alone for the first 24 hours of therapy, followed by a soy-based, lactose-free formula alternating with oral rehydration solution (control group). Twenty-nine infants were randomly assigned to the early-feeding group and 27 to the control group. Twenty-one (72%) of 29 in the early-feeding group resolved their diarrhea at the end of 48 hours of therapy compared with 12 (44%) of 27 in the group fed oral rehydration solution only ($P = .02$). It is concluded that the introduction of a soy-based, lactose-free formula from the beginning of therapy for acute diarrhea in children treated as outpatients is safe and may shorten duration of diarrhea while maintaining adequate caloric intake. *Pediatrics* 1991;87:619–622; *diarrhea, infants, lactose-free formula, soy-based formula, oral rehydration solution.*

Since the early part of this century, disagreement has existed regarding the advantages of feeding children during the acute phases of diarrheal illness ("early feeding").[1-3] In practice many pediatricians continue to recommend against early feeding during diarrhea in infants. Oral rehydration solutions given for the recovery and maintenance of hydration, while clearly beneficial, do not provide adequate nutrition if given as the only intake during acute diarrhea. Currently available oral rehydration solutions in the United States do not reduce the volume or duration of diarrhea when given alone.

In a recent study,[4] we demonstrated that the use of a soy-based, lactose-free formula during the initial phase of acute diarrhea among hospitalized patients in the United States resulted in the significant reduction of duration of diarrhea and stool output compared with a control group given oral rehydration solution alone for 24 hours. Similar data, however, are lacking for infants treated as outpatients, who account for the majority of those ill with diarrhea in the United States. Therefore, we conducted a randomized, controlled trial comparing the use of a soy-based, lactose-free formula vs oral rehydration solution alone during the first 24 hours in patients treated at home.

PATIENTS AND METHODS

Infants aged 2 through 12 months with acute (less than 7 days' duration) watery diarrhea (at least five watery stools in the previous 24 hours) were enrolled in the study if they were clinically assessed to have less than 7% dehydration using standard criteria.[5] Infants were recruited from the outpatient clinic of the US Public Health Service Hospital in Whiteriver, Arizona, and the private

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practice of Dr J. Crosson O'Donovan and a city health clinic in Baltimore, Maryland. The study was conducted from March 1983 to September 1983.

After initial examination by the primary physician or by one of the investigators, written informed consent was obtained from the parents of eligible patients. Infants were then block randomized by groups of 4, according to a random table of numbers, to group A or B. Patients in group A were provided with both a soy-based, lactose-free formula (Nursoy, Wyeth Laboratories) and an oral electrolyte solution (Resol, Wyeth Laboratories; composition, per liter: sodium, 50 mEq; potassium, 20 mEq; chloride, 50 mEq; citrate, 34 mEq [11 mmol/L as citric acid]; glucose, 20 g; magnesium, 4 mEq/L; calcium, 4 mEq/L; and phosphate, 5 mmol/L) at equal volumes (approximately 100 mL/kg per 24 hours of each). Mothers were instructed to alternate ad libitum feedings with each liquid during the first 24 hours. Patients in group B were given Resol alone, at approximately 200 mL/kg per 24 hours. Mothers of these patients were instructed to offer the Resol ad libitum (alternating with water for the first 24 hours). These volumes of fluids were intended to provide adequate amounts for daily maintenance (150 mL/kg per day), in addition to 50 mL/kg per day to compensate for anticipated diarrheal losses in the next 24-hour period. After 24 hours, group B patients were given half-strength soy formula alternating with oral rehydration solution for the subsequent 24 hours. After 48 hours of therapy, group B patients were given the same formula as patients in group A, and both groups continued to receive ad libitum alternate feedings with formula and Resol until diarrhea resolved. Resolution of illness was defined as absence of watery stools for a 16-hour period.

All infants were seen daily either at clinic or at home until resolution of diarrhea. Patients were weighed at the time of admission to the study, daily until symptoms resolved, and at 2 weeks after initial presentation. At the time of the daily follow-up visit, the volume of rehydration solution or formula remaining was measured by the study staff, and additional Resol or formula was dispensed. After resolution of symptoms, mothers were instructed to resume their normal feeding practices.

A patient was considered to be a treatment failure if the degree of dehydration was clinically assessed to be greater than 5% after 24 hours of therapy or if diarrhea persisted for more than 7 days after the start of therapy.

Admission laboratory studies included determinations of concentrations of serum sodium, potassium, chloride, bicarbonate, blood urea nitrogen, glucose, and total protein.

A t test was performed on appropriate variables among treatment groups. Chi-square analysis was used on frequency data except when Fisher's exact analysis was more appropriate.

RESULTS

Fifty-nine patients were enrolled in the study. Three patients were dropped from the study within 24 hours because of noncompliance with the study regimen. Fifty-six patients were enrolled in the study and followed the treatment regimen according to protocol, 29 in group A (16 from Whiteriver, 13 from Baltimore) and 27 in group B (16 from Whiteriver, 11 from Baltimore). There were no significant differences in the admission characteristics between the two groups nor were there significant differences between patients enrolled in Baltimore or Whiteriver (Table 1).

The duration of diarrhea and intake of fluids is shown in Table 2. The number of patients whose illness resolved within 24 hours of initial therapy was greater in group A than in group B, but this difference was not statistically significant ($P = .09$). At the end of 48 hours, 21 (72%) of 29 group A patients had resolved their diarrhea, compared with 12 (44%) of 27 group B patients ($P = .02$). The diarrhea lasted longer than 48 hours after beginning treatment in 6 (20.7%) of the patients in group A,

TABLE 1. Admission Characteristics (Means ± SD)*

Characteristic	Group A (Early Feeding; n = 29)	Group B (Delayed Feeding; n = 27)
Age, mo	6.2 ± 3.3	6.3 ± 2.5
Male:female	1.6:1	1:1.2
Temperature, °C	37.9 ± 0.7	37.6 ± 0.7
Weight, kg	7.4 ± 2.0	7.2 ± 1.5
Mean no. of stools in the 24 h prior to admission	7.2 ± 2.3	8.6 ± 4.1
Sodium, mmol/L	137 ± 3.6	138 ± 3.5
Potassium, mmol/L	4.9 ± 0.6	4.9 ± 0.7
Chloride, mmol/L	111 ± 3.0	111 ± 2.9
Bicarbonate, mmol/L	14.9 ± 2.5	15.3 ± 2.4
Blood urea nitrogen, mg/dL	7.8 ± 3.9	8.5 ± 4.9
Glucose, mg/dL	100.3 ± 16.6	90.7 ± 18.7
Total serum protein, mg/dL	6.4 ± 0.6	6.3 ± 0.6
History of vomiting prior to entry	10	7
Degree of dehydration		
<5%	27	24
5–7%	2	3

* None of the differences between the groups were statistically significant.

TABLE 2. Features of Treatment Groups During Therapy

Feature	Group A (Early Feeding)	Group B (Delayed Feeding)	*P* Value
No. in study	29	27	
No. (%) resolved illness within 24 h of treatment	13 (44.8)	6 (22)	.09
No. (%) resolved illness within 48 h of treatment (cumulative)	21 (72)	12 (44)	.02
No. (%) resolved illness after 48 h of treatment	6 (20.7)	15 (55.6)	<.01
No. of treatment failures	2	0	.26
No. of days from entry into study until resolution of symptoms (mean ± SD)	2.0 ± 0.2	2.7 ± 1.3	.02
ORS* intake first 24 h, mL/kg (mean ± SD)	68 ± 38	155 ± 61	.001
Formula intake first 24 h, mL/kg (mean ± SD)	88 ± 43	. . .	. . .
Total intake first 24 h, mL/kg (mean ± SD)	160 ± 69	166 ± 67	.6
ORS* intake during illness, mL/kg (mean ± SD)	104 ± 81	260 ± 171	.001
Formula intake during illness, mL/kg (mean ± SD)	165 ± 116	364 ± 313	.02
Total fluid intake during illness, mL/kg (mean ± SD)	269± 176	624 ± 409	.02
No. of stools/day, first 24 h after beginning treatment (mean ± SD)	2.6 ± 2.8	3.4 ± 3.5	.21
% Weight gain† at 24 h after entry (mean ± SD)	1.5 ± 3.5	2.5 ± 3.7	.5
% Weight gain† at resolution (mean ± SD)	1.8 ± 3.5	1.2 ± 2.2	.5
% Weight gain† at 2 wk after therapy (mean ± SD)	3.0 ± 6.2	3.4 ± 2.9	.8

* ORS, oral rehydration solution.

† % Weight gain = $\frac{\text{weight at time of observation}}{\text{admission weight}}$.

compared with 15 (55.6%) of the patients in group B ($P < .01$).

Group A patients consumed significantly ($P = .001$) less oral rehydration solution than group B patients, both in the first 24 hours and during the entire illness (Table 2). The total fluid intake during therapy was also significantly ($P = .02$) less in group A than in group B. No significant differences were detected in the percentage of weight gain during any of the intervals. Sodium intake was within the range of normal daily requirements in both groups. In the first 24 hours of therapy, group A received 3.4 mEq/kg of sodium, while group B patients received 7.8 mEq/kg. Parents of patients in group B reported giving very little additional water (only 11 mL/kg in the first 24 hours). No patients were reported to have had recurrence of diarrhea within the 2-week follow-up period.

Two patients were considered treatment failures. One patient in group A was admitted to the hospital 24 hours after treatment began, for intravenous fluid therapy because of poor oral intake due to severe oral thrush. A second patient in group A was considered a treatment failure because of persistent diarrhea for more than 7 days.

DISCUSSION

Our previous study performed with hospitalized infants[4] demonstrated that the introduction of a soy-based, lactose-free formula during the acute phase of diarrheal illness resulted in reduction of stool output and in duration of diarrhea. In the present study, we have demonstrated that the duration of diarrhea can also be reduced in outpatients if early feeding with a soy-based, lactose-free formula is used. This finding is particularly relevant because most episodes of acute diarrhea in the US population occur in infants treated at home.

Large volumes of fluid intake have been suggested to induce or prolong diarrhea.[6] In the current study, although the delayed-feeding group consumed larger total amounts of fluid, no patient took more than 200 mL/kg per day. It appears unlikely, therefore, that fluid intake alone accounts for the observed differences between groups. Inasmuch as feeding was delayed by only 24 hours, it also seems unlikely that the longer duration of diarrhea in the delayed-feeding group was accounted for by "starvation stools." Etiologic agents were not determined in this study. Previous studies by us have shown *Rotavirus* to be the dominant pathogen in

both the Whiteriver[7] and Baltimore pediatric populations.[8]

Many pediatricians continue to recommend a clear liquid diet consisting of fluids such as fruit juices or gelatin water. Such solutions contain relatively high carbohydrate concentrations. The higher carbohydrate concentrations in these fluids are not optimal for the absorption of sodium and water from the gut.[9] They may actually exacerbate diarrhea by imposing a high osmotic load and may ultimately lead to hypernatremic dehydration.[10] The findings in the present study provide support for recommending early feeding with a soy-based, lactose-free formula, instead of clear liquids, in the acute phase of diarrheal illness in children.

It is probable that the reduction in duration of diarrhea in patients fed early in the course of their treatment is the result of enhancement of sodium and water absorption by the products of digestion of the soy formula (glucose and amino acids) in the gut. Such enhanced sodium transport forms the physiologic basis for oral rehydration itself. Substances besides glucose serve as substrates for facilitated cotransport of sodium (eg, certain amino acids) and have been proposed to be useful in improving the absorption of oral rehydration solution.[11]

Because soy-based formulas may be unavailable or prohibitively expensive in developing countries, studies are under way in a number of countries to evaluate the use of locally available foods during diarrheal episodes. Some recent studies have supported the use of diluted lactose-containing formulas or foods in well-nourished infants with mild to moderate diarrhea.[12,13] Continued breast-feeding during diarrheal episodes has also been shown to reduce stool output.[14] Therefore, all breast-feeding infants should be encouraged to continue to do so.

We conclude that for outpatients with diarrhea in the United States, the early introduction of a soy-based, lactose-free formula is safe and may shorten the duration of diarrhea while maintaining adequate caloric intake.

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