Feeding of Children with Protracted Diarrhea in Developing Countries

Alejandro M. O’Donnell and Marina Orsi

Centro de Estudios sobre Nutrición Infantil (CESNI), 1425 Buenos Aires, Argentina

Acute infectious diarrhea with dehydration is among the two main causes of infantile morbidity and mortality in less developed countries. The complex etiology of childhood diarrhea and its close relationship with environmental conditions and nutritional status must be stressed in designing and evaluating possible treatments. In the present chapter, we attempt to express some of our thoughts and reports of our work on patients with diarrhea, the product of many years of work in Argentina and in other Latin American countries.

After 2 years of systematic use of the WHO–UNICEF oral rehydrating solution (ORS), we feel that it has been a true breakthrough in the management of acute infectious diarrhea. The effectiveness of the method clearly dispelled our initial skepticism. A controlled study done by our group showed the ORS to be effective in 92% of the cases (102 patients) irrespective of age, nutritional status, or severity of diarrhea. It was even given to patients with severe dehydration, and only two children showed plasma sodium slightly above the normal level. The average sodium intake for the whole group was 9 mg/kg per day, which is similar to or less than what is used in i.v. rehydration regimens. An evaluation of the i.v. rehydration of diarrheic patients was performed in the same hospital in 1978. Patients in this study are comparable in age, nutritional status, and severity of diarrhea to the ones rehydrated with ORS. Table 1 shows the obvious advantages of the latter method. Currently, oral rehydration is used routinely in this hospital with excellent results. We consider it safe, inexpensive, and effective, and it allows the mother or caretaker to participate in the treatment of the child.

We have always been concerned with the question of how and with what a diarrheic patient should be refed, since the outcome of the diarrhea is so closely linked to the improvement of nutrition and vice versa. The very rapid clinical recovery (sense of well-being and appetite) of the child rehydrated with the WHO–UNICEF ORS is conducive to an earlier introduction of food, raising some questions as to the advisability of this modality. The classical studies of Chung et al. (1) demonstrated that feedings could increase fecal losses but simultaneously promote absorption of nutrients to an extent that could be helpful in preserving the nutritional condition of the child.
In 1968, we developed a lactose-free formula to treat diarrheic patients in the hope of improving nutrient intake without increasing fecal losses. Its composition is shown in Table 2. It cannot be considered an elemental diet because it was formulated with sodium caseinate, corn, coconut, and sunflower oils, and three different carbohydrates (glucose, sucrose, and rice maltodextrins). The importance of the concentration and type of carbohydrates to be included, the osmolality, and some other aspects that are currently prevalent were not understood at the time the formula was developed. Although it was designed on
a rather empirical basis, our present understanding of the pathophysiology of diarrhea supports its use.

The formula was first tested in children with severe diarrhea and malnutrition. Initially, we were concerned by the increase in fecal losses of water and electrolytes that could result if the patients were fed liberal amounts of the formula. When the first metabolic balances were available and showed acceptable absorption of nutrients, we felt more confident in increasing the feedings considerably with the idea of preserving the nutritional status of the children. Positive nitrogen balance was used as an indicator of acceptable nutrition. The results of the two different studies are shown in Table 3. In the second trial, 20 out of 30 of nitrogen balances were positive, in contrast to 7 out of 28 in the initial trial.

To assess the nutritional importance of vegetable oils against butterfat in infants with severe protracted diarrhea, metabolic balances were performed. The formulas were identical except for the fat composition (Table 4). Fecal loss expressed as percentage of absorption was 17.7 (±3.1) for butterfat \( (n = 14) \) and 6.7 (±1.3) for vegetable oil \( (n = 36) \) \( (p < 0.01) \) (Table 4). No significant correlations were found in these metabolic studies between nitrogen or fat intake and absorption and the diarrheal losses (Figs. 1–4). On the other hand, a highly significant correlation was found between fat intake and its absorption \( (r = 0.82, p < 0.01) \). The same was true for nitrogen (Figs. 5, 6).

Although the experimental design was not intended to establish nutrient requirements in diarrheic children, it can be seen from Fig. 5 that all balances became positive on intakes above 350 mg/kg per day of N equivalent to 2.2 g of protein/kg per day. This figure is higher than the FAO–WHO safe intakes for such age groups, and such differences can be explained to some extent by malabsorption.

<table>
<thead>
<tr>
<th>Source of ingested fat</th>
<th>Fecal fat (%)</th>
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<tbody>
<tr>
<td>Butterfat ( (n = 14) )</td>
<td>17.7 ± 3.1*</td>
</tr>
<tr>
<td>Vegetable oil blend ( (n = 36) )</td>
<td>6.7 ± 1.3</td>
</tr>
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</table>

* \( p < 0.01 \).

From O'Donnell et al. (3), with permission.
That estimation was confirmed by the urinary excretion of urea. As depicted in Fig. 6, urinary area excretion has the shape of an ellipse with the lowest value of excretion on nitrogen intakes of 350 to 400 mg/kg per day, similar to that obtained from nitrogen balances. On higher intakes, urea excretion increased exponentially, expressing waste of nitrogen that could not be efficiently metabolized. The highest nutritionally useful level of nitrogen intake seems to be 800 mg/kg per day of N (5 g protein).

An additional consideration is energy intake and its relation to protein intake. From Fig. 7, we can infer that all but two infants had positive nitrogen balances with a protein calorie percent ≥10. The formula used contains 13% of the calories as protein at full-strength dilution.

In the clinical evaluation, we randomly assigned the formula to refeed 100
diarrheic rehydrated infants and gave another 100 other milk-based formulas. Two important conclusions were obtained from this simple clinical study. The group fed the lactose-free formula had significantly shorter hospitalizations than the group fed the other milk-based formulas \( (p < 0.01) \). These differences were more significant among those patients with evident carbohydrate malabsorption (fecal pH 5.5 and positive Clinitest®). The formula is expensive for the Argentinian health system and for the lower socioeconomic groups. However, if we consider the above-mentioned differences, its higher cost is compensated by savings related to shorter hospitalizations. Over many years, the formula has proven its usefulness. However, because of its popularity among pediatricians, it is overprescribed to patients belonging to the lowest income groups of our society, which are, as everywhere, the most affected by diarrhea and malnutrition. At times, the health system cannot afford to purchase the formula for public hospitals and primary care centers.
We are, therefore, charged with the development and evaluation of less expensive alternatives, ideally with components available in almost every household or sanitary facility. This is a real challenge and a high priority for research in the less developed countries. We cannot follow guidelines for treatment of intractable diarrhea in developed countries, where parenteral nutrition and many diagnostic aids are always at hand. Similarly, elemental formulas and infusion pumps for continuous intragastric feeding are prohibitively expensive. For example, 100 g of whole dry cow's milk costs $0.50; 100 g of the lactose-free formula costs $1.00; 100 g of soy-isolate-based formula costs $1.50; 100 g of a well-known elemental formula marketed in the United States costs $4.00. The evaluation of a formula made in our hospital containing egg white, corn oil, sucrose, corn starch, and egg yolk as an emulsifier in percentages similar to the lactose-free formula is under progress. The initial results have been encouraging.

Another alternative that needs to be properly evaluated is the use of cereal purees and gruels with small amounts of cow's milk, vegetable oil, and sucrose. They have the advantages of being available almost everywhere and have been used traditionally in infant feeding. The use of purees and gruels has the additional advantage of hygiene, which deserves special consideration in ambulatory patients. We have recently studied the contamination of infant foods in a poor section of Buenos Aires. Samples of milk from bottles were obtained during

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**FIG. 3.** Correlation between fecal weight and fat malabsorption (as percent of intake) (n = 28, balance studies). (From O'Donnell et al., ref. 3, with permission.)
home visits immediately prior to its being offered to infants. Samples of purees and milk–cereal gruels were also studied. As can be seen from Fig. 8, 46% of milk samples were contaminated. A contaminated milk (e.g., not suitable for human consumption) was defined according to FAO criteria (more than 100,000 colonies/ml of nonpathogenic bacteria). Furthermore, about half the samples were contaminated whether dried cow's milk or fluid pasteurized milk was used and whether or not the families owned a refrigerator. This was a surprising finding, because it is generally felt that dry milk is safer than the pasteurized milk sold as a liquid in such environments. Every mother boiled milk from 2 to 20 min. This shows that health education messages were incorporated by most people.

Environmental contamination may be so overwhelming that boiling milk and leaving it at room temperature is no different from unboiled milk kept in
An amazing finding was that samples from bottles prepared with milk and cereals (not precooked) that needed some cooking before being offered to the baby were uniformly sterile. The same happened with purees and gruels. The culinary properties of some cereals requiring cooking were more effective than attempts to preserve the sterility of milk through boiling as recommended by health education campaigns. This is an interesting finding that needs further research.

Another argument of the future use of cereals derives from our findings in a longitudinal collection of milk samples in three families who consumed the same brand of milk, which was also purchased in the same market (Table 5). Contaminated samples were collected on 8 out of 10 days in a follow-up of a low-income family not owning a refrigerator. In a medium- to high-level family, cultures were all negative.
As a previous step for an ongoing study on cereals, gruels, and purees for diarrheic infants, we evaluated the capacity of a child between 2 to 3 months to accept food from a spoon. Figure 9 shows that after the second day of being fed, babies were able to obtain 75% of their recommended energy intake from semisolid foods.

The usual definition of protracted diarrhea is persistence of diarrheal stools for more than 2 weeks. Some investigators have suggested that at this point, patients should be put on total parenteral nutrition. This is generally impossible in hospitals in the underdeveloped countries despite the fact that more than 20% of hospitalized patients fall into the category of severe protracted diarrhea according to this definition. If we add the deficit of diagnostic aids and the previous malnutrition of infants, it is easy to understand the high mortality of the disease and the empirical basis of many treatments.
FIG. 7. Nitrogen balance versus protein calories. (From O'Donnell et al., ref. 3, with permission.)

FIG. 8. Bacterial contamination of pasteurized milk: family follow-up with milk samples over 20 consecutive days. Arrows indicate days on which contaminated milk samples were obtained. (From Barilaro et al., ref. 4, with permission.)
TABLE 5. Contamination of milks at the household*

<table>
<thead>
<tr>
<th>Type of milk</th>
<th>Number of contaminated samples (%)</th>
<th>E. Coli</th>
<th>Klebsiella</th>
<th>EPEC</th>
<th>Serratia</th>
<th>Pseudomonas aeruginosa</th>
<th>Proteus</th>
<th>Strep D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole, dry (n = 50)</td>
<td>21 (42)</td>
<td>10 (48)</td>
<td>10 (24)</td>
<td>5 (24)</td>
<td>3 (14)</td>
<td>3 (14)</td>
<td>0 (0)</td>
<td>3 (14)</td>
</tr>
<tr>
<td>Fluid, pasteurized, w/refrigerator (n = 50)</td>
<td>18 (36)</td>
<td>7 (39)</td>
<td>9 (50)</td>
<td>2 (11)</td>
<td>3 (15)</td>
<td>1 (6)</td>
<td>0 (0)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Fluid, pasteurized, no refrigerator (n = 50)</td>
<td>20 (40)</td>
<td>9 (45)</td>
<td>8 (40)</td>
<td>3 (15)</td>
<td>5 (25)</td>
<td>1 (5)</td>
<td>3 (15)</td>
<td>3 (15)</td>
</tr>
</tbody>
</table>

* More than 10^6 col/ml and/or enterobacteria present.
 Modified from Barilaro et al. (4), with permission.
An additional area requiring urgent research is the use of antibiotics in protracted diarrhea, which is advocated by many and denied by an equal number. Our policy has been based on the prevalence of rotavirus and enteropathogenic E. coli infections and on the slower turnover of the epithelial cells in malnourished infants. We prescribe nonabsorbable antibiotics after 10 days of diarrhea not explained by carbohydrate malabsorption or known pathogens. We do not have, as yet, data from a controlled study to assess the usefulness of this regimen.

When diarrhea persists, the mechanisms underlying it are difficult to determine with the exception of obvious carbohydrate malabsorption. Food intolerance can be suspected if the patient, on withdrawal of enteral feedings for 24 to 36 hr while receiving i.v. fluids and glucose, has resolution of diarrhea. If significant diarrhea still persists after 24 hr of fasting, a secretory process or deconjugation of bile acids can be suspected. Antibiotic and cholestyramine therapy has not, however, been useful in our experience. Milk protein intolerance is present in no more than 2% of patients with protracted diarrhea. Lactose intolerance is fairly common, with many infants showing long-lasting malabsorption.

Hospital-made formulas (casein, chicken meal, egg white, plus corn oil) are used to initiate feedings after the i.v. period. Carbohydrates (glucose, sucrose) are added in initially low concentrations (2%) that are slowly increased according to tolerance and to the detection of sugar in feces.

The problem of feeding children with protracted diarrhea is far from being solved. Protracted diarrhea represents a major health problem in less developed
countries, where its prevalence is increasing since a greater percentage of infants survive the initial dehydration because of better management. The WHO–UNICEF ORS has made a substantial contribution in decreasing mortality from dehydration. Future research will be needed, particularly contributions of microbiologists, nutritionists, clinicians, and public health specialists. The food industry could make substantial contributions through the development of inexpensive and safe foods. Economic support for such research is crucial.

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REFERENCES