Frozen Oral Hydration as an Alternative to Conventional Enteral Fluids

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Background: Oral hydration therapy is effective in dehydration, but is often bypassed or may fail.

Objective: To compare the tolerance (amount accepted minus amount vomited) of a frozen solution (FS) (Revital-ICE, PTS Labs, Deerfield, Ill) with the conventional glucose electrolyte solution (CS).

Design: Prospective, controlled crossover trial.

Setting: Pediatric emergency department.

Participants: A convenience sample of 91 children with enteritis, 6 months to 13 years of age, with mild to moderate dehydration.

Intervention: Children were offered either FS or CS. Each group was offered 10 mL/kg of either product during a 90-minute trial period, in 3 equal aliquots, and was monitored for the quantities consumed and vomited. Complete treatment failures (absolute refusals) were crossed over to the alternate product and intake was recorded.

Main Outcome Measures: Tolerance of the full 10 mL/kg of the original product offered and, for treatment failures, the percentage who tolerated the alternate product.

Results: Of the patients who initially received FS, 23 (55%) tolerated the full amount offered, compared with 5 (11%) in the CS group (P < .001). Of the 57% who completely refused CS, after crossover, 20% tolerated the full amount of FS and 33% tolerated between 5 and 9 mL/kg of FS and were discharged from the hospital. The original treatment failures for FS (12%) were crossed over to CS; none tolerated more than 5 mL/kg.

Conclusions: Children with mild or moderate dehydration are more likely to tolerate FS than CS. Conventional solution failures crossed over to FS had a greater tolerance rate than the reverse.

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The first physiologic oral hydration fluids were introduced in 1946. The first controlled trials of oral rehydration therapy were performed in 1967, and included studies in adults, children, and infants. These studies demonstrated the efficacy of oral rehydration therapy for mild to severe acute diarrheal disease of various causes. In the United States, infant diarrhea is associated most frequently with mild dehydration and responds to oral hydration therapy. However, it still accounts for 200,000 hospitalizations and 400 deaths per year, according to a recent article from the US Centers for Disease Control and Prevention, Atlanta, Ga.

Despite the endorsements of such organizations as the American Academy of Pediatrics (AAP), the World Health Organization (WHO), and the United Nations Children’s Fund (UNICEF), appropriate oral therapy for diarrhea and vomiting remains underused in the United States. The WHO estimates that worldwide, fewer than 25% of people who could benefit from oral therapy are treated with appropriate oral hydration fluids.

In the United States, even with commercially available rehydration and maintenance solutions, common practice continues to consist of the administration of clear liquids like fruit juices (such as apple...
PATIENTS AND METHODS

This study was conducted in the emergency department at Hasbro Children’s Hospital, a tertiary care facility in Providence, RI. Approximately 35,000 patients each year visit this emergency department, which is staffed 24 hours a day by pediatric emergency medicine attending physicians. The children were enrolled during a 6-month period, from October 1995 to March 1996. The standard of care for children with mild to moderate dehydration at this institution involved either an attempt at oral hydration using the CS or the administration of intravenous fluids.

METHODS

This was a prospective, controlled, convenience-sample trial approved by the Institutional Review Board for the hospital. Patients were enrolled in the study if the family gave informed consent and if the child (if of appropriate age) provided assent. Children aged 6 months to 13 years were eligible if they presented with an uncomplicated history of diarrhea, vomiting, or both. All children with mild, mild to moderate, and moderate dehydration were included provided they had not received prior intravenous therapy. Enrollment was dependent on the availability of either of the investigators (A.C.A. and K.A.S.).

Complete medical histories were obtained and physical examinations were performed, with an emphasis placed on the presence of vomiting and diarrhea and their onset, duration, and character. A standard table adapted from the WHO7 was used to assess the degree of dehydration of each enrolled child (Table 1). The column that contained 5 or more characteristics determined the degree of dehydration for each child. Children eligible for the study fell into the mild to moderate (shared characteristics of the mild and moderate groups), and moderate dehydration categories.

Exclusion criteria included the presence of severe dehydration or diminished perfusion requiring immediate intravenous fluid resuscitation, grossly bloody stools, systemic infections, suspected surgical illness (such as acute abdomen), severe malnutrition, or underlying chronic illness.

The caretakers of the participants were asked to complete a study questionnaire, which consisted of demographic information as well as specifics about their child’s presenting complaints: duration of symptoms, presence of vomiting and/or diarrhea and the frequency of each over the preceding 24 hours, the presence or absence of fever, the fluid type being offered at home, time of last emesis, time of last urination, and the parents’ expectations for treatment in the emergency department.

TREATMENT GROUPS

Patients enrolled on even-numbered days were offered CS and those enrolled on odd-numbered days received FS. The FS has the same electrolyte composition as the CS, but is naturally fruit-flavored and comes in a clear plastic package of 63-mL aliquots per ice pop. Both solutions contain 45-mEq/L sodium, 20-mEq/L potassium, 35-mEq/L chloride, 30-mEq/L citrate, 25-g dextrose, and 100 calories per liter.

Each of the groups was offered a total of 10 mL/kg of the respective solution, either CS or FS. The total amount was divided into 3 separate aliquots and a single aliquot was offered to the participants at 0, 30, and 60 minutes. The objective was to provide the fluid slowly and in small amounts. Parents giving their child the CS were instructed to provide small aliquots (3-10 mL) every 1 to 5 minutes. Five milliliters every minute is the recognized standard for infants; the fluid was offered less aggressively in this study. Parents supervised their child’s intake of the FS.

The researchers monitored both groups for intake, vomiting, and refusal. Children who retained the fluid were eligible to be discharged.

At each 30-minute interval, the total amount of fluid consumed and the amount vomited or refused by the child was tabulated. Children were monitored by the investigators during the 90-minute trial period to safeguard against familial consumption of the product and to assess vomiting or refusal. Those children who tolerated 10 mL/kg or more of the product offered were considered treatment successes. They were discharged with advice on refeeding and instructions to return to the emergency department if the child stopped drinking or had persistent vomiting. A complimentary sample of the product they tolerated in the emergency department was provided and, as is routine in our emergency department, a recommendation for follow-up with the primary care provider was made.

Children were permitted 30 minutes for the consumption of the first portion of the initial product. Patients who either completely refused the initial product or had persistent vomiting with that product were then crossed over to the alternate product and considered a treatment failure for the first product. These children were started at time 0 with the alternate product and permitted to continue through the 90-minute timeline. If children who were crossed over failed with the second product, they were reevaluated for intravenous fluid administration.

juice), carbonated beverages (such as ginger ale), and the more recently popularized sports drinks. These products are not suitable for rehydration or maintenance therapy in patients with ongoing losses because of their high osmolality and inappropriate ratio of sodium to carbohydrate content.7,8

Two of the solutions (with the appropriate electrolyte composition) available in the United States are Pedialyte (Ross Products Division, Abbott Laboratories, Columbus, Ohio) and Infalyte (Mead Johnson & Co, Evansville, Ind) and are best suited for use as maintenance solutions. These products have sodium concentrations ranging from 45 to 50 mEq/L.9 They can satisfactorily rehydrate otherwise healthy children who are mildly or moderately dehydrated10,12; however, at times there is resistance associated with their use.

There are many possible reasons why oral hydration and rehydration products are underused. In the emergency department, there may be a reluctance to introduce a regimen of oral rehydration because of time constraints, space limitations, and the difficulties associated with providing 5 mL of fluid by mouth every 1 to 5 minutes.9 Proper training and the exercise of patience may obviate these perceived obstacles.
Intravenous therapy has been used successfully in US hospitals for many years. Furthermore, parents and referring pediatricians may not be inclined to seek the same type of therapy they have been trying at home or in the office. At times, an appropriate hydration product is already being offered at home and the child either dislikes and refuses it or, less frequently, may have had “persistent” vomiting, leading to failure of this method. In 1996, there was some speculation that glucose electrolyte solutions could be frozen into an ice-pop form, which may appeal to some children and facilitate the administration of the product.9

This study was designed to determine if, within the confines of the emergency department, a frozen product might facilitate the initiation of oral rehydration or maintenance hydration, without the use of intravenous fluids, in children with ongoing losses. The frozen solution (FS) (Revital-ICE, PTS Labs, Deerfield, Ill) is a naturally flavored ice-pop solution with the same electrolyte composition as the conventional solution (CS) (Pedialyte), a clear glucose electrolyte solution commonly used to help restore and maintain hydration in children with mild or negligible physical signs of dehydration.

We compared the tolerability (quantity accepted minus the quantity vomited) of the FS with the CS in a population of children with mild to moderate dehydration secondary to enteritis.8

Table 1. Dehydration Status*

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mild</th>
<th>Mild-Moderate</th>
<th>Moderate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>Normal</td>
<td>Increased</td>
<td>Greatly increased</td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>Normal</td>
<td>Normal</td>
<td>Hyperpnea</td>
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<tr>
<td>Blood pressure</td>
<td>Normal</td>
<td>Orthostatic</td>
<td>Decreased pulse pressure</td>
</tr>
<tr>
<td>Capillary refill</td>
<td>Normal</td>
<td>Normal or slow</td>
<td>Slow</td>
</tr>
<tr>
<td>Eyeballs</td>
<td>Normal to dry</td>
<td>Normal</td>
<td>Sunken</td>
</tr>
<tr>
<td>Mucous membranes</td>
<td>Normal</td>
<td>Dry</td>
<td>Dry</td>
</tr>
<tr>
<td>Mental status</td>
<td>Normal</td>
<td>Normal to irritable</td>
<td>Lethargic</td>
</tr>
<tr>
<td>Urine output</td>
<td>Normal to decreased</td>
<td>Decreased to none</td>
<td>None</td>
</tr>
</tbody>
</table>

* Adapted from World Health Organization guidelines.7

RESULTS

A total of 91 children were enrolled during the 6-month study period. Forty-six children (51%) received CS and 45 (49%) received FS. Their ages ranged from 6 months to 13 years, with a mean age of 44.4 months for the CS group and 42.3 months for the FS group. The 2 groups were comparable for age, duration of illness, degree of dehydration, and percentage with fever (Table 2).

The presenting complaints of patients in the CS group consisted of vomiting in 35%, diarrhea in 20%, and a combination of vomiting and diarrhea in 45%. For the FS group, the presenting complaints were vomiting in 51%, diarrhea in 4%, and a combination in 45%. Notably, more children in the FS group presented with vomiting than in the CS group.

Five (11%) of the 46 children initially offered the CS tolerated a total of 10 mL/kg and were successfully discharged with instructions for continuing oral hydration at home. Parents were told that feeding should be reintroduced initially with rice or rice cereal, bananas, or other carbohydrate-rich foods. Twenty-three (55%) of the 45 children initially offered the FS tolerated 10 mL/kg of the ice pops and were discharged home (P < .001) with similar guidelines (Figure 1).

Twenty-six children (57%) were treatment failures for CS (complete refusal or intolerance of the CS) and were crossed over to FS. Five (20%) of these original treatment failures tolerated the full 10 mL/kg of the FS, 9 (33%) tolerated between 5 and 9 mL/kg, and 4 (15%) tolerated 5 mL/kg; all of these children were deemed well enough to be discharged for continuous oral hydration at home. None of these children were moderately dehydrated and all were discharged with the FS and advice on refeeding. Eight (32%) had complete intolerance or refusal and were evaluated by the emergency department physician for intravenous hydration.

The original complete treatment failures for FS (12%, n = 5) were similarly crossed over to CS and none of these children tolerated more than 5 mL/kg. One

Table 2. Comparison of Study Groups*

<table>
<thead>
<tr>
<th>CS</th>
<th>FS</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>46</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>44.4</td>
</tr>
<tr>
<td>Duration of symptoms, d</td>
<td>3.4</td>
</tr>
<tr>
<td>Degree of dehydration, %</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td>Mild-moderate</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Equivocal</td>
</tr>
</tbody>
</table>

* CS indicates conventional solution (Pedialyte); FS, frozen solution (Revital-ICE, PTS Labs, Deerfield, Ill). All P > .05.

Figure 1. Tolerance of products.
patient tolerated 5 mL/kg and was discharged with anticipatory guidance and the other 4 had complete intolerance or refusal and were evaluated for intravenous hydration by the emergency department physician (Figure 2).

**COMMENT**

The success rate of oral hydration therapy for infants and children with enteritis and mild to moderate dehydration is approximately 90% worldwide. There is an enormous discrepancy between our data and that previously reported. In our study, the CS group demonstrated an 11% success rate for the consumption of the full 10 mL/kg and the FS group had a 55% success rate. The study methods catered to the limitations of the confines of a busy emergency department. The quantity of 10 mL/kg and the 90-minute trial period were predetermined. The investigators deemed these to be reasonable gauges regarding the predictability of potential continued success with oral hydration.

Children seemed to prefer the FS, but even for this experimental group the success rate deviates from previously reported values by a wide margin. One possible explanation for the deviation is our sample population. The investigators intentionally excluded younger infants who invariably do well with oral hydration, and focused on toddlers and preschool-aged children. They are possibly a more discriminating subset of children. They composed 53% of the CS group and 68% of the FS group. Many of these participants were being offered more palatable but less physiologically effective liquids at home (eg, apple juice and soda) prior to coming to the emergency department and were refusing and/or vomiting these. In the emergency department, we introduced a formula that is accepted to be constitutionally optimal for the absorption of sodium and water, yet may not be the most attractive to children. We offered the solution in its previously accepted liquid form, but also offered it to a sample group as a colorless frozen ice pop with natural fruit flavoring. Participants receiving the FS had a higher percentage of overall acceptance in the emergency department during the 90-minute trial period, perhaps secondary to the ice pop’s appeal, its perceived better taste, or because it is cool and potentially soothing to a child with nausea, vomiting, and enteritis.

A second explanation for our higher failure rates could be an overestimation of the degree of dehydration of study participants. The guidelines we used could have incorporated some bias toward an overestimation of dehydration and without the benefit of a recent accurate weight in each of the children, the assessment of dehydration is difficult to corroborate. Additionally, because the study was performed in an emergency department setting, a follow-up weight measurement would have been impractical because the study time frame was only 90 minutes in many cases, and a maximum of 3 hours in the crossover cases.

A third possible explanation is that some of the children (30%) who were enrolled in the study were referred by their pediatricians after being assessed in their offices, where they were deemed to have failed with oral hydration. More than half of this subset successfully tolerated the FS and were discharged with a supply of the product and refeeding instructions. The overall failure rates witnessed by the researchers vary greatly from those previously reported in the literature but not from those witnessed by our institution, potentially because of selection bias. Children who are doing well with oral hydration at home or after being seen by their pediatricians will not be referred to our emergency department. Therefore, there is an institutional bias built into the study that might help explain our high failure rates.

A fourth possible cause for our exceptionally high failure rates is that perhaps the “failure criteria” were set in such a way as to perpetuate some myths about oral hydration. Refusal or persistent vomiting during the initial 30 minutes was sufficient to label a child an oral hydration “failure” for that study product. In reality, this 30 minutes may be the time required for a family to begin to learn to administer the solution, and may be the refractory period after the last emesis of the child.

The criteria for oral rehydration failure for this study should not and must not be used for assessing failure of oral hydration in general. Our criteria are relevant only to the study protocol and success and failure rates are predetermined for this study within the realm of the emergency department and its intrinsic constraints.

It is well accepted that children with any real degree of dehydration will not refuse oral hydration and that vomiting for less than 1 to 2 hours does not constitute true failure of oral hydration. Our study was directed toward the implementation of the initiation of a physiologic oral hydration solution in frozen form and investigating if this might prove to be a therapeutic option in children who present with vomiting, diarrhea, and often refusal of all fluids.

In this study, we were able to demonstrate a difference between the tolerance of FS as compared with CS in children presenting to the emergency department with enteritis and mild to moderate dehydration. More than half of the children initially randomized to the FS group tolerated the full 10 mL/kg of solution offered as compared with 11% of the children receiving CS. Additionally, two thirds of the children who initially failed therapy with CS and were later offered FS successfully
tolerated the FS and were discharged home. None of the original treatment failures for FS were successful crossovers to CS.

Oral rehydration has considerable potential advantages over intravenous therapy for dehydration and diarrhea. The cost of this mode of hydration therapy is lower, most of the treatment can be administered by the caretaker, and the discomfort and potential morbidity associated with intravenous fluids may be avoided. Oral rehydration therapy has been proved effective in multiple clinical trials, but remains underused by the public and health care professionals. We believe that FS has value as an alternative and an addition to CS, but not as a replacement for that which has already proved efficacious. In our study, FS may represent a useful alternative to CS for assisting in maintaining hydration and preventing further dehydration. The frozen product might facilitate administration of an appropriate maintenance fluid, because children seem to be attracted to its form and flavoring. Nationally it costs 20% to 30% less than CS; however, one would need access to a freezer to obtain the full benefit of the product. Its frozen state may provide a self-limiting administrative mode that provides a slower consumption rate, which could potentially decrease the frequency of emesis. (There was a greater percentage of children with an initial chief complaint of vomiting in the FS group than for CS, yet participants receiving FS still consumed more volume per kilogram with full retention.)

The limitations of this study include the type of randomization used and the lack of product blinding. The randomization schedule was chosen to help alleviate potential patient envy of the alternative product. This randomization method did allow for possible enrollment bias, yet analysis of the 2 study groups proved that they were statistically similar. Additionally, the investigators used unflavored liquid and compared this to a colorless but flavored ice pop. Ideally, a flavored variety of CS should have been used; the unflavored liquid was chosen because it was the standard solution used by the study site.

It seems reasonable that the next study (already under way) should include a comparison of the acceptance rate of a flavored variety of CS to FS, with 24- to 48-hour follow-up. We are exploring the possibility of performing similar studies at several centers.

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REFERENCES