formulations. Examples include the unique needs of patients undergoing small bowel regeneration and adaptation, those of the neonatal and aged patients and of patients with incapacitating food allergies. An interesting dividend of the extended use of total parenteral nutrition may also be the recognition of additional trace mineral requirements in man and the impetus to study further nutrient-drug and nutrient-hormone interactions.

Conclusions

There is an exciting future for parenteral nutrition, both in patient care and in clinical research. Its use for individual patients is still a matter of the highest clinical judgment and demands knowledgeable pharmacy support, with adequate equipment for preparation and testing of solutions, an understanding by the responsible physician of the metabolic and mechanical aspects of the technic, a skilled nursing staff that can monitor individual patients' responses and ability of the institution to monitor its overall results and complications.

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COMPARISON OF SUCROSE AND GLUCOSE IN THE ORAL ELECTROLYTE THERAPY OF CHOLERA AND OTHER SEVERE DIARRHEAS

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ORAL glucose electrolyte solution is now established as simple, effective and relatively inexpensive fluid-replacement therapy[1-5] for severe diarrheal disease, the leading cause of morbidity in the developing world. Cholera, the illness with most massive stool loss, has been treated successfully with oral solution in the hospital as well as in the field situation,[6,7] and in children[8-10] as well as in adults. The electrolyte components (table salt, sodium bicarbonate and a potassium salt) are cheap, available and easily stored. Glucose, which is necessary to promote intestinal absorption of sodium and concomitantly of water,[11] is relatively expensive and may not be available in the countries with the highest incidence of cholera. Sucrose has been suggested as a possible alternative. Potential disadvantages of this disaccharide sugar include insufficient glucose generation to effect electrolyte fluid absorption[11] owing to rapid transit or disaccharidase deficiency (or both) in acute diarrhea[12] or malnutrition.[13]

This study compares the effectiveness of sucrose and glucose electrolyte solutions as fluid replacement in cholera and severe diarrheas from other causes.

Materials and Methods

Study subjects were male and female patients five years of age and above with severe dehydration (estimated to be at least 8 per cent or more of body-weight loss) and clinical cholera entering the Cholera Research Hospital or its field hospital in Bangladesh. If diarrheal volume was greater than 10 ml per kilogram per hour during the initial interval of four to six hours of intravenous fluid rehydration,[14] the patient was entered into the study after giving informed consent to a Bengali-speaking physician. At that point, intravenous fluids were stopped, and the patient was randomly assigned to one of the two oral fluids. Both had concentrations of 96 meq of sodium, 25 meq of potassium, 72 meq of chloride, 24 meq of bicarbonate, and 25 meq of citrate; one had 40 g of sucrose, and the other 20 g of glucose per liter. The dry components had been weighed and packaged by the clinical laboratory in coded polyethylene bags in amounts sufficient to make 2 liters of fluid.

Urine, stool and vomitus were measured at four-hour intervals; replacement was given equal to the preceding four-hour total of stool and vomitus. All patients received tetracycline,[15] (1 g per day for adults and 500 mg per day for children), and a standard sugar-free diet was started within 24 hours of admission. A nasogastric

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tube was used to give the oral electrolyte solution in 17 patients unable to keep up with stool loss by drinking. The sole criterion of the success or failure of oral fluid therapy was the ability to maintain adequate hydration without return to intravenous fluids. When either the intake-output records or the four-hour clinical assessment indicated a negative balance, the plasma specific gravity* was determined. If this value was greater than 1.030, intravenous fluids were given to restore hydration to normal, after which oral fluids were resumed.

At admission and each morning thereafter, plasma specific gravity was determined, the patient was weighed, and stool collected and frozen in a fluoride-containing tube for sugar analysis. Stool sugar was quantified by the Nelson–Somogyi method[15] before and after acid hydrolysis; sucrose concentration was calculated as the difference between samples before and after hydrolysis. Height and weight were measured at discharge and nutritional status calculated as weight for height expressed as a percentage of international standards.[16] A rectal-swab culture was taken at admission to determine the diarrheal pathogen. During the latter half of the study, 31 stool cultures yielding only *Escherichia coli* were assayed by the Chinese-hamster ovary-cell method[17] for heat-labile enterotoxin production.

Results

In total, 138 patients were started on oral fluids, 108 in the Cholera Research Laboratory hospital, and 30 at the rural treatment center. On subsequent analysis, no statistically significant differences were found between these populations, and results were combined. Sixteen patients were treated successfully, but required less than 1 liter (seven on sucrose and nine on glucose solutions) of oral therapy; these cases were excluded from analysis as of insufficient severity to evaluate effectiveness of the solutions. Of the 122 patients remaining in the analysis when the code was broken, 69 were found to have been given sucrose electrolyte solution, and 53 glucose electrolyte solution.

The patient characteristics of each treatment group are shown in Table 1. Except for a larger number of men in the sucrose group, there were no statistically significant differences. In addition, no differences in degree of initial dehydration were detected between patients with and those without cholera; at admission, both averaged about 8 per cent total weight loss, and were without discernible radial pulse in about half the cases. Figure 1 compares treatment groups for success or failure of hydration maintenance without reversion to intravenous fluids. The total success rate of 86 per cent for sucrose electrolyte solution and 87 per cent for glucose electrolyte solution were identical (chi-square = 0.04). When restricted to patients with cholera, the outcome with both oral fluids also showed no difference between solutions (68 per cent success on sucrose and 78 per cent success on glucose — chi-square = 0.27). Failures (as shown in Figure 1) were all in those whose stool rates were greater than 10 ml per kilogram per hour; most failures (13 of 17) occurred in those with rates over 20 ml per kilogram per hour during the first 24 hours.

Total volumes of each oral fluid needed per successful treatment course were essentially identical, averaging 6.0±0.5 (± S.E.M.) liters for sucrose and 5.7±0.7 liters for glucose. In 10 of the 17 failures (seven sucrose and three glucose) the same oral solution was started again at a later period after intravenous

*T.S. meter, AO Instrument Co., Buffalo, New York.

Table 1. Comparison of Sucrose and Glucose Therapy Groups on Admission.

Item Compared	Sucrose Electrolyte Solution	Glucose Electrolyte Solution
Total No.	69	53
Sex:		
Male	42*	26
Female	27	27
Age:		
Median	35	30
Range	6–80	6–80
Initial plasma specific gravity	1.038 ±0.001†	1.037 ±0.001
% weight gain after hydration	8.6 ±0.4†	8.4 ±0.6
Bacteriologic findings:		
Vibrio cholerae	28 (41%)	27 (51%)
Enterotoxigenic *Esch coli*‡	14 (20%)	7 (13%)
Other pathogen	3 (4%)	3 (6%)
No pathogen found	24 (35%)	16 (30%)
% of standard weight & height	75.4 ±1.2†	74.3 ±1.3

*None of the differences between groups were significant except for the sex distribution.

†Mean ± SE.

‡Assay for enterotoxin was performed only during the latter half of the study; this isolation rate may be inappropriately low.

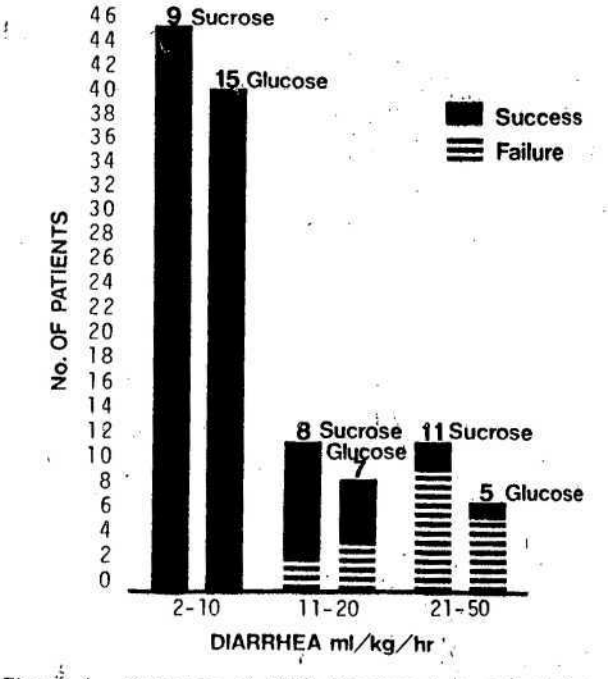

Figure 1. Outcome of Fluid Treatment as a Function of First-Day Diarrhea Rate.

"Success" or "failure" (see text for definitions) in maintaining hydration was related to diarrhea rate, not choice of sugar electrolyte solution. Average diarrhea rate was the same in both fluid treatment groups but was significantly higher ($P<0.005$) in failures. Most failures occurred in patients with rates greater than 20 ml per kilogram per hour. Numbers at the top of each column indicate patients with cholera in each group.

dehydration. Only two of these again failed, one with each solution. Both of the latter were children who vomited large portions of the prescribed fluid. Comparison of diarrheal severity after start of treatment showed no statistically significant differences between treatment groups despite a slightly higher rate of stool production among patients with cholera receiving sucrose solution.

In both treatment groups, stool sugar content increased markedly during the first day, and concentration was maximal on the morning after the beginning of oral therapy. Those on glucose solution averaged 0.7 g of total stool glucose per day, thus passing only inconsequential amounts of the sugar in the several liters consumed (20 g of glucose per liter). Of patients receiving sucrose solution (40 g per liter), the average monosaccharide sugar excreted per day was 5.4 g, which was 5.7 per cent of the average ingested. On the average, only 1/20 of the sucrose was not hydrolyzed in the intestine, and about the same proportions of the total monosaccharides generated were not absorbed.

The degree of protein-calorie malnutrition found (average of 75 per cent expected weight for height of the international standard) was comparable to that generally found in this hospital.[18] In an effort to determine if either glucose malabsorption or a presumptive disaccharidase deficiency might be more prevalent in the malnourished, total stool sugars (monosaccharide and disaccharide) were examined in the upper and lower nutritional quartiles. No statistically significant differences were found, nor did more hydration failures occur among the more malnourished.

Discussion

The results of this study conducted in a double-blind, prospective fashion indicate that sucrose can effectively replace glucose in an oral electrolyte solution for severe diarrhea in patients over five years of age. Conditions of the study were designed to match those in ordinary therapeutic circumstances. Thus, solutions were made up and administered by the nursing staff from tap or well water and preweighed packets made from salts and locally available table sugar; a rural treatment center was used for a portion of the trial; nasogastric tubes were used infrequently; all patients were given tetracycline to shorten duration of diarrhea; patients were fed as soon as vomiting stopped, since malnutrition is common; and all patients with severe cholera-like diarrhea, regardless of subsequent culture, were included.

The overall failure rates of 13 and 15 per cent are similar to those found by other workers using oral glucose electrolyte solution in severe diarrheal disease. Nalin et al.,[2] reported a failure rate of four in 19 (21 per cent) despite orogastric tubes. Pierce et al.[3] had a rate of 10 per cent (one of 10), and Sack et al.[4] found that three of 22 (14 per cent) had to receive additional intravenous fluids. In a study of sucrose electrolyte solution, three of 18, or 17 per cent, failed.[19] When totaled, these studies give a failure rate of 16 per cent. In our study, for cholera alone, 32 and 28 per cent of patients could not keep up hydration by mouth. This rate was higher (although not significantly) than that reported elsewhere, but failure was a function of the rate of fluid loss and not solution used (Fig. 1). This important relation is not discussed in most published studies but is true for the failures in Nalin's report[19] regardless of the sugar used. In patients both with and without cholera, dehydration was equally severe on admission; patients who could not maintain hydration by mouth continued to have early fluid loss rates of 10 to 20 ml per kilogram per hour (10 to 20 liters per day in a 40-kg patient) or greater. In our study, none of the 21 patients with enterotoxigenic *Esch. coli* diarrhea lost more than 12 ml per kilogram per hour, and none were fluid-maintenance failures. Two patients without cholera were failures, one with each solution.

In a study comparing both solutions in children with non-cholera diarrhea by Suprapto et al.[20] the failure rate was 12 per cent with glucose and 19 per cent with sucrose electrolyte solution. Among Bengali children treated with glucose solution by Nalin et al.[10], four of 12 (33 per cent) had to be given additional intravenous hydration after oral fluids were started. In our study there were a total of 11 children between five and 10 years of age, among whom all six on sucrose solution were successfully treated.

Failure of hydration maintenance may occur in either children or adults with severe diarrhea for several reasons. Stool output may increase up to 20 per cent after glucose electrolyte therapy is begun.[1,3] Occasionally, clinical signs of dehydration may arise even in the presence of apparently adequate fluid balance and may reflect a large, unabsorbed gastric or intestinal reservoir, which may subsequently be vomited. More commonly, the child or adult with very large stool output is simply unable to drink the volume needed, which may average 6 liters per four hours, as seen in several adult patients in this study. This may pose a special problem early in the course of fluid repletion when there may be incompletely corrected acidosis or potassium depletion. Continued close supervision of all patients by trained personnel is necessary regardless of solution choice, with judicious use of intravenous fluids to supplement oral therapy.

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VITAMIN D RESISTANCE IN OSTEOMALACIA AFTER URETEROSIGMOIDOSTOMY

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OSTEOMALACIA after ureterocolic anastomosis has been recognized for 25 years.[1] Its cause is uncertain, but both renal damage and acidosis may contribute.[2-4] A requirement for vitamin D is variable: although vitamin D "resistance" has been documented[3] other workers have suggested that only correction of acidosis, with little or no added vitamin D, is necessary.[5]

25-Hydroxycholecalciferol is several times more potent than the parent vitamin in the treatment of various forms of rickets[6,7] and is effective in renal osteodystrophy.[8-10] The reason for its superior potency has been somewhat clarified by recent comparison of relative plasma 25-hydroxyvitamin D levels produced in different subjects.[11] The analogue 1α-hydroxycholecalciferol[12] closely resembles 1,25-dihydroxycholecalciferol, the active hormonal form of the vitamin that is synthesized only in kidney, and is even more potent [illegible]droxycholecalciferol.[13,15] There are no reports of the use of these metabolites in the treatment of osteomalacia after ureterocolic anastomosis, nor has the relative efficacy of all three compounds been compared in any one patient with osteomalacia of renal origin.

In the patient described below, the degree of "vitamin D resistance" was measured by the level of circulating 25-hydroxyvitamin D required to overcome it. Our findings thus explain the superior potency of 25-hydroxycholecalciferol over vitamin D that was found and also indicate that vitamin D resistance in this condition was of renal rather than end-organ origin.

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METHODS

We performed metabolic balances in the classic manner,[16] using barium sulfate as an internal marker and carmine markers to separate successive four-day fecal-collection periods. Dietary calcium was based on the patient's calculated previous long-term intake. In contrast to other metabolic studies in patients with ureterocolic anastomosis the combination of a permanent colostomy and rectosigmoid bladder allowed complete separation of urine and feces. Plasma 25-hydroxyvitamin D was measured by the protein-binding method of Haddad and Chyu,[17] which recognizes equally the 25-hydroxy derivatives of vitamin D_2 and vitamin D_3.[18] 25-Hydroxycholecalciferol was supplied by the UpJohn Company and 1α-hydroxycholecalciferol by Leo Laboratories.

CASE REPORT

In 1965 a 58-year-old woman underwent total cystectomy and ureterocolostomy, followed by radiotherapy, for anaplastic bladder carcinoma. Recurrent loin pain and pyrexia, and persistent hyperchloremic acidosis subsequently developed, and she was treated with intermittent antibiotics and sodium bicarbonate, 6 g daily. In 1969 a permanent colostomy with ureteric transplantation to the rectosigmoid was performed, and infective symptoms subsequently were better controlled. Nevertheless, acidosis persisted, and plasma calcium between 1970 and 1972 ranged from 5.0 to 6.0 mg per deciliter. In 1972 progressive muscle weakness and increasing bone pain developed. Sodium bicarbonate was increased, but she took medication irregularly and acidosis and hypocalcemia persisted.

On admission to the hospital in February, 1975, she had dry, inelastic skin and was unable either to rise from a chair or to walk because of bone pain and muscle weakness. Dietary history showed an inadequate vitamin D intake of less than 50 IU daily. The hemoglobin was 8.4 g, plasma calcium 6.1 mg (albumin 3.5 g), and phosphorus 4.9 mg per deciliter, alkaline phosphatase 19 King-Armstrong Units, and the sodium 142, potassium 3.0, chloride 118, and total carbon dioxide 6 meq per liter; blood urea was 102 mg per deciliter. The pH was 7.30. Plasma 25-hydroxyvitamin D was low at 5 ng per milliliter, but serum parathyroid hormone (kindly assayed by Dr. J. L. H. O'Riordan) was normal, 0.3 ng per milliliter (antiserum 199 [Bu 211-32] — normal range, 0.15 to 1.0[19]). Urine was infected on culture, there was no aminoaciduria, and 24-hour urine calcium excretion was 68 mg. X-ray examination showed pseudofractures in the pubic rami and both femoral necks, together with increased density in the thoracolumbar spine. An intravenous pyelogram showed moderate bilateral hydronephrosis. Iliac-crest biopsy showed gross osteomalacia without hyperparathyroidism; quantitation by Dr. P. D. Byers demonstrated the total area occupied by bone to be 17.6 percent (normal range, 4.9 to 30.0), by osteoid 39.4 per cent (normal, 0 to 14.3) and by bone plus osteoid 57.1 per cent (normal, 4.9 to 30.0); the proportion of trabecular surface covered by osteoid was 99.1 per cent (normal, 0 to 30.0), with resorption of 0.0 per cent (normal, 4 to 20.0) (normal ranges were derived from the literature[20]).