SUCROSE IN ORAL THERAPY FOR CHOLERA AND RELATED DIARRHEAS

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Introduction

Enhancement of intestinal sodium and water absorption by glucose is the basis for an oral glucose-electrolytes maintenance solution for cholera and related diseases (1,2). Practical alternatives to glucose could be of value because glucose is not always available. Sucrose was thought to be worthy of trial since its intestinal hydrolysis releases glucose. Fructose is also released but is not believed to enhance absorption.

Patients and Methods

The study included 18 patients (17 males and 1 female) admitted for treatment of severe dehydration due to diarrhea and vomiting. Thirteen patients had a positive rectal swab culture for *V.cholerae* and one patient's culture revealed non-agglutinable vibrios. Four cultures revealed no recognized pathogen. Stated age was 32 (11-65) years; body weights (admission/discharge) were 38.9/41.6 (16.7-50) kg., and duration of diarrhea in hospital was 43 (16-64) hours (means and ranges).

Initial intravenous rehydration (equivalent to 10% of body weight) restored fluid and electrolyte balance, pulse and blood pressure to normal. I.V. therapy was slowed or stopped after the start of oral (or nasogastric) maintenance therapy with the sucrose-electrolytes solution. The solutions used contained either 48 grams of sucrose per liter (5 patients or 38 grams of sucrose per liter (13 patients, of whom five received the solution from day two). Both solutions contained (g. per 1.): NaCl(4.2), $NaHCO_3$(2.0) and K Citrate (2.7). In addition to the oral solution patients were allowed measured amounts of oral water and milk ad libitum.

During oral maintenance periods an average of 4 plasma specific gravity and electrolyte determinations were made.

Intake and output volumes were monitored constantly and recorded at 8-hour intervals. Data are based on complete 8-hour periods when oral therapy was in use.

All patients received tetracycline 250 mg. P.O. every 6 hours for 4 days from the start of the oral maintenance period. Stool samples were obtained in bottles containing fluoride and analyzed for reducing sugar and sucrose (3,4).

Results

Fifteen out of 18 patients could be maintained in fluid balance during oral therapy periods using the sucrose-electrolytes solution. However, two cholera patients and one non-cholera patient developed increases in net water and electrolyte losses (and in 2 cases recurrent vomiting) associated with inability to absorb the solution. In these cases plasma specific gravity increased over 1.031, necessitating additional intravenous fluid therapy. Plasma electrolytes remained normal because oral maintenance was discontinued and I.V. therapy resumed when balance data showed significant increases in net diarrhea fluid losses.

After drinking the sucrose solution gross diarrhea rates of 3 other patients also increased markedly (2 to 4 fold from pre-oral to first oral period) but in these and the remaining cases net gut fluid and electrolyte balance could be maintained. In two cases, however, the degree of net absorption was too small to compensate for insensible losses, and plasma specific gravity rose up to (but not over) 1.030 during oral maintenance.

Stool samples of 12 patients were analyzed and all were found to contain reducing sugar (pre-hydrolysis: 436. mg.%; 2-1857 mg.%; post-hydrolysis: 957 mg.%; 175-2175 mg.%; means and ranges). The break-down of sucrose by intestinal enzymes or by bacteria accounts for the presence of reducing sugar in the stool. The results during oral therapy administration are summarized in Table I.

Discussion

In the case of cholera and related illnesses, patients are often admitted in shock; fluid and electrolyte balance can be most rapidly restored (within 60-90 minutes) by the

intravenous route. The balance achieved with initial intravenous rehydration must be maintained until diarrhea ceases in order to prevent a recurrence of dehydration. The goal of maintenance therapy (oral or intravenous) is to quantitatively replace the post-rehydration losses of water and electrolytes.

The measurement and oral or intravenous replacement of post-rehydration diarrhea and vomitus provide a practical and rational method of maintenance therapy. In practice it is desirable for the patient to remain in slight positive fluid balance until treatment ceases, in order to replace insensible losses, generate adequate urine flow and correct any residual deficits (usually small) which remain after rehydration.

Oral maintenance therapy using a solution of glucose and electrolytes has been extensively tested in hospital and field situations and meets the criteria for a successful maintenance solution (1,2,5-8). Oral or nasogastric intake of the glucose-electrolytes solution almost always promotes positive fluid balance within 8 hours after starting therapy. Treatment failures (i.e. persistent negative balance leading to recurrent dehydration) are rare. In one series of 580 cases only one patient could not be maintained on the oral glucose electrolyte solution (due to vomiting and inability to tolerate a nasogastric tube)(5).

The results of the present sucrose study, though preliminary, are in marked contrast to previous results with the oral glucose-electrolytes solution.

Although the five patients treated with the sucrose-electrolytes solution during convalescence absorbed it, three of 13 patients treated during acute diarrhea could not absorb the solution adequately. Possibly these three patients could not hydrolyze sufficient sucrose to yield the amount of glucose needed for adequate absorption; this could account for the presence of sugar in the stool and could be attributed to the type of disaccharidase deficiency reported to occur during and after diarrheal episodes (9).

The explanation may be that some sucrose may fail to come in contact with the diminished sucrase in the brush

border of the intestinal mucosa. Intestinal transit time is decreased during severe diarrhea, and if hydrolysis is delayed the solution may be propelled to the terminal gut where glucose does not enhance absorption. If fructose absorption is decreased during diarrhea it could further aggravate the osmotic effect of unabsorbed sucrose in the intestinal lumen: Diarrhea would increase due to the osmotic effect of the unabsorbed molecules. In contrast, glucose given orally or by tube to diarrheal patients is almost entirely absorbed in the upper small bowel (1).

The present study shows that the oral sucrose-electrolytes solution could be used successfully to treat most patients under emergency conditions in which I.V. fluid supplies would have to be conserved. However, the sucrose solution should be used only when glucose is not available, because the data suggest that there may be more treatment failures using the oral solution with sucrose than is the case using oral solution with glucose. This could discredit oral therapy using glucose, which only now is coming to be accepted as a cheap and available means of reducing intravenous fluid requirements. Furthermore, the use of the sucrose solution will demand particularly close monitoring of intake and output so that nonabsorbers can be quickly recognized. Such nonabsorber patients should then be treated with intravenous maintenance alone. In this manner total I.V. fluid needs for a given group of patients could be reduced as is the case when oral glucose-electrolytes solutions are used for maintenance therapy.

The recent decrease in availability of world sucrose supplies and accompanying marked price increases also reduce the advisability of recommending sucrose for routine oral diarrhea therapy instead of glucose. It seems more appropriate to recommend that sufficient glucose be stockpiled to anticipate future requirements in areas affected by cholera and related disorders; this will avoid the extra hazard which would accompany any recommendation for sucrose therapy.

References

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Culture*	Duration (Hrs.)	Oral Solution (L.)	Water/Milk (L.)	Stool/Vomitus (L.)	Urine	GNB
c	24	9.0	0/0.6	7.4/0	1.9	+2.2
c	16	5.0	0/0.3	3.5/1.1	0.7	+0.7
c	16	6.5	0/0.6	3.6/0	0.7	+3.5
c	48	19.0	0/1.2	11.9/0.6	6.5	+7.9
c	48	11.0	1.9/1.8	9.1/0	4.4	+5.6
c	16	2.0	0.9/0.3	1.2/0	0.3	+2.0
c	16	4.0	0.3/0.6	3.3/0	0.6	+1.6
c	32	5.0	0.1/1.0	5.6/0	1.1	+0.5
c	32	11.0	0.8/0.6	8.7/0	2.1	+3.7
c	32	8.0	0.3/0.6	3.7/0	1.7	+5.2
c	24	6.0	1.0/0.9	4.8/0	2.7	+3.1
n	24	8.0	0.3/0.6	5.0/0	2.6	+4.9
i	16	4.0	1.3/0.6	1.5/0	1.1	+4.4
i	24	10.6	0/0.6	9.6/0	0.5	+1.6
i	24	10.0	0/0.6	5.5/0	3.3	+5.1
c	16	8.0	0.0/0.0	9.9/1.0	0.5	-2.9
c	32	9.4	0.4/1.2	10.9/2.0	4.7	-1.9
i	24	16.0	0.4/0.6	16.5/0	0.9	+0.5**

* c = cholera; n = NAG vibrio; i = idiopathic

** Although overall GNB was slightly positive, -2.0L. negative balance developed from 16th to 24th hour.

TABLE - I

Balance data during the periods of oral maintenance therapy with the sucrose-electrolyte solution. dnb = fluid net balance; this is the balance left after subtracting volume of stool plus vomitus from oral intake. Patients received an average of 1.1 L. I.V. fluids to keep the I.V. drip open during the oral therapy period. The last three patients represent treatment failures.

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