The Effect of Intestinal Solute Load on Water Secretion in Infants with Acquired Monosaccharide Intolerance

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Summary

The osmotic effect of unabsorbed glucose on intestinal secretion of water and electrolytes was investigated by jejunal perfusion in eight infants ranging from 2 to 17 months of age. All infants had or were recovering from acquired monosaccharide intolerance. Isocaloric solutions of glucose and glucose polymer containing 1% polyethylene glycol as a nonabsorbable marker were tested. The osmolalities of the glucose polymer solutions were $\frac{1}{3}$ to $\frac{1}{2}$ that of the glucose. No major differences were noted in carbohydrate absorption whereas mean water flux changed from secretion of 0.37 ml/min to absorption of 0.023 ml/min when glucose was replaced by glucose polymer. Sodium and potassium flux followed the same pattern. The results of this study indicate that the increased intestinal secretion in acquired monosaccharide intolerance may be a function of osmolar load in the presence of a reduced absorptive capacity.

Speculation

Formulas presently used to treat infants with absorptive disorders of the small bowel frequently include those which are elemental and have high osmolalities. This study implies that there is a need to further develop dietary products which are well absorbed but have a lower osmotic load.

Acquired monosaccharide intolerance is a reversible clinical syndrome commonly seen in the first 6 months of infancy. This syndrome is initiated by acute diarrhea or surgical manipulation of the intestine and results in chronic acidic diarrhea, generalized malabsorption, and failure to thrive. It was first reported by Burke and Danks (1) in 1966 and further described by Lifshitz *et al.* (5) in 1970. The small intestinal mucosa in affected infants is characterized by atrophy or blunting of the villi causing a reduced mucosal absorptive surface which we previously reported (4) to be responsible for the malabsorption which is characterized by total carbohydrate intolerance. The oral ingestion of sugar results in a profound fermentative diarrhea with an acidic pH.

In an attempt to enhance absorption, these infants are frequently treated with chemically defined formulas which contain glucose as the carbohydrate and amino acids as the protein source. These formulas have a very high osmolality and are difficult to feed to infants with this syndrome without producing diarrhea. Even though it appears that the malabsorption of nutrients is the major stimulus for diarrhea in these infants, the osmolality of the feeding mixture may enhance the secretion of water into the intestinal lumen, worsening the symptom. The following study was designed to evaluate this phenomenon.

PATIENT SELECTION

Eight patients as described in Table 1 were selected for study. Six were male, and two were female. The age at the time of study

ranged from 2 to 17 months. All patients either at the time of the study or within several months had monosaccharide intolerance as defined by the presence of glucose in the stool, a fecal pH of less than 5, watery diarrhea after ingestion of 5% glucose in water, and failure to thrive. Six patients developed this intolerance after what was presumed to be an infectious gastroenteritis. One patient developed it after surgical manipulation of the intestinal tract. The final patient developed necrotizing enterocolitis at 3 days of age which precipitated the monosaccharide intolerance. All patients were at some stage of recovery, whereas two were essentially recovered as evidenced by normal jejunal mucosa. Two patients did not have adequate biopsy material available.

Informed consent was obtained from parents of all infants, and the studies were performed with approval of the Human Investigation Committee.

MATERIALS AND METHODS

A double lumen silastic perfusion catheter with a 2 ml mercury bag on its distal end was introduced into the small intestine by peristalsis. This catheter consisted of two lumens with ports located 20 cm apart. Before the study, catheter position was checked by fluoroscopy so that the proximal port was within 5 cm of the ligament of Treitz. All test solutions contained 1% polyethylene glycol as a nonabsorbable marker and were perfused at rates ranging from 1 to 1.5 ml/min through the proximal port. The composition and osmolalities of the solutions used are listed in Table 2. Each patient was perfused with a pair of solutions containing either 5 or 10 g/dl carbohydrate. The order of the solutions was randomly assigned between glucose and glucose polymer. The glucose polymer used is sold under the brand name Polycose (Ross Laboratories) and is prepared by controlled acid-enzyme hydrolysis of cornstarch. The polymer is predominantly medium chain length amylose with a chain length of 5 to 9 glucose units comprising almost 50% of the product. Free glucose concentration is less than 2%. The average molecular weight is 1080 resulting in an osmolality while in solution of approximately one-sixth that of glucose. After an equilibration period of 1 hr, four samples were collected from the distal port at 15-min intervals for each solution tested.

Glucose concentrations were analyzed by the *o*-toluidene method. Glucose polymer was analyzed by the same method after acid hydrolysis. Polyethylene glycol was determined by the method of Malawer and Powell (6). Sodium and potassium were determined by flame photometry. Glucose and glucose polymer absorption and water flux rates were calculated by the method of Jacobson *et al.* (3).

RESULTS

Water flux rates changed dramatically when the hypotonic maltodextrin solutions were perfused in comparison to the glucose solutions as shown in Figure 1. Only one patient (patient 4)

Table 1

Patient	Sex	Age (mo)	Etiology	Status during study	Jejunal biopsy	Perfusion solutions
1	M	5	Infectious diarrhea	Acute	Inadequate tissue	A and B
2	F	3	Infectious diarrhea	Convalescent	None available	A and B
3	F	7	Infectious diarrhea	Convalescent	Normal	A and B
4	M	17	Infectious diarrhea	Convalescent	Normal	A and B
5	M	6	Laceration of duodenum	Acute	Villous atrophy	C and D
6	M	11	Infectious diarrhea	Convalescent	Villous atrophy	C and D
7	M	2	Necrotizing enterocolitis	Acute	Villous atrophy	C and D
8	M	5	Infectious diarrhea	Convalescent	Villous atrophy	C and D

Table 2

Solutions	A ¹	B	C	D
Sodium (mEq/liter)	30	30		
Potassium (mEq/liter)	20	20		
Chloride (mEq/liter)	30	30		
Citrate (mEq/liter)	31	31		
Magnesium (mEq/liter)	4	4		
Calcium (mEq/liter)	4	4		
Glucose (g/liter)	50		100	
Glucose polymer ² (g/liter)		50		100
pH	5.0-6.0	5.0-6.0	5.0-6.0	5.0-6.0
Osmolality (mOsm/kg)	380	135	556	93

¹ Pedialyte (Ross Laboratories).

² Polycose (Ross Laboratories).

absorbed water during the glucose perfusions whereas only two patients (patients 1 and 5) continued to secrete water when the perfusions were switched to the glucose polymer solutions. The mean water flux changed from secretion of 0.37 ml/min to absorption of 0.023 ml/min when glucose was replaced by glucose polymer.

Figures 2 and 3 show that there was an enhancement in the absorption of both sodium and potassium during the glucose polymer perfusions in the four patients who received the electrolyte containing solutions.

Glucose polymer was not absorbed as efficiently as glucose (Fig. 4) in spite of the enhancement of absorption demonstrated for water and the electrolytes sodium and potassium. The mean absorption fell from 32 mg/min for glucose to 28 mg/min for polycose. This difference, however, is probably not of biological significance.

DISCUSSION

Even though the glucose polymer solutions were hypotonic solutions, secretion occurred in two of the patients. This can at least be partially attributed to the fact that an average of 40% of the perfused polymer was hydrolyzed to free glucose by enzymatic activity within the lumen of the gut enhancing the osmotic effect.

The results of this study indicate that intestinal secretion in acquired monosaccharide intolerance correlates well with the osmolar load presented to the gut. This could certainly play a role in the perpetuation of diarrhea in these patients because unabsorbed carbohydrates are present in their stool and therefore exert an osmotic effect along the entire intestinal tract. The use of an isocaloric solution of a glucose polymer with a larger molecular weight, hence a lower osmolality, resulted in a significant reduction in water secretion. This hypotonic solution also enhanced the absorption of sodium and potassium even though the rate of absorption of the polymer was similar to that of glucose.

The osmotic theory states that when a solution is separated from another solution of a different concentration by a semipermeable membrane, molecules of the solvent will diffuse through the membrane from the more dilute to the more concentrated solution. Under normal circumstances, this effect is minimized, and less water enters the intestinal tract because the intestinal mucosa is not a semipermeable membrane for glucose but one that actively absorbs this solute, rapidly diminishing the osmotic effect within the lumen. In infants with monosaccharide intolerance, the intestinal mucosa is damaged, and glucose absorption is impaired, thus more closely resembling a true semipermeable membrane. Glucose tends to remain in the intestinal lumen, and these unabsorbed osmoles enhance the movement of water into the lumen. The

osmolality itself, however, remains close to isotonic, provided the gut is not overwhelmed with solute. Isotonicity of intraluminal fluid was observed in this study.

Daum *et al.* (2) have shown that rats have a significant decrease in duodenal osmolality and water content after an acute injection of 5 or 10% glucose polymer into their duodenum as compared to equivalent concentrations of glucose. The mucosal uptake of polymer also was better than glucose. They implied that glucose polymer may be useful in the oral nutritional rehabilitation of infants with diarrhea. This study supports their impression even though the data can not be directly compared because of differences in experimental design.

In infants with acquired monosaccharide intolerance, absorp-

Fig. 1. Individual patients are connected. Mean water flux changed from -0.37 ml/min (secretion) to $+0.023$ ml/min (absorption) over a 20 cm segment of jejunum when glucose perfusions are compared to glucose polymer.

Fig. 2. Individual patients are connected. Mean sodium flux remained in secretion but decreased from 0.066 to 0.016 mEq/min over a 20 cm segment of jejunum when the perfusion was switched from glucose to glucose polymer.

POTASSIUM ABSORPTION

Fig. 3. Individual patients are connected. Mean potassium flux increased from a mean absorption of 0.0015 to 0.01 mEq/min over a 20 cm segment of jejunum when the perfusion was switched to glucose polymer.

CARBOHYDRATE ABSORPTION

Fig. 4. Individual patients are connected. Mean carbohydrate absorption was 32 mg/min for glucose and 28 mg/min for polycose.

tion of nutrients is limited by a damaged intestinal mucosa. Previous studies done by us (4) have shown that glucose absorption can be as low as one-sixth normal. Undoubtedly, other nutrients such as protein and fat can also be significantly malabsorbed. The formulas presently being used to treat them are far from optimal in that they are elemental or predigested resulting in high osmolalities which may potentiate diarrhea. Further study is needed to develop dietary products which are well absorbed but have a lower osmotic load.

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