Original articles

Hydrolysed wheat based oral rehydration solution for acute diarrhoea

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SUMMARY A randomised three cell study was carried out in 78 children with acute diarrhoea to evaluate the relative efficacy of oral rehydration solution (ORS) made from partially hydrolysed wheat grain, cooked rice powder, or glucose. Twenty six patients with comparable age, body weight, duration of diarrhoea, and degree of dehydration were studied in each of the three groups. Initial rehydration was carried out by using intravenous Dhaka solution within one to two hours followed by administration of oral rehydration solution. The mean ORS intake during the first and second 24 hours of treatment in patients with cholera receiving wheat-ORS and rice-ORS was significantly less compared with those receiving glucose-ORS. The stool output during the same period in patients receiving wheat-ORS and rice-ORS was significantly less compared with those receiving glucose-ORS. Similar trends in both ORS intake and stool output were observed during the next 24 hours.

The efficacy of oral rehydration treatment in replacing the loss of water and salts in stools in cases with watery diarrhoea has been well established.¹⁻⁴ It has almost eliminated the need for treatment with intravenous fluids, except in very severe cases. The discovery of glucose facilitated transport of sodium and water in the small intestine⁵ led to the use of glucose-salt solution for effective rehydration of patients with acute watery diarrhoea. The absorption of glucose is, however, rate limiting, and increasing its concentration leads to osmotic diarrhoea. A number of possible ways of further enhancing the absorption of sodium (and water) in acute diarrhoea have been tried. Studies by Molla *et al*^{6,7} and subsequently by Patra *et al*⁸ have shown that rice powder was as effective as, or even superior to, glucose for the treatment of acute diarrhoea as far as both requirements of oral rehydration solution (ORS) and stool volume were concerned. Rice and other cereals are inexpensive and, being staple foods, are easily available and acceptable. In the intestine they yield glucose and amino acids slowly, reducing the risk of osmotic diarrhoea. To our knowledge, no study has been undertaken using hydrolysed wheat as a substitute for glucose in ORS, although wheat is a staple source of energy and proteins for a considerable proportion (about 43%) of the total world population.

Wheat extract prepared by enzymatic digestion⁹ was obtained from the late Professor A Dahlqvist. The preparation is rich in protein (11.5%) and low in lactose and fat (0.5%) content, with linoleate as the main component. Lysine is the limiting amino acid. It also contains vitamins and minerals (including thiamin, niacin, iron, zinc, and calcium). In preliminary studies we have tested its acceptability and digestibility¹⁰ and its use as an alternative source of nitrogen and energy during rehabilitation of malnourished children. (Alam AN, Khanum S, Khatun A, Molla A, Rahaman MM. Unpublished observations.) The present study was undertaken to evaluate the relative efficacy of this hydrolysed wheat based electrolyte solution compared with other available oral rehydration solutions in the management of dehydrating diarrhoea.

The composition of the wheat grain extract was verified in our biochemistry laboratory and consists of carbohydrates 87%; protein 11.5%; fat 0.5%; and ash 1.8%. The carbohydrates in the extract include glucose (dextrose) 3%, maltose 60%, maltotriose 15%, higher maltosaccharides 15%, and isomaltose, sucrose, and fructose (2% of total carbohydrate).

The wheat extract was obtained as a slightly coloured spray dried powder (about 2% water). The extract was completely soluble in water.

In vitro acid hydrolysis converts about 80% of the wheat extract into glucose so that if 50 g is added to a litre of ORS about 40 g of glucose can be expected to be released in the intestinal lumen. The osmolality of a 5% solution of the wheat extract as measured after adding electrolytes recommended by the World Health Organisation (WHO) was found to be 280 mmol, which is iso-osmolar with plasma.

Patients and methods

Seventy eight children aged 1–8 years who attended the treatment centre at our hospital from April 1983 to April 1984 were studied. They had a history of watery diarrhoea of less than 72 hours' duration with moderate to severe dehydration. Clinical examination was performed on admission. Patients with severe malnutrition (<60% weight for age of 50th centile of National Center for Health Statistics) or systemic illnesses, such as bronchopneumonia, otitis media, and meningitis, and those who had received antibiotics before admission were excluded. Written consent was obtained from the legal guardian of each child before the study. The children were randomised according to the permuted block design to ensure equal numbers of subjects in each treatment group.

Electrolyte content of the solutions was the same as that recommended by the WHO (Na^+ 90 mmol/l, K^+ 20 mmol/l, Cl^- 90 mmol/l, and HCO_3^- 30 mmol/l) in all three groups. One group received the electrolyte solution with 50 g/l wheat powder (wheat-ORS), the second group with 50 g/l rice powder (rice-ORS), and the third group with 20 g/l glucose (glucose-ORS) (Table 1). The wheat extract or rice powder and the electrolytes were packaged separately. The solutions were prepared by adding the electrolytes to the wheat powder dissolved in or the rice powder cooked in a litre of water. Normal

hospital diet (rice and chicken) was allowed soon after initial rehydration. Nursing mothers were encouraged to continue breast feeding. The oral rehydration preparations and plain water were offered ad libitum. All patients were rehydrated initially by intravenous Dhaka solution (Na^+ 133 mmol/l, K^+ 13 mmol/l, Cl^- 88 mmol/l, and HCO_3^- 48 mmol/l) within one to two hours, in accordance with WHO guidelines,¹¹ and were offered the study solutions after initial rehydration.

Body weight was recorded on admission and every eight hours thereafter. Any vomitus was measured and recorded. No antibiotics were given during the study. On admission 3 ml blood were drawn for the estimation of electrolytes, packed cell volume, and specific gravity. This was repeated after 24 hours and before discharge. Eight hourly intake/output charts were maintained. Plastic uribags were used to collect urine separately. Microscopic examination and culture of stool samples were carried out on admission for *Vibrio cholerae*, *Salmonella* spp, *Shigella* spp, and enterotoxigenic *Escherichia coli*. Isolates of *E. coli* were tested for heat labile and heat stable enterotoxins.^{11 12} Rotavirus was tested by an enzyme linked immunosorbent assay method.¹³

The rate of purging, change in body weight, serum specific gravity, urine output, sugar content of stool before and after hydrolysis were measured every 24 hours to compare the efficacy of the three kinds of oral treatment. Patients were discharged after passing the first formed stool.

Patients who required intravenous fluid after beginning treatment with oral fluid because of recurrence of signs of severe dehydration with decreased body weight up to or below the admission weight were declared failures and treated as a separate group. They were excluded from analysis.

Statistical analysis. One way analysis of variance was

Table 1 Admission clinical data on the study children. Values are mean (SEM) except for sex and aetiology (No)

	Treatment group		
	Glucose-ORS (n=24)	Wheat-ORS (n=24)	Rice-ORS (n=24)
Age (months)	40.1 (5.2)	48.6 (4.02)	48.5 (4.6)
Sex (M/F)	23/3	24/2	22/4
Admission body weight (kg)	10.2 (0.6)	11.2 (0.6)	10.9 (0.4)
Weight/height (% NCHS)	78 (2.8)	76 (30)	78 (2.6)
Weight/age (% NCHS)	63 (1.7)	64 (1.9)	63 (1.7)
Duration of diarrhoea before admission (hours)	14 (4.1)	15.4 (2.3)	15 (2.1)
Duration of vomiting before admission (hours)	21.8 (6.4)	18.4 (3.6)	15.3 (2.5)
Aetiology of diarrhoea (cholera/non-cholera)	19/7	20/6	20/6
Admission serum specific gravity	1.0320 (0.00003)	1.0316 (0.0004)	1.0306 (0.0004)
Admission packed cell volume (%)	41 (1.5)	40 (1.5)	38 (0.9)
Volume of initial intravenous treatment (ml/kg)	90 (5.3)	87 (7.8)	82 (5.9)

NCHS=National Center for Health Statistics.

performed to establish general significance between the three groups. When significance was established Duncan's multiple range test was applied to detect differences between two groups.

Results

The admission clinical data of the study children are shown in Table 1. Patients in all three groups were comparable for sex, age, weight, duration of diarrhoea and vomiting before admission, degree of dehydration, and fluid required for initial rehydration. Most of the patients in all three groups had cholera (Table 1). Except for two patients with shigellosis (one in the glucose-ORS group and one in the wheat-ORS group), the remaining patients had diarrhoea due to *E. coli* infection. The children

receiving rice-ORS were, however, less dehydrated, as assessed by their admission serum specific gravity and packed cell volume value, compared with the other two groups, although the difference was not significant.

Twenty four hourly ORS intakes and purging rates in the patients with cholera are shown in Figure 1. There was a progressive decrease in stool volume in all the groups. Compared with patients receiving glucose-ORS, the other two groups had significantly decreased rates of purging at the first and second 24 hours ($p<0.01$). The glucose-ORS group, however, had significantly higher ORS intakes compared with the other two groups ($p<0.01$) during the first 24 hours. Similar observations were made between the groups in both ORS intake and stool output during the 48-72 hour period, although the difference was less significant ($p<0.05$).

In children with diarrhoea not due to cholera, however, no significant difference was observed at any interval between the groups with regard to ORS consumption and rate of purging (Fig. 2).

Table 2 provides additional information regarding duration of diarrhoea after admission to hospital,

Fig. 1 Mean (SEM) 24 hourly oral rehydration solution intake (ORS) and stool output in patients with cholera.

Fig. 2 Mean (SEM) 24 hourly oral rehydration solution intake (ORS) and stool output in patients without cholera.

Table 2 Comparison of various characteristics after treatment with different oral rehydration solutions. Values are mean (SEM)

	Treatment group		
	Glucose-ORS	Wheat-ORS	Rice-ORS
Duration of diarrhoea after admission to hospital (hours)	90 (8.7)	80 (6.0)	78 (5.8)
Sugar content in stool after hydrolysis (mmol/l):			
24 h	11.2 (4.5)	10.0 (5.9)	12.7 (5.5)
48 h	12.2 (3.6)	9.3 (4.5)	15.3 (3.8)
72 h	15.5 (3.5)	10.4 (2.8)	16.0 (2.7)
Urine output (ml/kg/day):			
24 h	32.8 (7.6)	65.3 (8.8)	60.3 (6.3)
48 h	42.9 (6.6)	37.4 (7.0)	45.5 (6.7)
72 h	47.6 (9.9)	46.5 (7.5)	43.6 (5.9)
Weight gain:			
24 h	7.0 (1.0)	7.3 (1.2)	6.5 (1.2)
48 h	7.0 (1.5)	6.9 (1.6)	6.0 (1.5)
72 h	8.0 (1.0)	7.6 (1.3)	6.0 (1.7)

sugar content in stool after hydrolysis, 24 hourly urine output, and percentage weight gain in the three groups. Sugar content after hydrolysis in the wheat-ORS group was lower compared with the other two groups, although the difference was not significant. Duration of diarrhoea after admission to hospital was comparable in all three groups. Urine output was significantly less in patients receiving glucose-ORS compared with the other two groups during the first 24 hours ($p < 0.05$). Children receiving wheat-ORS and glucose-ORS had, on average, gained more weight at the time of discharge than the children receiving rice-ORS, but the difference was not significant. There were six therapeutic failures (as described above), two in each of the groups. All six patients had positive results of culture for cholera on admission, with severe dehydration (mean specific gravity = 1.0330) and vomiting during the early period of rehydration.

Discussion

This study shows that hydrolysed wheat-ORS, like rice-ORS and glucose-ORS, can be used effectively in the treatment of cases of acute diarrhoea. Both of the cereal based ORS were found, however, to be superior to glucose-ORS, considering the decreased rate of purging as well as consumption of ORS.

The carbohydrate of cereals is predominantly starch, and it is speculated that this starch is digested by intraluminal enzymes, slowly releasing the glucose molecules that stimulate optimum absorption of sodium without imposing an 'osmotic penalty'. In a recent study a significant reduction of both stool volume (about 50%) with less intake of ORS was observed by using 80 g rice powder to replace

sucrose or glucose in the standard electrolyte solution.⁷ In another recent study wheat extract mixed with milk was found to be effective in the management of severe diarrhoea in malnourished children after initial rehydration.¹⁴ No untoward effects—for example, osmotic diarrhoea, hypernatraemia, etc—were observed after the intervention.

We attempted to ensure that this study comprised mainly patients with acute watery diarrhoea. Of these patients with diarrhoea not due to cholera, however, all had infection with enterotoxigenic *E. coli*, except for two with shigella infection (one each in the rice-ORS and wheat-ORS groups). Wheat extract used in this study was partially hydrolysed, resulting in a lower sugar content in the stool after hydrolysis. Urine output was significantly lower during the last 24 hours of treatment in patients receiving glucose-ORS compared with those receiving wheat-ORS. This may have been due to an increased rate of purging in the glucose-ORS group. Less weight gain in the rice-ORS group may be explained by the fact that they were initially less dehydrated and had less intake of ORS.

It is believed that the incidence of gluten enteropathy may increase with the use of wheat products, though in our limited study diarrhoea was not aggravated in any of our patients by the use of the wheat solution.

In developing countries acute diarrhoea leads in many children to both fluid-electrolyte malnutrition and protein energy malnutrition. Glucose polymers are known to be powerful carrier molecules of sodium and water absorption in healthy subjects. Converting any starch (like wheat in this study) into soluble carbohydrates, the preparation of ORS will be simple. It may also be possible to formulate ORS

that is energy dense and facilitate early rehabilitation of malnourished children with diarrhoea. This study illustrates that an oral solution of electrolytes and wheat extract could maintain fluid and electrolyte balance in patients with acute dehydrating diarrhoea. Cereal based ORS has been found to be superior to glucose-ORS. All the cereal ORS preparations so far tested, however, need boiling and are suitable for use as a home solution in cases of diarrhoea. This is the first cereal product that can be used as cold water preparation and therefore has the prospect of being available in packet form, although the cost of extract preparation may be a constraint.

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