Oral rehydration solution without bicarbonate

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SUMMARY The efficacy of oral rehydration solution without bicarbonate was compared with World Health Organisation oral rehydration solution in 98 young children in a double blind and randomised clinical trial. These children had varying degrees of dehydration and acidosis caused by acute watery diarrhoea. The mean serum bicarbonate concentration on admission was 13.3 mmol(mEq)/l in the former and 13.1 mmol(mEq)/l in the latter group of children. All but three children who received the rehydration solution without bicarbonate were successfully treated; three treatment failures were attributed to persistent vomiting and severe diarrhoea (greater than 10 ml/kg/hour). Correction of acidosis was slower in the non-bicarbonate treated than the control group during the first 24 hours' treatment ($P < 0.001$). By 48 hours, however, acidosis was corrected and mean serum bicarbonate had risen to 17.1 mmol(mEq)/l compared with 18.9 mmol(mEq)/l in the control group ($P > 0.05$). Some failures due to sustained acidosis and persistent vomiting and diarrhoea should be expected. Oral rehydration solution without bicarbonate may be used where complete formula solution is not available.

The evolution of oral rehydration solution has been a major treatment advance in modern medicine. A single oral rehydration solution with a bicarbonate content of 30 mmol(mEq)/l has been recommended by the World Health Organisation (WHO) for acute diarrhoea in all age groups.¹ This universal formula has been derived largely from studies in adult cholera patients and has subsequently been used in children.² Bicarbonate is directly absorbed from the gut and corrects acidosis. Although oral rehydration solution with bicarbonate is effective for correction of acidosis, it has some disadvantages as bicarbonate reacts with glucose and sucrose in humid climates, resulting in a brownish furfural compound. This appearance makes some patients hesitant to use the solution. Molla *et al* observed that the average faecal bicarbonate content in children suffering from rotavirus and *Escherichia coli* diarrhoea was only 6 and 18 mmol(mEq)/l respectively.³ This amount of faecal bicarbonate loss may be handled physiologically in most patients by renal compensation, suggesting that a successful oral rehydration solution could be developed without adding bicarbonate. This makes the formulation simple, inexpensive, and suitable for presentation with a prolonged shelf life. In this study we compared the efficacy and safety of oral rehydration solutions with and without bicarbonate in the treatment of diarrhoea in children.

Materials and methods

This study was carried out at the International Centre for Diarrhoeal Disease Research, Bangladesh between April and September 1982. Children aged below 5 years who attended the treatment centre with a mild or moderate degree of dehydration due to acute diarrhoea of less than 7 days duration were randomly selected for the study. Dehydration was assessed clinically, and children were grouped into mild, moderate, and severe according to the WHO guidelines.⁴ After parental consent had been obtained and brief clinical histories and physical examinations undertaken, the children were assigned to either WHO oral rehydration solution (with bicarbonate) or oral rehydration solution without bicarbonate, using a random number table. The WHO solution used as a control provided Na^+ 90, K^+ 20, Cl^- 80, and HCO_3^- 30 mmol(mEq)/l and glucose 111 mmol/l (2000 mg/100 ml). Oral rehydration solution without bicarbonate provided Na^+ 90, K^+ 20, and Cl^- 110 mmol(mEq)/l, and glucose 110 mmol/l (1981 mg/100 ml). Biochemistry laboratory personnel prepared two types of oral solution packets, confirmed their chemical concentrations, coded, and blinded them. Nursing staff dissolved the contents of the packets according to the random schedule before giving the solution to the patients.

Table 1 Composition of oral rehydration solutions (ORS)

WHO ORS		ORS without bicarbonate	
NaCl	3.5 g	NaCl	5.3 g
KCl	1.5 g	KCl	1.5 g
NaHCO ₃	2.5 g	Glucose	20 g
Glucose	20 g	Water	1000 ml
Water	1000 ml		

No intravenous fluid was allowed at any stage of treatment. Children received oral rehydration solution in a volume of 50 ml/kg for mild dehydration and 100 ml/kg body weight for moderate dehydration for initial rehydration, followed by a free intake to match stool output as long as diarrhoea continued.⁴

Each patient was placed in a cholera cot covered with a plastic sheet specially designed to collect liquid stool in a bucket underneath. Breast milk, when available, or half strength cows' milk where it was not, were allowed from four hours after admission. The amount of milk ingested was measured by weighing the child before and after the breast feed. Children were closely observed in the clinical research ward by experienced and qualified nurses and attending physicians. Intake of oral rehydration solution and milk and output of stool, urine, and vomitus were measured at four hour intervals. Blood samples for measurement of haematocrit, plasma specific gravity, and electrolytes were drawn on admission, before starting oral rehydration treatment, and at 24 and 48 hours after the initiation of this. Na⁺ and K⁺ were determined on an IL-443 flame photometer, the bicarbonate content of blood was measured on a Cl/CO₂ auto-analyser, and plasma specific gravity was determined by a Goldberg refractometer. Stool samples were collected through rectal catheter on admission and at 24 and 48 hours for estimation of faecal Na⁺, K⁺, and HCO₃ concentrations by the above mentioned techniques. Urine samples were collected for Na⁺ and K⁺ estimation at 24 and 48 hours. A stool sample was cultured for salmonella, shigella, and *Vibrio cholerae*. Enterotoxigenic *E coli* colonies were tested for heat labile⁵ and heat stable⁶ enterotoxins. Detection of rotavirus in stool was carried out by an ELISA method.⁷ The effect of treatment was assessed by measuring the oral rehydration solution intake, output of stool and urine, gain in body weight, changes in haematocrit and plasma specific gravity, and correction and maintenance of the electrolyte balance.

Children whose initial rehydration or maintenance of hydration could not be achieved with oral rehydration solution and required intravenous fluid treatment were considered as oral treatment fail-

Table 2 Admission characteristics of children treated with WHO oral rehydration solution (ORS) and ORS without bicarbonate

Characteristics	WHO ORS (n=48)	ORS without bicarbonate (n=50)
Sex (boys/girls)	30/18	25/25
Age (months). Mean (SEM)	18.6 (2.1)	19.4 (1.9)
No breast fed (%)	50	43
Duration of diarrhoea before admission (hours). Mean (SEM)	54.4 (9.5)	54.7 (6.5)
Body weight (kg). Mean (SEM)	7.2 (0.3)	7.2 (0.2)
Clinical dehydration (%)		
Mild	25	21
Moderate	75	79
Acidosis (bicarbonate ≤ 15 mmol (mEq/l) (%))	67	72
Stool culture		
<i>Vibrio cholerae</i>	3	5
Shigella	1	2
<i>Escherichia coli</i>		
LT	2	1
ST	9	7
Rotavirus	12	10

ures. The criteria for failure of treatment were based on clinical assessment supported by intake and output balance and failure to gain body weight. Data were analysed by χ^2 and two tailed normal test (Z test). Data from the three children who failed treatment with oral rehydration solution without bicarbonate were excluded from analysis but are included in Table 2.

Results

The two groups of children were comparable for epidemiological, clinical, and diagnostic features (Table 2). Nearly 75% of children were admitted with moderate degrees of dehydration and acidosis. All 48 children (100%) receiving WHO oral rehydration solution and 47 of 50 children (94%) receiving the solution without bicarbonate were successfully rehydrated and maintained their hydration status until diarrhoea stopped. The three treatment failures were withdrawn from the study because of persistent vomiting and severe diarrhoea (greater than 10 ml/kg/hr). One of them had severe hypokalaemia (Serum K⁺ 1.7 mmol(mEq)/l) and bronchopneumonia. These children were subsequently treated with intravenous fluid.

The children treated with oral rehydration solution without bicarbonate consumed less than the control group and also passed less liquid stools, but the difference was not statistically significant ($P > 0.05$) (Table 3). All patients passed urine within 12 hours of beginning treatment. Seventeen patients (32%) in the oral rehydration solution without bicarbonate group and 15 patients (31%) in the control group had vomiting, mostly during the

rehydration phase. In those who vomited, the mean volume of vomitus/kg body weight was more in the group treated without bicarbonate (22 ml/kg) than those who received the WHO solution (12 ml/kg) ($P<0.001$).

Table 3 Comparison of intake of oral rehydration solution (ORS) and milk, output of stool, and urine; hour of first micturition; and duration of diarrhoea in patients treated with WHO ORS and ORS without bicarbonate. (Values mean (SEM)).

	WHO ORS (n=48)	ORS without bicarbonate (n=47)
ORS intake (ml/kg)		
1st 24 hours	309.7 (28.8)	259.2 (18.7)
2nd 24 hours	217.6 (31.8)	163.1 (13.9)
Total intake	567.8 (60.1)	436.2 (35.4)
Milk intake (ml/kg)		
1st 24 hours	91.4 (12.1)	82.6 (6.9)
2nd 24 hours	87.4 (8.6)	82.8 (7.1)
Total intake	200.6 (19.5)	187.4 (15.0)
Stool output (ml/kg)		
1st 24 hours	168.8 (22.8)	144.6 (13.8)
2nd 24 hours	148.7 (25.3)	112.9 (11.4)
Total output	348.8 (48.9)	269.4 (26.5)
Urine output (ml/kg)		
1st 24 hours	32.1 (4.1)	24.9 (3.2)
2nd 24 hours	40.6 (8.0)	39.6 (5.6)
Total output	83.5 (13.4)	68.0 (8.4)
1st micturition (hours)	5.1 (0.3)	6.3 (0.4)
Duration of diarrhoea after admission (hours)	50.5 (2.1)	50.3 (1.1)

Table 4 Comparison of bodyweight gain, haematocrit, plasma specific gravity, and serum Na^+ , K^+ , and HCO_3^- at 0, 24, and 48 hours after treatment with WHO oral rehydration solution (ORS) and ORS without bicarbonate. (Values mean (SEM)).

	WHO ORS (n=48)	ORS without bicarbonate (n=47)
Bodyweight gain (%)		
At 24 hours	6.4 (0.5)	5.6 (0.4)
At 48 hours	6.1 (0.5)	6.0 (0.5)
Haematocrit (%)		
On Admission	37.3 (0.6)	38.5 (0.6)
At 24 hours	30.6 (0.6)	31.1 (0.5)
At 48 hours	31.5 (0.6)	31.6 (0.6)
Plasma specific gravity		
On Admission	1.0279 (0.0003)	1.0271 (0.0003)
At 24 hours	1.0243 (0.0003)	1.0239 (0.0002)
At 48 hours	1.0239 (0.0002)	1.0240 (0.0002)
Serum Na^+ (mmol(mEq)/l)		
On Admission	132.6 (0.9)	134.5 (0.5)
At 24 hours	136.2 (0.9)	137.8 (0.6)
At 48 hours	136.2 (0.8)	137.2 (0.4)
Serum K^+ (mmol(mEq)/l)		
On Admission	3.5 (0.1)	3.7 (0.1)
At 24 hours	3.9 (0.1)	4.0 (0.1)
At 48 hours	4.2 (0.1)	4.1 (0.1)
Serum HCO_3^- (mmol(mEq)/l)		
On Admission	13.3 (0.6)	13.1 (0.5)
At 24 hours	18.1 (0.6)*	15.1 (0.4)*
At 48 hours	18.9 (0.8)	17.1 (0.5)

* $P<0.001$ (Z test).

Success of hydration in both groups was determined by appreciable weight gain and fall in haematocrit and plasma specific gravity at 24 and 48 hours after oral treatment had begun. Children treated without bicarbonate, however, failed to correct acidosis as efficiently as control children during the first 24 hours of treatment ($P<0.001$).

By 48 hours acidosis was similar in both groups with a rise in the mean serum bicarbonate concentration from 13.1 to 17.1 mmol(mEq)/l in the study group and from 13.3 to 18.9 mmol(mEq)/l in the control group ($P>0.05$) (Table 4).

The sodium, potassium, and bicarbonate concentration in stool as well as the sodium and potassium concentration in urine at 24 and 48 hours showed no significant differences between the two groups.

Discussion

This study indicates that oral rehydration solution without base may be used when complete formula, recommended by the WHO, is not available. In many developing countries WHO oral rehydration solution is not available for a variety of reasons: nor is sodium bicarbonate always available. Simple salt and sugar solution has been found effective in the treatment of both infantile diarrhoea⁸ and adult diarrhoea.⁹ Hypokalaemia rather than acidosis, however, was found to be three times more frequent in patients treated without bicarbonate than in WHO solution treated patients.⁸ Children treated with oral rehydration solution without bicarbonate may remain biochemically acidotic for up to 24 hours without any clinical evidence of acidosis. By 48 hours acidosis is usually corrected, probably by the homeostatic mechanism of the body through lungs and kidneys. Some oral rehydration treatment failures may be expected in children treated with a bicarbonate-free solution due to sustained acidosis associated with persistent vomiting, severe diarrhoea, and non-acceptance of sufficient rehydration solution.

In this study, the laboratory personnel measured the salts and so their electrolyte concentrations were controlled, but in a rural situation where mothers prepare the salt-sugar solution using household measurements, there may be considerable variations in the electrolyte concentrations.¹⁰ Mothers, however, may be taught to prepare a simple home made salt-sugar oral solution containing a reasonable and safe concentration of sodium.¹¹ Thus a simple salt-sugar solution without bicarbonate but with adequate potassium supplementation either in the oral solution or in the diet, may be used as an alternative in childhood diarrhoea, but should be reserved for situations where WHO oral rehydration

solution is not available. Green coconut water, which is available in many developing countries, contains a sufficient amount of natural potassium and is well absorbed.¹² Mothers may be instructed to use oral rehydration solution and coconut water in a 2:1 ratio which will allow free water as well.

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