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A comparison of oral replacement solutions containing sodium in concentrations of 120 m mols/ L and 60 m mols/L in paediatric diarrhoea

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The efficacy and safety of two types of oral replacement solutions (ORS) were tested in 65 children aged 6 months to 2 years, with histories of acute watery diarrhoea and dehydration of comparable severity. 40 children were maintained with ORS containing low sodium (60 m. mols/L) and 25 with ORS containing high sodium (120 m. mols/L) after initial intravenous rehydration. Hydration and electrolyte balance could be maintained in all children. Two children receiving ORS with 120 m. mols/L sodium developed hypernatremia. Children receiving ORS with high sodium excreted significantly more sodium in urine and stool after 24 & 48 hours of oral therapy. Despite the presence of effective homeostatic mechanism of the body, we do not recommended ORS with 120 m. mols/L. We still consider the WHO recommend ORS with 90 m. mols sodium/L as the appropriate oral solution for general use in all types of diarrhoea including cholera. However, a lower concentration of sodium in ORS would also be safe and effective for most of the non-cholera pediatric diarrhoeas.

Key words : Low sodium, high sodium in oral replacement solution (ORS) ; hypernatremia ; hyponatremia.

One of the recent advances in last decade in the field of diarrhoeal disease research has been the discovery of oral rehydration solution for the treatment of dehydrating diarrhoeal diseases[1-6]. A single oral hydration solution having a sodium concentration of 90 m.mols/L has been recommended by WHO/ UNICEF in all age groups and in all causes of diarrhoea. This oral rehydration solution is recommended largely from the studies in adult patients with acute cholera and subsequently has been used in children. It has been shown that average concentration of sodium in stool in paediatric diarrhoea is 37 m. mols/L in rotavirus infection, 53 m.mols/ L in enterotoxigenic E. coli, and 88 m.

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mols/L in cholera infection[7]. The possible risk of hypernatremia after the use of high sodium containing oral solution in children has discouraged many paediatricians against its wider use since excess salt load may cause cerebral haemorrhage convulsions and death [8,-11]

Preparation of oral rehydration solution at home is being encouraged where wider ranges of sodium concentration have been observed. In this context, It has become very important to determine the safety range of sodium concentration in oral rehydration solution in a scientific way. Hence this study was designed to assess the relative risk of "high" sodium (Na 120 m.mols/L) with "low" sodium (60 m.mols/L) containing oral solution in children under 2 years of age suffering from acute watery diarrhoea.

Materials and Methods

65 children aged 6 months to 2 years (40 in low sodium and 25 in high sodium group) were studied in two separate six month periods in the study ward of International Centre for Diarrhoeal Disease Research. These children had uncomplicated watery diarrhoea of less than 7 days duration and had not taken any antibiotics before admission. Their clinical sings showed moderate dehydration according to WHO criteria[12]. Low sodium ORS group were studied first and the high sodium ORS groups were studied later in the same year. They were selected with comparble age, duration of diarrhoea and severity of illness in both the groups. On admission after physical examination and clinical assessment of the degree of dehydration, intravenous Dacca solution was given for initial replacement of fluid loss. Amount of intravenous fluid given was determined from the clinical assessment of dehydration of the patient (6—9%/body weight for moderate dehydration)[12].

Intravenous rehydration was done within 4 hours of admission. After that children received either "high" (120m. mols/L) or "low" (60 m.mols/L) sodium containing oral replacement solution until diarrhoea stopped. The compositions of these two types of oral solutions used are shown in Table 1. We have used a combination of bases, sodium citrate and sodium bicarbonate in two different concentrations but, in equal proportions for correction of base deficit acidosis (Table1). Intravenous Dacca solution contains sodium cholride 5 gm, potassiam chloride 1 gm in one litre distilled water wich provides Na^+ 133, K^+13, Cl^-98 and HCO_3 48 m.mols/L. No antibiotics were used in any of the study patients. Vital signs, body weight, intake of oral replacement solution and diluted milk, output of stool and urine as far as possible were measured every 8 hourly from the beginning of oral therapy until diarrhoea stopped. Mothers were specifically instructed to offer oral fluid in small amounts frequently either by spoon or feeding bottle. Cow's milk diluted 1:1 with water was offered every four hourly to both groups of children. Samples of blood were drawn on admission and after four hours when the oral therapy started and subsequently at 24 hours, 48 hours and at discharge for estimation of serum specific gravity and electrolytes. Adequate samples of stool

Table 1. Composition Of low And high Sodium Oral Replacement Solutions (ORS)

	Low Sodium ORS	High Sodium ORS
	m. mols/L	m. mols/L
Na^+	60	120
K^+	25	25
Cl^-	55	95
$HCO3^-$	15	25
Citrate	15	25
Glucose	111	111
Total	281	401
Ingredients		
Nacl	1.75 gm	4.2 gm
Kcl	1. 9 gm	1.9 gm
NaHCO3	1.25 gm	2.1 gm
Na Citrate (Tribasic)	1.47 gm	2 45 gm
Glucose	20 gm	20 gm
Water	1 litre	1 litre

and urine were sent simultaneously for estimation of sodium concentration/L along with serum electrolyes. Stool was cultured for *V. cholereae*, *Salmonella* species and *Shigella* species. Oral therapy was considered successful when adequate hydration was maintained in the face of continuing stool losses and when the serum sodium concentration at the end of the 48 hour study period was within the range of 130-150 m.mols/L.

Results

40 children in the "low" (Na^+60m. mols/L) and 25 in the "high" (Na^+120m. mols/L)sodium ORS group were studied. Clinical characteristics of the two groups of children are shown in Table 2. Both groups were comparable in age, duration of diarrhoea, blood and stool laboratory values etc. This comparative clinical study showed that mean serum sodium was significantly higher after 24 hours administration in the high sodium group than in the low sodium group ($P<0.05$), as shown in Table 3. In fact, hypernatremia ($Na^+<150$m.mols/L) developed in 2 children whose sodium concentration rose from 146 to 161 and the other 146 to 152 m mols/L after 24 hours of oral therapy. These two children did not show any signs and symptoms of hypernatremia. Use of sodium citrate in combination with sodium bicarbonate in equal proportion was found quite effective for correction of acidosis (Table 3). We have not observed any biochemical or clinical signs of alkalosis in those children receiving 50 m. mols of base/litre of oral solution. No differences between the two groups were observed in total oral solution intake, milk intake, purging rates per kilogram body weight and the duration of hospitalization (Table 4). Significant differences were found in the excretion of sodium in urine and stool after 24 and 48 hours of oral therapy in high sodium ORS group (Table 5). Bacterial pathogens were isolated in 6 cases (2 cholera, 2 non-agglutinating vibrios and 2 shigella) in the low sodium ORS group and 4 (2 non-agglutinating vibrios and 2 shigella) in high sodium ORS group. Detection of enterotoxigenic *E. coli* and rotavirus was not attempted.

Discussion

This study demonstrated a wide range of safety for the concentration of

Table II : Clinical Data of Patients treated with low and high sodium Oral Replacement Solution (ORS) before intravenous rehydration

	Low Sodium ORS	High Sodium ORS
Number of patients	40	25
Age (months)	11±1	12±1
Duration of diarrhoea before admission (hours)	62±6	56±8
Laboratory values :		
Serum Na^+ (m. mols/L)	134±1	136±1
K^+ ,,	3.6±0.2	3.7±0.1
Cl^- ,,	103±1	108±1
Co_2^- ,,	12.7±0.6	14.1±0.8
Specific gravity	1.026±0.001	1.026±0.001
Stool Na^+ (m. mols/L)	56±	57±8

Results in Mean±S.E.M.

Table III : Clinical Course of patients treated with low and high Sodium Oral Replacement Solution (ORS)

	Low sodium ORS	High sodium ORS
Serum Specific Gravity		
on admission	1.026±<0.001	1.026±<0.001
at 4 hours	1.023±<0.001	1.024±<0.001
at 24 hours	1.023±<0.001	1.024±<0.001
at 48 hours	1.023±<0.001	1.023±<0.001
Serum Na (m. mols/L)		
on admission	134±1	136±1
at 4 hours	138±1	138±1
at 24 hours	137±1	140±1*
at 48 hours	137±1	137±1
Serum TCO_2 (m. mols/L)		
on admission	12.7±0.6	14.1±0.8
at 4 hours	16.9±0.6	16.9±0.8
at 24 hours	20.1±0.7	21.3±0.6
at 48 hours	22.6±0.8	23.0±1.0

Results in Mean± S.E.M.

* Mean serum sodium concentration was significantly greater than the mean serum sodium concentration in the group treated with low sodium ORS after 24 hours, by students' "t" test ($P<0.05$).

Table IV : Purging rates and Oral fluid intake in Patients treated with low and high Sodium Oral Replacement Solution (ORS).

	Low sodium ORS	High sodium ORS
Purging (ml/kg)		
First 4 hours	23±4	21±4
First 24 hours	113±9	123±19
Second 24 hours	81±7	86±12
Total until discharged	276±31	275±38
Duration of purging in hospital (hrs).	58±5	54±4
Oral rehydration fluid intake (ml/kg)		
First 4 hours	31±7	34±4
First 24 hours	131±8	139±12
Second 24 hours	78±8	85±13
Total ORS intake	261±26	263±23
Total milk intake during hospitalization (ml/kg)	241.9±22	210±15

Results in Mean± S.E.M.

Table V: Excretion of Sodium in Stool and urine of patients treated with low and high Sodium Oral Replacement Solutions (ORS)

	Low sodium ORS		High sodium (ORS)	
	Stool	Urine	Stool	Urine
Na (m.mols/L)				
On admission	56± 5(30)	—	57±8(20)	—
at 4 hours	53±6(34)	31±10(25)	52±7(16)	25±8(16)
at 24 hours	36±3(26)	26±9(19)	59±6(25)*	70±15(21)**
at 48 hours	42±7(16)	33±10(15)	55±11(14)	81±20(9)***

Results in Mean ± S.E.M.

Figures in parenthesis indicate number of patients' sample tested.

* Mean stool sodium concentration was significantly greater than the mean stool sodium concentration in the group treated with low sodium ORS after 24 hours, by students' "t" test ($P<0.001$).

** Mean urine sodium concentration was significantly greater than the mean urine sodium concentration in the group treated with low sodium ORS after 24 hours, by students' "t" test ($P<0.01$).

*** Mean urine sodium concentration was significantly greater than the mean urine sodium concentration in the group treated with low sodium ORS after 48 hours, by students' "t" test ($P>0,05$).

sodium in oral replacement solution. Studies in late 1960's and early 1970's have shown that oral solutions with concentration of sodium within the range of 90-120m. mols/L was safe and effective in the management of diarrhoea in both adults and children[5-3]. WHO recommended formula was found to be safe even in neonates when oral fluid and free water were allowed in 2 : 1 ratio[13]. Problems of measuring appropriate amount of water and electrolyte ingredients in the field remains to be resolved in the developing countries. Different techniques have been tried and wide range of sodium concentration have been observed. Although, the range of 20-120 m.mols of sodium/litre of oral solution is generally considered to be safe and effective,[14] few field studies have been carried out to assess how children under two years respond to the solutions prepared by mothers at home.

This study showed that the kidney as well as intestine excreted partly the extra load of sodium in the high sodium ORS group. The low sodium concentrations in the stools of these patients suggest that the high sodium content in oral replacement solution is unnecessary but even then symptoms of hypernatremia is a rare problem as the kidney protects the patients by excreting extra load of sidium. However, from this study, serum sodium value allows us to say that hypernatremia can occur with ORS containing sodium of 120m. mols/L when the excess sodium is not excreted by some patients indicating that sodium concentration accumulates in the body when measured between intake versus output. Thus despite the presence of excellent homestatic mechanisms a lower sodium containing ORS is desirable for children suffering mostly from non-cholera diarrhoea losing relatively less sodium in the stool.

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Smallpox Vaccination

Following the global eradication of smallpox, the Thirty-Fourth World Health Assembly of the World Heath Organization (WHO) by resolution amended the International Health Regulations to remove smallpox from the diseases subject to the regulations, effective January 1, 1982.

According to WHO, the collaboration of national health administration in withdrawing the requirement for smallpox vaccination certificates has been very positive. All the countries of the world except Chad, in Africa, have advised WHO that an International Certificate of Vaccination against smallpox is no longer required from any traveller. However, WHO reports that some local authorities in Democratic Kampuchea may require proof of vaccination. Because of the risk of complications of vaccination to both vaccinees and their contacts, physicians should give travelers to any country, in which a certificate may be required a signed statement that vaccination is medicalls contraindicted. Smallpox vaccination should not be given for international travel.

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