ORIGINAL ARTICLE

Oral Rehydration Therapy in Young Infants less than 3 Months with Acute Diarrhoea and Moderate Dehydration

by

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Abstracts

Oral rehydration therapy (ORT) as an appropriate technology in the treatment of acute diarrhoeal diseases (ADD) has been accepted throughout the world. It has been proved that besides lifesaving, ORT has reduced about 70-80% of the use of intravenous solution and average cost of the treatment of ADD. If there is still problem, question or doubtfulness, is the use of WHO ORS in full concentration for the neonates and young infants less than 3 months of age.

During one-year period it has been treated 72 cases of ADD in young infants less than 3 months of age with moderate dehydration. They were divided into 3 groups. The first group was treated with 100 ml/kg bw of fluid consisting of twothirds as WHO ORS in full concentration for 4 hours period and the rest, one-third, was given as plain water for 2 hours period. The second group was treated with kristalyte with the Na concentration of 51 mEq/L and the third group was treated with intravenous Ringer's lactate for 6 hours period.

After the end of the study only 18 patients in each group could be matched and evaluated. From clinical observation and laboratory examinations, the result of the treatment in general, statistically shows no significant difference. Diarrhoea and vomiting stopped in all groups on the second day of treatment. Hyponatremia which occurred in 3 patients in Group I and 2 patients each in Group II and III improved after 6 hours of treatment. Acidosis was corrected in all of the treatment groups in 6 hours period. Weight gain up to 6-9% of body weight on admission was achieved after 6 hours of treatment in all groups. No complication of hypernatremia, convulsion nor hypoglycaemia in all the treatment group.

From this study it could be concluded that WHO ORS is quite safe and effective as ORS with low sodium concentration and intravenous treatment, as far as it is given slowly, little by little with a strict supervision.

Introduction

Oral rehydration therapy (ORT) based on the knowledge of couple absorption between sodium and glucose has been accepted troughout the world as the main treatment in acute diarrhoeal diseases (ADD) with dehydration. Since the use of ORT, promosing results in decreasing the CFR (Case fatality rate) due to ADD have been reported everywhere.

Before 1974, before ORT was used as the main treatment of ADD, CFR of ADD in the Department of Child Health, Medical School University of Indonesia, was 17.5% per year (Sutoto et al., 1974). With the IMR (Infant mortality rate) 137 per thousand live-birth, 40 - 50% of them were due to or accompanied by diarrhoea, the number of death due to diarrhoea were estimated about 600,000 - 900,000 annually (Brotowasisto, 1974).

In 1980, after introducing ORT, besides improving nutrition programme, family planning and economical income, the IMR in Indonesia has decreased to 100%. (House Hold Survey, 1980; Central Statistic Bureau, 1980). Diarrhoea has played role as it is causing of death in 24%.

In 1986, the IMR could be reduced again up to 71%., 15% of them were due to diarrhoea (House Hold Survey, 1986; WHO, 1986). Among the deaths due to ADD in infants were mainly neonates and young infants less than 3 months of age.

Oral rehydration therapy using low sodium concentration (pedialyte, kristalyte) in infants more than 3 months of age had been done by authors with good results (Sunoto et al., 1978; 1981). ORT using WHO-formula in one-third dilution had been done also in neonates with promising results (Kustiman et al., 1977; Adnan S. Wiharta et al., 1980).

Several reasons of not using WHO ORS in neonates and young infants less than 3 months of age were due to:

1. The body homeostasis of the neonates and young infants were still imperfect.
2. The high sodium content of WHO ORS i.e. 90 mEq/L which may cause hypernatremia and convulsion. The low sodium concentration of 30 - 60 mEq/L was preferred.

Anyway, several studies done by Pizarro et al. (1980, 1983), Sutjiningsih et al. (1982), Roy et al. (1984), Mehta et al. (1985) revealed that WHO ORS could be given to neonates and young infants alternated with plain water and or breast milk with good results.

The purpose of this study is to prove that the body homeostasis including the kidney function of the neonates and young infants less than 3 months of age is not as poor as it was thought and to show that WHO ORS formula could be given in full concentration, as far as it can be done by giving plain water and or breast feeding.

Materials and Methods

During one-year period, from January 1986 to January 1987, there had been treated 72 young infants less than 3 months of age with a working diagnosis of acute diarrhoea with moderate dehydration. Diarrhoea is defined as the passage of 3 or more loose or watery stool within 24 hours. Moderate dehydration is defined as the loss of body weight in approximately 8% (with the range of 6 - 10%) or from clinical observation using scoring system of King (1974) and WHO (1980) as can be seen in Table 1 and Table 2.

They were divided at stratified random into 3 groups consisting of 24 patients in each group. The first group (Group I) was treated with ORS (Oral rehydration salts) using WHO formula, according to the guideline for clinical treatment of acute diarrhoea (1984) and the method of Pizarro et al. (1981, 1983).

The dose of the solution was 100 ml/kg bw which was given in 6 hours period. Two-thirds of the solution consisted of WHO ORS were given in the first 4 hours' period. Whereas one-third of the solution was given as plain water in 2 hours' period.

Those who were on breast feeding, breast milk was given on demand. Those who were on formula feeding, formula milk was stopped and started after 6 hours' period. The composition of the WHO ORS were: Na 90 mEq/L, K 20 mEq/L, Cl 30 mEq/L and glucose 111 mEq/L.

The second group (Group II) was treated with ORS using kristalyte (Squibb) with the following composition: Na 51.2 mEq/L, K 25.0 mEq/L, Cl 37.5 mEq/L, citrate 57.5 mEq/L, dextrose 100.0 mOsm/L and sucrose 52.0 mEq/L. The dose of the solution was the same as in group I, i.e. 100 ml/kg bw which was given in 6 hours' period. No additional plain water was given during this period. Those who were on breast feeding and those who were fed on formula, were similarly done as in group I.

The third group (group III) was treated with Ringer's lactate solution intravenously with the dose of 100 ml/kg bw and were given during 6 hours' period. Those who were on breast feeding and formula feeding were similarly done as in group I and II.

No other food were allowed to be given in all the 3 groups. No antibiotics nor anti diarrhoeal agents were given in all the treatment groups. Each patient's weight and the volume of fluid administered were recorded at 6 hours, 24 hours and every day until discharge. Stools volume were measured by determining the difference in weight between dry and wet napkins covered by thin plastics to prevent the leakage of the stools. For vomiting it was used dry linnen. Urine output was separately measured from stool output by using special urine collector. Physical examinations were done on admission, at 6 hours after treatment, 24 hours and every day until discharge (4th day).

Laboratory examinations performed on admission were included routine blood analysis, Ht (Hematocrit), serum electrolytes (Na, K, and Cl) blood gas analysis, blood glucose and urea nitrogen, serum osmolality, stool analysis (macroscopic, microscopic, pH, reducing substance), and routine analysis. Follow-up laboratory examinations were done at 6, 24 hours and before discharge (Ht, Na, K, and Cl), base deficit, blood glucose, blood urea nitrogen and serum osmolality).

Excluding the study were patients with acute diarrhoea with mild and severe dehydration, severe PEM, hyperpyrexia (temperature over 39° C on admission), severe accompanying diseases (bronchopneumonia, septicaemia, meningitis, encephalitis, etc.) and history of diarrhoea for more than 7 days and or chronic diarrhoea. Patients with mild systemic infection such as common cold, rhinitis, pharyngitis without hyperpyrexia were included in the study.

Statistical analysis for significancy test were performed using the t test and or the Chi-Square test.

Results

At the end of the study there were only 18 patients in each group which could be matched and evaluated. Excluding the study were 18 patients of all the treatment groups, consisting of 6 patients for each group due to misdiagnosed of severe dehydration in 4 patients, severe accompanying diseases (bronchopneumonia in 3 patients, septicaemia in 3 patients and purulent meningitis in 1 patient), and incomplete clinical and laboratory examinations in 7 patients.

The results of the clinical observations and laboratory examinations on admission could be seen in table 3 and 4. On admission, from the table 3 and 4, it can be seen that there were no significant differences ($p > 0.05$) in clinical characteristics and laboratory findings within the 3 groups. All of the 54 patients were successfully rehydrated within 6 hours' period according to the clinical observations (no sunken fontannel and sunken eyes, restoration of moist mucous membrane, normal skin turgor, return of urine flow, normal heart rate and pulse rate, normal respiration rate and gaining weight).

The results of the treatment on clinical characteristics and laboratory findings after 6 hours' period, 24 hours and before discharge on the forth day, can be seen in table 5 and 6. Increase of body weight was expressed as percent of weight gain on admission, not befote the patients suffering from diarrhoea because the body weight of most of the patients before illness were unknown.

Table 1 : *Scoring system of dehydration (King, 1974)*

Where to look	Points to score for the sign was found		
	0	1	2
1. The whole child (well or ill)	well	Restless, irritable, or abnormality quiet, drowsy or floppy	Delirium, comatose or shocked, very ill
2. Skin	Normal elasticity	Moderate reduced elasticity	Severely reduced elasticity
3. Eyes	Normal	Moderately sunken	Severely sunken
4. Respiration	20 - 30	30 - 40	40 - 60
5. Mouth	Normal	Dry	Dry and cyanosed
6. Pulse	Strong, less than 120	120 - 140	Over 140

Total score :
0 - 3 = mild dehydration
4 - 6 = moderate dehydration
7 - 12 = severe dehydration

Table 2 : *Assessment of dehydration and fluid deficit (WHO, 1980).*

Signs and symptoms	Mild dehydration	Moderate dehydration	Severe dehydration
General appearance and condition			
- infants and young children	Thirsty; alert; restless	Thirsty; restless or lethargic but irritable when touched	Drowsy; limp, cold, sweaty, cyanotic extremities; may be comatose
- older children and adults	Thirsty; alert; restless	Thirsty; alert; giddiness with postural changes	Usually conscious; apprehensive; cold, sweaty cyanotic extremities; wrinkled skin of fingers and toes; muscle cramps
Radial pulse	Normal rate and volume	Rapid and weak	Rapid, feeble, sometimes impalpable
Respiration	Normal	Deep, may be rapid	Deep and rapid
Anterior fontanelle	Normal	Sunken	Very sunken
Systolic blood pressure	Normal	Normal - low	Less than 10.7 kPa (80 mmHg); may be unrecordable
Skin elasticity	Pinch retracts immediately	Pinch retracts slowly	Pinch retracts very slowly(2 second)
Eyes	Normal	Sunken	Deeply sunken
Tears	Present	Absent	Absent
Mucous membranes	Moist	Dry	Very dry
Urine flow	Normal	Reduced amount and dark	None passed for several hours; empty bladder
% body weight loss	4 - 5%	6 - 9%	10% or more
Estimated fluid deficit	40 - 50 ml per kg	60 - 90 ml per kg	100 - 110 ml per kg

Table 3 : *Clinical features of the treatment groups on admission*

Features	Group I	Group II	Group III	Significancy
No. of the patients	18	18	18	
Sex : Male	15	14	14	P > 0.05
Female	9	10	10	
Age (days)	46.50 ± 32.10	44.13 ± 31.19	35.79 ± 26.38	p > 0.05
Body weight (kg)	3.27 ± 0.95	3.46 ± 1.23	2.92 ± 1.11	p > 0.05
Body temperature (°C)	37.18 ± 1.18	37.11 ± 1.24	37.27 ± 1.39	p > 0.05
Duration of diarrhoea before admission (days)	2.19 ± 1.21	2.31 ± 1.37	2.40 ± 1.53	p > 0.05
Frequency of diarrhoea before admission (times/day)	12.70 ± 6.99	9.79 ± 6.48	12.04 ± 8.11	p > 0.05
Stool output before admission (ml/day)	296.09 ± 172.17	333.54 ± 156.65	322.92 ± 184.40	p > 0.05
No. of the patients with vomiting	6 (33.3%)	6 (33.3%)	7 (38.8%)	p > 0.05
Frequency of vomiting before admission (times/day)	2.8 ± 0.6	3.0 ± 0.5	3.1 ± 0.6	p > 0.05
Kind of feeding :				
Breast fed (B)	7	6	7	
Bottle fed (F)	10	10	9	p > 0.05
Mixed (B + F)	1	1	2	
No. of accompanying diseases				
ARI	5	1	4	
Underweight	2	4	2	p > 0.05
LBW	1	1	1	
Anemia	3	6	6	
No. of sugar intolerance	3	6	6	
No. of fat malabsorption	14	12	14	p > 0.05
No. of intestinal fungal (Candida) infection	9	5	4	p > 0.05

Table 4 : *Laboratory finding of the treatment groups on admission*

Features	Group I	Group II	Group III	Significancy
Haemoglobin content (g/dl)	11.52 ± 2.80	10.85 ± 1.75	12.16 ± 2.60	p > 0.05
Haematocrit content (%)	39.33 ± 2.55	38.92 ± 2.80	38.21 ± 2.86	p > 0.05
Serum sodium (mEq/L)	134.17 ± 2.81	134.17 ± 2.81	133.71 ± 2.99	p > 0.05
Serum potassium (mEq/L)	3.78 ± 0.48	3.70 ± 0.35	3.75 ± 0.44	p > 0.05
Serum chloride (mEq/L)	103.08 ± 5.78	105.88 ± 5.86	105.21 ± 5.92	p > 0.05
Base deficit (mEq/L)	6.79 ± 2.06	6.77 ± 2.74	7.13 ± 2.56	p > 0.05
Blood glucose (mg/dl)	76.96 ± 13.07	78.63 ± 12.38	78.00 ± 12.47	p > 0.05
Blood urea (mg/dl)	24.70 ± 10.07	22.90 ± 11.70	20.80 ± 12.44	p > 0.05
Serum osmolality (mOsm/L)	303.17 ± 16.10	302.96 ± 11.66	301.71 ± 12.33	p > 0.05

Table 5 : *Intake of fluid, stool output and vomiting, weight gain of the 3 groups, 6 hours after treatment, 24 hours and before discharge (4th day)*

	Group I	Group II	Group III	Significancy
Intake of fluid				
During first 6 hours (ml)	328.13 ± 89.86	347.92 ± 121.40	247.92 ± 108.12	p > 0.05
During 24 hours (ml)	691.26 ± 168.93	764.48 ± 160.77	644.67 ± 193.00	p > 0.05
Before discharge (ml/day)	490.80 ± 133.55	519.30 ± 96.00	439.35 ± 171.25	p > 0.05
Stool output and vomiting				
During first 6 hours (ml)	24.58 ± 0.70	25.23 ± 0.80	24.30 ± 0.58	p > 0.05
During 24 hours (ml)	86.9 ± 13.06	90.05 ± 10.96	82.60 ± 1.26	p > 0.05
Before discharge (ml/day)	25.08 ± 5.78	30.88 ± 7.68	23.88 ± 5.07	p > 0.05
Weight gain (% of admission's weight)				
After 6 hours of treatment	8.63 ± 1.54	7.34 ± 0.95	7.82 ± 1.02	p > 0.05
After 24 hours of treatment	9.51 ± 1.18	7.59 ± 0.91	7.79 ± 0.86	p > 0.05
Before discharge	10.37 ± 0.49	10.29 ± 1.02	9.77 ± 1.02	p > 0.05

Table 6 : *Laboratory findings of the 3 groups on admission, after 6 hours of treatment, 24 hours of treatment and before discharge (4th day)*

	Group I	Group II	Group III	Significancy
Haematocrit (%)				
On admission	39.33 ± 2.55	38.92 ± 2.80	38.21 ± 2.86	p > 0.05
6 hours after treatment	37.33 ± 2.20	36.92 ± 2.08	36.92 ± 2.69	p > 0.05
24 hours after treatment	36.33 ± 1.18	35.54 ± 2.40	36.17 ± 2.73	p > 0.05
Before discharge (4th day)	36.01 ± 0.49	35.05 ± 1.31	35.09 ± 1.73	p > 0.05
Serum sodium (mEq/L)				
On admission	134.17 ± 2.81	134.40 ± 2.20	133.71 ± 2.99	p > 0.05
6 hours after treatment	135.63 ± 2.62	135.42 ± 2.30	135.88 ± 2.72	p > 0.05
24 hours after treatment	135.50 ± 2.06	137.50 ± 2.19	137.08 ± 2.84	p > 0.05
Before discharge (4th day)	133.92 ± 2.15	135.64 ± 2.52	136.69 ± 2.46	p > 0.05
Serum potassium (mEq/L)				
On admission	3.78 ± 0.48	3.70 ± 0.35	3.75 ± 0.44	p > 0.05
6 hours after treatment	3.81 ± 0.28	3.63 ± 0.29	3.73 ± 0.34	p > 0.05
24 hours after treatment	3.65 ± 0.22	3.46 ± 0.15	3.63 ± 0.20	P > 0.05
Before discharge (4th day)	3.34 ± 0.42	3.58 ± 0.20	3.72 ± 0.30	p > 0.05
Base deficit (mEq/L)				
On admission	6.79 ± 2.06	6.77 ± 2.74	7.13 ± 2.56	p > 0.05
6 hours after treatment	0.36 ± 2.29	0.38 ± 2.55	0.74 ± 2.27	p > 0.05
24 hours after treatment	0.64 ± 2.87	1.01 ± 2.58	0.97 ± 2.64	p > 0.05
Before discharge (4th day)	0.49 ± 2.34	0.87 ± 2.66	0.78 ± 2.36	p > 0.05
Blood glucose (mg/dl)				
On admission	76.96 ± 13.07	78.63 ± 12.38	78.00 ± 12.47	p > 0.05
6 hours after treatment	85.08 ± 12.75	85.21 ± 11.70	78.63 ± 13.53	p > 0.05
24 hours after treatment	85.21 ± 10.67	86.88 ± 9.07	85.38 ± 11.36	p > 0.05
Before discharge (4th day)	86.07 ± 9.88	87.12 ± 8.98	86.01 ± 10.06	p > 0.05
Serum osmolality (mOsm/L)				
On admission	303.17 ± 16.10	302.96 ± 11.66	301.71 ± 12.33	p > 0.05
6 hours after treatment	290.54 ± 13.15	287.58 ± 12.66	284.46 ± 9.36	p > 0.05
24 hours after treatment	283.17 ± 11.76	282.96 ± 11.66	281.71 ± 9.21	p > 0.05
Before discharge (4th day)	282.67 ± 10.36	281.17 ± 9.37	281.21 ± 8.37	p > 0.05

Not significant differences were found between the 3 groups during the first critical 6 hours of treatment (deficit replacement period) and thereafter regarding the fluid intake, stool output and vomiting, weight gain during rehydration period and laboratory indicators or rehydration. No patients needed intravenous therapy in group I and group II, indicating that both groups could drink enough ORS. All of the patients in the 3 groups gain weight satisfactorily, more than 8% of the body weight on admission.

Vomiting which was present in 33.3% of the patients in group I and II, and 38.8% in group III with the frequency of once or twice during therapy were stopped after 24 hours of treatment. Acidosis were corrected in all of the patients after 6 hours of treatment. Hyponatremia (Na < 130 mEq/L), occurring in 3 patients in group I and 2 patients each in group II and III were corrected within 6 hours of rehydration.

Hypokalemia (K < 3.0 mEq/L), which occurred in 5 patients in group I and 4 patients each in group II and III were also improved after 6 hours of treatment, but there was 1 patient in group I and 2 patients each in group II and III, were still present after 24 hours of treatment. Anyway all of them were already close to normal and became normal on the fourth day (before discharge).

Hypoglycaemia (blood glucose < 60 mg/dl) occurred in 2 patients in group I and I patient each in group II and III all of them were LBW and underweight infants. Sugar intolerance were found in group I, II and III in 2, 4 and 1 patient respectively.

Fungal (Candida) infection were found in group I, II and III in 9, 5 and 4 patients respectively. LBW infant were found in one patient in each group, whereas underweight was found in 2 patients in group I and III, and 4 in group II. The number of neonates in group I, II and III, were 7, 8 and 9 patients respectively. The number of neonates who were breast fed in groups I, II and III were 8, 8 and 10 patients respectively. Mild acute respiratory infection was found in group I, II and III in 5, 1 and 4 patients respectively. Whereas anemia was found in group I, II and III in 3, 6 and 6 infants respectively.

Discussion

From the results of the study in all the 3 groups as it is demonstrated, that ORS, WHO formula with high Na (90 mEq/L) is as safe and effective as ORS treatment with lower Na concentration (51.2 mEq/L) or intravenous solution using Ringer's lactate solution, for the rehydration of neonates and young infants less than 3 months of age. Two-thirds of the replacement solution of moderate dehydration could be given orally either by spoon or bottle little by little in full concentration for 4 hours' period, which is then followed by plain water as the rest calculated solution needed. Almost all of the patients in groups I and II could consume approximately 100 ml/kgbw in 6 hours' period without any complication (oedema of the eyelids, hypernatremia or convulsion).

Diarrhoea stopped in almost all of the patients on the first day on admission. In the groups I, II and III, diarrhoea was still present in 1, 2 and 1 patient respectively on the 2nd day and on laboratory examination, all of these patients revealed suffering from lactose intolerance. Vomiting which was present in the groups I and II, did not interfere nor becoming a problem

in giving ORS. All of the patients in groups I and II who suffered from vomiting could accept ORS if given little by little, particularly by using spoon. Vomiting was stopped after 24 hours of treatment. Weight gain as much as 6 - 9% of body weight on admission were acquired in all the treatment groups, with no significant difference between the groups I, II and III ($p > 0.05$).

Hyponatremia which occurred in 3 patients in group I and 2 patients each in groups II and III were corrected satisfactorily after 6 hours rehydration period. No hypernatremia was found as a complication in all the treatment groups.

Pizarro et al. (1983) in the treatment of 242 neonates with dehydration diarrhoea with the same method found 19 patients with hypernatremia and 5 patients with hyponatremia on admission who were corrected after complete rehydration and after 24 hours of treatment.

In the earlier studies, Pizarro et al. (1981) found also that WHO ORS solution and plain water in a 2 : 1 ratio could be successfully treated in both hyponatremia and hypernatremia patients. Also in the earlier studies Pizarro et al. (1983) successfully treated 61 patients with hypernatremia dehydration, 16 of them were neonates and 27 patients were children below 6 months of age. Complication resulting from rapid correction of hypernatremia were more likely to occur in patients with intravenous solution. No iatrogenic hypernatremia nor hyponatremia occurred as results of ORT in the 78 patients tested (Clements et al., 1980).

Roy et al. (1984) had also successfully treated 64 breast-fed children of age 3 months to 2 years with WHO ORS in full concentration without any additional of plain water. After 2 hours of ad libitum ORS and breast milk intake, 61 children had normal serum sodium level and only 3 children had marginal hypernatremia with sodium level of 150 - 151 mEq/L.

However, in contrast, Bhargava et al. (1984) in their study with 65 young infants less than 3 months of age, 22 of them were treated with WHO ORS, 6 infants resulting in hypernatremia at 8 hours of treatment and another 5 patients developed it at 24 hours. Among these 11 patients, 6 were neonates. Generalized convulsions occurred 12 hours after admission in a neonate who had a serum sodium of 167 mEq/L. In 2 patients asymptomatic and clinical manifestations of hypernatremia (periorbital oedema, mild pedal oedema and irritable) resolved within 12 to 36 hours period.

Hypokalemia which occurred in 5 patients in group I and 4 patients each in group II and III improved within 6 hours' period. There was 1 patient in group I and 2 patients each in group II and III, and still persisted after 24 hours of treatment. On clinical examinations all of them were low birth weight and underweight infants, and the serum potassium close to normal on the 2nd day and become normal before discharge on the 4th day. So, the hypokalemia in these infants were more or less due to the nutritional state of the patients rather than as a complication of the treatment.

Similar condition with the hypoglycaemia occurred in 2 patients in group I and 1 patient each in the groups II and III, all of them were LBW and undernourished infants. Mild acidosis which occurred in all of the 3 groups were also successfully corrected with all the 3 solutions after 6 hours of treatment.

Sugar intolerance, and steatorrhoea which occurred in all of the treatment groups were not becoming problem in the clinical management on the refeeding. Breast feeding and formula feeding could be given in full concentration without worsening the condition. All of the patients gained weight satisfactorily as expected.

Fungal infection which occurred in 18 patients successfully treated with nystatin with the dose of 4 × 100 000 IU for 3 - 5 days. The 2 LBW and 2 underweight infants in groups I and II could be treated with both of ORS in the hospital as far as given little by little by using spoon or bottle with a good supervision. For community operational and or home treatment this approach may still have limiting factor.

Mild acute respiration without high fever as found in groups I and II could be treated with both ORS without any problems or complications. Anemia found in 15 of these patients were not treated during the 3 days period of treatment, but will be evaluated ambulatorily further after discharge.

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