EFFECTS OF RICE POWDER SALT SOLUTION AND MILK-RICE MIXTURE ON ACUTE WATERY DIARRHEA IN YOUNG CHILDREN

C Sirivichayakul[1], W Chokejindachai[1], N Vithayasai[2], P Chanthavanich[1], K Pengsaa[1], P Wisetsing[1], S Harikul[2], H Rathvuth, A Sabchareon[1]

[1]Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand; [2]Queen Sirikit National Institute of Child Health, Ministry of Public Health, Bangkok 10400, Thailand

Abstract. A randomized pilot study was carried out to compare the safety and effectiveness of rice powder salt solution (RPSS) in combination with milk-rice mixture (RPSS-MR group, n = 17) with other two regimens, glucose-based oral rehydration solution (ORS) combined with MR (ORS-MR group, n = 17) and ORS combined with formula milk (ORS-milk group, n = 14) in the treatment of acute watery diarrhea with mild to moderate dehydration in 48 boys younger than 2 years. Results showed that in the first 24 hours patients in the RPSS-MR group had significantly smaller amounts of stool weight (32.7 g/kg) than those in the ORS-MR group (67.5 g/kg) and ORS- milk group (59.2 g/kg) ($p< 0.05$ for both measurements). Patients in the RPSS-MR group also had significantly shorter duration of diarrhea (29.6 hours) than the other two groups (43.8 hours and 49.6 hours, respectively) ($p < 0.05$ for both measurements). The stool weight and duration of diarrhea between the ORS-MR group and the ORS-milk group were not significantly different. The positive effect of milk rice mixture was not demonstrated in the study due to the significantly more severe diarrhea in the ORS-MR group. The effectiveness of the RPSS-MR is therefore likely due to mainly RPSS.

INTRODUCTION

Over two million children in developing countries die from diarrheal disease each year, making it the second most serious killer of children under five worldwide (WHO, 1997). Children under 2 year-old may suffer up to 10 diarrheal episodes each year (Bern *et al*, 1992). Rotavirus is the most common cause of acute diarrhea in children aged between 6 months and 2 years old (Sack *et al*, 1978; Wasi *et al*, 1984). The virus may destroy intestinal epithelial cells and cause secondary disaccharidase, mainly lactase deficiency (Cheney and Wong, 1993).

After the widely use of glucose-based oral rehydration solution (ORS) recommended by the World Health Organization for treatment of diarrheal episodes, the mortality due to acute diarrhea has been decreased significantly (WHO, 1984). The ORS formulation has, however, no effect on decreasing the volume, frequency, and duration of diarrhea. This causes the necessity to search for other formulations of oral rehydration solution (Mahalanabis, 1985). Cereal-based ORS has been used in acute childhood diarrhea with more effectiveness in reducing stool volume when compared to glucose-based ORS (Molla *et al*, 1989). However, cereal-based ORS is not generally available. Subsequently a rice-powder salt solution containing rice-powder 30 g/l and salt 3.5 g/l (RPSS), a more simple solution that can be prepared at home, was found by our group to be safe and more effective than glucose-based ORS in treatment of acute diarrhea in young children with mild to moderate dehydration as shown by significantly lower stool frequency, lower rate of stool output, and a shorter duration of diarrhea (Sabchareon *et al*, 1992).

As malabsorption of and intolerance to lactose occur frequently after acute enteric infections and diarrhea (Brown *et al*, 1988; Santosham *et al*, 1985), continuing formula milk feeding that contains lactose may cause in prolongation of diarrhea in some children. Non-lactose containing milk is likely to be useful in these children but it is expensive. To find a cheap and appropriate low lactose formulation, during 1994 - 1995 we conducted a preliminary study on effects of RPSS plus milk-rice mixture (RPSS-MR), ORS-MR, and ORS-milk in 21 boys aged between 2 and 24 months who suffered acute watery diarrhea with mild to moderate dehydration. The results showed that the group treated with RPSS-MR had the smallest mean stool weight in the first 24 hours (50 ± 28 g/kg) and the shortest mean duration of diarrhea (36 ± 13 hours). The

Correspondence: Prof Arunee Sabchareon, Faculty of Tropical Medicine, 420/6 Ravithi Road, Bangkok 10400, Thailand.
Tel: (662) 245-7197; Fax: (662) 248-2589; E-mail: tmasc@mahidol.ac.th

duration of diarrhea in the ORS-MR group (43 ± 9 hours) was shorter than those treated with ORS-milk (55 ± 22 hours) (Rathavuth, 1995). The data suggested that RPSS-MR is safe, and could be very effective for the treatment of acute diarrhea with or without lactose intolerance. The present study therefore was conducted to further evaluate effect of RPSS-MR on acute diarrhea in young children.

MATERIALS AND METHODS

A randomized, open, comparative study of RPSS-MR, ORS-MR and ORS-milk in 48 boys aged 4 to 24 months who had acute watery diarrhea of not more than 7 days duration with signs of mild or moderate dehydration and had no underlying diseases (such as pneumonia, sepsis, second to third degree malnutrition, and immunodeficiency) was conducted at Queen Sirikit National Institute of Child Health, Bangkok, Thailand, during 1997 to 1999. The study was approved by the Ethical Committee of Ministry of Public Health, Thailand. Written informed consent was obtained from all of the parents or guardians.

RPSS was prepared from separately pre-bagged rice powder (30 g) and salt (3.5 g). These would approximately be one and one-third tablespoonfuls of rice powder and one and one-fourth teaspoonfuls of salt. A fresh preparation was made by adding 1 packet of rice powder to a small amount of water and boiled for 10 minutes while stirring once in a while to make a uniform solution, and water was added up to 1 liter. The solution was then cooled and the salt was dissolved. The final solution contains sodium 63.4 mmol/l, chloride 62.4 mmol/l (Sabchareon *et al*, 1992). *In vivo* hydrolysis by intraluminal enzymes converts 80-85% of rice to glucose, amino acids and oligopeptides (Molla *et al*, 1982). Therefore 30 g/l of rice powder would liberate approximately 24 g (133mmol/l) of glucose in the intestinal lumen. MR was freshly prepared by adding 1 bag of the rice powder to 250 ml of water and boiled for 10 minutes. The final volume would be about 200 ml and then mixed with formula milk in a proportion of 1:2. The mixture contains approximately 19 calories per ounce that is slightly less than those of formula milk (20 calories per ounce). RPSS and MR were discarded four hours after preparation if not consumed. ORS was prepared by mixing one packet of ORS (Thai Government Pharmaceutical Organization) with 750 ml of cool boiled water. The contents of ORS were glucose 111 mmol/l, sodium 90 mmo1/1, chloride 80 mmol/l, potassium 20 mmol/l and bicarbonate 30 mmol/l. The ORS was discarded 24 hours after preparation if not consumed.

Children were randomized into one of the three treatment groups, RPSS-MR (n = 17), ORS-MR (n = 17), and ORS-milk (n = 14). Illness history was taken and physical examination was performed for each child. Venous blood samples from each child for hematocrit, electrolytes (sodium, potassium and chloride) were drawn on admission and 24 hours later. Complete blood count, blood urea nitrogen and creatinine were measured on admission.

Fecal sample obtained from each child on admission was examined microscopically for leukocytes, parasites and ova, and cultured for Enteropathogenic *Escherichia coli*, *Shigella*, *Salmonella*, and vibrios by the standard methods. Due to laboratory limitations, stool reducing substances and stool for rotavirus detection (using Slidex® test) were done on admission in 39 and 33 cases, respectively.

The children were initially rehydrated orally in the first 4 hours with RPSS for RPSS-MR group, or with ORS for both ORS-MR and ORS-milk groups. The oral fluid was administered mainly by the mothers or by attendants, the amount given followed the WHO guidelines (WHO, 1984). As soon as the calculated fluid deficit was replaced and there was clinical evidence of improving hydration status, the study diets (milk-rice or formula milk) were begun (approximately 5 hours of admission). Children in the RPSS-MR and ORS-MR groups were fed with milk-rice mixture and the children in ORS-milk group were fed with formula milk. On going "excess losses" (liquid stool and vomitus) were replaced volume for volume with RPSS or ORS in the corresponding group.

The volume of fluids intake was measured from pre-marked containers at 4 hours and 8 hours after initiation of treatment and every 8 hours thereafter. Stool frequency was recorded and stool output was weighted from pre-weighted disposal absorbent pads, which were changed according to patient's stool frequency. To prevent spillage of urine to the absorbent pads, disposable urine collectors were used. Vomiting frequencies were also recorded.

Duration of diarrhea in the hospital was defined as number of hours after admission until passing of the last liquid or semi-liquid stool that not

followed by another liquid or semi-liquid stool in 24 hours. Treatment failure was defined as recurrent dehydration (an evidence of > 5% dehydration after a successful initial rehydration), or no recovery over 72 hours after initial treatment.

Baseline and outcome data from each group were compared and analyzed by analysis of variance (ANOVA) (continuous variables) or Kruskal-Wallis test for quantitative data and Fisher Exact test for qualitative data with small cell sizes.

RESULTS

Patients in the three groups were more or less similar in mean values of age, body weight, duration of diarrhea before admission, history and frequency of vomiting, presence of fever, and hydration status. However, patients in the ORS-MR group had significantly more frequent diarrhea than the other two groups ($p < 0.05$ for both measurements). It was noted that history of vomiting was frequent, approximately 80%. Before admission most of the patients (78 to 94 %) received oral rehydration therapy and a considerable number of patients received oral antibiotics (29 to 47%) and/or antidiarrheal drugs (17 to 41%) but these parameters were not significantly different among the three groups (Table 1).

Bacterial enteropathogens were found in seven cases (14.6%) including one case each for *Vibrio cholera, Campylobacter, Salmonella B, Aeromonas hydrophila,* and *Aeromonas caviae* and two cases for *Aeromonas sobria*. Out of 34 patients whose stools were tested for rotavirus, 14 patients (41.2%) showed positive results. Of these 4, 4, and 6 cases were in the RPSS-MR, ORS-MR, and ORS-milk groups, respectively. Stool reducing factor was positive in 11 out of 39 patients (28.2%) (Table 2). All of biochemical laboratory values including blood urea nitrogen and creatinine on admission, and electrolytes on admission and 24 hours later were within normal limits. Reduction in hematocrit values 24 hours after treatment in the ORS-MR group (6.4%) was greater than those in the other two groups (0-3%) (Table 3).

MR, RPSS and ORS were well tolerated. In the first 24 hours the mean ORS intake in the ORS-MR group (94 ± 64 ml) were approximately two fold more than the ORS intake in the ORS-milk

Table 1
Characteristics of patients.

Characteristics	RPSS-MR (n=17)	ORS-MR (n=17)	ORS-milk (n=14)
Mean (SD) age (month)	10.2(4.5)	9.5(5.4)	10.1(4.3)
Mean (SD) body weight (kg)	8.1(1.6)	7.6(2.2)	8.1(1.0)
Mean (SD) duration of diarrhea before admission (day)	3.2(1.7)	2.5(1.8)	3.1(1.8)
Mean (SD) frequency of diarrhea before admission[a] (time/day)	7.4(2.6)	10.2(3.6)	6.9(2.8)
Presence of vomiting (% patient)	88.2	88.2	78.6
Mean (SD) frequency of vomiting (time/day)	2.8(2.6)	2.8(2.0)	2.5(2.6)
Presence of fever (% patient)	23.5	23.5	28.6
Hydration status (% patient)			
Mild dehydration	88.2	82.4	71.4
Moderate dehydration	11.8	17.6	28.6
Pre-admission therapy (% patient)			
Oral rehydration	88.2	94.1	78.6
Antibiotics	47.1	29.4	42.9
Antidiarrhea	17.6	41.2	35.7

[a]Significantly greater in the ORS-MR group than those in the RPSS-MR and ORS-milk groups ($p<0.05$ for both measurements).

Table 2
Laboratory profile of stool examination [number of cases/total cases tested (%)].

Findings	RPSS-MR	ORS-MR	ORS-M
Positive reducing factor	4/15 (26.7)	5/13 (38.5)	2/11 (18.2)
Stool leukocytes			
None	14/17 (82.4)	14/17 (82.4)	10/14 (71.4)
≥1/HPF[a]	3/17 (17.6)	3/17 (17.6)	4/14 (28.6)
Presence of rotavirus	4/11 (36.4)	4/11 (36.4)	6/12 (50)
Presence of bacterial enteropathogens	3/17 (17.6)	1/17 (5.9)	3/14 (21.4)

[a]HPF = high power field

Table 3
Results of hematological and biochemistry studies [mean (SD)] on admission and at 24 hours later.

Laboratory values	RPSS-MR	ORS-MR	ORS-milk
Blood urea nitrogen (mg/dl)	9.8 (4.3)	14.1 (11.7)	11.4 (5.9)
Creatinine (mg/dl)	0.50 (0.14)	0.41 (0.14)	0.47 (0.08)
Hematocrit (%)			
On admission	34.0 (4.1)	35.8 (4.0)	34.9 (3.1)
24 hours	34.3 (3.5)	33.5 (3.9)	33.8 (2.4)
Sodium (mEq/l)			
On admission	136.4 (4.2)	138.4 (4.7)	135.8 (6.4)
24 hours	137.4 (3.2)	137.7 (3.1)	137.0 (4.2)
Potassium (mEq/l)			
On admission	4.3 (0.7)	4.6 (0.8)	4.4 (0.9)
24 hours	4.1 (0.6)	4.2 (0.6)	4.3 (0.8)
Chloride (mEq/l)			
On admission	112.1 (6.1)	113.8 (8.1)	111.5 (9.4)
24 hours	112.1 (7.5)	112.3 (5.8)	112.4 (7.0)

Table 4
Outcome measures of treatments [mean (SD)].

Variables	RPSS-MR	ORS-MR	ORS-milk
Frequency of diarrhea in the 1st 24 hours (time)	5.3 (2.2)	7.5 (3.8)	5.3 (2.6)
Duration of diarrhea after initiation of treatment[a] (hour)	29.6 (17.4)	43.8 (17.2)	49.6 (21.7)
Stool weight in the 1st 24 hours[a] (g/kg bodyweight)	32.7 (27.0) (n = 17)	67.5 (47.4) (n = 17)	59.2 (51.5) (n = 14)
Stool weight in the 2nd 24 hours (g/kg bodyweight)	29.5 (41.4) (n = 5)	49.8 (43.6) (n = 12)	56.4 (48.8) (n = 11)

[a]Statistically significant ($p<0.05$).

group (45 ± 40 ml), and the RPSS intake in the RPSS-MR group (46 ± 39 ml), however the differences were not statistically significant. Vomiting was gradually ceased. Frequencies of vomiting recorded during the first 24 hours of admission were 0.4, 0.4, and 0.6 times/day for the RPSS-MR, ORS-MR and ORS-milk groups, respectively. Their hematocrit and electrolyte values at 24 hours after initiation of treatment also did not differ significantly. Patients in the RPSS-MR group had significantly less stool weight in the first 24 hours of treatment (32 ± 27 g/kg body weight) than those in the ORS-MR group (67 ± 47 g/kg body weight) and the ORS-milk group (59 ± 51 g/kg body weight) ($p < 0.05$ for both measurements). In the second 24 hours the mean stool weight of the RPSS-MR group (30 ± 41 g/kg body weight) was approximately half of those in the other two groups but the differences did not reach statistic significance. Patients in the RPSS-MR group had significantly shorter duration of diarrhea after initiation of treatment (30 ± 17 hours) than the ORS-MR group (44 ± 17 hours) and the ORS-milk group (50 ± 22 hours) ($p < 0.05$ for both measurements) (Table 4). Twelve out of 17 patients (70.6%) in the RPSS-MR group recovered within 24 hours after initiation of treatment while such the recovery occurred in the ORS-MR and ORS-milk groups only 29.4% and 21.4%, respectively. Treatment failures (no recovery over 72 hours of treatment) were recorded in 8 cases (16.6%). Patients in the RPSS-MR group had lower treatment failure (1 case, 5.9%) than those in the ORS-MR (3 cases, 17.7%) and the ORS-milk group (4 cases, 28.6%), but the differences were again not significant. Among eight patients who had treatment failures, three were infected by rotavirus (one patient was in ORS-MR group and two patients in ORS-milk group).

DISCUSSION

The fact that lactose intolerance after acute diarrhea occurs frequently (Brown *et al*. 1985), the finding of appropriate feeding formulation therefore is important in management of acute childhood diarrhea in developing countries.

Rice is cheap, easily obtained in most of tropical countries where acute diarrhea is also prevalent. Preparing milk-rice mixture and rice powder salt solution is convenient in most of households. Starch from rice is digested by salivary and pancreatic amylase to be dextrins, maltotriose and maltose. Maltose is digested into glucose by intestinal maltase (Auricchio *et al*, 1967; Eggermont, 1969). Milk-rice mixture contains lower lactose content and rice is digestible by young children (Molla *et al*, 1989). Milk-rice mixture therefore should be less affected by secondary lactase deficiency caused by intestinal infections. The effectiveness of MR, however, is not clearly seen in this study, as there was as no significant reduction in stool weight and the duration of diarrhea in the patients who received ORS-MR as compared to those received ORS-milk. This is most likely due to the significantly greater severity of diarrhea in the ORS-MR group than the other two groups as shown by the significantly greater mean frequency of diarrhea before admission and the greater amount of ORS intake on the first 24 hours in the ORS-MR group. In addition, lactose intolerance may not be the major clinical problem in the subjects studied as most of them had mild diarrhea. Small sample size could be also a major factor in failure of demonstration of the effectiveness of MR. Further studies are therefore needed before making conclusion of its effectiveness.

The finding that patients in RPSS-MR group had significantly less stool output, greater proportion in recovery in the first 24 hours, and significantly shorter duration of diarrhea comparing to the ORS-MR and ORS-milk groups is therefore due to the effect of RPSS. This supports our previous study that RPSS is superior to ORS for treatment of diarrhea with mild or moderate dehydration (Sabchareon *et al*, 1992). Recovery within the first 24 hours of initiation of treatment of majority of the patients make the sample size in the second 24 hours for the RPSS-MR group to be too small for comparison with the other two groups.

Milk-rice mixture contains nearly equal calories when compared with formula milk and it has adequate calories for diarrheal children. Combination of RPSS and MR may be useful in children who suffered diarrhea with secondary lactase deficiency, especially in children from developing countries who can not afford for more expensive low or non-lactose milk. Pilot study on the effectiveness of RPSS - MR on diarrhea in young children with lactase deficiency is warranted.

ACKNOWLEDGEMENTS

The authors would like to thank staff of Department of Pediatrics, Queen Sirikit National

Institute of Child Health for their assistance throughout the study. This study was supported by the National Research Council of Thailand.

REFERENCES

Auricchio S, Pietra DD, Vegnente A. Studies on intestinal digestion of starch in man, II. Intestinal hydrolysis of amylopectin in infants and children. *Pediatrics* 1967; 39: 853-62.

Bern C, Martines J, de Zoysa I, Glass RI. The magnitude of the global problem of diarrheal disease: a ten years update. *Bull WHO* 1992; 70: 705-14.

Brown KH, Gastanaduy AS, Saavedra JM, *et al*. Effect of continued oral feeding on clinical and nutritional outcomes of acute diarrhea in children. *J Pediatr* 1988;112:191-200.

Cheney CP, Wong KH. Acute infectious diarrhea. *Med Clin North Am* 1993; 77: 1169-96.

Eggermont E. The hydrolysis of the naturally occurring alphaglycosides by the human intestinal mucosa. *Eur J Biochem* 1969; 9: 483-7.

Mahalanabis D. Development of an improved formulation of oral rehydration salts (ORS) with antidiarrhoeal and nutritional properties. Geneva: World Health Organization CCD/85.3, 1985.

Molla AM, Molla A, Nath SK, Khatun M. Food-based oral rehydration salt solution for acute childhood diarrhoea. *Lancet* 1989; 2: 429-31.

Molla AM, Sarker SA, Hossain M, Molla A, Greenough III WB. Rice-powder electrolyte solution as oral therapy in diarrhoea due to *Vibrio cholerae* and *Escherichia coli*. *Lancet* 1982; 1: 1317-9.

Rathvuth H. Effects of milk-rice mixtures and rice powder salt solution on acute watery diarrhea in young children. Bangkok: Faculty of Tropical Medicine, Mahidol University, 1995. Thesis for MCTM (Trop Ped).

Sabchareon A, Chongsuphajaisiddhi T, Kittikoon P, Chanthavanich P. Rice-powder salt solution in the treatment of acute diarrhea in young children. *Southeast Asian J Trop Med Public Health* 1992; 23: 427-32.

Sack DA, Chowdhury A, Eusof A, *et al*. Oral rehydration in rotavirus diarrhea: a double blind comparison of sucrose with glucose electrolyte solution. *Lancet* 1978; 2: 280-3.

Santosham M, Foster S, Reid R, *et al*. Role of soy-based, lactose-free formula during treatment of acute diarrhea. *Pediatrics* 1985; 76: 292-8.

Wasi C, Louisirirotchanakul S, Ghakerngol K. Epidemiological study on viral diarrhea in Thailand. *J Med Assoc Thai* 1984; 7: 369-75.

WHO. Diarrheal Diseases Control Program. A manual for the treatment of acute diarrhoea. WHO/CDD/SER/80.2 Rev 1, 1984.

WHO. Improving Child Health, IMCI: the integrated approach. WHO/CHD/97.12 Rev 1, 1997.