Is a 2 : 1 Ratio of Standard WHO ORS to Plain Water Effective in the Treatment of Moderate Dehydration

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Summary

Increased amounts of plain water have been recommended *ad libitum* during rehydration treatment with oral rehydration solutions (ORS) in moderately dehydrated cases in order to decrease the hypertonicity of ORS. However, we could not encounter any study demonstrating its effectiveness objectively. In this study, moderately dehydrated children admitted to Hacettepe University Ihsan Doğramacı Children's Hospital Diarrheal Disease Training and Treatment Unit were administered either standard WHO ORS treatment or two parts of standard WHO ORS and one part of plain water alternately at a dose of 100 ml/kg, according to the period they were admitted to the center. The frequency of vomiting, stool purging rate, and unscheduled intravenous treatment rate of the two different regimens were compared. There were 51 children in the standard ORS group and 79 children in the 2 : 1 ratio ORS group. The admission characteristics of the children were similar. The children with a stool purging rate over one per hour during treatment was higher in the standard ORS group (29.4 vs. 15.2 per cent, $p = 0.051$), as well as the children with vomiting (56 vs. 30 per cent, $p = 0.007$). The children who required unscheduled intravenous treatment was also higher in the standard ORS group (20 vs. 14 per cent, $p = 0.2$). A regimen of two parts of WHO ORS and one part of plain water may be an alternative treatment for moderately dehydrated children with non-cholera diarrhea in areas where hypotonic ORS is not yet available.

Introduction

Oral glucose electrolyte solution containing 90 mmol/l of sodium and 111 mmol/l of glucose (total osmolarity, 311 mmol/l) has been recommended for all cases (children, adult) of moderate dehydration by the World Health Organization (WHO) and the United Nations International Children's Emergency Fund (UNICEF) for the past 25 years,[1] although the content was designed originally for cholera cases. Since the implementation of ORS use, there has been a dramatic decrease in dehydration-related mortality in many developing countries[2] but ORS use is still not at the desired level worldwide.[3] The concerns about standard WHO ORS use may be related to the risk of hypernatremia or an osmotically driven increase in stool output, especially in infants and young children.[4,5] Therefore for the past 20 years there were many ongoing studies to develop an improved ORS.

Although the effectiveness of reduced osmolarity ORS has been demonstrated in both well-nourished and malnourished children with or without cholera,[6,10] there is still concern about the risk of an increased incidence of hyponatremia especially in cholera cases.[11–13] One of the suggestions was to produce two types of ORS, but this may cause confusion among healthcare workers and mothers.[11,14,15]

Recently a group of experts at WHO has concluded that the policy of a single solution be maintained and that this ORS solution contain 75 mEq/l of sodium and 75 mmol/l of glucose and have a total osmolarity of 245 mOsm/l.[16] However, in many parts of the world, the only available ORS is the hyperosmolar standard WHO ORS.

One of the earliest studies about the effectiveness of the hypotonic ORS was performed by diluting standard ORS packages in 1.5 l of water, which was shown to be effective.[5] In their study, El-Mougi, *et al*.[5] recommended increased amounts of plain water until a new formulation for ORS comes up. As we have also observed many cases with high purging rate during standard WHO ORS treatment,[17] we changed our treatment policy to use standard WHO ORS alternatively with plain water in a ratio of two parts of WHO ORS and one part plain water. Although increased amounts of plain water has been recommended *ad libitum* during rehydration treatment, we could not encounter any study demonstrating its effectiveness objectively. In this study the results of the two treatment regimens are compared.

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Materials and Methods

This study compared the results of the two different treatment regimens between October 1998 and April 2001 at Hacettepe University Ihsan Doğramacı Children's Hospital Diarrheal Disease Training and Treatment Unit, where more than 3000 cases are admitted annually and the dehydration of children has been evaluated and treated according to WHO criteria for more than 10 years.[18] We started giving standard WHO ORS in a 2 : 1 ratio (two parts ORS and one part plain water) at 100 ml/kg dose to moderately dehydrated children under 2 years of age in March 2000. In this study moderately dehydrated children under 2 years of age admitted between October 1998 and March 2000 were given standard ORS at 100 ml/g, and those admitted between March 2000 and April 2001 were treated with a 2 : 1 ratio ORS again at a 100 ml/kg dose. Children who were breastfed continued breastfeeding during rehydration treatment. Blood samples were collected from all cases that were considered to be moderately dehydrated for the determination of blood pH and bicarbonate level, as well as electrolytes, on admission. After treatment, blood samples were collected only from children who had a blood pH or electrolyte imbalance on admission.

The children given the two different regimens were compared for frequency of vomiting, stool purging rate, and unscheduled intravenous treatment rate. Intravenous treatment after ORS was given to patients during either regimen according to the following criteria: persistence of clinical signs for more than 12 h after oral rehydration has been initiated, failure to maintain positive fluid balance with oral fluids because of persistent vomiting (more than 3/h), or a high stool purging rate (more than 1/h).[9]

Statistical analysis was performed by SPSS version 9.0. Parametric values were compared by Student's *t*-test and non-parametric values by the chi-squared test.

Results

During the first period of the study when the patients were treated with standard ORS there were 51 patients. For the second period when the patients were treated with a 2 : 1 ratio ORS regimen there was 79 cases. The demographic characteristics are displayed in Table 1. The mean age, sex, weight, and duration of diarrhea were similar in both regimens.

The clinical and laboratory findings of the regimens during and at the end of the treatment are shown in Table 2. The mean serum sodium, chloride, potassium, blood pH, and bicarbonate levels on admission and after treatment were similar in both regimens.

The frequency of vomiting and stool purging rate were also similar on admission and during treatment for both regimen. Although on admission there was no children in either group with a stool purging rate over 1/h, 15 children (29.4%) in standard treatment regimen and 12 children (15.2%) in the 2 : 1 ORS treatment regimen had high purging rate (> 1/h) (p = 0.051) during treatment. On admission the ratio of children with vomiting were similar in both groups (15/51, 29.4 per cent; 28/79, 35.4 per cent; p = 0.8). However, during treatment, children with vomiting were higher in the standard ORS group (22/51 children, 56 per cent) compared with the 2 : 1 ORS group (20/79 children, 30 per cent) (p = 0.007).

TABLE 1
Demographic characteristics of children according to treatment regimens

	Standard ORS (n = 51)	2 : 1 ORS (n = 79)
Male/female	35/16	45/34
Age (months)	10.6 ± 5.7	12.7 ± 6.8
Weight (kg)	9.24 ± 6.3	9.06 ± 1.98
Duration of diarrhea on admission (days)	3.83 ± 4.6	3.52 ± 2.6

$p > 0.05$ for all comparisons.

The mean weight gain, total amount of fluid received, and rehydration time were similar in both regimens. Total ORS intake was less and the total water intake was more in the 2 : 1 ORS regimen than the standard ORS regimen (Table 2).

The number of children who required unscheduled intravenous treatment was also higher in the standard ORS regimen (10/51, 20 per cent; 11/79, 14 per cent; p = 0.2), although the difference was not statistically significant.

Discussion

In this study standard ORS treatment was compared with two parts WHO ORS and one part plain water treatment given alternately. The number of cases with high purging rate, vomiting, and unscheduled intravenous treatment was less in the 2 : 1 ORS regimen.

Although very effective in the treatment of dehydration, the current WHO ORS may cause hypernatremia and increase purging rate, and there is therefore still concern about the optimal content of ORS.[19] Studies in animal models and human volunteers have shown that the osmolarity of ORS is a critical factor influencing absorption of water and electrolytes from the small intestine.[20,21] Hypotonic solutions with an osmolarity of 200–250 mmol/l perform better than hypertonic or isotonic solutions. It has been demonstrated that a sodium

TABLE 2
Clinical and laboratory characteristics of children according to treatment regimens

	Standard ORS (n = 51)	2 : 1 ORS (n = 79)
Frequency of vomiting (per h)		
On admission	0.16 ± 0.10	0.17 ± 0.10
During treatment	0.32 ± 0.30	0.19 ± 0.12
Stool purging rate (per h)		
On admission	0.27 ± 0.17	0.29 ± 0.15
During treatment	0.45 ± 0.31	0.40 ± 0.27
Blood pH		
On admission	7.27 ± 0.07	7.28 ± 0.06
After treatment	7.33 ± 0.07 (n = 28)	7.32 ± 0.07 (n = 45)
Blood HCO_3 (mmol/l)		
On admission	14.7 ± 3.7	15.3 ± 3.6
After treatment	17.1 ± 2.8 (n = 28)	17.6 ± 2.9 (n = 45)
Serum sodium (mmol/l)		
On admission	137 ± 4.6	138 ± 4.4
After treatment	137 ± 2.4 (n = 8)	139 ± 3.7 (n = 10)
Serum potassium (mmol/l)		
On admission	4.39 ± 0.8	4.32 ± 0.8
After treatment	3.6 ± 0.7 (n = 8)	4.2 ± 0.7 (n = 11)
Oral fluid intake rate (ml/kg/h)	19.37 ± 6.19	18.81 ± 6.17
Total fluid intake (ml/kg)	148 ± 81	157 ± 78
Total ORS intake (ml)	1334 ± 833	952 ± 496*
Total plain water intake (ml)	10.6 ± 47.7	402 ± 243**
Weight gain (% of admission)	4.61 ± 3.59	4.40 ± 11.4
Rehydration time (h)	7.8 ± 4.2	8.9 ± 4.9
Unscheduled i.v. treatment n (%)	10 (20)	11 (14)

*$p < 0.01$; ** $p < 0.0001$.

concentration around 60 mmol/l and a glucose concentration between 50 and 100 mmol/l are optimal for water absorption.[21]

After several studies with reduced osmolarity ORS, three final papers that have come to a conclusion have been published.[11–13] One study[13] including children with acute diarrhea, concluded that reduced osmolarity ORS (75 mmo/l sodium, osmolarity 245 mosm/l) in children decreased the need for unscheduled i.v. treatment by 33 per cent without any effect on stool output or duration of illness. Similarly, in our study we found a 30 per cent reduction in the percentage of cases requiring unscheduled i.v. treatment without an effect on mean stool purging rate. In the above study no risk for increased incidence of hyponatremia was detected, as well as in our study. However, the risk of hyponatremia is increased in malnourished children; in our study there were no children with malnutrition. On the other hand the study conducted among adult cholera patients[12] concluded that although there was no difference in the effectiveness of treatment, asymptomatic hyponatremia was more common among the cases treated with reduced sodium, reduced osmolarity ORS. Finally the results of a meta-analysis performed to study the overall effectiveness of reduced sodium, reduced osmolarity ORS solutions, including 15 randomized controlled trials conducted among children, showed a decreased need for unscheduled i.v. treatment, decreased stool volume, and vomiting without an apparent increase in cases with hyponatremia.[11]

In our study, standard WHO ORS was administered with an increased amount of water, similar to a hypotonic ORS, to moderately dehydrated children less than 2 years old. In fact this was suggested earlier[7,8] to be as effective as hypotonic ORS, but no study was encountered. It is also well known that WHO recommends 100–200 ml of plain water during rehydration treatment in children under 6 months of age who are not breastfed.[18] In this study it was shown that among children given a less amount of WHO ORS but with an increased amount of plain water, there were less cases with high purging rate, less cases with vomiting, and less need for unscheduled intravenous treatment. Although a 30 per cent reduction was detected in the need of i.v. treatment we could not find a statistical significance for the decrease, but we believe that this may be due to the limited number of patients. As mentioned in the study above,[13] in order to show the statistical significance of a 33 per cent reduction in unscheduled i.v. treatment at least 700 cases in each treatment group are required.

Transient glucose intolerance is one the most common complications of standard G-ORS treatment[17,22] requiring i.v. treatment. In the CHOICE

study[13] the decrease in i.v. treatment was speculated to be related to the decrease in cases with glucose malabsorption, which was explained by the decrease of cases with a high purging rate. Similarly in our study, cases with high purging rate was decreased in the 2 : 1 ORS regimen. The cases with vomiting also decreased in the 2 : 1 ORS group, which we believe may have an impact on decreased i.v. need.

Recently a group of experts at WHO concluded that the new recommended ORS solution should contain 75 mEq/l of sodium and 75 mmol/l of glucose and have a total osmolarity of 245 mOsm/l. However, it will take time for its availability worldwide. The limited number of cases and the retrospective design of the study are the main constraints of this study. Meanwhile, we suggest that the 100–200 ml of plain water along with WHO's recommendation of ORS during the treatment of moderately dehydrated children under 6 months of age, corresponding to two parts of WHO ORS and one part plain water treatment, may be an alternative treatment for older, moderately dehydrated, non-malnourished children with non-cholera diarrhea in areas where hypotonic ORS is not yet available.

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