ASSESSMENT OF THE EFFECTIVENESS OF ORAL REHYDRATION THERAPY AGAINST SEVERE DIARRHEAL DEHYDRATION

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Abstract. A hospital based case-control study for assessing the effectiveness of oral rehydration therapy (ORT) preparation against severe dehydration due to diarrhea was conducted at the Infectious Diseases Hospital, Jakarta, Indonesia. A total of 202 children aged 24 months or less who attending the hospital were suffering from acute watery diarrhea were recruited in the study. Those who were severely dehydrated as assessed by WHO criteria were accounted as cases; those who were non-severely dehydrated were accounted as controls. There were 59 cases and 143 controls. A questionnaire was used to interview all study subjects' mothers about ORT usage and various risk factors. Mothers who used ORT were asked to show how they prepared either oral rehydration solution (ORS) or sugar salt solution (SSS). Effectiveness of ORT against severe diarrheal dehydration was based on the formula for assessment of vaccine efficacy by using the odds ratio (OR). With the use of the logistic regression method, an adjusted OR was obtained after controlling various confounders. The effectiveness of ORT against severe diarrheal dehydration was 72.1% for proper ORT preparation and was decreased to 63.2% when ORT was improperly prepared.

INTRODUCTION

Death in acute diarrhea is often due to dehydration which results from excessive loss of body fluids and electrolytes in stools. The composition of the lost fluid depends on the age of the patient, the rate of stool loss and the causative agent. Younger children tend to lose more potassium and less sodium in their stools. The higher the rate of the stool lost, the more the sodium electrolyte level tends to approach serum level (Philips, 1964). The optimal absorption of sodium and water occurred in the small intestine when oral rehydration solution contained 110 to 140 mmol/l of sodium and 2% to 2.5% glucose (Sladen and Dawson, 1969). It was later shown that the absorption of glucose in the small intestine and its cotransport with sodium remained intact during acute diarrhea (Hirschhorn, 1980). Therefore the incorrect dilution of ORS and SSS would result in either high or low concentrations of sodium and glucose which would decrease the effectiveness of ORT for the treatment of dehydration in acute diarrhea.

In a recent study of ORT usage in Indonesia, it was reported that 30% and 10% of mothers with diarrheal children used ORS and SSS packages, respectively. Among ORS users, 64.3% showed how to mix the electrolyte powder correctly, while of SSS users, 50% made the solution correctly (Bunjamin *et al,* 1990; Ismail and Nazir, 1990). Thus the present study sought to assess the effectiveness of ORT against severe dehydration in acute diarrhea.

MATERIALS AND METHODS

Study subjects

The study was carried out in the Infectious Diseases Hospital in North Jakarta Municipality, Jakarta during November 1990 to February 1991. The present research is a hospital-based case-control study. The eligible subjects were children aged 24 months or younger attending the hospital with acute watery diarrhea.

Criteria for dehydration assessment

The assessment of diarrheal children for dehy-

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dration was based on the following features (WHO, 1990):

1. General condition - *lethargic or unconscious
   - *floppy
2. Eyes - very sunken and dry
3. Tears - absent
4. Mouth and tongue - very dry
5. Thirst - *drink poorly
   - *not able to drink
6. Skin pinch - *goes back very slowly

The diarrheal children who had two or more signs as mentioned above including at least one *sign were classified as diarrheal patients with severe dehydration.

Selection of cases and controls

The study subjects were examined and the severity of dehydration assessed by attending physicians. Those who had severe dehydration were admitted and accounted as cases. Subjects who had non-severe dehydration were treated as outpatients and accounted as controls. At least two controls were selected for each case either on the same day or on the subsequent day. Matching on an individual basis was not performed but restriction of age to 24 months or less among cases and controls was done.

Sample size estimation

The present study was designed to have a power of 80% to detect statistical significance at the 5% level (one-tailed test) with the ratio of cases to controls of 1 : 2. It was assumed that 50% of diarrheal children with non-severe dehydration got ORT and that the effectiveness of ORT against severe diarrheal dehydration was 60%. Therefore, on this basis a sample size of 52 cases and 104 controls was required (Schlesselman, 1982).

Ascertainment of ORT preparation

All study subjects' mothers were asked whether they gave ORT to their diarrheal children or not. Among mothers who were ORT users, all were asked to prepare one glass of either ORS or SSS depending on their answers. For ORS preparation, a commercial package of ORS was used and the amounts of ORS powder and water for dilution were recorded. In SSS preparation, mothers were requested to use a home-available spoon to measure sugar and salt. After that it was assessed whether the amount of sugar and salt were properly measured or not by using the blue-spoon, a standard measurement of sugar and salt for 200 ml SSS. The volume of water for dilution either ORS or SSS was measured by using a measuring glass.

Data collection

Besides the ascertainment of ORT preparation, all study subjects' mothers were interviewed with a structured questionnaire in order to obtain information which may confound the association between ORT and severe diarrheal dehydration. These included general characteristics of study subjects, maternal demographic and socioeconomic factors, maternal practice and knowledge on diarrhea, diarrheal management, and clinical signs and symptoms of study subjects. The study questionnaire was pretested before administration to ascertain the validity of the questions. Pretesting was done on mothers who brought their diarrheal children to the Infectious Diseases Hospital before the actual survey.

Data analysis

Point and 95% interval estimates of odds ratio (OR) were calculated to determine the magnitude of association between ORT and severe diarrheal dehydration (Greenberg and Kleinbaum, 1985). Chi-square test with Yates correction (Mantel and Haenzel, 1959) and Fisher's exact test (Fisher, 1934; Irwin, 1935) were used to assess which variables were associated with severe dehydration due to diarrhea. The association between simultaneous risk factors and diarrhea with severe dehydration was examined with the use of logistic regression analysis (Kleinbaum *et al,* 1982) by stepwise selection on the basis of maximum likelihood ratio (MLR). Adjusted OR between ORT and severe diarrheal dehydration was determined by using BMDP software (Dixon *et al,* 1985). Calculation of the effectiveness of ORT against diarrhea with severe dehydration was based on the formula for assessment vaccine efficacy (Smith, 1988) as follows :

Effectiveness of ORT = 100* (1-R) %
where R = relative risk, which in the present study was estimated by odds ratio (OR)

Eventually the effectiveness of ORT against diarrhea with severe dehydration based on crude OR and adjusted OR was compared.

RESULTS

There were 202 children of 24 months old or less with acute watery diarrhea enrolled in the present study. Out of 202 study subjects, 59 (29.2%) were suffering from acute watery diarrhea with severe dyhydration and required hospital admission, while 143 (70.8%) had acute diarrhea with non-severe dehydration and received ambulatory treatment. As indicated above, a minimum of 52 cases and 104 controls was needed, however with the aim of increasing the power of the study, it was decided to include all cases and controls in the analysis.

Among 202 subjects, it was noted that during onset of diarrhea, 134 (66.3%) received ORT, comprising 107 (79.9%) with ORS, 20 (14.9%) with SSS and 7 (5.2%) with both ORS and SSS. No information about the use of other types of household fluid such as coconut juice or rice soup was obtained. Two levels of ORT preparation ascertainment, improper and proper, were classified. Table 1 shows that 20.3% and 22.4% of cases and controls, respectively, received improper ORT preparations, while 28.8% and 51.0% of cases and controls had proper ORT dilutions, respectively. There was no significant association between improper ORT preparation and diarrhea with severe dehydration ($p > 0.05$), however the strength of association was quite noticeable (OR = 0.47). Conversely, significant association between proper ORT dilution and severe diarrheal dehydration was obtained ($p < 0.05$) with the strength of association (OR) of 0.29.

From cross tabulations between various potential risk factors and severe diarrheal dehydration, it was revealed that age, maternal age, maternal education, family size, breast feeding, maternal knowledge on diarrhea, fever and frequency of vomiting were significantly associated with severe dehydration due to diarrhea ($p < 0.05$), as presented in Table 2. After allowing all covariates to be explored simultaneously in stepwise logistic regression (Table 3), the best model was selected on the basis of maximum likelihood ratio (MLR). Five factors : age, family size, breast feeding, fever and frequency of vomiting were found to be confounding variables. Table 3 compares the crude OR and adjusted OR between ORT and severe diarrheal dehydration after controlling for these confounding variables. It was noted that controlling for these confounding factors resulted in some changes to the OR but did not alter the main finding. Tests for interaction of the effects on severe diarrheal dehydration of ORT and age, ORT and family size, ORT and breast feeding, ORT and fever and ORT and frequency of vomiting were performed (Table 4). There was no evidence that effect of ORT on severe diarrheal dehydration varied according to age, family size, breast feeding, fever or frequency of vomiting.

Based on crude OR and adjusted OR, the effectiveness of ORT, either improper or proper preparations, on severe diarrheal dehydration was calculated (Table 5). It was shown that the effectiveness of proper ORT dilution on diarrhea with severe dehydration was 72.1% and the effectiveness was decreased to 63.2% when ORT was improperly prepared.

Table 1

Association between the ascertainment of ORT preparation and severe diarrheal dehydration.

Variables	Cases		Controls		OR	p-value
	No.	(%)	No.	(%)	(95%CI)	
Ascertainment of ORT preparation						
Proper ORT	17	28.8	73	51.0	0.29 (0.14-0.64)	0.0011
Improper ORT	12	20.3	32	22.4	0.47 (0.19-1.16)	0.1099
No ORT	30	50.9	38	26.6	1.00	

Table 2

Association between significant risk factors and severe diarrheal dehydration.

Variables	Cases		Controls		p-value
	No.	(%)	No.	(%)	
Age group (months):					0.0430
< 6	24	40.7	36	25.2	
> 6	35	59.3	107	74.8	
Maternal age (years):					0.0118
> 25	35	52.3	55	39.2	
< 25	24	40.7	87	60.8	
Maternal education:					0.0467
No school	9	15.3	8	5.6	
Primary school and higher	50	84.7	135	94.4	
Family size:					0.0347
> 2 child	29	49.2	46	32.2	
< 2 child	30	50.8	97	67.1	
Breast feeding:					0.0248
No	24	40.7	34	23.8	
Yes	35	59.3	109	76.2	
Knowledge on diarrhea*					0.0171
Low	38	64.4	64	44.8	
High	21	35.6	79	53.2	
Fever:					0.0002
>38.5°C	25	42.4	24	16.8	
<38.5°C	34	57.6	119	83.2	
Frequency of vomiting in last 24 hours					0.0134
> 5	22	37.4	28	19.6	
< 6	37	62.7	115	80.4	

* Based on 7 questions, knowledge on diarrhea was categorized as low (< 3 corrected answers) and high (> 4 corrected answers).

DISCUSSION

It has been shown in many studies that ORT is effective in treating dehydration due to diarrhea (Cash *et al,* 1970; Nalin *et al,* 1979; Sharifi and Ghavani, 1984). The present study was sought to assess the effectiveness of ORT preparation against severe diarrheal dehydration among children under 2 years with the aim of confirming the previous findings and gaining encouragement in continuing use of ORT not only for treating but also for preventing severe dehydration due to diarrhea. It was noted that 66% of diarrheal children in the present study received ORT from the onset. This proportion (66%) was rather high when compared with the ORT usage rate (40%) reported from other studies in Indonesia (Bunjamin *et al,* 1990; Ismail and Nazir, 1990). This difference was probably due to the accessibility and availability of ORS packages being greater in the present area which is located in the capital city.

As the result of univariate analysis, eight factors besides ORT were found to be related with severe dehydration due to diarrhea. Nevertheless, after being analyzed by the logistic regression method, five factors remained significant : age, family size, breast feeding, fever and frequency of vomiting. The finding that age younger than 6 months was a risk factor for severe diarrheal dehydration in the present study was consistent with the findings from previous reports (Griffin *et al,* 1988; *Ryder et al,* 1988). This was because this age group is the

Table 3

Comparison on crude and adjusted odds ratio of ORT preparation and severe diarrheal dehydration.

	OR (95% confidence interval)	
	Crude	Adjusted for covariates*
ORT preparation:		
Proper ORT	0.29 (0.14-0.64)	0.279 (0.13-0.61)
Improper ORT	0.47 (0.19-1.16)	0.368 (0.15-0.92)
No ORT	1.00	

* Covariates selected by logistic regression analysis in the assessment of ORT preparation against severe diarrheal dehydration are as follows :
- age group
- family size
- breast feeding
- fever
- frequency of vomiting

The logistic model :
In (odds) of severe diarrheal dehydration = - 1.5188 + 0.62716 age group + 0.70438 family size + 0.7718 breast feeding + 1.4627 fever + 0.762559 frequency of vomiting - 1.0008 improper ORT - 1.2730 proper ORT.

Table 4

Test for interaction of effect of ORT preparation on severe diarrheal dehydration according to age group, family size, breast feeding, fever and frequency of vomiting.

Variables	Model					
	1	2	3	4	5	6
Age group	#	#	#	#	#	#
Family size	#	#	#	#	#	#
Breast feeding	#	#	#	#	#	#
Fever	#	#	#	#	#	#
Vomiting	#	#	#	#	#	#
Improper ORT	#	#	#	#	#	#
Proper ORT	#	#	#	#	#	#
ORT * Age group		#				
ORT * Family size			#			
ORT * Breast feeding				#		
ORT * Fever					#	
ORT * Vomiting						#
Log likelihood	-100.170	-99.686	-98.365	-99.403	-98.562	-99.196
p-value of chi-square improvement in relation to model 1		>0.05	>0.05	>0.05	>0.05	>0.05

Table 5

Assessment of the effectiveness of ORT preparation against severe diarrheal dehydration.

	Effectiveness of ORT	
	based on crude OR	based on adjusted OR
ORT preparation :		
Improper	53.0%	63.2%
Proper	71.0%	72,1%

most susceptible to diarrhea (Snyder and Merson, 1982; Sunoto, 1982) as well as other diseases. Large family size was another variable identified as a risk factor for severe dehydration due to diarrhea. It is possibly related to two explanations: (1) inadequate time to take care diarrheal child as the mother had to look after other children as well; (2) the effect of crowding in the family on the sanitation conditions. Rahman *et al* (1985) reported that the risk of postnatal mortality in the household of large family size was higher than the small family size household.

On the basis of either univariate or multivariate analysis of the present data, breast feeding was found to be associated negatively with severe dehydration due to diarrhea which was similar to many previous reports. Many studies had shown that breast-fed infants who got diarrhea were less likely to develop complications such as severe dehydration (Lapage *et al,* 1981; Clemens *et al,* 1986). The protective effect of breast milk against diarrhea may be due to the unique anti-infective properties of breast milk (Mata and Wyatt, 1971; Jelliffee and Jelliffee, 1978).

Regarding clinical signs and symptoms, it was noted that two clinical features: fever (38.5°C or higher) and history of vomiting (more than 5 times during 24 hours prior attending hospital) were identified as risk factors for severe dehydration due to diarrhea. Similar results were also reported from studies of risk factors for fatal diarrhea and severe-life threatening diarrhea in African children (Griffin *et al,* 1988). This was probably due to diarrheal children with high fever or frequent vomiting losing body salts and fluid through sweat and vomitus. Moreover, they tended to lose appetite with the result of low intake of food and water.

In the present study, it was revealed that the effectiveness of proper ORT preparation on severe diarrheal dehydration was 72.1% and this effectiveness was reduced to 63.2% when ORT was improperly prepared. This implied that 72% of severe diarrheal dehydration could be prevented when diarrheal children received ORT of correct dilution but the protective effect was decreased to 63% when ORT of incorrect dilution was used, even though the use of an improper ORT preparation could prevent about 63% of diarrheal children going on to develop severe dehydration. It is important to stress that the higher protective effect of 72% could be obtained if ORT was properly diluted: thus emphasis on how to prepare ORT correctly was essential as well as promotion of the use of ORT in diarrheal programs.

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