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Original Article

Benefits of gum arabic supplementation to oral rehydration solution in managing acute diarrhea

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Abstract

Background Oral rehydration solution (ORS) has been proven successfully to overcome dehydration in diarrhea. The improvement of the effectiveness of ORS is still needed to overcome some failures. Gum Arabic (GA), an indigestable starch, can enhance ORS absorption in mice with diarrhea. It is worthy to explore its benefits in human. Since GA is non toxic to human being, it is regarded ethical to conduct effectiveness study directly in clinical setting.

Objective To evaluate the effectiveness of GA supplementation to ORS in managing inpatients diarrheal cases .

Methods A double blind clinical trial was conducted during March to September 2004 in the Department of Child Health of M. Hoesin Hospital, Palembang. The subjects were randomly enrolled to GA-ORS (GA) group or ORS (SO) group. Indirect measurements were conducted on ORS absorptive enhancement by evaluating the duration of diarrhea after hospitalization, frequency of defecation during hospitalization, ORS consumption during hospitalization, and time laps of stool consistency conversion. The effectiveness analysis was controlled for confounders.

Results Supplementation of 0.5 gram GA to 200 ml ORS could decrease the duration of diarrhoea 15.65 hours (P=0.000) during hospitalisation, frequency of defecation during hospitalization 1.171 times/days (P=0.002), ORS consumption 38.39 ml/kg BW (P=0.029), time of stool consistency to become semisolid 15.84 hours (P=0.000), and become solid 14.45 hours (P=0.002). Vomiting during hospitalization and aged group of 6-11 months were significant confounder. However, after controlling the outcome with these confounding factors, the benefits of GA supplementation were still significant.

Conclusions GA supplementation to ORS significantly shorten the duration of diarrhea, decreases the frequency of defecation, consumption of ORS, time of stool consistency to become semisolid and solid in inpatients diarrheal cases. **[Paediatr Indones 2007;47:265-269]**.

Keywords: *ORS, acute diarrhoea, gum arabic, supplementation, effectiveness study*

Oral rehydration therapy (ORT) to maintain normal hydration and electrolyte balance is the mainstream of diarrheal disease (DD) case management. WHO's standard formula of Oral Rehydration Solution (ORS) is widely used for this purpose because of its proven effectiveness and safety. It is also cheap, easy to use, and readily available.[1-3] However, some failures of ORT have been observed. The cases become dehydrated and deteriorated.[2,4] The failures could be due to the rejection from the patient to consume ORS, profuse vomiting, lack of compliance of the caregivers, or the absorbed water and electrolyte could not fulfill the lost. The last cause of failure is being overcome by formulating more effective ORS.[2,5]

Some modalities have been explored to formulate the more effective ORS, such as using polysaccharide as organic carrier, adding additional carrier on top of glucose, using rice base ORS and others.[2] Gum arabic

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(GA), a complex polysaccharide consisted of D-Galactopyranose, D-Glucoronic acid, 4-o-methyl gluconic acid, L-Arabinase, and L-rhamnose, has been shown to improve absorption of ORS in diarrheal rat, resulting in shortened duration of the diarrhea, decreased frequency of defecation, decreased ORS consumption, decreased fecal mass, and improved stool consistency conversion.[6-8] GA is safe to be consumed as it is widely use in many kinds of food such as bubble gum.[9-13] It has been used in some studies[14-17] about chronic renal failure in human without causing any bad effect on health.[14] Based on these facts, it is worthy to explore the effectiveness of adding GA into ORS formula. Due to any technical limitation, this effect would be measured indirectly by measuring the duration of diarrhea, frequency of defecation, ORS consumption, and time needed to change the fecal consistency from liquid to semisolid and solid. Since GA is safe, it is ethical to conduct the effectiveness study of GA supplementation in human directly in clinical setting.

Methods

Patients suffering from acute diarrhea, hospitalized in the Department of Child Health RSMH Palembang between March 27th to September 29th 2004 were enrolled. Inclusion criteria were acute diarrhea with dehydration and aged 6–59 months. Exclusion criteria were severe malnutrition, bloody stool, and severe accompanying disease. Sample size was calculated based on the assumption of the influence in giving GA supplementation toward dependent variables, based on animal study. The calculated sample size was 56 for each the case and control groups.

The study was a double blind randomized clinical trial. Blinding was carried out through preparation of 2 kinds of ORS by third party, ORS with GA supplementation and standard ORS. ORS supplemented with GA was prepared by adding 0.5 gram of GA to 200 ml standard ORS formula. Both preparations were packed in similar sachets, and coded. The code was opened after finishing all data collection. Randomization was carried out into two groups. The first was the subjects with severe dehydration, and the second with mild-moderate dehydration. Using randomization number, subjects within each group were allocated into GA1 or GA2 subgroups. Each subgroup received ORS (with GA supplementation or standard ORS) within the same code. The analysis was carried out thoroughly, combining group 1 and 2. After opening the code, they were grouped as GA group (received ORS with GA supplementation), and SO group (received standard ORS).

A thorough history and physical examination were done on admission. Degrees of dehydration was assessed according to the National Diarrhoeal Diseases Control Program (CDD) DD case management regiment.

Subjects with mild-moderate dehydration were rehydrated with oral solution 75 ml/kgbw for 4 hours, followed by maintenance dose, which depends on the estimation of water loss per each defecation or vomiting. Subjects with severe dehydration were rehydrated intravenously, and then followed with the same oral maintenance therapy. Other treatment, if needed, was given according to the CDD regiment.

Mothers were asked to observe the stools. If she noticed any changes in stool appearance, she should put the stool sample in a small bottle and record the time. The main investigator determined whether the stool was liquid, semi-solid or solid.

Duration of diarrhea was calculated from the time of admission until the last liquid stool passing. The time needed for stool to become semi-solid /solid was calculated from the time of admission to the first semi-solid/ solid stool passing.

Data was analyzed using chi-square or student t-test. Multiple regression was done to analyze the effect of confounders.

Table 1. Subject's characteristics in GA and SO groups

Characteristics	Groups	
	GA (N=58)	SO-(N=57)
Male / Female	26 /32	34/23
Age (month)		
6–11/12–59	27 /31	35/22
Nutrional Status:		
Good/Underweight	18 /40	23/34
Average	86.7±10.24	87.9±11.98
Beastfeeding Yes / No	44/14	41/16
Residence: Urban / Rural	44/14	49/8
Parents education:		
High school / lower	34/24	32/25
Parents income: rich / poor	8/50	13/44

Results

One hundred and fifteen subjects were eligible, enrolled, and finished the study, 58 in GA and 57 in SO group. Characteristics of the subjects of the 2 groups were not significantly different. (**Table 1**)

The clinical features of diarrhea at home and at the time of enrollment were not significantly different between the 2 groups (**Table 2**).

The comparison of the duration of diarrhea, frequency of defecation, ORS consumption, and time of fecal conversion in GA and SO groups are shown in **Table 3**.

Table 2. Clinical features of diarrhea at home / enrollment

	Groups	
	GA- (N=58)	SO- (N=57)
Duration of diarrhea at home (hour)	58.6 (SD 39.6)	60.7 (SD 32.9)
Frequency of diarrhea (times/day)	8.8 (SD 3.25)	8.8 (SD 3.95)
Liquid /Semi solid stool last 24 hr	57/1	56/1
Previous treatment		
Antibiotic / ORS / others	24/12/1	26/18/0
Degree of dehydration		
Mild-moderate / Severe	31/27	27/30
Accompanying symptoms		
Previous vomiting	50	48
On going vomiting	8	14
Fever	30	34
Cough-runny nose	12	10

Duration of diarrhea in GA group was 15.65 hours shorter than SO group. Overall, the average frequency of defecation in GA group was 1.2 times less than SO group. Daily figure shows that, although GA group always had less defecation, the difference was only significant on day 2 and 3 (**Figure 1**). ORS consumption in group GA was 38.39 ml/kgbw less than SO group. Daily figures shows that the GA group always consumed less ORS since day 2, but the difference was only significant on day 2 (**Table 4**).

Out of 7 potential confounders which had been tested by multiple logistic regression analysis were: breastfed prior to illness, prior antibiotic treatment, age, underweight, still vomit on admission, fever on admission and leukocytosis. Two variables, namely aged 6-11 month group and vomiting on admission, were found to have significant effect toward the outcome variables. It is seen, that after controlling with the potential confounders, the different outcomes between the GA group and SO group was still significant.

Discussion

The study showed that, when 0.5 gram GA was added to 200 ml standard ORS, there was an improvement in all observed parameters of DD healing process,

Table 3. Average duration of diarrhea, frequency of defecation, ORS consumption and time laps for fecal conversion in GA and SO groups

Dependent Variables	GA Group (N=58)			SO group (N=57)			
		95% CI			95% CI		
	Average ± SD	Lower limit	Upper limit	Average ± SD	Lower limit	Upper limit	P*
Diarrhea duration (hour)	19.53±18.195	14.85	24.21	35.18±25.133	28.66	41.71	0.000
Freq of defecation (x/day)	3.429±1.823	3.000	3.858	4.600±2.170	4.037	5.163	0.002
ORS consumption (ml/kg)	117.26 ± 56.77	102.65	131.87	155.65±117.55	125.13	186.17	0.029
Fecal conversion							
To semisolid (hour)	25.02 ± 18.454	20.271	29.769	40.86 ± 26.229	34.051	47.669	0.000
To solid (Hour)	46.90 ± 20.465	41.633	52.167	61.35 ± 27.375	54.243	68.457	0.002

Note: * = t-test

Table 4. Daily average of ORS consumption (ml/kgBW) in GA and SO groups

Day	n	Mean (SD)	95% CI	n	Mean (SD)	95% CI	P
1	58	82.9 (37.91)	73.2; 92.7	57	80.0 (40.89)	69.38; 90.62	0.691
2	40	36.8 (23.60)	29.4; 44.1	46	53.2 (37.62)	42.28; 64.02	0.016
3	11	27.2 (14.83)	18.4; 36.0	28	46.1 (56.99)	25.00; 67.22	0.288
4	5	33.8 (22.32)	14.2; 53.4	16	34.5 (41.27)	14.28; 54.72	0.972
5	2	19.0 (15.56)	2.6; 35.4	4	20.8 (9.74)	11.20; 30.30	0.869

Note: * = t- test

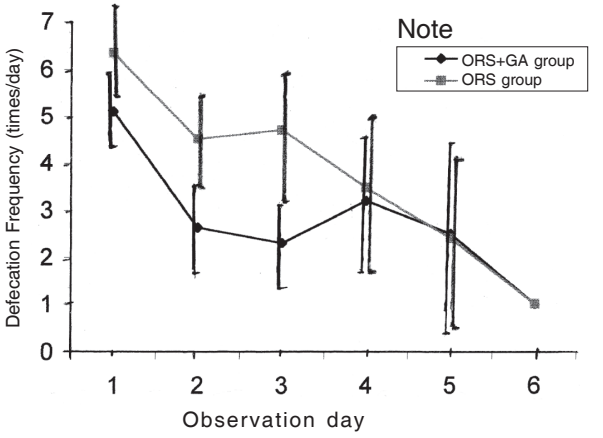

Figure 1. The daily average of defecation frequency during hospitalization in GA and SO groups

compared to using WHO standard ORS. The average duration of diarrhea was shortened by 15.65 hours which is roughly 44.5% of the average duration of diarrhea in a group treated with standard ORS. The frequency of diarrhea significantly decreased on day 2 and 3 of hospitalization, along with the shorter time of feces to become semi-solid and solid. This benefit was achieved by consuming less quantity of ORS.

The role of confounders had been excluded statistically using multiple logistic regression analysis controlling method. Despite above mentioned as a source of bias, it is believed that GA supplemented ORS have some beneficial effects in improving the healing process of DD. All of the analyzed subjects in this study were recovered. However, further study with larger number of subjects is needed to prove the safety of GA supplementation.

There is lack of data on the benefit of GA supplementation to ORS in managing human DD. Alam has studied the benefit of supplementing partially hydrolyzed guar gum, with the similar outcome: shortening the duration and frequency of diarrhea significantly.[18] There are 4 strategies in improving the performance of ORS in managing DD: 1) improving the palatability such as using rice based ORS; 2) diminishing the side effects, such as using lower sodium content of ORS; 3) increasing the nutrient benefits, such as using rice base ORS; and 4) improving the water and electrolyte absorption.[5] GA supplementation is aimed to improve water and electrolyte absorption ,in order to reduce the failure rate of ORT. Operationally, it is aimed to decrease the duration of hospitalization, and also applicable for home-based DD case management. This study was conducted on the inpatient setting. To achieve the above objective, this study should be regarded as a preliminary effectiveness study, which should be followed up by ambulatory setting effectiveness study, before conducting any implementation study.

Although the exact mechanism is unknown, GA had been proved to increase ORS absorption in mice with diarrhea.[6-8] Ramakhrisna *et al*[19]added amylase resistant starch, a substance that is similar to GA, and found an increased of ORS effectiveness for treating patients with cholera. Under the auspice of ESPGHAN, non-digestible carbohydrate has been supplemented to improve the performance of standard ORS. The rationale of the study was non-digestible carbohydrate will be digested by bacteria in the colon with all of its beneficial gain, which may improve the DD healing process. The study could not prove significant outcome.[20]

The pharmacodynamics of GA are not well documented yet. GA is an indigestable starch, so then it will not function as a co-carrier.[6] However GA supplementation to ORS in Teichberg animal study showed that there was morphological changes in small intestine, increasing interstitial space in lamina propria.[7] WHO International Program on Chemical Safety do not limit the ADI (Acceptable Daily Intake) of GA.[12] GA has been used as food adjuvant including ingredient of medicinal capsule, and this had been studied for its benefit to manage several diseases such to control hypercholesteronemia.[21] It is reasonable to consider GA is safe to be consumed.

The cost of adding GA to 200 ml standard ORS was Rp 95.00. This will increase the price of ORS, not more than 20% of standard ORS sachet cost. Although GA is regarded as a stable carbohydrate, the stability of GA should be studied in ORS packaged which contains glucose, electrolyte and base, in exploring the shelve life of GA supplemented ORS. This study used old standard ORS with hyper-osmolarity. Marshintauli[22] have proven that adding GA to the new standard ORS with hypo-osmolarity showed similar outcomes with that found by this study (unpublished data).

In conclusion, addition of GA to standard ORS is effective in improving the performance of

standard ORS in managing DD in the inpatient setting. This treatment is a cheap and safe way to increase the effectiveness of ORS. Further study should be conducted before implementing it operationally.

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