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Original Article

Selenium for acute watery diarrhea in children

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Abstract

Background Acute watery diarrhea remains a major health problem affecting infants and children in developing countries. Selenium deficiency may be a risk factor for diarrhea and vice versa. Few studies have been conducted on the effectiveness of selenium for the treatment of diarrhea in children.

Objective To determine the effectiveness of selenium in reducing the severity of acute watery diarrhea in children.

Methods A single-blind, randomized clinical trial was done in children with acute watery diarrhea, aged six months to two years, and who visited the community health center in Simalungun from May to August 2012. Children were randomized into either the selenium or placebo (maltodextrin) group. We monitored diarrheal frequency, stool consistency, and duration of diarrhea. Mann-Whitney, Fisher's, and Kolmogorov-Smirnov tests were used to compare the two groups.

Results Sixty-five children were recruited into the study, of whom 36 children received selenium and 29 children received a placebo. The selenium group had significantly lower frequency of diarrhea (bouts per day) than the placebo group on days 2, 3, and 4 after treatment onset [day 2: 3.5 *vs.* 4.1, respectively (P=0.016); day 3: 2.7 *vs.* 3.4, respectively (P=0.002); day 4: 2.1 *vs.* 2.8, respectively (P<0.001)]. On day 2, stool consistency had significantly improved in the selenium group compared to the placebo group (P=0.034). In addition, the median duration of diarrhea was significantly lower in the selenium group than in the placebo group (60 vs. 72 hours, respectively; P=0.001). Median recovery time from the the first day of diarrhea was also significantly lower in the selenium group than in the placebo group (108 vs. 120 hours, respectively; P=0.009).

Conclusion In children with acute watery diarrhea, those treated with selenium have decreased frequency of diarrhea, improved stool consistency, as well as shorter duration of diarrhea and recovery time than those treated with a placebo. **[Paediatr Indones. 2016;56:139-43.]**

Keywords*: acute watery diarrhea; selenium; frequency diarrhea; stool consistency*

Acute watery diarrhea is one manifestation of gastrointestinal tract dysfunction[1] and the leading cause of death in infants and children, especially in Indonesia.[2] Most episodes of diarrhea are acute.[1] Since the 1980s, researchers have questioned whether deficiencies of specific micronutrients might affect the risk of diarrhea.[3] Selenium, as an essential micronutrient, is thought to have a role in gastrointestinal tract dysfunction, but research on a relationship between selenium and acute diarrhea has been limited.[4]

Recently, the concept of free radical-mediated oxidative stress (OS) has gained tremendous scientific momentum with many studying its role in the pathophysiology of disease.[5] The pro-oxidant–antioxidant balance in aerobic organisms is critical. Overabundance of pro-oxidants leads to a damaging condition known as oxidative stress. Oxidants can directly damage tissue and initiate cellular signaling cascades, expanding the process of destruction by oxidants. To reduce the negative impact of free radicals

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and to protect tissues from oxidants, the body needs antioxidants.[6,7] One such antioxidant is selenium-containing gastrointestinal glutathione peroxidase, an enzyme commonly found in the mucosal epithelium of the gastrointestinal tract.[8] Selenium deficiency concurrent with diarrhea can increase oxidative stress and decrease the differentiation and proliferation of T cells as well as the increase toxicity of T lymphocytes.[9,10] This condition has led to the rise of the hypothesis that selenium plays a role in the healing process of acute diarrhea.[4] The aim of this study was to compare selenium to a placebo for reducing the severity of acute watery diarrhea in children.

Methods

We conducted a single-blind, randomized clinical trial from May to August 2012 at a community health center in Tiga Balata, Simalungun District, North Sumatera Province. Children aged 6-24 months with acute watery diarrhea, some dehydration according to the WHO criteria[11] and no leukocytes or blood in the stool on microscopic examination were included. Exclusion criteria were children who received selenium supplementation, or suffered from severe comorbidities such as malnutrition, encephalitis, meningitis, sepsis, bronchopneumonia, or tuberculosis. All subjects' parents provided informed consent after receiving an explanation of the study. Subjects were given oral rehydration solution. This study was approved by the Research Ethics Committee of the University of Sumatra Utara Faculty of Medicine.

Subjects who met the inclusion criteria were divided into two groups using simple randomization. In the selenium group, subjects aged 6-12 months were given 15 μg/day of selenium and those aged >12-24 months were given 20 μg/day of selenium, orally for seven days. The placebo group was given maltodextrin in similar amount. Monitoring was carried out every day until the subject recovered.

Data processing was performed with SPSS version 15.0. Mann-Whitney test was used to analyze for relationships between selenium and frequency and duration of diarrhea. Fisher's exact and Kolmogorov-Smirnov tests were used to analyze for a relationship between selenium and stool consistency. Statistical significance was set at $P<0.05$. Intention-to-treat analysis was performed.

Results

A total of 73 children with acute diarrhea were examined, but 8 were excluded from the study. Of 65 subjects, 36 children were treated with selenium and 29 children were treated with placebo (**Figure 1**).

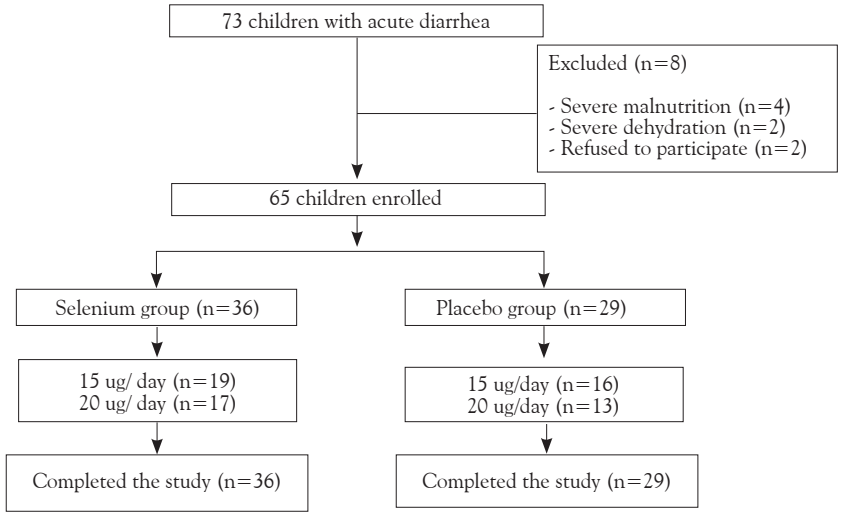

Figure 1. Study profile

Table 1. Baseline characteristics of subjects

Characteristics	Group	
	Selenium (n=36)	Placebo (n=29)
Gender, n (%)		
Male	19 (52.8)	17 (58.6)
Female	17 (47.2)(53.8)	12 (41.4)
Mean age (SD), years	12.22 (5.5)	13.66 (6.3)
Mean body weight (SD), kg	8.29 (1.5)	8.34 (2.1)
Mean body height (SD), cm	71.03 (5.7)	71.17 (8.3)
Mean (SD) BW/BH	92.67 (3.4)	93.45 (4.9)
Duration of diarrhea, n (%)		
1-2 days	28 (77.8)	24 (82.8)
3-4 days	5 (13.9)	5 (17.2)
>4 days	3 (8.3)	0
Frequency of diarrhea, n (%)		
3-5x/day	28 (77.8)	24 (82.8)
6-10x/day	5 (13.9)	4 (13.8)
≥ 10x/day	3 (8.3)	1 (3.4)
Dehydration status, n (%)		
Well-hydrated	27 (75)	22 (75.9)
Some dehydration	9 (25)	7 (24.1)

The mean diarrheal frequency per day was significantly lower in the selenium group than in the placebo group on days 2, 3, and 4 (P<0.05) (**Figure 2**). On day 5 of treatment, the mean diarrheal frequency had reached <2 times/day in both groups.

The selenium group had significantly improved (soft or normal) stool consistency compared to the placebo group, on days 2 , 4, and 5 (P<0.05) (**Table 2**).

The Mann-Whitney test revealed that the median duration of diarrhea from treatment onset to recovery was significantly shorter in the selenium group than in the placebo group [60 hours (2.5 days) vs. 72 hours (3 days), respectively; (P=0.001)]. Also, the median duration of the first day of diarrhea until recovery was significantly shorter in the selenium group than in the placebo group (**Table 3**).

In our study, we monitored subjects for side effects of selenium use, including nausea, vomiting,

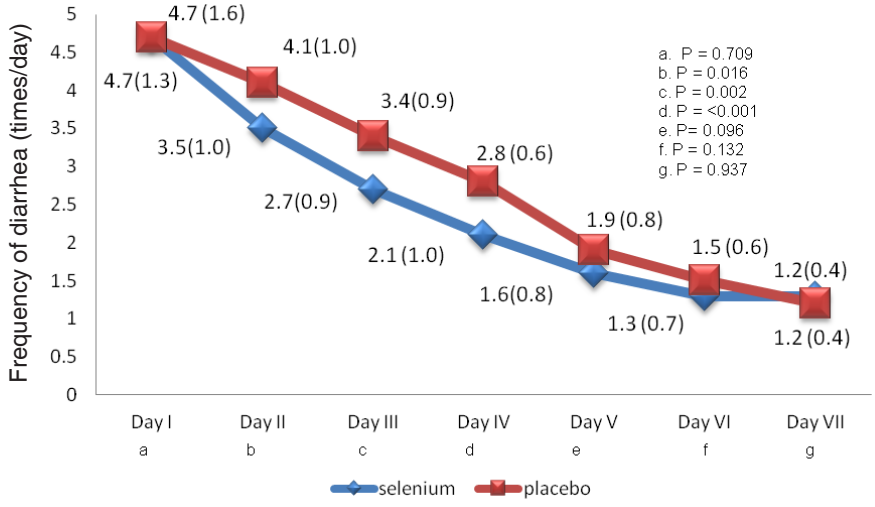

Figure 2. Mean frequency of diarrhea [times per day (SD)] after treatment onset

As shown in **Table 1**, subjects' mean ages in the selenium and placebo groups were 12.22 and 13.66 months, respectively, with a majority of boys (52.8% and 58.6%, respectively). The majority of subjects in both groups had diarrheal frequency of 3-5 times per day, diarrheal duration of 1-2 days at the time of presentation, and no dehydration (75%). There were no clinically significant differences in characteristics of diarrhea between the two groups.

hair loss, and garlic odor of the breath, but we found no side effects in any subjects.

Discussion

Selenium is an essential micronutrient which is necessary for specific and non-specific immunity. Selenium deficiency affects the virulence, or

Table 2. Stool consistency after treatment

	Selenium (n = 36)			Placebo (n = 29)			P value	OR	95% CI
	Watery n (%)	Soft n (%)	Normal n (%)	Watery n (%)	Soft n (%)	Normal n (%)			
Day									
1	36 (100)	0	0	29 (100)	0	0	-		
2	27 (75)	9 (25)	0	28 (96.6)	1 (3.4)	0	0.034[a]	0.107	0.013 to 0.904
3	9 (25)	21 (58.3)	6 (16.7)	14 (48.3)	14 (48.3)	1(3.4)	0.349[b]		
4	3 (8.3)	14(38.9)	19 (52.8)	6 (20.7)	20 (68.9)	3 (10.4)	0.006[b]		
5	3 (8.3)	5(13.9)	28 (77.8)	0	17 (58.6)	12(41.4)	0.028[b]		
6	0	3 (8.3)	33(91.7)	0	8 (27.6)	21(72.4)	0.51[a]	0.239	0.057 to 1.002
7	0	0	36(100)	0	0	29(100)	-		

[a] Fisher's exact; [b]Kolmogorov-Smirnov

Table 3. Duration of diarrhea

Duration of diarrhea	Selenium (n= 36)		Placebo (n=29)		P value
	Median	Range	Median	Range	
From treatment onset to recovery, hours	60	18-120	72	36-132	0.001
From 1st day of diarrhea to recovery, hours	108	60-132	120	48-132	0.009

disease progression of some viral infections.[4] This micronutrient is an important part of selenium-dependent enzymes, also known as selenoproteins, such as gastrointestinal glutathione peroxidase (GPx2/GPxGI). Most GPx2/GPxGI are found on the muscosal epithelium of the intestinal tract.[8] Lesions of the intestinal epithelium caused by diarrhea can result in selenium deficiency.[12]

In this study we found that the mean age of children suffering from acute watery diarrhea was 13 months. The most common cause of acute diarrhea in children less than five years is rotavirus.[13] A Kupang, East Nusa Tenggara study in 2002 found that most diarrhea in children was caused by rotavirus.[14] Incidence rates were higher among infants aged 6-11 months (12.65%) and 12-17 months (14.43%).[2]

Research on the role of selenium for diarrhea management has been limited. A Turkish study found that serum selenium levels were lower in the group suffering from acute watery diarrhea compared to the control group, at the time of hospital admission. After recovery, selenium levels significantly increased in the diarrhea group compared to the control group.[4] A New York study reported that mice with diarrhea had a 40-50% decrease in selenium-dependent glutathione peroxidase (GPx 1 and GPx2). This reduction leads to disruption of the immune system in the digestive tract.[15] A New Zealand study found that selenium-deficiency in bulls was associated with severe diarrhea, while selenium supplementation could prevent and treat the diarrhea.[16] Furthermore, administration of a selenium supplement to pigs with dysentry had a positive effect, which was most clearly illustrated by a greater weight gain during the post-inoculation period compared to control.[17] In addition, a study in England found that patients with chronic diarrhea had a lower median plasma selenium and plasma GPx compared to controls.[12]

Most cases of acute watery diarrhea caused by viruses are self-limited and clear up after a few days, therefore, antibiotics are not recommended. Uncontrolled and irrational use of antibiotics may lead to prolonged diarrhea, because of the disruption of normal intestinal flora and the growth of *Clostridium difficile*.[18] In our study, subjects were not given antibiotics during the intervention.

The side effects of selenium supplementation may be observed in those who exceed the recommended dosage. Side effects may include nausea, vomiting, hair loss, and garlic odor of the breath.[19] However, we observed no side effects in our subjects during the intervention.

The present study has several limitations. We did not measure plasma selenium levels before and after treatment, nor did we directly observe daily patient improvement as we used parental information in our

data collection. Also, the identity of the diarrhea-causing microorganisms should also be explored in further study.

In conclusion, in children with acute watery diarrhea, those treated with selenium have decreased frequency of diarrhea, improved stool consistency, as well as shorter duration of diarrhea and recovery time than those treated with a placebo.

Conflict of interest

None declared.

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