Zinc Supplementation in Children with Acute Diarrhea of Invasive Bacterial and Non-bacterial Infection

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ABSTRACT

Background: *Diarrhea is one of the manifestations of gastrointestinal disorder. In Indonesia, diarrhea is still one of the leading causes of death in infants and children. Diarrhea requires a rational and comprehensive management to deliver an optimal result. This study was aimed to assess the effectiveness of zinc supplementation in children with acute diarrhea of invasive bacterial infection.*

Method: *A cross-sectional study was performed in 74 children aged 2-14 years with acute diarrhea, who visited the Outpatient Clinic, Pasar Rebo Hospital Jakarta, between January and June 2011. The inclusion criteria were patients had suffered diarrhea for 1-7 days. Based on fecal analysis results, subjects were divided into group A (non-infectious) and group B (infectious). All children received zinc supplementation.*

Results: *The mean value of subject age was 46.6 months in group A and 81.3 months in group B. The mean frequency of diarrhea prior to zinc supplementation was 7.5 times/day in group A and 7.8 times/day in group B. Duration of diarrhea before zinc supplementation was 52.6 hours in group A and 45.4 hours in group B. On the seventh day, there was no subject of both groups who still suffered from diarrhea. Although the duration of diarrhea in group A was shorter than group B, no significant difference was found (62.4 hours vs 66.8 hours, p = 0.07).*

Conclusion: *Zinc supplementation shows similar efficacy in children with acute diarrhea caused by invasive bacterial infection and those without bacterial infection as well.*

Keywords: *acute diarrhea, invasive diarrhea, zinc supplementation*

ABSTRAK

Latar belakang: *Diare merupakan salah satu menifestasi gangguan saluran cerna. Di Indonesia, diare masih merupakan penyebab kematian terutama pada bayi dan anak. Diare memerlukan perawatan rasional dan tatalaksana yang komprehensif untuk mencapai hasil optimal. Penelitian ini bertujuan untuk melihat keefektifan suplementasi seng pada pasien anak dengan diare akut akibat infeksi bakteri.*

Metode: *Dilakukan studi potong lintang pada 74 pasien anak usia 2-14 tahun dengan diare akut di klinik rawat jalan Rumah Sakit Pasar Rebo Jakarta untuk periode Januari sampai Juni 2011. Semua pasien anak penderita diare akut selama 1-7 hari diikutsertakan dalam penelitian. Pasien dibagi ke dalam kelompok A (tidak terinfeksi) dan kelompok B (terinfeksi) berdasarkan hasil pemeriksaan feses dan semua mendapat suplementasi seng.*

Hasil: *Usia rata-rata pasien anak di grup A yaitu 46,6 bulan dan grup B sebesar 81,3 bulan. Frekuensi rata-rata diare setelah suplementasi seng 7,5 kali/hari pada grup A dan 7,8 kali/hari pada grup B. Rata-rata lama diare grup A yaitu 52,6 jam sedangkan grup B 45,4 jam. Pada hari ketujuh, tidak ada lagi penderita diare pada kedua kelompok. Walaupun lama diare pada grup A lebih singkat dibanding grup B tetapi tidak dijumpai perbedaan bermakna (62,4 vs 66,8 jam; p = 0,07).*

Simpulan: *Suplementasi seng pada pasien anak penderita diare akut karena infeksi bakteri maupun non bakteri menunjukkan efikasi yang sama.*

Kata kunci: *diare akut, diare invasif, suplementasi seng*

INTRODUCTION

Diarrhea is one of the manifestations of gastrointestinal disorder. Generally, the episode of diarrhea is acute, and in certain circumstances, it may last up to weeks and become persistent.[1] In Indonesia, diarrhea is still one of the leading causes of death in infants and children. Diarrhea ranks second (17%) as the cause of death in children under age of 5 years, after the neonatal problems.[2,3] Therefore, diarrhea requires a rational and comprehensive management to deliver an optimal result. Rational therapy is expected to have maximum results because it is effective, efficient, and also affordable.

Zinc supplementation has been assessed as part of a rational therapy on acute diarrhea in children by World Health Organization (WHO). The assessment is performed on diarrhea in general, regardless the cause of diarrhea. Zinc supplementation to the diet of infants under 12 months of age who suffered from acute diarrhea showed less in severity and duration of diarrhea.[4,5] Similarly, a meta-analysis study on zinc supplementation in children with acute diarrhea showed a decrease of frequency, severity and morbidity significantly.[4] The aim of this study was to assess the effectiveness of zinc supplementation in children who suffered from acute diarrhea with invasive bacterial infection.

METHOD

A cross-sectional study was performed in 74 children aged 2-14 years with acute diarrhea, who visited the outpatient clinic, Pasar Rebo Hospital, Jakarta during the period of January until June 2011. The inclusion criteria were patients suffered diarrhea for 1-7 days, no dehydration or mild to moderate dehydration, no zinc consumption, probiotics, prebiotics, and antibiotics at least two weeks before participating the study, did not suffer from co-morbidities that requires special care, such as malnutrition, encephalitis, meningitis, bronchopneumonia, sepsis, and the parents agreed to participate the study until completion.

Invasive bacterial infection was defined indirectly by findings of leukocytes above 10^{10}/high power field (HPF) on fecal analysis using Giemsa staining. Zinc supplementation was given at a dose of 20 mg once daily for 10 days. Based on fecal analysis results, subjects were divided into group A (non-infectious) and group B (infectious). Oral rehydration was given to each patients who suffered from watery diarrhea. In this study, we divided the subjects into two groups based on the number of leukocytes in the stool. One group consisted of children with no bacterial infection or with stool leukocyte ≤ 10/HPF (group A) and the other group consisted of children with invasive bacterial infection or with stool leukocyte > 10/HPF (group B). Monitoring was done by home visit or telephone call to patients who lived away from the hospital. Chi-square test was performed to determine the correlation between zinc supplementation and patients with invasive bacterial and non-bacterial infection. All data was analyzed with computer using SPSS version 14.0.

RESULTS

Seventy four children were participated in this study and divided into two groups: group A (no bacterial infection) of 35 children and group B (infected with invasive bacteria) of 39 children. In the subsequent monitoring, 4 children from group B did not continue their participation in the study because their clinical condition required additional treatment such as antibiotics and other drugs. The rest of thirty-five children continued to be monitored. Baseline characteristics of the children are shown in Table 1.

Tabel 1. Baseline characteristics of patients

Characteristics	Group A	Group B
	Mean (SD)	Mean (SD)
Age (month)	46.6 (26.56)	81.3 (22.46)
Sex* (n)		
Boys	13 (28.9)	19 (54.3)
Girls	22 (71.1)	16 (45.7)
Dehydration status* (n)		
No dehydration	15 (42.8)	10 (28.6)
Mild-medium dehydration	20 (57.2)	25 (71.4)
Leukocytes in stool (mean)	1.8 (1.22)	12.9 (3.02)
Diarrhea frequency before treatment (times/day)	7.5 (1.06)	7.8 (0.99)
Diarrhea duration before treatment (hour)	52.6 (13.78)	45.4 (16.1)

* n (%)

The mean values on frequency of diarrhea during zinc supplementation in both groups are listed in Table 2. On the seventh day, there was no subject from both groups who still suffered from diarrhea.

Tabel 2. Frequency of diarrhea after zinc supplementation

Monitoring days	Daily diarrhea frequency		p*
	Group A Mean (SD)	Group B Mean (SD)	
Day-1	9 (0.88)	8.2 (0.81)	1.000
Day-2	6.2 (0.82)	6 (0.85)	0.842
Day-3	2.7 (0.82)	2.8 (0.80)	0.726
Day-4	1.1 (0.82)	1.2 (0.63)	0.524
Day-5	0.4 (0.55)	0.5 (0.53)	0.063
Day-6	0.1 (0.16)	0.2 (0.28)	0.223
Day-7	0.0 (0.00)	0.0 (0.00)	-

*Chi-square; $p < 0.05$

Although the duration of diarrhea in group A was shorter than group B, there was no significant difference (62.4 vs 66.8 hours; p = 0.07) (Table 3).

Tabel 3. Frequency and duration of diarrhea after zinc supplementation

	Group A	Group B	p*
	Mean (SD)	Mean (SD)	
Diarrhea frequency (times/day)	2.5 (0.34)	2.8 (0.31)	0.34
Diarrhea duration (hour)	62.4 (11.32)	66.8 (10.86)	0.07

*Chi-square; p < 0.05

DISCUSSION

Diarrhea in children remains a major health problem in Indonesia with a still high mortality rate, which is around 17%.[2,3] Therefore, a comprehensive and proper care is needed.[6-8] In previous studies, the severity of diarrhea was assessed by four aspects, such as frequency, duration, volume, and stool consistency.[9-14] In this study, the severity of diarrhea was assessed by two aspects, the frequency of defecation (times/day) and duration of diarrhea (hours). The stool consistency and volume of diarrhea were not included in the assessment since it was difficult to set a scoring system for those two aspects.

Zinc supplementations in children are more often directed to diarrhea in general, regardless of specific causing microorganism. As has been widely reported, the most common cause of diarrhea in children under 5 years old is Rotavirus (60-70%).[15,16] Some studies of zinc supplementation in children with diarrhea, showed the effectiveness of zinc supplementation in decreasing the stool frequency and duration of diarrhea significantly.[14-16]

The mean value of stool leukocytes in group A was 1.8/HPF, while in group B was 12.9/HPF. Stool leukocyte analysis was only used to distinguish the two groups, and it was not used to assess the efficacy of zinc supplementation. We did not perform culture examination since stool culture is not a routine investigation in acute diarrhea.

By chance, the mean age of children in group A was lower than the mean age of children in group B (47.8 months vs. 82.4 months). These data support the existing epidemiological data, which indicates that bacterial infection is more common in children with diarrhea above 5 years old.

The results obtained in this study were not significant in terms of the frequency of defecation (2.5 times/day vs. 2.8 times/day) after receiving zinc supplementation. Similarly, although the duration of diarrhea in group A (no bacterial infection) was shorter than in group B (invasive bacterial infection) after zinc supplementation, but the difference was not statistically significant (62.4 and 66.8 hours). Similar data has also been reported in previous studies, which reported 2.34 ± 0.71 and 2.84 days.[17,18] One meta-analysis of zinc supplementation in children with acute diarrhea also showed decreased duration of diarrhea by 16% compared with placebo.[4]

Some positive effects of zinc supplementation have been demonstrated in subjects with acute diarrhea. Zinc is needed for growth, regeneration, and restoring the function of the intestinal mucosa, and leads to increase absorption of water and electrolytes. Zinc is also needed to enhance the immune system, including cellular and humoral antibody; thus, speeding up the clearance of pathogens causing intestinal diare.[9,18] To determine the direct effect of zinc on the severity of diarrhea, it's ideal to examine the levels of zinc in the plasma. However, it was not done in this study because of its high cost. Moreover, the study was also more conducted as a community study.

Side effects have been reported as complaints of nausea, vomiting, abdominal pain and fever.[18] These effects generally occur in the supplementation of more than 2 g/day dose and in those who had prolonged treatment.[14-17] A study in Nepal reported that side effects occurred in children with diarrhea who received zinc supplementation with a dose of three times the amount recommended by WHO.[19] In the present study, the dose given was only 20 mg/day, which is consistent with WHO recommendations and no side effects were reported.

The interesting point of the present study was the findings that showed no significant differences in terms of frequency and duration of diarrhea after zinc supplementation in group A (without bacterial infection) and group B (with invasive bacterial infection). These results require further study with larger number of subjects to support the initial conclusions obtained from this study. Zinc supplementation in patients with acute diarrhea and stool leukocyte count above 10/HPF (a marker of bacterial infection) may improve the severity of diarrhea, both in frequency and duration. It also delivers similar results in patients with acute diarrhea, who had no signs of bacterial infection.

CONCLUSION

Zinc supplementation shows similar efficacy in children who have acute diarrhea caused by invasive bacterial infection or those without bacterial infection.

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