The Effect of Zinc Supplementation in Adult Patients with Acute Diarrhea

Deskian Kostermans, Marcellus Simadibrata*, Irsan Hasan**, Laras Budiyani****

* Department of Internal Medicine, Pertamina Central Hospital, Jakarta
** Division of Hepatology, Department of Internal Medicine, Faculty of Medicine University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital, Jakarta
*** Department of Internal Medicine, Faculty of Medicine University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital, Jakarta

ABSTRACT

Background: *Acute diarrhea is a common problem in developing country such as Indonesia with quite high morbidity andmortality rate. It was revealed that the level of zinc deficiency in adult acute diarrhea patients in several hospitals in Jakarta was 69.3%. Although zinc has been proven to be beneficial in the treatment of acute diarrhea in pediatric patients, the effect of zinc supplementation is not fully understood. The objective of this study was to discover the effectiveness of zinc supplementation as an adjuvant therapy in acute diarrhea for adult patients.*

Method: *A double blind randomized controlled trial was done to discover the effect of zinc supplementation to the duration, signs and symptoms on acute diarrhea in hospitalized adults patients in Pertamina Central Hospital, Jakarta from January to December 2013. The data was analyzed using Chi-square test to compare the duration of diarrhea and general linear model (GLM) to assess changes of the symptoms accompanying diarrhea.*

Results**:** *Data analysis from 84 patients, 30 males (19 zinc, 11 placebo) and 54 females (23 zinc, 31 placebo) with p = 0.111 showed that zinc supplementation significantly reduced the duration of acute diarrhea (p = 0.027) and nausea (p = 0.032). In addition there is a tendency of improvement in several acute diarrhea associated symptoms.*

Conclusion: *Zinc supplementation significantly reduces the duration of diarrhea, nausea, as well as improving some symptoms accompanying acute diarrhea.*

Keywords: *zinc supplementation, acute diarrhea, adult patient*

ABSTRAK

Latar belakang: *Diare akut adalah masalah umum di negara berkembang seperti Indonesia dengan angka morbiditas dan mortalitas yang cukup tinggi. Pada beberapa rumah sakit di Jakarta ditemukan bahwa pasien diare akut dewasa mengalami defisiensi kadar seng sebesar 69.3%. Pemberian seng terbukti bermanfaat untuk pengobatan diare akut pada anak. Namun, efek suplementasi seng pada pasien dewasa belum diketahui sepenuhnya. Tujuan penelitian ini adalah untuk mengetahui dampak suplementasi seng sebagai terapi alternatif/ adjuvant untuk pengobatan diare akut pada pasien dewasa.*

Metode: *Double blind randomized controlled trial diterapkan pada penelitian ini untuk mengetahui efek suplementasi seng terhadap durasi dan gejala gastrointestinal pada pasien diare akut rawat inap di Rumah Sakit Pusat Pertamina, Jakarta selama periode Januari hingga Desember 2013. Analisis data dilakukan dengan menggunakan uji Chi-square untuk perbandingan durasi diare dan uji model linear umum untuk menilai tren perubahan gejala penyerta diare.*

Hasil: *Analisis data dari 84 pasien yang dikelola, yaitu 30 pasien laki-laki (seng 19, plasebo 11) dan 54 pasien perempuan (seng 23, plasebo 31) dengan p = 0.111 memperlihatkan pemberian suplementasi seng bermakna*

mengurangi durasi diare akut (p = 0.027) dan bermakna mengurangi gejala mual (p = 0.032). Selain itu ada tren perbaikan pada sebagian gejala penyerta diare akut.

Simpulan: *Pemberian suplementasi seng bermakna mengurangi durasi diare dan gejala mual, serta perbaikan pada sebagian gejala gastrointestinal.*

Kata kunci: *suplementasi seng, diare akut, pasien dewasa*

INTRODUCTION

Acute diarrhea is a common problem in developing countries, such as Indonesia. The morbidity and mortality rate of diarrhea in Indonesia are relatively high.[1-2] According to studies taken in Indonesia, diarrhea is the 13th leading cause of death.[2] Diarrhea is frequently accompanied with gastrointestinal symptoms such as nausea, vomiting, abdominal pain, fever, bloody stool, and rectal tenesmus.[3] In most of cases, acute diarrhea is a self-limiting disease, but in some cases, it can be severe and life threatening. Therefore, an effective and precise therapy is needed to reduce the morbidity and mortality rate.

In developing countries, diarrhea is often related with zinc deficiency. In a study carried out in Division of Gastroenterology, Cipto Mangunkusumo Hospital, Jakarta in 2011, proportion of zinc deficiency in adult with acute diarrhea was 69.3%.[4] This founding is consistent with zinc deficiency in children with acute diarrhea.[5] Recent meta-analysis showed that zinc supplementation reduce the incidence of diarrhea to 20%, particularly in children below 1 year old.[6] Although the mechanism of zinc in diarrhea is not fully understood, zinc showed great benefit in strengthening immunity against infection and reducing the duration and risk of diarrhea.[4] It is suggested that zinc increases intestinal fluid absorption, aids organism elimination, and enhances mucosal integrity and regeneration as well as interrelated with the immune system.[6]

There is a shortage of data about zinc deficiency in adult population with diarrhea. National data about zinc deficiency, including subclinical deficiency in adults, is scarce. Hence, this study aimed the symptoms related with zinc deficiency in adult patients with diarrhea, as well as the effects of zinc supplementation towards recovery and relieving diarrhea associated symptoms.

METHOD

This is a double blind randomized control trial study. This study, which investigated the effects of zinc supplementation in adult acute diarrhea patients compared with placebo, was a continuation of the study that evaluate zinc level in adult diarrhea patients in Jakarta.[4] This study was conducted in Pertamina Central Hospital from January 2013 until December 2013.

The inclusive criteria that were included were age between 18 to 60 years old and acute diarrhea without complication. Meanwhile the exclusive criteria were patients with irritable bowel syndrome, inflammatory bowel disease and chronic diarrhea, colon disease such as inflammatory bowel due to radiation, bowel adhesion, colon cancer, gastrointestinal operation within 3 months, patients who received antibiotics, kidney failure, metabolic acidosis, hypovolemic shock, immunosuppressant and/or immunomodulator recipients, not cooperative, every disease that could endanger patient, known or suggestive allergic to the research or related products, for women in childbearing age: currently pregnant, breastfeed, or intent to get pregnant, and patients who underwent chemotherapy and/or radiotherapy.

Sample recruitment was carried out consecutively for all patients who were admitted in Pertamina Central Hospital. Patients who met the inclusive and exclusive criteria were randomized into zinc group and placebo group. The zinc group received 20 mg zinc sulphatetwice a day for 7 days. Patients were given a diary to monitor their conditions and symptoms.

The patients fulfilled the criteria underwent several steps that included history taking, and physical examination. The data collected were age, sex, body mass index (BMI), the severity of acute diarrhea, length of diarrhea, and other symptoms such as fever, abdominal pain, nausea, vomiting, tenesmus, bloody stool, thirst, stool consistency, mucus in stool, less urination, disturbed daily activities, and headache.

SPSS for Windows version 17 was used to data analysis. The data was presented using texts, tables or graphics; Chi-square was used to analyze the duration of diarrhea, and general linear model (GLM) was used to analyze the diarrhea associated symptoms.

This study was approved and received ethical clearance from the Medical Committee of Ethics, Faculty of Medicine, University of Indonesia. Every data collected from medical records were classified.

RESULTS

A total of 84 patients with acute diarrhea that fulfill the inclusion and exclusion criteria, were enrolled in this study, with a proportion of 30 male and 54 females. There were neither significant difference of the subjects' characteristics nor the diarrhea types between two groups. The proportion of symptoms before the treatment was not significantly different, except for the fever (p = 0.028).

Table 1. Patients characteristics and the type of diarrhea

Variable	Group n (%)	
	Placebo	Zinc
Sex		
Male	11 (26.2)	19 (45.2)
Female	31 (73.8)	23 (54.8)
Age (years)		
< 20	1 (50.0)	1 (50.0)
20-30	11 (52.4)	10 (47.6)
31-40	17 (58.6)	12 (41.4)
41-50	6 (42.9)	8 (57.1)
51-60	8 (44.4)	10 (55.6)
Diarrhea type		
Infectious diarrhea	10 (23.8)	18 (42.9)
Non-infectious diarrhea	32 (76.2)	18 (42.9)
Etiology of infection		
Virus	5 (11.9)	4 (9.5)
Bacteria	0 (0.0)	1 (2.4)
Fungus	3 (7.1)	8 (19.0)
Parasite	0 (0.0)	1 (2.4)
Non-infectious causes		
Not specific	30 (71.4)	27 (64.3)
Food	4 (9.5)	1(2.4)
Stool color		
Brown	6 (14.3)	9 (21.4)
Green	3 (7.1)	2 (4.8)
Yellow	32 (76.2)	31 (73.8)
White	1 (2.4)	0 (0.0)
Blood in stool		
None	42 (50.6)	41 (49.4)
Present	0 (0.0)	1 (100.0)

Through the data collected from 84 patients during 7 days of treatment, there was a significant difference of diarrhea duration reduction between the two groups (p = 0.027). Regarding the analysis of diarrhea associated symptoms, there was only significant difference in nausea (p = 0.032). However, zinc supplementation showed trends of improvement in some diarrhea associated symptoms, consisting of abdominal pain, frequency of bowel movement, stool consistency, vomiting, flatulence, and disturbed daily activities. Meanwhile, there was no difference in thirst, less urination, and fever parameters in both groups before and after the study.

Table 2. Proportions of diarrhea associated symptoms before the treatment

Variable	Group n (%)	
	Placebo	Zinc
Frequency of bowel movements		
3-5	11 (64.7)	6 (35.3)
6-10	11 (50.0)	11 (50.0)
> 10	20 (44.4)	25 (55.6)
Stool consistency		
Liquid	32 (58.2)	23 (41.8)
Watery (½ liquid, ½ solid)	10 (34.5)	19 (65.5)
Mucus		
Mone	38 (51.4)	36 (48.6)
Mild	2 (25.0)	6 (75.0)
Average	2 (100.0)	0 (0.0)
Tenesmus		
None	40 (49.4)	41 (50.6)
Present	2 (66.7)	1 (33.33)
Abdominal pain		
None	7 (63.6)	4 (36.4)
Mild	14 (53.8)	12 (46.2)
Average	21 (44.7)	26 (55.3)
Severe	0 (0.0)	0 (0.0)
Nausea		
None	2 (40.0)	3 (60.0)
Mild	16 (50.0)	16 (50.0)
Average	23 (53.5)	20 (46.5)
Severe	1 (25.0)	3 (75.0)
Vomiting		
None	17 (53.1)	15 (46.9)
Mild	14 (46.7)	16 (53.3)
Average	11 (50.0)	11 (50.0)
Severe	0 (0.0)	0 (0.0)
Flatulence		
None	3 (30.0)	7 (70.0)
Mild	21 (51.2)	20 (48.8)
Average	18 (54.5)	15 (45.5)
Severe	0 (0.0)	0 (0.0)
Fever		
Present	24 (64.9)	29 (61.7)
None	18 (38.3)	13 (35.1)
Headache		
None	18 (52.9)	16 (47.1)
Mild	23 (51.1)	22 (48.90
Average	1 (20.0)	4 (80.0)
Severe	0 (0.0)	0 (0.0)
Less urination		
Present	39 (51.3)	37 (48.7)
None	3 (37.5)	5 (62.5)
Thirsty		
Present	29 (53.7)	25 (46.3)
None	13 (43.3)	17 (56.7)
Disturbing daily activities		
None	4 (100.0)	0 (0.0)
Mild	22 (52.4)	20 (47.6)
Average	16 (42.1)	22 (57.9)
Severe	0 (0.0)	0 (0.0)

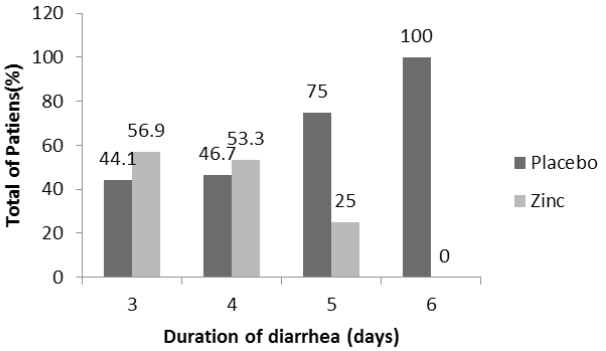

Figure 1. The comparison of diarrhea duration between zinc and placebo group (p= 0.027)

DISCUSSION

This study focused on the effect of zinc supplementation to adult patient with acute diarrhea. Zinc is one of essential micronutrients needed for the body processes.[7] Zinc is known for its anti-inflammatory and antioxidant effect as well as the role in immunity. Zinc effect towards acute diarrhea is due to its function in cellular works in increasing water and electrolyte intestinal absorption, enhancing intestinal epithelial regeneration, and improving brush border enzyme in the enterocyte.[8] Zinc also has a role in immunity. Zinc deficiency is e health problem in developing countries. Zinc supplementation significantly reduces the rate of diarrhea.[7,9]

After conducting the experimental study with adjustment to age, comorbid, and history of medical treatment using the bivariate analysis, we found that the zinc supplementation significantly reduce the diarrhea duration (p = 0.027). Besides that, it also significantly improve nausea in acute diarrheal patient (p = 0.032).

This study is concordance with previous study conducted in India which showed that zinc supplementation reduce the severity of diarrhea in children in India.[10] Zinc was found to lower the severity and incidence of persistent diarrhea in adults with HIV-1 infection.[11] Meta-analysis reported by Galvao et all also concluded that zinc supplementation gave a significant effect in reducing the duration of diarrhea.[12] A double blind randomized controlled trial using 20 mg zinc or placebo daily showed a decrease of diarrhea prevalence and incidence by -48% (p = 0.20) and -50% (p = 0.17) respectively.[13]

This double blind randomized controlled trial experimental study was done with 84 samples treated either as zinc group or placebo group. However, the limitation in this study was that most of the patients were discharged from hospital on the third day of admission. Therefore, the data were collected using phone calls that were not enough detail and laboratory analysis was not possible because many patients did not control after 1 week. Furthermore, the data was gathered from one hospital that only included patients from moderate to higher social status.

CONCLUSION

From this study, we can conclude that zinc supplementation could enhance the improvement of acute diarrhea, reduce nausea, and have trends in improving several diarrhea associated symptoms, such as abdominal pain, frequency of bowel movements, stool consistency, vomiting, flatulence, and disturbed daily activities. Because of that, zinc supplementation can be considered to be an additional therapy in adult acute diarrhea patients. Furthermore, another study with better methodology which consists of every social strata should be carried out following this study.

Table 3. The comparison of diarrhea associated symptoms between zinc and placebo group

Variable	Group	Day							p
		1	2	3	4	5	6	7	
Abdominal pain	Placebo	1.6 (0.09)	1.31 (0.09)	1.11 (0.06)	1.00 (0.03)	1.00 (0.0)	1.00 (0.0)	1.00 (0.0)	0.194
	Zinc	1.71 (0.09)	1.43 (0.09)	1.17 (0.06)	1.09 (0.03)	1.00 (0.0)	1.00 (0.0)	1.00 (0.0)	
Frequency of bowel movement	Placebo	3.12 (0.15)	2.64 (0.12)	2.21 (0.13)	2.05 (0.7)	1.98 (0.06)	1.98 (0.05)	1.98 (0.05)	0.276
	Zinc	3.43 (0.15)	2.93 (0.12)	2.33 (0.13)	2.09 (0.79)	2.12 (0.07)	1.95 (0.05)	1.95 (0.05)	
Stool consistency	Placebo	1.76 (0.08)	1.93 (0.06)	1.93 (0.15)	2.43 (0.14)	2.45 (0.14)	2.76 (0.12)	2.76 (0.12)	0.833
	Zinc	1.76 (0.07)	2.00 (0.66)	2.14 (0.15)	2.26 (0.14)	2.5 (0.13)	2.78 (0.12)	2.78 (0.12)	
Mucus present	Placebo	1.048 (0.04)	1.024 (0.02)	1.00 (0.017)	1.00 (0.0)	1.00 (0.0)	1.00 (0.0)	1.00 (0.0)	0.393
	Zinc	1.95 (0.04)	1.024 (0.02)	1.02 (0.017)	1.00 (0.0)	1.00 (0.0)	1.00 (0.0)	1.00 (0.0)	
Nausea	Placebo	1.64 (0.11)	1.40 (0.08)	1.31 (0.06)	1.09 (0.05)	1.05 (0.04)	1.00 (0.0)	1.00 (0.0)	0.032
	Zinc	1.88 (0.11)	1.50 (0.08)	1.20 (0.06)	1.20 (0.05)	1.11 (0.04)	1.00 (0.0)	1.00 (0.0)	
Vomiting	Placebo	1.476 (0.10)	1.20 (0.06)	1.14 (0.045)	1.048 (0.03)	1.00 (0.0)	1.00 (0.0)	1.00 (0.0)	0.570
	Zinc	1.48 (0.10)	1.21 (0.06)	1.05 (0.045)	1.024 (0.03)	1.00 (0.0)	1.00 (0.0)	1.00 (0.0)	
Flatulence	Placebo	1.50 (0.10)	1.24 (0.07)	1.12 (0.06)	1.00 (0.02)	1.00 (0.0)	1.00 (0.0)	1.00 (0.0)	0.538
	Zinc	1.60 (0.10)	1.31 (0.07)	1.21 (0.05)	1.05 (0.24)	1.00 (0.0)	1.00 (0.0)	1.00 (0.0)	
Disturbed daily activities	Placebo	1.67 (0.11)	1.29 (0.07)	1.09 (0.05)	1.00 (0.024)	1.00 (0.0)	1.00 (0.0)	1.00 (0.0)	0.148
	Zinc	1.93 (0.11)	1.54 (0.07)	1.09 (0.05)	1.05 (0.02)	1.00 (0.0)	1.00 (0.0)	1.00 (0.0)	

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Correspondence:
Deskian Kostermans
Department of Internal Medicine
Pertamina Central Hospital
Jl. Kyai Maja No. 43 Jakarta Indonesia
Phone: +62-21-7219176 Facsimile: +62-21-7219190
E-mail: deskian_kost@gmail.com