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The effect of zinc supplementation in adolescent patients with acute diarrhoea

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***Abstract*---**Background: Despite the recommendation of zinc in the management of acute diarrhoeal illness, the effect has been seldomly reported in adolescent population. Objective: To evaluate the efficacy of zinc supplementation in acute diarrhoea in adolescent population. Study Design: Randomized Controlled Trial. Settings: Department of Medicine and Paediatrics, Hayatabad Medical Complex. Study duration: This study was conducted from 1st February 2022 till 31st October 2022. Materials and methods: Both male and female patients presenting with acute diarrhoeal illness were enrolled. Patients were equally divided through block randomization into two groups. Elemental zinc at 20mg BD was administered orally to the study group. Control group received mineral and vitamin supplementation except zinc. Efficacy was evaluated in terms of reduction in stool frequency and hospital stay. Results: Age of the patients ranged from 10 to 18 years. Mean age of the patients in study group was 14.83±3.730 years versus 13.90±3.806 years in control group. Mean stool frequency on presentation in study versus control group were 5.904±1.052 versus 6.089±1.472 respectively while on day it was 1.472±0.130 versus 2.937±640 respectively. Recovery was observed in 29 patients (93.5%) in study group as compared to 21 patients (67.7%) in control group. Mean hospital in study versus group was 2.861±0.827 days versus 4.247±1.318 days. Conclusion: Zinc supplementation has better efficacy than placebo acute diarrhoeal Illness in adolescent patients.

***Keywords*---**acute diarrhoeal illness, zinc supplementation, efficacy.

Introduction

Adolescent age is the most vulnerable period in the life time during which individual is exposed to several hormonal and anatomical changes.[1] Energy and nutritional demands are increased for accelerated growth and developments changes.[2] A subtle deviation from the accustomed physiologic state like acute diarrhoeal illness could potentially prone the individual to nutritional deficiencies including micronutrients which could lead to long-lasting deleterious consequences including disturbances in growth and development.[3, 4]

Acute diarrhoeal illness has remained a major public health concern among patients of all age groups. To cope with the challenge of diarrhoeal illness related mortality below the age of 5 years is onerous, the consequences in adolescent population aren't gratifying. Nearly 10% of all mortalities under the age of 5 years is attributed to acute diarrhoeal illness.[5] Asian and African countries are among the worst affected countries.[6] On the other hand, the outcomes in adolescent population aren't glorifying. Though mortality in this age group is low, still it constitute a major cause of hospital admission, morbidity and nutritional deficiency especially in under developed countries.[7]

Rehydration is the mainstay of treatment and mortality reducing practice in diarrhoeal disease but WHO recommended elemental zinc as an adjunctive therapy with potential useful outcomes in 2004.[8] The impact range of zinc is broad and it is thought to exert its beneficial effects though several mechanisms ranging from enhancing immunity through strengthening and restoring the integrity of enterocytes along the entire GI mucosal wall to recruiting and stimulating lymphocytes and antibodies against the invading microorganism.[9, 10] Besides, it also activate several enzymes and ATP-generating systems.[11] Rerksuppapho et al reported recovery in 97.7% patients who received zinc compared to 69.8% patients in placebo group after 03 days of treatment.[12]

Zinc is routinely prescribed as integral part of while managing children under the age of 5 years in our setup. However, no comprehensive reports are available regarding its role in adolescent population. This study is aimed to assess the efficacy of zinc supplementation among adolescent patients presenting with acute diarrhoeal illness. It was hypothesized that zinc supplementation in acute diarrhoeal illness has better efficacy than placebo.

Materials and Methods

Study design and settings

This randomized controlled trial was conducted at department of department of Medicine and Paediatrics, Hayatabad Medical Complex, Peshawar. Participants were enrolled from 1st February 2022 till 31st October 2022. Approval was taken from hospital research review committee.

Sampling

A total of 62 patients, 31 patients in each group were enrolled based on previous study report (ref), i.e. recovery in zinc group = 97.7%, recovery in placebo group = 69.8%, Power of test= 80% and confidence level =95%. Both male and female patients within the age range of 10 to 18 years, presenting with acute diarrhoeal illness were recruited. Acute diarrhoeal was defined by the sudden onset, passage of more than three episodes of loose/watery stools in the last 24 hours for less than 2 weeks. Patients with acute hepatitis, chronic systemic illness and who received commercial rehydration containing zinc or elemental zinc in the last 03 months were excluded.

Data collection

Informed consent was taken from all participants after taking approval from the research review board of the hospital. Baseline information including age, gender, BMI, disease duration (days) were recorded. Patients were divided equally into two groups (A and B) though block randomization. Group A was called study/intervention group while group B was labelled control/placebo group. Elemental zinc was administered orally at 20mg BD during the hospital stay and then continued for a total of 14 days to patients in study group. Placebo (minerals other than zinc and iron with vitamins) was administered twice daily during the hospital stay and then continued for a total of 14 days to all patients in control/placebo group.

Study end point

The primary end point of the study was to determine the efficacy of zinc supplementation evaluated by reduction in the stool frequency to ≤2 stools day which was recorded on day 3 of treatment initiation. Primary end point was called efficacy. Secondary end point included the length of hospital stay and grave complications like deterioration of renal functions evident by rise in the serum creatinine from the baseline and mortality measured on day 3 of treatment initiation.

Data analysis

Categorical data was presented as frequencies and percentages while means and standard deviations were computed for numerical variables. Shapiro-Wilk test was used to assess normality of the data. Statistical test of significance included independent sample t test and pearson chi square tests which were applied to compare the means of continuous variables and categorical variables respectively. p value ≤0.05 was labelled statically significant. Data was recoded in statistical analysis program IBM SPSS version 25.

Results

A total 62 patients (31 in each group) were enrolled. Age of the patients ranged from 10 to 18 years. Baseline characteristics of patients in study groups versus control group included age (14.83±3.730 years versus 13.90±3.806 years), BMI

(21.373±1.322kg/m^2 versus 22.006±1.916kg/m^2), disease duration (8.009±2.049 days versus 7.882±2.394 days), mean stool frequency at presentation (5.904±1.052 versus 6.089±1.472) and baseline serum creatinine (1.205±0.629mg/dl versus 1.297±0.942 mg/dl). Mean stool frequency in study group versus control group on day 3 was (1.472±0.130 versus 2.937±640). Reduction in stool frequency to ≤2 per day (efficacy) was observed in 29 patients (93.5%) in study group as compared to 21 patients (67.7%) in control group.

Mean length of hospital stay was shorter in study group as compared to placebo group (2.861±0.827 days versus 4.247±1.318 days). Mean serum creatinine in study versus control group on day 3 were 0.989±0.049 mg/dl versus 1.036±0.521 mg/dl. Deterioration of renal functions were observed in 1 patient (3.2%) in study group and 4 patients (12.9%) in placebo group. No mortality was recorded in either group during the hospital stay.

Table 1. Baseline characteristics of patients in study group

	Minimum	Maximum	Mean	Std. Deviation
Age (years)	10	18	14.83	3.730
BMI (kg/m^2)	20.1	22.5	21.373	1.322
Disease Duration (days)	6	11	8.009	2.049
Baseline stool frequency	4	9	5.904	1.052
Leucocyte Count(per ml)	4873	17376	9831.65	5720.32
Creatinine (mg/dl)	0.9	3.3	1.205	.629

Table 2. Baseline characteristics of patients in control group

	Minimum	Maximum	Mean	Std. Deviation
Age (years)	10	17	13.90	3.806
BMI (kg/m^2)	20.3	23.1	22.006	1.916
Disease duration (days)	5	11	7.882	2.394
Baseline stool frequency	5	11	6.089	1.472
Leucocyte Count (per ml)	5083	23896	10452.46	7558.426
Creatinine (gm/dl)	0.7	4.1	1.297	.942

Table 3. Outcomes on Day 3

	Study Group	Control Group
Stool Frequency	1.472±0.130	2.937±640
Serum Creatinine (mg/dl)	0.989±0.049	1.036±0.521
Recovery (≤2stools)	29 (93.5%)	21 (67.7%)
Hospital Stay (days)	2.861±0.827	4.247±1.318
Renal Deteriorations	1 (3.2%)	4 (12.9%)
Mortality	0 (0.0%)	0 (0.0%)

Table 3. Sub-group analysis of patients in study group

		RECOVERY		Total	p value
		YES	NO		
Age	10-14 years	16 94.1%	1 5.9%	17 100.0%	0.886
	15-18 years	13 92.8%	1 7.2%	14 100.0%	
Gender	Male	17 89.5%	02 10.5%	19 100.0%	0.840
	Female	12 100.0%	0 0.0%	12 100.0%	
Disease duration	≤ 7 days	11 100.0%	0 0.0%	11 100.0%	0.934
	> 7 days	18 90.0%	02 10.0%	20 100.0%	
Serum creatinine	≤1.5mg/dl	16 94.1%	1 5.9%	17 100.0%	0.886
	>1.5mg/dl	13 92.8%	1 7.2%	14 100.0%	
Leucocyte Count	Less than 10,000	19 100.0%	0 0.0%	19 100.0%	0.734
	more than 10,000	10 83.3%	02 16.7%	12 100.0%	

Table 4. Sub-group analysis of patients in control group

		RECOVERY		Total	p value
		YES	NO		
Age	10-14 years	11 68.8%	05 31.2%	16 100.0%	0.901
	15-18 years	10 66.7%	05 33.3%	15 100.0%	
Disease Duration	≤ 7 days	10 71.4%	04 28.6%	14 100.0%	0.690
	>7 days	11 64.7%	06 35.3%	17 100.0%	
Serum Creatinine	≤1.5mg/dl	11 68.8%	06 31.2%	16 100.0%	0.599
	>1.5mg/dl	11 73.3%	04 26.7%	15 100.0%	
Gender	male	12 63.2%	07 36.8%	19 100.0%	0.492
	female	09 75.0%	03 25.0%	12 100.0%	
Leucocyte Count	Less than 10,000	10 71.4%	04 28.6%	14 100.0%	0.690

	More than 10,000	11 64.7%	06 35.3%	17 100.0%	

Discussion

To our knowledge, this was the first of its kind study evaluating efficacy of zinc supplementation in adolescent population. Age of the patient ranged from 10 to 18 years. Mean age of the patients was 14.83±3.730 years in study group and 13.90±3.806 years in control group. This is the hallmark of the study. We could not find any comparable study of this study population. Majority of the previous studies have been reported on pediatric population.

In this study, reduction in stool frequency to ≤2 per day was observed in 93.2% patients who received zinc as compared to 67.7% patients who received placebo. Moreover, amore accelerated recovery course was noted with zinc with overall mean duration of hospital stay was 2.861±0.827 days as compared to 4.247±1.318 days with placebo. Zinc was better tolerated by all patients and none of the patients reported any complaint. Previous studies have demonstrated variable results about the efficacy of zinc acute diarrhoeal illness. In a placebo controlled randomized trial by Trivedi and colleagues, efficacy of zinc recorded was 62% as compared 29% with placebo.[13] This observation is in coherence with the result of our study. Promising results were reported by Laghari and colleagues in terms of reduction in stool frequency from baseline 6.14±0.98 to 2.40± 0.81 on day 3 after zinc supplementation. However, this study included patients below the age of 5 years.[14] Borna P et al studied the pattern of acute diarrhoeal illness episodes in patients with and without zinc deficiency. Elemental zinc was provided to both groups. None of the groups showed statistically significant improvement in diarrhoeal episodes.[15] Of note, zinc deficient patients failed to show improvement after normalization of serum zinc with supplemental zinc. This is in contrast to our observation and the above mentioned studies. The difference in the pattern of underlying pathogenic organism among the Asian and European population may have imparted this effect.[16] Moreover these results cannot be generalized because the study population included children 6 months to 60 months only.

A large scale randomized trial performed on Indian population failed to show substantial evidence regarding the impact zinc, either alone or in combination with copper, on the reduction in diarrhoeal illness when compared with placebo.[17] However, the author admitted low dose zinc administration compared in contrast to fixed therapeutic dose of 20mg/day. In addition to its beneficial role in acute diarrhoeal conditions, a recent documents has entrusted its part in chronic diarrhoeal disorder as well.[18] This effect could be attributed to the fact that zinc is an essential component for maintaining the integrity and growth of enterocytes. Moreover, it also promote lymphocyte recruitment and trafficking towards hazardous microorganisms.[19] Study population is major strength of this study as it is the first of its kind study performed on this age group to our knowledge. Small sample size, lack of long term follow up are the main limitations of this study.

Conclusion

Zinc supplementation in adolescent patient with acute diarrheal illness has favorable outcomes in reducing stool frequency. It also shortens the length of hospital stay. The drug is well tolerated. Carefully designed large scale randomized trials should be performed to confirm the effect in this population along with long term follow up results.

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