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## EVALUATING EFFICACY OF ORAL ZINC AS ADJUVANT THERAPY IN ACUTE DIARRHEA IN CHILDREN.

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**ABSTRACT... Objectives:** To evaluate the efficacy of oral zinc as adjuvant therapy in acute diarrhea comparing frequency and volume of stool and duration of diarrhea in children. **Study Design:** Case Control study. **Setting:** Department of Paediatrics, Shaheed Muhtrama Benazir Bhutto Medical College Layari General Hospital, Karachi. **Period:** September 2017 to August 2018. **Material & Methods:** A sample of 200 children, age 5- 15 years, suffering from acute diarrhea was divided into control and cases (study group). Oral zinc therapy (20 mg once daily) was given 14 days and its efficacy was observed in terms of stool frequency, stool volume and duration of diarrhea. Variables were noted at 24 hours and 48 hours and on 7<sup>th</sup> day of hospitalization. Data was analyzed on SPSS statistical software (version 22.0) at 95% confidence interval ( $P \leq 0.05$ ). **Results:** Mean  $\pm$  SD age in control and study group was noted as  $9.1 \pm 5.43$  years and  $9.5 \pm 6.02$  years respectively ( $P=0.053$ ). 89% of children of study group were discharged on 3<sup>rd</sup> day of hospitalization compared to only 45% from control group. Zinc treated study group shows significant decrease in frequency of loose stools, stool volume and lesser duration of hospital stay. **Conclusion:** Oral zinc therapy was effective in decreasing the frequency of loose stools and volume and lesser duration of hospital stay in children.

**Key words:** Acute Diarrhea, Duration, Frequency Stool, Zinc Supplement.

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### INTRODUCTION

Various micronutrients are essential for the growth and cell functioning, zinc is one of them. Zinc (Zn) is needed for essential vital functions of living organisms. Such vital functions include water and electrolyte transport across intestinal Lumina, protein synthesis, cell differentiation and growth, and immune functions.<sup>1,2</sup> Zn is essential for physical growth and development of children. Zn deficiency has been linked to risk of gut infections, impaired immune system and altered anatomical and physiological behavior of intestinal epithelia.<sup>2</sup> Zn is reportedly common in developing countries because of low zinc content of diet and no food fortification. Dietary phytates impair zinc absorption.<sup>3</sup> Zn supplementation for the acute diarrhea has been reported in several studies. A previous systematic review and meta-analysis<sup>4,5</sup> concluded 20% decrease in mean duration of acute diarrhea after zinc supplements. Acute

diarrhea is a public health problem particularly in children. Millions of children are affected by diarrhea Worldwide. It is main cause of under 5 years childhood morbidity and mortality.<sup>6,7</sup> An estimate shows 3.3 million mortalities in developing countries occur each year in children suffering from diarrhea.<sup>7</sup> Oral rehydration solution (ORS) is the mainstay of diarrheal disease. World Health Organization (WHO) and United Nations International Children's Emergency Fund (UNICEF) guidelines recommend the oral rehydration. Practically, the ORS does not change stool frequency, volume and duration of diarrhea.<sup>6,7</sup> Probiotics and anti-secretory drug had studied but not found too much effective. Now the WHO and UNICEF recommended 10- 14 days zinc therapy with ORS for the acute diarrhea in children.<sup>7-9</sup> Many studies had reported efficacy of Zn adjuvant therapy in children under 5 years.<sup>7-10</sup> However, guidelines are lacking on the use of Zn

in acute diarrhea. The present study was planned to evaluate the effects of Zn adjuvant therapy in children in terms of improvement in stool frequency and volume and duration of diarrhea at our tertiary care hospital.

## MATERIAL & METHODS

A case control study was conducted at the Department of Paediatrics, Shaheed Muhtrama Benazir Bhutto Medical College Layari General Hospital, Karachi, Sindh from period of September 2017 to August 2018. Ethical issues were explained in research protocol and approval from the ethical review committee.

A sample of 100 control and 100 cases (study group) admitted children were enrolled according to the inclusion and exclusion criteria. Control and cases were age and gender matched. Children of age 5- 15 years, admitted in Pediatric department, with acute diarrhea and suffering from some or severe dehydration were included in the study protocol. Those suffering from malnutrition, metabolic or endocrine disease, chronic systemic illness, and acute bacillary dysentery were strictly excluded from study protocol. Control group were treated normally while Study group received zinc syrup (20 mg once daily) orally.

Zinc therapy was offered for 14 days to the study group. Compliance was ensured by checking the syrup bottles daily and attendants were asked to adhere. Clinical general and systemic examination was conducted daily. Efficacy of Zn as adjuvant therapy was calculated in terms of stool frequency and volume and duration of diarrhea. Urine output, vomiting and abdominal pain were checked. Hydration status of control and cases was calculated as some or severe dehydration. Intravenous fluids and oral rehydration was administered continuously as per clinical need of patients. Hydration was controlled as according to the given guidelines. Both groups were administered lactobacilli strains (*saccharomyces boulardii*) once daily for five days. Anti-secretory and anti-motility drugs were not used. Routine laboratory investigations were checked daily. Primary outcome measure was frequency and volume of stool. Secondary outcome measure

was dehydration that was categorized as some or severe dehydration. Variables were noted at 24 hours and 48 hours.

If patients were discharged they were given called for follow up in outpatient departments on 7<sup>th</sup> day of hospitalization. Volunteer parents and guardians were asked to sign the consent form. They were interviewed and informed that the study will not harm to their children and there will be no extra expenses. They were further informed to denial and withdrawal from study protocol at any time and this will not affect their drug therapy. A pre- structured Performa was designed for the data collection that was noted on daily basis as per study protocol. Data was analyzed on SPSS statistical software (version 22.0) for windows release. Continuous variables were compared by Student`s t-test and descriptive statistics. Outcome results were presented as mean +/- SD. Categorical variables were cross tabulated by Chi- square test (cross tabulation). Results were tabulated as frequency and%. Statistical analysis were performed at 95% confidence interval ( $P \leq 0.05$ )

## RESULTS

Mean  $\pm$  SD age in control and study group was noted as  $9.1 \pm 5.43$  years and  $9.5 \pm 6.02$  years respectively. Distribution of age categories of control and study group is shown in table-I. ( $P=0.053$ ). Cross tabulation shows male were noted as 53 vs. 47 and female as 49 vs. 51 in control and study group respectively ( $P=0.051$ ) (table 2). Some and severe dehydration was cross tabulated between control and study group. Control and study group revealed some or severe dehydration in 53 vs. 61 and 47 vs. 39 respectively ( $P=0.001$ ). Frequency of loss stool was calculated at 24, 48 hours and 7<sup>th</sup> day as shown in table 4, 5 and 6. Study groups showed improvement in frequency of loose stool at 24, 48 hours and day 7. The differences were statistically significant and study group shows best outcome in terms of frequency of loose stool that was decreased in large number of study group compared to control group. 89% of children of study group were discharged on 3<sup>rd</sup> day of hospitalization compared to only 45% from control group. Zinc

treated study group showed significant decrease in frequency of loose stools, early recovery and discharge and lesser hospital stay duration.

Age (Years)	Control	Study Group	P-Value
5.0 - 5.9	8	9	0.053
6.0 - 6.9	9	11	
7.0 - 7.9	11	7	
7.0 - 7.9	8	8	
8.0 - 8.9	12	11	
9.0 - 9.9	9	10	
10.0 - 10.9	8	7	
11.0 - 11.9	7	9	
12.0 - 12.9	11	10	
13.0 - 13.9	9	8	
14.0 - 14.9	8	10	
Total	100	100	

**Table-I. Age distribution of control and study groups.**

Gender	Control	Study Group	P-Value
Male	53	49	0.051
Female	47	51	
Total	100	100	

**Table-II. Gender distribution of control and study groups.**

Dehydration	Control	Study Group	P-Value
Some dehydration	53	61	0.001
Severe dehydration	47	39	
Total	100	100	

**Table-III. Degree of Dehydration in control and study groups.**

Loose Stools/Day	Control	Study Group	P-Value
9	31	41	0.001
8	27	25	
7	11	13	
6	19	11	
5	12	10	
Total	100	100	

**Table-IV. Frequency of loose stools at 24 hours in control and study subjects (n=200).**

Loose Stools/Day	Control	Study Group	P-Value
8	30	29	0.0001
7	26	19	
6	19	13	
5	19	27	
4	6	20	
Total	100	100	

**Table-V. Frequency of loose stools at 48 hours in control and study subjects (n=200).**

Loose Stools/Day	Control	Study Group	P-Value
8	11	5	0.001
7	18	9	
6	17	7	
5	13	8	
4	19	7	
3	12	23	
≤ 2	10	41	
Total	100	100	

**Table-VI. Frequency of loose stools at 7<sup>th</sup> day in control and study subjects (n=200).**

**DISCUSSION**

The present case control study evaluated the efficacy of zinc as adjuvant therapy in children with acute diarrhea. We report improvement in frequency of loose stool and stool volume and duration of diarrhea. Mean ± SD age in control and study group was noted as 9.1± 5.43 years and 9.5±6.02 years respectively (P=0.053). Cross tabulation shows male were noted as 53 vs. 47 and female as 49 vs. 51 in control and study group respectively (P=0.051). These findings are in agreement with previous studies.<sup>11-17</sup> In present study, 89% of children of study group were discharged on 3<sup>rd</sup> day of hospitalization compared to only 45% from control group. Zinc treated study group showed significant decrease in frequency of loose stools, early recovery and discharge and lesser hospital stay duration. The findings are in agreement with previous studies.<sup>11-17</sup>

In clinical practice, the zinc in acute and persistent diarrhea is used since 1990s. Since then many studies<sup>6,8-10</sup> were conducted worldwide to evaluate its efficacy in acute diarrheal disease. All of these studies<sup>8-17</sup> reported significant efficacies of zinc therapy in terms of decrease in frequency of loose stool and stool volume and lesser duration of hospital stay. The present study is in agreement with above studies. The findings of present study are also supported by recent studies from Pakistan.<sup>18,19</sup> A recent study<sup>18</sup> from Pakistan reported zinc therapy reduced stool frequency in 62% cases compared to 26% reduction in controls. The findings are highly consistent with present observations. They further added that the zinc group hospital stay was lesser compared

to control. They concluded that the oral zinc supplementation decreases frequency of acute diarrhea, stool volume and total duration of diarrhea.<sup>18</sup> Ahmed I et al<sup>19</sup> (2017) conducted study with 72 cases and 72 control. They reported the oral zinc supplementation decreased frequency of acute diarrhea and stool volume within 24 hours. Also the duration of diarrhea and hospital stay was decreased by zinc supplementation.<sup>19</sup>

The findings of Ahmed I et al<sup>19</sup> are consistent with the present study. In present study, decrease in frequency of stool and stool volume was noted within 24 hours in the zinc group compared to the control. Kurane et al<sup>20</sup> (2019) reported significant decrease in frequency and volume of stool. Duration of hospital stay was 2 days lesser in zinc group compared to control. These findings are in agreement with present study. We noted 89% discharge on 3<sup>rd</sup> day of hospitalization compared to only 45% from control group. However, Negi R et al<sup>21</sup> reported controversial findings of no efficacy of zinc as adjuvant therapy in childhood acute diarrhea. They used 40 mg zinc dose and reported no shortening of duration of diarrhea and stool frequency and volume. The findings are controversial and inconsistent to present and previous studies.<sup>11-17</sup> Zinc efficacy has been proven in animals.<sup>22</sup>

Hoque et al<sup>22</sup> reported that the zinc decreases the volume of stool through inhibition cAMP induced-Cl<sup>-</sup> dependent fluid secretion from enterocytes. K<sup>+</sup> channels in basolateral membrane of enterocytes are inhibited through cAMP induced changes. In the present study, stool frequency and volume were reduced significantly in study group compared to the control group. The strength of study lies in its inclusion and exclusion criteria and prospective study design. However, the limitation of present study includes; first- small sample size, second- children of specific ethnicity and race, third- randomization was not done. As the present study was a hospital based observation study; the findings cannot be generalized to other settings and other racial and ethnical groups.

## CONCLUSION

The present study reports oral zinc as adjuvant

therapy in acute diarrhea was effective in decreasing the frequency of loose stools and volume, early recovery and discharge and lesser duration of hospital stay in children.

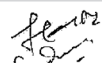
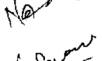
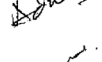
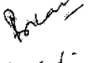

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## REFERENCES

1. Aggarwal R, Sentz J, Miller MA. **Role of zinc administration in prevention of childhood diarrhea and respiratory illnesses: A metaanalysis.** *Pediatrics* 2007; 119:1120–30.
2. Somji SS, Dhingra P, Dhingra U, Dutta A, Devi P, Kumar J, et al. **Effect of dose reduction of supplemental zinc for childhood diarrhea: study protocol for a double masked, randomised controlled trial in India and Tanzania.** *BMJ Paed Open* 2019; 3:e000460.
3. Haider BA, Bhutta ZA. **The effect of therapeutic zinc supplementation among young children with selected infections: A review of the evidence.** *Food Nutr Bull* 2009; 30:S41–59.
4. Patel A, Mamtani M, Dibley MJ. **Therapeutic value of zinc supplementation in acute and persistent diarrhea: A systematic review.** *PLoS One* 2010; 5:e10386.
5. Lazzarini M, Wanzira H. **Oral zinc for treating diarrhoea in children.** *Cochrane Database Syst Rev* 2016; 20:CD005436.
6. Sazawal S, Black R, Bhan M, Bhandari N, Sinha A and Jalla S; **Zinc supplementation in young children with acute diarrhea in India.** *N Engl J Med* 1995(333):839-44.
7. Lazzarini M, Wanzira H. **Oral zinc for treating diarrhea in children.** *Cochrane Database of Systematic Reviews* 2016.
8. Nazarullah R, Pillai S.K, Nair PMC. **Efficacy and effectiveness of zinc therapy in the treatment of acute diarrhea among children.** *J Evol Med Dent Sci* 2018; 4(10):6994-7003,
9. Lukacik M, Thomas R, Aranda J; **A meta-analysis of the effects of oral zinc in the treatment of acute and persistent diarrhoea;** *Pediatr* 2008 February;121(2);23-6.
10. Lamberti M, Fischer Walker C, Chan k, Jian W, and Black R; **Oral zinc supplementation for the treatment of acute diarrhea in children: A systematic review and meta-analysis.** *Nutrients* 2013; 5(11):4715-40.

11. Abbas J, Pandey DC, Verma A, Kumar V. **Management of acute diarrhea in children: Is the treatment guidelines is really implemented?** Int J Res Med Sci. 2018; 6(2):539-44.
12. Bhan MK, Bhandari N, Saksena M, Strand T, Kumar GT. **Efficacy of zinc-fortified oral rehydration solution in 6- to 35-month-old children with acute diarrhea.** J Trop Pediatr 2010; 141(5):677-82.
13. Patel AB, Dhande LA, Rawat MS. **Economic evaluation of zinc and copper use in treating acute diarrhea in children.** Cost Eff Resour Alloc 2003; 1(1):7-11.
14. Al-Sonboli N, Gurgel RQ, Shenkin A, Hart CA, Cuevas LE. **Zinc supplementation in Brazilian children with acute diarrhoea.** Ann Trop Paediatr 2003; 23(1): 3-8.
15. Bhatnagar S, Bahl R, Sharma PK, Kumar GT, Saxena SK, Bhan MK. **Zinc with oral rehydration therapy reduces stool output and duration of diarrhea in hospitalized children: A randomized controlled trial.** J Pediatr Gastroenterol Nutr 2004; 38(1):34-40.
16. Dutta P, Mitra U, Datta A, Niyogis K, Dutta S, Manna B. **Impact of zinc supplementation in malnourished children with acute watery diarrhoea.** J Trop Pediatr 2010; 46(5):259-63.
17. Yadav H, Mittal NK, Mittal SK. **A controlled trial on utility of oral zinc supplementation in acute dehydrating diarrhea in infants.** J Pediatr Gastroenterol Nutr 2008; 7:877-81.
18. Rao MY, Malik B, Raza A. **Role of zinc supplementation in acute diarrhea in pre-school children.** Pak Armed Forces Med J 2017; 67(1):117-21.
19. Ahmed I, Tahir A, Malik FR. **Zinc supplementation in malnourished children under 5 years with acute diarrhea.** J Rawal Med Coll 2012; 16(2):174-176
20. Kurane AB, Kavthekar SO, Bilagi VR, Hittangi PK. **Efficacy of oral zinc as an adjuvant therapy in acute diarrhea in children aged 5-15 years.** Int J Med Paediatr Oncol 2019; 5(1):1-5.
21. Negi R, Dewan P, Shah D, Das S, Bhatnagar S, Gupta P, et al. **Oral zinc supplements are ineffective for treating acute dehydrating diarrhea in 5-12 years old.** Acta Paediatrica 2014; 104(8):1-5.
22. Hoque KM, Rajenndran VM, Binder HJ. **Zinc inhibits cAMP stimulated Cl<sup>-</sup> secretion via basolateral K-channel blockade in rat ileum.** Am J Physiol 2005; 288:G956-63.

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2	Nadeem Noor	Materials handling, interpretation lab investigations, Manuscript write up, Proof reading.	
3	Adnan Bashir	Concept, materials handling, Collection of materials, compilation of results, statistical analysis, manuscript write up, correspondence.	
4	Bilawal Hingorjo	Literature review, Concept, Materials handling, Interpretation lab investigations, Manuscript write up, Proof reading.	
5	Arshad Ali	Concept, Materials handling, Interpretation lab investigations, Manuscript write up, Proof reading.	
6	Urooj Tabassum	Concept, materials handling, Collection of materials, compilation of results, statistical analysis, manuscript writing.	