Original Article

OPEN ACCESS

Effectiveness of Zinc Supplementation in Tablets versus Suspension Form in Acute of Diarrhea

Imtiaz Ali Channar[1], Marium Umrani[2], Farina Usman[3], Om Parkash[4], Saqib Raza[5], Kausar Keerio[6]

[1]Consultant pediatrician, Pediatric department LUMHS Jamshoro
[2]WMO, Pediatric department LUH Jamshoro, [3]Senior registrar, BMC for Boys /LUMHS Jamshoro
[4]Senior registrar, Liaquat institute of medical and health sciences LUMHS Thatta, Sindh, Pakistan
[3]Consultant Pediatrician, health department Government of Sindh
[6]Senior registrar, Pediatric department, LUMHS Jamshoro

Author`s Contribution

[1,2]Substantial contributions to the conception or design of the work; or the acquisition, [4,6]Active participation in active methodology, [2,3]analysis, or interpretation of data for the work, [5]Drafting the work or revising it critically for important intellectual content

Funding Source: None
Conflict of Interest: None

Received: May 16, 2024
Accepted: Nov29, 2024

Address of Correspondent
Imtiaz Ali Channar
Consultant pediatrician, Peads department LUMHS Jamshoro
drimtiazalichannar@gmail.com

ABSTRACT

Objective: To evaluate the effectiveness of zinc supplementation in the management of acute diarrhea among children more than six months of age, with a specific focus on its administration in tablet versus suspension form.

Methods: A cross-sectional comparative study was carried out in the department of Pediatrics, Liaquat University of Medical and Health Sciences Jamshoro/Hyderabad. Children of either gender, aged 5 months to 59 months coming with presentation of acute diarrhea/ recurrent episodes of diarrhea were included. Total 100 children of acute diarrhea were enrolled in this study and they were equally divided into two groups. All patients were treated according to current IMCI guideline for acute diarrhea. The children in group A were treated with zinc supplement in tablet form whereas those children in group B were treated with zinc supplement in suspension form 14 days. Children in both groups were assessed for duration and frequency of acute diarrhea. All the children were assessed on daily basis to determine the stool frequency and duration of acute diarrhea. All the data was entered and analyze by version 26.

Results: The majority (54%) of children were aged 6 to 12 months. Zinc supplementation significantly reduced stool frequency in children with acute diarrhea over a 5-day period. On day 1, the overall mean stool frequency was 5.6 ± 2.51, with Group A (tablet) at 5.2 ± 2.22 and Group B (suspension) at 6.0 ± 2.72. By day 2, the mean stool frequency decreased to 2.7 ± 1.63 (Group A: 2.6 ± 1.5; Group B: 2.9 ± 1.74). On day 3, the frequency further declined to 1.7 ± 0.94 (Group A: 1.8 ± 0.85; Group B: 1.7 ± 1.03). A statistically significant reduction in stool frequency was observed from day 1 to day 5 (p = 0.05), with stool frequency also decreasing as the children's age increased.

Conclusion: Zinc supplementation in tablet and suspension form is equally effective reducing frequency and severity of acute watery diarrhea in children.

Keywords: Acute diarrhea, zinc supplementation, stool frequency, duration of diarrhea.

Cite this article as: Channar IA, Umrani M, Usman F, Parkash O, Raza S, Keerio K. Effectiveness of Zinc Supplementation in Tablets versus Suspension Form in Acute of Diarrhea. Ann Pak Inst Med Sci. 2024; 21(1):71-75. doi. 10.48036/apims.v20i2.1258.

Introduction

Globally, diarrhea ranks as the second most common cause of death among children under the age of five.[1] The majority of diarrheal-related deaths occur in low-income regions, where limited access to clean water, sanitation, and healthcare services exacerbates the burden of the disease.[1] It is defined as the sudden onset of 3 or more frequent, loose, or watery stools per day lasting for less than 14 days may be caused by infectious agents, including bacterial, viral, or parasitic pathogens, or noninfectious factors, such as medication adverse effects or food intolerances.[2,3] The commonest pathogens including Rotavirus, Escherichia coli, and Salmonella;

transmission often occurs through contaminated water, food, or the direct contact of person to person.[4] Although most cases of diarrhea resolve on their own, severe diarrhea can result in dehydration, electrolyte imbalances, and potentially fatal complications if not treated immediately.

In accordance to the estimates of WHO, diarrheal diseases were responsible for approximately 444,000 deaths among children under five years old globally in 2021, accounting for 9% of all deaths in this age group.[5,6] The burden of diarrheal mortality is disproportionately high in low- and middle-income countries, account for nearly 90% of global childhood diarrheal deaths.[5] These regions continue to face significant challenges in healthcare access, sanitation, and disease prevention, making diarrheal disease a persistent public health concern.[5,7] The significance of zinc in human nutrition has grown considerably, as it is a crucial micronutrient essential for overall health, particularly in children.[8,9] Zinc plays a vital role in immune function, growth, and wound healing, making it especially important in pediatric health and disease management. Several studies have established a strong correlation between zinc levels and diarrheal disease, indicating that zinc deficiency may contribute to increased susceptibility and severity of diarrhea. However the Zinc therapy plays a crucial role in managing diarrheal diseases by promoting multiple physiological benefits. It enhances the absorption of water and electrolytes from the intestines, aiding in better hydration and faster recovery. Additionally, zinc stimulates epithelial regeneration, helping to restore the integrity of the intestinal lining. It also boosts intestinal enzyme activity, which supports digestive function, and strengthens the immune response, enabling the body to combat infections more effectively. These combined effects contribute to faster resolution of diarrhea and improved overall gastrointestinal health.[8,10]

However, there is still clinical interest considering the efficacy, compliance, and treatment outcomes between the various formulations the ease of swallowing tablets versus suspensions. Recent comparative studies suggest that dispersible zinc tablets could be superior to the suspension forms in reducing the duration and severity of diarrhea. Another study performed in Pakistan noticed that out of 280 children treated with tablets, 72% showed improvement in stool frequency by day 3 versus 43% in the suspension group leading to a conclusion that bioavailability and therefore superior effectiveness lies with the tablet form of zinc.[12]

On the other hand, another study in an emergency setting reported the improved observations and outcomes in group of administrated by the suspension form, possibly due to easy administration in the children.[13] Although both formulations are effective in decreasing the duration of diarrhea and are associated with improved recovery rates, the choice between the two may depend on the age of the patient and access to health care. However due to the above controversial finings and inadequate more data this study has been done to assess the effectiveness of zinc supplementation in the management of acute diarrhea among children with more than 6 months of age, with a specific focus on its administration in the form of tablet versus suspension.

Methodology

This cross-sectional comparative study was carried out in the department of Paediatrics, Unit I, Liaquat University of Medical and Health Sciences Jamshoro/Hyderabad, during six months from April 2020 to September 2020. All the children aged 6 months to 59 months presented with presentation of acute diarrhea of either gender were included. Additionally, some retrospective patient data was also incorporated. Children with parental diarrhea, diarrhea with sepsis, children with severe dehydration needed IV rehydration, zinc supplementation history in the past 2 weeks, children with severe malnutrition or immunodeficiency disorders and caretaker were not willing to take a part of study were excluded. After taking informed consent and explanation of study purpose, total 100 children of acute diarrhea were enrolled in this study and they were randomly assigned into two groups. 50 children in group A (Tablet) dissolved in a small amount of water before administration to ensure proper dosage and ease of consumption, while 50 children in group B (Suspension), which was administered directly in liquid form according to standard dosage guidelines. Both groups were also provided with oral rehydration therapy and symptomatic treatment, as recommended by the World Health Organization guidelines. The primary outcome of the study was the duration of diarrhea, measured in days, from the initiation of zinc supplementation until resolution. Secondary outcomes included the daily frequency of stools, the need for hospitalization, caregiver-reported adherence and acceptability of the zinc formulation, and the incidence of vomiting or other side effects related to zinc supplementation. The Data was entered and analyzed in statistical program SPSS version 26.0.

Results

The study included the 100 children, evenly divided between Group A (zinc tablets) and Group B (zinc suspension). Most of the cases (54.0%) were aged 6 to 12 months, followed by 40.0% in the 13 to 36 months group and 6.0% in the 37 to 59 months group, with no significant difference between groups (p=0.854). In terms of gender, 56.0% were male and 44.0% were female, with a similar distribution across groups (p=0.315). Table 1

Table 1: Age and gender distribution in both (n=100)

Variables	Zinc supplementation		Total	P-value
	Group A n=50	Group B n=50		
Age groups				
6 to 12 months	25 (50.0%)	29 (58.0%)	54 (54.0%)	0.854
13 to 36 months	21 (42.0%)	19 (38.0%)	40 (40.0%)	
>36 months	4 (8.0%)	2 (4.0%)	6 (6.0%)	
Gender				
Male	31 (62.0%)	25 (50.0%)	56 (56.0%)	0.315
Female	19 (38.0%)	25 (50.0%)	44 (44.0%)	

The average diarrheal stools per day were recorded over five days for both Groups A. On Day 1, the average number of episodes was 5.2 ± 2.22 in Group A and 6.0 ± 2.72 in Group B, with no significant difference (p=0.096). By Day 2, stool frequency decreased to 2.6 ± 1.52 in Group A and 2.9 ± 1.74 in Group B (p=0.364). On Day 3, Group A had 1.8 ± 0.85 episodes, while Group B had 1.7 ± 1.03, showing a statistically significant difference (p=0.022), suggesting a slightly faster reduction in diarrhea in Group A. By Day 4 and Day 5, stool frequency further declined in both groups, with no significant difference between them (p=0.685 and p=0.781, respectively). Table.2

Table 2: Frequency of stools in days among both groups (n=100)

Mean episodes of diarrhea /per day	Zinc supplementations		Total	P-value
	Group A n=50	Group B n=50		
Day 1	5.2.±2.22	6.0±2.72	5.6±2.51	0.096
Day 2	2.6±1.52	2.9±1.74	2.7±1.63	0.364
Day 3	1.8±0.85	1.7±1.03	1.7±0.94	0.022*
Day 4	1.4±0.51	1.5±1.01	1.5±0.52	0.685
Day 5	1.1±0.01	1.0±0.91	1.2±0.12	0.781

Among all of the participants, 50.0% had 1 to 3 stools per day, particularly 54.0% in Group A and 46.0% in Group B. A slightly higher proportion of patients in Group B (48.0%) had 4 to 6 stools per day, compared to 40.0% in Group A. The 7 to 9 stools per day category had an equal distribution in both groups (6.0% each), and no participants experienced more than 9 stools per day. The p-value (0.0973) indicates that the difference in stool frequency between the two groups was not statistically significant. **Table 3**

Table 3: Frequency of stools per day in both groups (n=100)

Frequency of stool per day (in groups)	Zinc supplementations		Total	p-value
	Group A n=50	Group B n=50		
1 to 3 times	27 (54.0%)	23 (46.0%)	50 (50.0%)	0.0973
4 to 6 times	20 (40.0%)	24 (48.0%)	44 (44.0%)	
7 to 9 times	3 (6.0%)	3 (6.0%)	6 (6.0%)	
> 9 times	0	0	0	

The average length of hospital stay was 2.21 ± 0.8 days in Group A (zinc tablets) and 2.42 ± 0.7 days in Group B (zinc suspension), with a total mean hospital stay of 2.5 ± 0.88 days across all participants. The p-value (0.71) indicates that there was no statistically significant difference between the two groups in terms of hospital stay duration. **Table 4**

Table 4: Hospital stay (in days) in both groups (n=100)

	Zinc supplementation		Total	P-value
	Group A n=50	Group B n=50		
Hospital stay (in days)	2.21 ± 0.8	2.42 ± 0.7	2.5 ± 0.88	0.71*

Discussion

In developing countries, acute diarrhea in children is a growing public health concern, leading to high morbidity and mortality rates. The extensive inappropriate use of antibiotics for the therapy of diarrhea in children has contributed to the increasing burden of antimicrobial resistance, rendering therapies less effective and threatening long-term control of the disease. This triggered a response and, so, probiotics and zinc supplementation surfaced as promising evidence-based solutions that not only maintain gut health but also enhance immunity and improve post infection recovery. However, this study was conducted on **100 children with acute diarrhea** to evaluate the **effectiveness of zinc**

supplementation in management, with a particular focus on its **administration in tablet versus suspension form**. The **overall mean age** of the children was **4.2 ± 2.22 years in Group A** and **5.0 ± 2.72 years in Group B**, with a **slight predominance of male children.** Our findings were consistent with the studies by Mahyar A et al[14] and Abdulah DM et al[15], where the mean age of children was 1.79 years in the probiotic group and 1.69 years in the probiotic plus zinc group P = 0.645, with a predominance of male children. However, the minor variations in mean age and gender ratio across studies may be attributed to differences in study populations, sample sizes, or regional demographic factors.

In this study based on the effectiveness of zinc supplement as well as the comparison between zinc supplementation in the forms of tablet versus suspension in the treatment of acute diarrhea in children show that there is a very small, but statistically significant, advantage for zinc tablets over suspension in reducing stool frequency on Day 3 (p=0.022), while the differences are not statistically significant on other days (p= >0.05). These findings were in accordance with prior studies wherein zinc tablets were stated to expedite the diarrhea resolution process by Urooj et al[12] and in contrast to our findings, a study done by the Habib et al[13] in an emergency setting found that zinc suspension improved compliance and outcomes among selected populations. In the study by Larson CP et al[16] a 20 mg dispersible zinc sulphate tablet was used to assess the efficacy of the therapeutic agent in acute childhood diarrhea, and was found to carry a 14% increase risk of vomiting, which was not significantly related to any previous episodes of vomiting at 4.2% of the ZS and 2.6% of the placebo groups who had experienced a previous episode of vomiting, and regurgitation at 5.2% for dose-related or persistent vomiting, both of which occurred in the form of transient side effects occurring within a few minutes of administration. However, inconsistently a systematic review inconclusively reported that when zinc supplementation, given in pill or suspension form, was included, there was no benefit in limiting the duration of acute diarrhea in children from high income countries, with no statistically significant reduction in the incidence of diarrhea by 7 days of treatment.[17]

Additionally in this study there was no significant different in the hospital stay duration (2.21 ± 0.8 days, tablets; 2.42 ± 0.7 days, suspension; P=0.71). This is in contrast to the findings of Habib et al[13] reported a somewhat faster recovery with the suspension formulation in children under emergency conditions. Compliance, a powerful determinant of outcomes, can be affected by the need to use a liquid rather than a tablet formulation, especially in younger children. Zinc tablets have been shown to be better accepted by slightly older children.[13] Consistently Nuzhat S et al[18] conducted a study to evaluate the tolerability and adherence of an improvised zinc tablet formulation among children under five years old with acute diarrhea. Since zinc has an inherently unpleasant taste, children frequently experience nausea or vomiting, affecting compliance. Their findings revealed that the modified formulation with improved taste was well tolerated, with caregivers expressing a high willingness to use it in the future, highlighting its acceptability and better adherence.[18] Additionally in the study by Gregorio GV et al[19] observed that the the combination of zinc and oral rehydration solution (ORS) was found to lower both the overall cost and duration of acute diarrhea treatment. The incremental cost-effectiveness ratio (ICER) indicates that zinc supplementation is a cost-effective intervention.[19] Although the overall efficacy of zinc in reducing the duration and frequency of diarrhea is well established, our findings suggest a non-significant trend favoring the tablet form, particularly in the early phase of diarrhea resolution. However, due to variability in patient preference and adherence, either formulation may be suitable for managing acute diarrhea. Due to certain study limitations, further large-scale studies are recommended to identify specific subgroups of children (based on age, acceptability and nutritional status etc.) that may benefit more from one formulation over the other.

Conclusion

Findings revealed that the Zinc supplementation in both tablet and suspension forms effectively reduces the duration and frequency of acute diarrhea in children, reinforcing its role as a key intervention alongside oral rehydration therapy. Both formulations demonstrated comparable efficacy, suggesting that either form can be used based on availability and caregiver preference. While zinc supplementation has proven beneficial in lowering disease severity, further large-scale studies are needed to assess its long-term impact, cost-effectiveness, and adherence in different populations particularly in low-resource settings

References

1. Hartman RM, Cohen AL, Antoni S, Mwenda J, Weldegebriel G, Biey J, Shaba K, De Oliveira L, Rey G, Ortiz C, Tereza M. Risk factors for mortality among children younger than age 5 years with severe diarrhea in low-and middle-income countries: findings from the World Health Organization-coordinated Global Rotavirus and Pediatric Diarrhea Surveillance Networks. Clinical Infectious Diseases. 2023 Feb 1;76(3):e1047-53.
2. Liang D, Wang L, Liu S, Li S, Zhou X, Xiao Y, Zhong P, Chen Y, Wang C, Xu S, Su J. Global Incidence of Diarrheal Diseases—An Update Using an Interpretable Predictive Model Based on XGBoost and SHAP: A Systematic Analysis. Nutrients. 2024 Sep 23;16(18):3217.
3. Thompson R, Patel S, Gupta V. Advances in acute diarrhea management: Epidemiology, pathophysiology, and emerging treatments. J Clin Gastroenterol. 2024;58(2):123-135
4. Khan M, Raza T, Alam S. Gastrointestinal infections: A comprehensive review on acute diarrheal pathogens and control measures. Int J Infect Dis. 2023;112:89-102
5. Ali AA, Naqvi SK, Hasnain Z, Zubairi MB, Sharif A, Salam RA, Soofi S, Ariff S, Nisar YB, Das JK. Zinc supplementation for acute and persistent watery diarrhoea in children: A systematic review and meta-analysis. Journal of Global Health. 2024 Dec 6;14:04212.
6. Unite Nations Children's Fund. Diarrhoea. 2024. Available: https://data.unicef.org/topic/child-health/diarrhoeal-disease/. Accessed: 19 November 2024
7. Baral R, Nonvignon J, Debellut F, Agyemang SA, Clark A, Pecenka C.Cost of illness for childhood diarrhea in low- and middle-income countries: a systematic review of evidence and modelled estimates. BMC Public Health. 2020;20:619
8. Ahmadipour S, Mohsenzadeh A, Alimadadi H, Salehnia M, Fallahi A. Treating viral diarrhea in children by probiotic and zinc supplements. Pediatric Gastroenterology, Hepatology & Nutrition. 2019 Mar 11;22(2):162.
9. Mitra H, Shokoufeh A, Homa B, Azam M. The effect of oral zinc sulfate on hepatitis b vaccine immunogenicity in premature infants. Life Sci J. 2012;9:3359–3361
10. Berni Canani R, Buccigrossi V, Passariello A. Mechanisms of action of zinc in acute diarrhea. Curr Opin Gastroenterol. 2011;27:8–12
11. Urooj S, Memon HU, Memon Y, Ali BS. Comparison of the effectiveness of zinc supplementation in tablet form with that of the suspension form in the treatment of acute diarrhoea. J Pak Med Assoc. 2017;67(2):214-218
12. Habib MA, Soofi SB, Bhutta ZA. Effect of zinc in tablet and suspension formulations in the treatment of acute diarrhoea among young children in an emergency setting of an earthquake-affected region of Pakistan. J Coll Physicians Surg Pak. 2010;20(12):837-841
13. Mahyar A, Ayazi P, Chegini V, Sahmani M, Oveisi S, Esmaeily S. Serum zinc concentrations in children with acute bloody and watery diarrhoea. Sultan Qaboos University Medical Journal. 2015 Nov 23;15(4):e512.
14. Abdulah DM, Sulaiman SJ, Ahmed ZW. Effect of probiotics plus zinc supplementation on clinical outcomes of infants and children with acute infectious diarrhea: A randomized controlled trial. Clinical and Experimental Pediatrics. 2024 Feb 19;67(4):203.
15. Larson CP, Hoque AM, Larson CP, Khan AM, Saha UR. Initiation of zinc treatment for acute childhood diarrhoea and risk for vomiting or regurgitation: a randomized, double-blind, placebo-controlled trial. Journal of health, Population and Nutrition. 2005 Dec 1:311-9.
16. Revoredo T, Alves LV, Victor DR, Alves JG. Zinc Supplementation in the management of acute diarrhea in high-income countries–A systematic review and meta-analysis. medRxiv. 2024 Jul 9:2024-07.
17. Nuzhat S, Ahmed T, Alam J, Billal SM, Khan AI, Hossain MI. New formulation zinc sulphate acceptability and adherence in children with acute diarrhoea: a prospective, open-label, interventional study in Bangladesh. Journal of paediatrics and child health. 2022 Jul;58(7):1215-20.
18. Gregorio GV, Dans LF, Cordero CP, Panelo CA. Zinc supplementation reduced cost and duration of acute diarrhea in children. Journal of clinical epidemiology. 2007 Jun 1;60(6):560-6.