Original Article

Comparison of Zinc Supplementation versus Placebo in Addition to Standard Therapy for Management of Children with Pneumonia: A Randomized Controlled Trial

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Abstract

Objective: To compare the mean hospital stay with zinc supplementation vs placebo in standard therapy for management of pneumonia in children. In children with pneumonia, zinc supplements have been shown to enhance the remission of clinical symptoms.

Study Design: Randomized controlled trial

Duration and place of study: Pediatric department Nishtar Hospital Multan From Jan 2019 to Feb 2020.

Methodology: Two hundred and forty children were enrolled and divided into two groups. In group I, children were given 20mg per 5ml solution of zinc supplementation with standard therapy for pneumonia, while in group II, children were given 20 mg of placebo along with standard therapy for pneumonia. The patients were discharged, and the resolution of symptoms and total stay in the hospital were noted. Data was collected, and statistical analysis was performed using SPSS-20.

Results: The mean age of patients was 4.42±2.71years, and there were 85 (70.8%) males and 35 (29.2%) females in group 1, while the mean age of patients was 4.71±3.04 years, and there were 82 (68.3%) males and 38 (31.7%) females in group II. The mean duration of hospital stay in the zinc group was 100.14±16.83 hours, and in the placebo group was 123.34±15.38hours. The difference was highly significant (p <0.05).

Conclusion: Thus, zinc supplementation is beneficial in the early resolution of symptoms of pneumonia, and there is a reduction in the hospital stay of children.

Keywords: Pneumonia, pediatric population, zinc supplement, placebo, standard therapy, hospital stay

Introduction

Pneumonia in pediatric patients is still the leading cause of mortality, accounting for around 20 percent of the 10 million yearly fatalities worldwide.[1] In developing nations, pneumonia kills about 740,180 children below the age of 5 every year and accounts for 14% of all fatalities in this age bracket.[2] About 158 million cases of pneumonia develop all around the world; 124 million of them belong to developing countries, and about 25% of them are less than five years old.[3] The yearly incidence rates of pneumonia were 4 per 100 in the preschool age group, 2 per 100 in the 5-9-year-old age group, and 1 per 100 in the 9-15-year-old age group, according to a large community-based research by Denny and Clyde.[4] Antibiotics are given on an "empirical" basis, and other therapies (such as oxygen, IV fluids, and nebulization) are used as needed. Zinc supplementation used for adjunctive therapy in the management of pneumonia is debated. Zinc adjunctive treatment decreases the case mortality rate in very ill children with pneumonia and respiratory-related disorders.[5] Zinc is a vital mineral for proper development and immune system function. Inadequate zinc levels may lead to stunted development, loss of appetite, altered behavior, and weakened resistance to infections.[6]

Zinc supplementation of normal therapy for pneumonia is helpful in shortening the duration of treatment. Additionally, it is beneficial in shortening the time spent dealing with sickness.[7] Zinc supplementation is often advised in addition to standard antibiotic therapy for these young patients. In addition, it helps mitigate the harmful effects of using numerous antibiotic treatments simultaneously.[8] Zinc supplementation has been shown to shorten the duration of hospitalization for patients with severe pneumonia, and it has also been shown to reduce the severity of the disease.[9] Much research has been performed to determine whether zinc is effective in treating severe pneumonia, but the findings have been contradictory.[10,11] Controversial results have been found in the literature, and not much work has been done on this subject. No local evidence has also been found in the literature, and that is why zinc is not given in addition to standard treatment. This study was conducted to evaluate whether or not the addition of zinc to standard therapy for pneumonia is beneficial. So that better strategies can be planned and implemented to improve patients' conditions, lessen hospital stays, and decrease the burden on hospitals and physicians. The objective of our study was to evaluate the mean hospital stay with zinc supplementation versus placebo in standard therapy for management of children with pneumonia.

Methodology

This was a randomized controlled trial with a double-blind study (patient and outcome assessor). It was conducted at the Paediatric department, Nishtar Hospital Hospital Multan, from January 2019 to February 2020. A total sample size of 240 cases was taken with the WHO sample size calculator, with a 95% confidence level, 80% and taking the magnitude of mean hospital stay, i.e., 167.3±47.19 hours with zinc and 188.19±65.92 hours with placebo for management of children with pneumonia.[12]

Inclusion Criteria: Children of age 1-10 years of either gender presented with pneumonia were enrolled. Pneumonia was defined as the presence of rapid respiratory rate (> 50 breaths per minute), fever (temperature >100 F, oxygen saturation<90%, and inflammation of lungs on x-ray.

Exclusion Criteria: Children admitted with recurrent pneumonia within one month of previous treatment, Malnourished children (< -2SD based on weight for height Z scoring on WHO classification), already taking zinc supplementation before admission or anemia (Hb<10g/dl) were excluded.

After Informed consent, the parents were explained the purpose of the research, and demographic information (age, gender, weight, and duration of symptoms) was obtained. The patients were divided into two groups randomly by using sealed envelopes. A non-probability consecutive sampling technique was used. In group I, children were given 20mg per 5ml solution of zinc supplementation for seven days with standard therapy for pneumonia. In group II, children were given 20mg of placebo (saline solution without zinc supplementation) along with standard therapy for pneumonia. Standard treatment includes a combination of Ampicillin (50- 100mg/kg/day IV every 8 hours) and Amikacin (15-22.5mg/kg/day IV twice daily). Then, all children were followed up in the pediatric ward till discharge. Children were discharged on resolution of symptoms, and total stay in hospital was noted (as per operational definition). The hospital stay was assessed in terms of hours from the time of admission till the discharge of the child. The child was discharged on the basis of resolution of symptoms, i.e., respiratory rate<50 breaths per minute, temperature <100oF, and oxygen saturation>90%. The information was noted in the proforma (attached).

Data analysis was done using SPSS-20. Mean and SD were calculated for the age, weight of the child, duration of symptoms, and hospital stay. Frequency and percentage were calculated for gender. An Independent sample t-test was applied to compare the mean hospital stay in both groups, taking p-value ≤0.05 as significant. Post-stratification, an independent sample t-test was applied. P value ≤0.05 was taken as significant.

Results

In group 1, the mean age of patients was 4.42±2.71years, there were 85 (70.8%) males and 35 (29.2%) females, the mean weight of patients was 17.53±6.04kg, and the mean duration of symptoms was 9.65±3.48days. In group 2, the mean age of patients was 4.71±3.04 years with 82 (68.3%) males and 38 (31.7%) females, the mean weight of patients was 17.63±6.85kg, and the mean duration of symptoms was 9.39±3.45days. Table 1. In group 1, the mean duration of hospital stay was 100.14±16.83hours. In group 2, the mean duration of hospital stay was 123.34±15.38hours. The difference was highly significant (p<0.05). Table 2.

In patients aged 1-5 years, the mean duration of hospital stay was 99.08±16.73hours with zinc and 123.87±14.94 hours with placebo. The difference was highly significant (p<0.05). In patients aged 6-10 years, the mean duration of hospital stay was 102.20±17.03hours with zinc and 122.43±16.25 hours with placebo. The difference was highly significant (p<0.05). Data was stratified based on the gender of patients. In male patients, the mean duration of hospital stay was 100.42±16.58 hours with zinc and 122.78±16.05 hours with placebo. The difference was highly significant (p<0.05). In female patients, the mean duration of hospital stay was 99.46±17.64 hours with zinc and 124.55±13.98 hours with placebo. The difference was highly significant (p<0.05). Data was stratified based on the weight of patients. In patients weighing 8-15kg, the mean duration of hospital stay was 96.16±15.87 hours with zinc and 122.50±14.77 hours with placebo (p<0.05). In patients weighing 16-32kg, the mean duration of hospital stay was 102.89±17.03 hours with zinc and 124.03±15.94 hours with placebo (p<0.05). Data was stratified for the duration of symptoms. In patients having symptoms from ≤ 7 days, the mean duration of hospital stay was 99.26±16.53 hours with zinc and 124.44±15.19 hours with placebo (p<0.05). Table 3

Table 1. Demographic characteristics of children

	GROUP	
	I Zinc	II Placebo
N	120	120
Age (years)	4.42 ± 2.71	4.71 ± 3.04
Male	85 (70.8%)	82 (68.3%)
Female	35 (29.2%)	38 (31.7%)
Weight (kg)	17.53 ± 6.04	17.63 ± 6.85
Duration (days)	9.65 ± 3.48	9.39 ± 3.45

Table 2. Comparison of length of hospital stay

		GROUP	
		Zinc (n=120)	Placebo (n=120)
Hospital stay (hours)	Mean	100.14	123.34
	SD	16.83	15.38
	Minimum	72	96
	Maximum	130	150
Duration (days)		9.65 ± 3.48	9.39 ± 3.45

Independent Samples Test = 11.147 p-value = 0.0001
CI 95%

Table 3. Hospital stay in both groups for effect modifiers

Age (years)	Hospital stay		p-value
	Zinc	Placebo	
1-5	79	76	123.34
	99.08±16.73	123.87±14.94	15.38
6-10	41	44	96
	102.20±17.03	122.43±16.25	150
Male	85	82	9.39 ± 3.45
	100.42±16.58	122.78±16.05	
Female	35	38	
	99.46±17.64	124.55±13.98	
Weight 8-15 kg	49	54	
	96.16±15.87	122.50±14.77	
Weight 16-32 kg	71	66	
	102.89±17.03	124.03±15.94	
Duration ≤7 days	38	39	
	99.26±16.53	124.44±15.19	
Duration >7 days	82	81	
		122.81±15.54	

Discussion

Zinc supplementation administered with empiric antibiotic treatment has been shown in a recent clinical study in Bangladesh to dramatically reduce the severity of pneumonia and length of hospital stay for pediatric patients with pneumonia.[13] One study showed that the mean hospital stay was 167.30±47.19hours with zinc supplementation and 188.19±65.92hours with placebo in standard therapy for management of pediatric

patients with pneumonia. The difference was insignificant (p=0.0521), which was near to significance.[2] One more study showed that the mean hospital stay was 73.5(49.5-107.5) hours with zinc supplementation and 72(48.0-87.7) hours. The difference was insignificant (p=0.193). Several nations have studied zinc's effectiveness as a complementary treatment for pneumonia. Among 96 Chinese patients aged 1-12 months hospitalized with severe pneumonia, those with low blood zinc levels were allocated to either a therapy group or a control group. While the treatment increased serum zinc levels, it did not affect the duration of hospital stay between the groups.[14] Among 94 hospitalized Tanzanian children aged 6 - 36 months with radiology-confirmed acute pneumonia, zinc supplement with antibiotics resulted in no significant reduction in hospitalization duration.[15]

A 2011 meta-analysis of 3200 pediatric patients aged between 2 and 35 months in Bangladesh, Nepal, and India found that adjunctive zinc supplementation had no effect on clinical recovery from severe or non-severe pneumonia.[16] In 2016, another meta-analysis of 3000 children under five years old was conducted to further evaluate the significance of zinc supplements as an adjunct therapy to antibiotics for the treatment of severe pneumonia.[17]

In another meta-analysis of 1066 pediatric patients from developing countries hospitalized with severe lower respiratory tract infection.[18] When compared to placebo, zinc supplementation did not significantly decrease recovery time, there were no significant differences in mortality, adverse events (vomiting and worsening). Hospitalization length and time to recovery from severe illness (standardized mean difference were not significantly different between groups.

Conclusion:

Our study have shown that hospital stay in adjunctive zinc group was significantly less as compared to placebo group in children with pneumonia. Thus, zinc supplementation is beneficial in the early resolution of symptoms of pneumonia and reduces the hospital stay of children.

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