The Effect of Zinc Supplementation On Resolution Of Symptoms In Pediatric Pneumonia

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Abstract

Objective: To compare the mean duration of resolution of pneumonia in pediatric patients (from 2 months to five years) using zinc as an adjuvant therapy to those receiving only standard treatment of pneumonia.

Methods: It is a randomized control trial that has been carried out at the Department of Pediatrics, Hameed Latif Teaching Hospital, Lahore. The study involved 60 children (30 in each group), within the age bracket of 2 months to 5 years. Informed written consent was obtained from parents. Children were randomly divided by using the lottery method into groups "A" and "B". Group A received zinc supplementation as adjuvant therapy in addition to age-appropriate antimicrobial therapy. Group B received age-appropriate antimicrobial therapy only. The duration of the resolution of pneumonia was recorded from the commencement of therapy until the resolution of symptoms.

Results: The mean age of all the children was 2.75 ± 1.40 years. The mean age of cases in group A was 2.87 ± 1.41 years and the mean age of cases in group B was 2.63 ± 1.40 years. There were 16(53.33%) male cases and 14(46.67%) female cases in group A. In group B there were 18(60%) male and 12(40%) female cases. The mean duration of recovery time in group A was 3.80 ± 0.66 days and the mean duration of recovery in group B was 6.30 ± 0.75 days. The mean duration of recovery time was statistically less in group A as compared to group B, p-value < 0.05.

Conclusion: We conclude that the mean duration of resolution of pneumonia in patients under five years of age was significantly less in the zinc group as an adjuvant therapy when compared with those receiving only standard treatment of pneumonia. Hence, adding zinc can reduce the hospital stay which will surely reduce the related cost while enhancing parents' and physicians' satisfaction.

Keywords: Zinc supplementation, pneumonia, adjuvant therapy

Introduction

Pediatric pneumonia is regarded as an evident culprit of child mortality worldwide in sufferers in the first five years of life. The United Nations Children's Fund (UNICEF) reports that pediatric pneumonia causes the deaths of over 800,000 young children globally each year[1]. For one child death due to pneumonia in a first-world country, over two thousand children succumb to it in lower-middle income countries[1]. According to an estimate about 30% of deaths in the first five years of life are caused by pneumonia in Pakistan. In the year 2000, Pakistan was ranked fourth among the countries in terms of under-five mortality. The total estimate of child mortality under-five years of age was 565,000 [2]. In developing countries 95% of the children who die of pneumonia are also classified as having malnutrition according to the World Health Organization (WHO) criteria for malnutrition[2]. According to the World He-

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alth Organization (WHO) statistics,740180 children under the age of five years lost their lives to pneumonia in the year 2019. This comprises about 14% of age-specific mortality. According to an estimate about 22% of all child deaths in the first five years of life are caused by pneumonia[3]. Zinc is present in essentially all the systems of the human body and is considered an integral part of numerous processes. At the enzymatic level, it is either an essential part of enzyme structure or stimulates various biochemical reactions. Deficiency of zinc is quite prevalent in less privileged areas of the world i.e. lower-middle income countries. Like many other nutrient deficiencies, poverty is the main factor responsible for zinc deficiency. Most of the children in third-world countries are malnourished and have limited access to a balanced diet required for proper growth and function of the body. In contrast to other nutrients, zinc is not stored in the body and needs to be taken in the diet on a routine basis. In addition to poor oral intake, sometimes there are certain elements in diet such as calcium and phytates which hamper the absorption of zinc. Another well-known contributor is frequent gastrointestinal infections which augment the already existing deficiency by increasing zinc losses through stools[4]. Zinc has been studied as having a potential effect in reducing the burden of pneumonia. There are two possible ways of modes of action of zinc in pneumonia. Firstly it has a role in prevention of pneumonia. The other role is in the reduction of disease intensity and duration when given in combination with routine antibiotics in pediatric pneumonia[5]. Zinc acts as an anti-oxidant and stabilizes the cell membranes. It can reduce inflammation by halting the free radical production[6]. Zinc is essential for gene expression, manufacturing of proteins, and multiplication of cells and regeneration of tissues. It is also crucial to boost up immunity and protect against organisms responsible for different infections[7].

Research has proven that taking zinc along with standard treatment not only shortens the duration of disease symptoms but also reduces the overall length of hospital stay in children afflicted by pneumonia[8]. Lassi et.al did an analysis of studies that used prophylactic zinc administration for the prevention of pneumonia. These trials included about five thousand children from South Asia and Africa. The age group of children was between two and 59 months. It was evident that zinc intake not only decreased the occurrence of pneumonia but also reduced the death count in children with very severe disease[9]. A study conducted by Houman et all in Iran was intended to see the impact of augmentation therapy with zinc in pediatric patients with pneumonia who had severe symptoms. Two study groups collectively included 120 children. One group received oral zinc and the other was given a placebo for one week. The report concluded that in pediatric pneumonia, zinc intake leads to swift recovery in under five children having severe disease[10]

Traditional treatments of pneumonia focus only on antibiotics and supportive care. Pneumonia is a deadly disease in early years of life and is responsible for impaired quality of life. Considering the high occurrence of disease and its related complications in children, it is prudent to look for additional therapeutic options. This will help to reduce the disease burden. The study aims to compare the mean duration of resolution of pneumonia in children receiving zinc as an adjuvant therapy to those receiving only standard treatment. It is expected to have a potentially beneficial impact on the management of pneumonia.

Methodology

It is a randomized control trial that has been conducted at the Department of Paediatrics, Hameed Latif Teaching Hospital, Rashid Latif Khan University Medical & Dental College (RLKUMC) Lahore.

The study period was of six months with effect from September 2023 to February 2024.

The study sample comprised sixty children (30 per group) with a confidence interval of 95% and 80% power of test and taking the expected mean duration of the zinc group is 4.34±1.06 and without zinc groups is 5.94±1.20[9]. Cases who were admit-

ted with pneumonia through outpatient and emergency departments were considered for the study. Patients were randomly chosen by using the lottery method of sample collection. Children of either gender between the ages of 2 months and 5 years suffering from pneumonia were enrolled in the study. All the patients were immunized following the recommended schedule of routine early childhood vaccinations according to the Expanded Program of Immunization (EPI). Those who were already taking zinc supplements, had active tuberculosis, measles, asthma, diarrhea, cardiac or chronic pulmonary disease, severe malnutrition as per WHO criteria (weight for height > -3 standard deviation of WHO standard) and documented use of antibiotics 48 hours before admission were excluded from the study.

After getting informed written consent from the parents or guardians, children who fulfilled the inclusion criteria were registered for the study. Demographic data (name, gender, age and address) of all the patients was recorded. Cases were randomly divided by using the lottery method into groups A and B. Group A received zinc supplementation as adjuvant therapy along with routine treatment while Group B received age-appropriate antimicrobial therapy only. The choice of antibiotics was according to the World Health Organization (WHO) age appropriate recommendations of antibiotics for childhood pneumonia[11]. All the children in Group A (zinc group) received oral zinc once daily for 10 days (10mg for infants, 20 mg for older children). Pneumonia was defined as cough and tachypnea with or without breathing difficulty and fever. Breathing difficulty was defined as the presence of a lower chest in drawings, nasal flaring and/or cyanosis[3]. The effect of zinc supplementation was calculated in terms duration of the resolution of symptoms. Duration of resolution of pneumonia was taken as time from initiation of therapy until symptom eradication. Resolution of pneumonia was considered if fever, tachypnea and signs of respiratory distress settled for at least 24 hours after interviewing the mothers and examination of the patient. Bronchiolitis and foreign body aspiration were excluded based on clinical and radiographic findings. All the patients were cal-

called for follow-up after 7 days of discharge from the hospital. The data was documented in a predesigned structured Performa.

Data analysis was done using SPSS version 26. Qualitative variables like gender were recorded as frequency and percentage. Quantitative variables like age, and Duration of recovery were recorded as mean and standard deviation. An independent sample t-test was applied for comparison between variables. A p-value of d" 0.05 was taken as statistically significant. Data was stratified for age, gender and duration of pneumonia. Considering the p-value d"0.05, a post-stratification t-test was applied

Results

In this study, the average age of all cases was 2.75 ± 1.40 years. The mean age of cases in Group A (zinc group) was 2.87 ± 1.41 years and the mean age of patients in Group B (Non-zinc group) was 2.63 ± 1.40 years. Table -1.

We found out that the mean duration of recovery time in group A (zinc group) was 3.80 ± 0.66 days whereas the mean duration of recovery time in group B (non-zinc group) was 6.30 ± 0.75 days. It is inferred that the mean recovery time in group A (zinc group) was significantly less as compared to group B (non-zinc group), with a p-value of less than 0.05. Table -2

Considering the duration of disease, it was observed that in patients who had pneumonia for less than two weeks, the mean duration of recovery time was 4.09 days in group A(zinc group) whereas it was 6.16 days in group B (non-zinc group). It shows that in patients who had pneumonia for less than two weeks, the mean duration of recovery time was statistically less in group A (4.09 ± 0.54 days) as compared to group B (6.16 ± 0.76 days), p-value < 0.05.

In patients who had pneumonia for more than two weeks, the mean duration of recovery time was 3.63 days in group A (zinc group), whereas it was 6.55 days in group B (non-zinc group). This shows that the mean duration of recovery time in patients who had pneumonia for more than two weeks was

statistically less in group A (3.63 ± 0.68 days) as compared to group B (6.55 ± 0.69 days), with p-value < 0.05. Table -3

Table 1. Age related descriptive statistics of patients ingroup A(zinc group) and group B (non zinc group)

Study group	Age(2 months-5 years)			
	Mean	S.D	Minimum	Maximum
Group A A(2months -5years)	2.87	1.41	1.00	5.00
Group B B(2months -5 years)	2.63	1.40	1.00	5.00
Total	2.75	1.40	1.00	5.00

Table 2. Mean duration of the recovery time in group A (zinc group) and group B (non zinc group)

Study group	Duration of recovery time (days)				t-test	pvalue
	Mean	S.D	Minimum	Maximum		
Group A(2 months -5 years)	3.80	0.66	3.00	5.00	-13.670	<0.001
Group B(2 months -5 years)	6.30	0.75	5.00	7.00		
Total	5.05	1.44	3.00	7.00		

Table 3. Stratification with respect to mean duration of recovery time and duration of pneumonia

Duration of symptoms of pneumonia	Study groups	Duration of recovery time (days)			
		Mean	S.D	t-test	p-value
<2 weeks	Group A	4.09	0.54	-7.876	<0.001
	Group B	6.16	0.76		
>2 weeks	Group A	3.63	0.68	-11.223	<0.001
	Group B	6.55	0.69		

Discussion

The prevalence of pediatric pneumonia is quite high. In addition to a notable frequency of occurrence, the disease-related mortality and morbidity is also worthy of due attention. Particularly in children of the developing world, pneumonia is considered an important factor associated with case fatality. It has been found that approximately one-third of deaths in under-five children are caused by pneumonia[12].

In the current study, the mean age of all the cases was 2.75 ± 1.40 years. The mean age of cases in group A (Zinc group) was 2.87 ± 1.41 years and the mean age of patients in group B (non-zinc group) was 2.63 ± 1.40 years. A similar study from Egypt conducted by Dina Mustafa and colleagues identified the patients with pneumonia who had low levels of zinc in their blood. All the children were admitted in the hospital and received zinc therapy. The average age of patients was 12.906±11.23 and the majority of the children were males (56.3%)[13].

In present study, there were 16(53.33%) male cases and 14(46.67%) female cases in group A(zinc group), while in group B (non-zinc group) there were 18(60%) male patients and 12(40%) female cases. These figures are relatable to another similar research in which the gender distribution was 68% males and 32% females in the zinc supplementation group, and 70% males and 30% females in the other group[14].

In the current study, the mean duration of recovery time in group A(zinc group) was 3.80 ± 0.66 days and the mean duration of recovery time in group B (nonzinc) was 6.30 ± 0.75 days. The mean time of recovery was shorter in group A(zinc group) as compared to group B (non-zinc group) , p-value < 0.05. Another study reported similar findings which showed that the mean duration of resolution of pneumonia in the zinc group was 4.34±1.06 days and the mean duration of recovery time in patients with no zinc supplementation was 5.94±1.20 day[9]. A study conducted in Jamshoro, Pakistan reported that zinc therapy in addition to standard treatment of pneumonia results in symptom reduction and short hospital stay. A hundred children participated in the research. All of them were less than five years old and hospitalized for the treatment of pneumonia. It was concluded that there was no notable change in symptoms between the two study groups i.e. zinc and nonzinc groups. On the other hand, the length of hospitalization was much reduced in patients who received zinc than those who did not receive zinc treatment[15].

We found out that the mean duration of recovery time was statistically less in group A(zinc group) as compared to group B (non-zinc group). These results are comparable with another study which quoted that the mean duration of recovery time in zinc group was 4.34 ±1.06 days and the mean duration of recovery time in non zinc group was 5.94±1.20 days. This difference is statistically significant[16]. Our results are in contradiction with a meta-analysis of different randomized control trials comparing the effect of zinc supplementation in children with pneumonia. It was reported that there was no significant difference in the recovery time between zinc and nonzinc groups[17].

We found that in patients who had pneumonia for less than two weeks, the average time to recover from the disease was statistically less in group A (4.09 ± 0.54 days) as compared to group B (6.16 ± 0.76 days), with p-value < 0.05. On the other hand, the mean duration of recovery time in patients who had pneumonia for more than two weeks was statistically less in group A (3.63 ± 0.68 days) as compared to group B (6.55 ± 0.69 days), p-value < 0.05. This shows that patients were benefited from zinc supplementation irrespective of the duration of disease symptoms before getting the therapy. To our knowledge, there are no comparable studies that observed this association.

According to the study by Linlin and Yuanlin, there was no impact of zinc supplementation on treatment failure (RR = 0.97, p= .71). However a considerable reduction in mortality was observed in patients having severe disease who received zinc as an adjunct therapy (RR = 0.43, p = .01). Hence it was inferred that adding zinc to the standard treatment has beneficial effect in terms of reduced mortality and no effect on treatment failure and need to change the antibiotics[18].

A research was performed by Baruah et al to study the response of adjunct zinc therapy on symptoms, length of hospitalization and relapse in pediatric patients with pneumonia. It was observed that in the zinc group there was speedy recovery of pneumonia (p =0.042) which led to a shorter hospi-

tal stay (p =0.035). However, there was no considerable association between zinc fortification and recurrence of disease symptoms (p =0.52). Therefore, including zinc in the treatment of pneumonia can lead to fast recovery and early discharge from the hospital. However, it is not recommended as a preventer therapy[19].

A randomized control trial conducted by Stephen et all studied the correlation between zinc administration and persistence of symptoms of severe pneumonia i.e. poor response to treatment. It was observed that in both groups, the percentage of patients who failed to respond to the treatment was same (14% and 14.1%).There was no significant difference between the two groups concthe total time taken for complete resolution of symptoms (p-value 0.242) . This trial does not support the idea of using zinc in addition to routine antibiotics in the treatment of pneumonia in children[20].

Tie at al observed that zinc supplementation in severe pneumonia had no beneficial effect in under five children[21].

A noteworthy limitation of our study is that we were not able to determine the zinc deficiency status of study groups because the diagnostic tests are inaccessible and not cost-effective. Further research in this regard is recommended.

Conclusion

It is concluded that the mean duration of resolution of pneumonia in patients between two months and five years was significantly shorter in those who received zinc than those who received only standard treatment of pneumonia. Hence, adding zinc along with conventional medications can contribute to swift recovery which will reduce the hospital stay. Early discharge from the hospital will reduce the economic burden on patients and enhance satisfaction among parents and treating physicians.

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