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Research Article

The Role of Zinc as an Adjuvant Therapy in Acute Pneumonia in Children in Age of 2 Months to 2 Years

Rajagembeeran VI*, Basavaraja GV[2], Nijaguna[3], Govindraj M[4]
[1]Assistant Professor, Department of pediatrics, Melmaruvathur Adhiparasakthi Institute of Medical Sciences & Research, Melmaruvathur, Tamilnadu, India
[2]Associate Professor, Department of pediatrics, Indira Gandhi Institute of Child Health, Bangalore, Karnataka, India
[3]Associate Professor, Department of pediatrics, Indira Gandhi Institute of Child Health, Bangalore, Karnataka, India
[4]Professor, Department of pediatrics, Indira Gandhi Institute of Child Health, Bangalore, Karnataka, India

***Corresponding author**
Rajagembeeran VI
Email: rajagembeeran01@gmail.com

Abstract: Worldwide pneumonia is leading cause of pediatric morbidity and mortality WHO has estimated that each year pneumonia kills up to 2.4 million children, which accounts for 19% of all deaths in the under-five age group. The incidence of pneumonia is more than 10-fold higher and the number of childhood-related deaths due to pneumonia approximately 2000-fold higher in developing countries than in developed countries. Approximately 95% of the pneumonia related deaths occur in developing countries and the youngest age group has the highest risk of death. India contributes nearly 20%. The aim was to study the effect of zinc as an adjuvant therapy on recovery from pneumonia. Children in the age group 2-24 months presenting with features of pneumonia as per IMNCI guidelines were included. Eligible children were allotted to zinc (n=21) groups. Zinc group received 20 mg of elemental zinc per day. Outcome was measured in terms of time taken for resolution of distress, time to become asymptomatic and duration of stay. The mean time for resolution of distress was less in zinc group. It was 52.4 hrs in zinc and 74.4 hrs in non zinc (p=0.053). The mean time to became asymptomatic was 65.5 hrs in zinc and 88.0 hrs in non zinc (p=0.053). The mean duration of stay was 6.1 days in zinc and 7.14 days in non zinc (p=0.368). The results suggest that adjuvant treatment with zinc accelerates recovery from pneumonia.
Keywords: Children, Zinc, Pneumonia, Supplementation, Adjuvant therapy.

INTRODUCTION

Zinc deficiency is common among children in developing countries because of inadequate food intake, particularly from animal sources; limited zinc bioavailability from the local diets [1, 2]. Zinc deficiency can impairs the immune system [3] and can increase the rate of serious infections such as pneumonia [4]. Animal products and sea foods constitute the rich sources of dietary zinc [5] but are expensive and inaccessible for many of the world's poorest populations. Zinc deficiency is a widespread disorder in Asia and Africa [6].

There are certain social, economic, and environmental factors which are responsible for pneumonia. Socioeconomic status; severe malnutrition and lack of breast feeding particularly in early months of life contribute to development of pneumonia [7]. Elimination of most of the environmental risk factors of pneumonia is very difficult, but some nutritional factors need a simple intervention.

Zinc is reported to prevent pneumonia, and to prevent and treat diarrhea [8, 9]. It might act in the acute phase response to infection [10], helping to boost the body immune response through a defense cascade, beginning with mobilization and sequestration of zinc to metallothinenin-rich tissue, rapid up regulation of immune defense specific protein synthesis, activation of immune defense activity such as macrophages, lymphocytes, and nature killer cells and antibody-dependent cytotoxicity [11, 12]. The role of zinc in immunity also involves T cell independent aspects of the immune system including natural killer (NK) and B cells [13]. Zinc appears to be a potent immune regulator in that proinflammatory cytokines (TNF, IL6 and ILI) were all lowered during lip polysaccharide (LPS) stimulation [14].

Children with good zinc status may have a more robust immune response than with poor zinc status [15]. Zinc given together with antimicrobial therapy to young children with pneumonia was associated with a significant reduction in the duration of

pneumonia [16]. Zinc supplements are the most effective of all the available nutritional supplements to prevent pneumonia [17]. Zinc efficacy trials conducted in children with mild to moderate zinc deficiency have shown significant efficacy in the prevention of pneumonia and improved outcomes during episodes of severe diseases [18]. Recommended zinc nutritional intake is 10 – 20 mg per day for children [19]. Normal serum zinc level in children is 70-120 microgram/dl [20].

MATERIALS AND METHODS

All children in the age group of 2-24 months who presented with features of pneumonia defined by IMNCI to our Indira Gandhi Institute of Child Health were approached. For children in the age group of 2 months to 12 months respiratory rate of more than 50 is considered tachypnea. And for children 12 months to 24 months respiratory rate of more than 40 is taken as tachypnea. Further danger signs and retractions were taken into account as per IMNCI and grouped as pneumonia and severe pneumonia. Other pneumonias, which have the risk factors for recurrent pneumonia like Congenital Heart Disease, Cerebral Palsy, Congenital lung deformities, myopathies, HRAD etc. were excluded from the study. At admission we calculated respiratory rate for one minute and chest in drawing was observed. The oxygen saturation (by pulse oximetry), auscultation findings (crepts, wheeze, bronchial breath sounds) and danger signs (cyanosis, inability to feed, lethargy, unconsciousness, convulsions, stridor) were recorded. Eligible children were grouped into two studies group by stratified randomization. One was kept as zinc group and another group was kept as control. Enrolled children were given standard treatment for pneumonia in the form of oxygen, intravenous fluids, bronchodilators and parenteral antibiotics. Intravenous fluids were removed once respiratory distress had settled and child accepting orally. Zinc group received 20 mg of elemental zinc per day as a single dose. Two ml of blood was collected from all the 42 children in plain container on day one of admission. It was then centrifuged and zinc estimation was made by colorimetric method. Reference range of normal zinc level was set as 65-150 microgram/dL. This study was approved by ethical committee of our institute. Observations are made in terms of time taken for resolution of distress defined by resolution of tachypnea and retractions, time to became asymptomatic defined by resolution of distress and disappearance of danger signs and SpO_2>90 in room air, finally duration of stay in each group.

Statistical Analysis

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups. Leven 1s test for homogeneity of variance has been performed to assess the homogeneity of variance Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. We constructed Kaplan-Meyer plots of duration of each outcome for zinc and Non zinc groups.

RESULTS

Each group was allotted 21 each by stratified randomization. Along with standard therapy, zinc was given to one group and no zinc was given to other group. The baseline parameters were comparable. The mean age was 15.33 months in zinc and 13.54 months in Non zinc groups respectively. The gender distribution was nearly 2:1 favoring male. About 66.7% were male. The region distribution was more from urban region constituting 73.4%. Thirteen (30.95%) were exclusively breast fed and twenty seven (64.2%) were breast fed plus received normal family diet. Two (4.7%) were artificially fed children. About required oxygen supplementation in zinc and non zinc group. All these variables were not different between the groups. The time taken for resolving all the symptoms of patients in zinc supplemented group was significantly lesser than in non zinc group. The mean time for resolution of distress was 52.4 hrs in zinc and 74.1 hrs in non zinc group (p=0.053) respectively. The mean time to become asymptomatic was 65.5 hrs in zinc and 88 hrs in non zinc group. (p=0.053). The duration of stay was 6.14 day in zinc and 7.14 days in non zinc (p=0.368). The zinc supplemented group had a significantly accelerated recovery.

Zinc deficiency was found in about 11 children accounting for 26. 1% of study population. Of these 7 belong to severe pneumonia, accounting 63.6%. Zinc distribution is statistically similar in two groups with p=0.734. Time for resolution of distress is significantly in zinc with p=0.053. Mean duration of stay is less in Zinc group with p = 0.368.

DISCUSSION

This study showed significant reductions in time required for recovery from symptoms of severe pneumonia and reduction in the overall duration of hospital stay in children who received zinc supplementation along standard antimicrobial therapy.

There are several reports on the impact of supplementation with nutrients such as zinc and vitamin A for the treatment of pneumonia [21, 22]. Zinc as a micronutrient plays a key role in the development and maintenance of host defenses against infectious diseases [23] and zinc deficiency seems to enhance the airway inflammation and cellular damage in respiratory infections [24].

The reduction in recovery time from symptoms of severe pneumonia in the present study can be attributable to the function of zinc in protection of the lungs in inflammatory states. The mean time for resolutions of distress is 52.48 hrs in zinc group when compared with Non zinc group. It took about 6.14 days in zinc group and 7.14 days for non-zinc group

(p=0.368). It is about 4 Vs. 5 days. In our study 78% belonged to severe pneumonia group and 22% belong to Non severe pneumonia group. The zinc efficacy in our study may be because most of our children belong to severe pneumonia. All these studies concluded that zinc role as an adjuvant is significant in severe pneumonia [25].

Our study showed clinically and statistically reductions in the time required for recovery from symptoms of pneumonia. There is reductions in the mean time required for disappearance of danger signs, mean time required to reach O_2>90, mean time for resolution of distress, mean time to became asymptomatic and mean duration of days of hospital stay.

Table: 1 Baseline characteristics of 42 children were enrolled in the study

Personal history	Zinc (n=21)	Non zinc (n=21)	p value
Age (months)	15.33	13.57	0.388
Male	14(2:1)	14(2:1)	1.00
Rural / Urban	5/16	6/15	0.726
Breast fed exclusively	7(21)	6(21)	0.346
Artificially fed	1 (21)	1 (21)	1.000
Breast fed and family diet	13(21)	14 (21)	0.747
Fully immunized	19 (21)	17 (21)	0.378
Respiratory rate	61.57	59.33	
Chest in drawing	19(21)	18(21)	0.634
O2 at admission<90	10(21)	13(21)	0.352
Danger signs	12(21)	14(21)	0.525
Crepts / Wheeze	19/11	19/7	0.665
Diagnosis Pneumonia Sever pneumonia	4 (21) 17 (21)	5 (21) 16 (21)	 0.707
Anemia (Hb <10%)	8 (21)	10 (21)	0.536
Leukocytosis	10 (21)	5 (21)	0.335
Zinc	87.56	84.59	0.775

Table 2: Comparison of study variables in two groups:

Variables	Zinc	Non zinc	p value
Respiratory rate	61.86±11.13	59.33±9.54	0.435
O2 at RA	88.71±8.25	85.81±7.78	0.247
Zinc	87.57±41.95	84.60±22.07	0.775
time for resolution of distress	52.47±33.99	74.17±37.76	0.053+
time to be asymptomatic	65.52±36.03	88.00±37.97	0.053+
Duration of stay	6.14±3.55	7.14±3.57	0.368

Table: 3 Showing zinc levels in two groups of patients studied

Zinc level	Zinc		Non zinc	
	No.	%	No.	%
<65	6	28.5	5	23.8
65-150	14	66.7	16	76.2
>150	1	4.7	0	0.0
Total	21	100.0	21	100.0

Table 4: Table showing the time for resolution of distress in two groups of patients studied

Time for resolution of distress (hrs)	Zinc		Non zinc	
	No.	%	No.	%
24-48	12	57.1	4	19.0
48-72	5	23.8	8	38.0
72-96	3	14.2	3	14.2
96-120	0	0.0	1	4.7
120-144	0	0.0	3	14.2
144-168	0	0.0	2	9.5
>168	1	4.7	0	0.0
Total	21	100.0	21	100.0
Mean ± SD	52.47±33.99		74.47±37.45	

Table 5: Table showing the duration of stay in two groups of patients studied

Duration of stay	Zinc		Non zinc	
	No.	%	No.	%
<7 days	18	85.7	16	76.1
8-14 days	2	9.5	3	14.2
>14 days	1	4.7	2	9.5
Total	21	100.0	21	100.0
Mean ± SD	6.14±3.55		7.14±3.57	

CONCLUSION

The results suggest that adjuvant treatment with zinc 20 mg per day accelerates the recovery from severe pneumonia in young children and significantly reduces the duration of hospital stay.

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