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THE IMPACT OF ZINC SUPPLEMENTATION ON THE LENGTH OF HOSPITAL STAY OF SEVERE PNEUMONIA IN CHILDREN 2 MONTHS TO 2 YEARS OF AGE

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Abstract:

Introduction: *Pneumonia is an illness usually caused by infection in which lung parenchyma become inflamed and congested reducing oxygen exchange and leading to cough and breathlessness. Zinc is an important trace element in body. Meat, shellfish, legumes, cheese and whole grains are sources of zinc. Zinc plays an important role in maintaining normal immune function. Mild to moderate zinc deficiency impairs the function of immune response thus reduces the resistance to infection and reduces the lymphocyte effectiveness.*

Objective: *The objective of this study was to Compare the mean length of hospital stay in children 2- 24 months of age with severe pneumonia, treated with antibiotics with and without zinc supplementation.*

Material and Methods: *It was a Randomized Controlled Trial. This study was carried out in the medical unit of The Children Hospital and Institution of child Health, Lahore and the duration of this study was 6 months' period after the approval of synopsis from 06 September 2014 to 05 march 2015.*

Results: *In our study, out of 200 cases(100 in each group), 38%(n=38) in Zinc Group and 32%(n=32) without Zinc group were between 2-12 months of age while 62%(n=62) in Zinc and 68%(n=68) in without Zinc were between 13-24 months of age, mean±sd was calcualted as 13.90±6.02 and 15.27±5.97 years respectively, 54%(n=54) in Zinc Group and 58%(n=58) without Zinc group were male while 46%(n=46) in Zinc and 42%(n=42) in without Zinc were females, comparison of mean length of hospital stay in children in both groups was recorded as 3.69±0.98 in Zinc and 4.7±1.09 days in without Zinc group, p value was calculated as 0.0001 showing a significant difference.*

Conclusion: *We concluded that the mean length of hospital stays in children 2- 24 months of age with severe pneumonia, treated with antibiotics with zinc supplementation is significnatly lower when compared without zinc supplementation.*

KEYWORDS: *Severe Pneumonia, Management, Antibiotics with and Without Zinc Supplementation, Comparison, Hospital Stay.*

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INTRODUCTION:

Pneumonia is an illness in which the lungs become inflamed and congested, reducing oxygen exchange and leads to cough and breathlessness [1]. It is the single largest cause of death in children worldwide [2]. Every year, it kills an estimated 1.6 million children under the age of five years, accounting for 18% of all deaths of children under five years old [3]. While <1% of these deaths occur in developed countries, over 90% of deaths in children <5 years of age occur in south Asia and sub-Saharan Africa [2,3]. The United Nations General Assembly Millennium Development Goal number 4 (MDG4), aimed at reducing the under-5 mortality rate by two-thirds between 1990 and 2015, has in recent years become a rallying point for activities that are directed against childhood pneumonia [4,5]. UNICEF and WHO declared pneumonia to be "the forgotten killer of children" and, for the first time in history, the World Health Assembly passed a resolution recognizing pneumonia as the world's leading infectious killer of children on 21 May 2010, thus making pneumonia a global health priority [5].

Pneumonia can be caused by bacterial, viral, or parasitic infection as well as by noninfectious agents.[2,3] Streptococcus pneumonia, Haemophilus influenzae type b (Hib) and Respiratory syncytial virus are the most common causes of pneumonia in children below 5 years, while Pneumocystis jiroveci is one of the commonest cause of pneumonia in HIV-infected infants [1,3,6].

The clinical presentation of childhood pneumonia varies depending upon the responsible pathogen, the particular host and the severity [3]. No single symptom or sign is pathognomonic for pneumonia in children [6]. The combination of fever, cough and other respiratory findings (tachypnea, increased work of breathing) are suggestive of pneumonia [6]. Neonates and young infants may present with difficulty in feeding, restlessness, or irritability [6]. In children, who have cough and/or difficult breathing, with or without fever, pneumonia is diagnosed by the presence of either fast breathing or lower chest wall indrawing, supported by X-ray chest [2,6,5]. Pneumonia should be treated with antibiotics and most cases of pneumonia can get better with oral antibiotics [2,3,6]. Hospitalization is recommended only for severe cases of pneumonia, and for all cases of pneumonia in infants younger than two months of age [1,3,6].
Preventing pneumonia in children is an essential component of a strategy to reduce child mortality [1,3]. Immunization against Hib, pneumococcus, measles and whooping cough (pertussis) is the most effective way to prevent pneumonia [3].
Undernutrition is known to be associated with greater severity of pneumonia (higher frequency of complications, longer episodes of infection, and greater case fatality rates) [1]. Thus improvements in nutrition are a keystone of current global efforts to reduce the burden of mortality and morbidity due to pneumonia [1,5]. While much emphasis is placed on protein-energy status and vitamin A, it has been proposed that zinc has a real potential to prevent morbidity and mortality due to gastrointestinal and respiratory tract infections [6,8]. It plays an important role in the immune system and is essential for the normal function and development of innate and adaptive immune systems [8]. Two distinctive potential roles for zinc in modulating pneumonia burden exist; firstly, as a preventive element when administered prior to pneumonia disease; secondly, zinc when added as an adjunct to conventional antibiotic treatment, may potentially reduce the severity, duration and fatality of pneumonia in sufferers [8,4,12]. Although many trials have been conducted worldwide to evaluate the potential impact of zinc on the duration of illness in severe pneumonia, but the results are variable, ranging from a positive effect to no overall effect [4,8,12,14]. Only 4 out of these 10 trials carried out in the last one decade showed statistically significant reduction in the duration of hospital stay in children with severe pneumonia when supplemented with zinc in adjunct to antibiotics [8,12]. Consensus as to whether zinc supplementation provides therapeutic benefit to children with severe pneumonia has not yet been established, requiring additional information before policy recommendations can be made. A study in Multan showed mean duration of 4.6 ($\pm$0.125) against 6.84($\pm$0.269) days with zinc supplementation in pneumonia in children.

The rational of the study is, to date only two studies have been carried out in Pakistan to evaluate the therapeutic role of zinc in reducing duration of illness in children with severe pneumonia, [12,14] and the data is scanty. Imran et al carried out a study in Multan which showed 32 percent reduction in hospital stay in pneumonia sufferers supplemented with zinc [15]. While Haider et al's study carried showed no significant difference (60 hrs in zinc versus 54 hrs in controls) in duration of hospital stay with zinc supplementation in severe pneumonia patients [16]. Given what was previously mentioned about the beneficial effects of administrating zinc compounds for the treatment of pneumonia among children, this study is aimed to determine the effect of zinc on speeding up recovery of severe pneumonia in 2 to 24 months old children and reducing their duration of illness and stay in hospital.

MATERIALS AND METHODS:

It was a Randomized Controlled Trial. This study was carried out in the medical unit of The Children

Hospital and Institution of child Health, Lahore and the duration of this study was 6 months' period after the approval of synopsis from 06 September 2014 to 05 march 2015. A sample size of 200 cases (100 in each group) is estimated using 95% confidence level, 80% power of test with mean duration of illness in zinc group as 4.6±0.125 and in placebo group as 6.84±0.269.[12] It was non probability purposive sampling.

Ethical clearance was taken from the ethical committee of the Children hospital. A total of 200 children fulfilling the inclusion criteria were admitted in the medical unit. Informed consent was taken from the parents of children and explained in detail that their data was used and published but confidentiality was also maintained. Demographic profile of the patient in the form of name, age and sex were recorded. All enrolled children were randomly divided by lottery method into two groups after their admission in ward by using random number tables with 100 children in each group, children in one group received antibiotics with supplementation of elemental zinc 10mg/day, and the other received antibiotics with placebo. The lactose in powder form was used as placebo. The placebo and zinc powder was prepared and packed in similar small packets by the hospital pharmacy. All children were treated according to the standard protocol for treatment of severe pneumonia. Inj. Ceftriaxone was given to all the children and inj. Vancomycine was only added if there was evidence of staphylococcal infection (pleural effusion or abscess). Patients were reviewed after every 12 hours and followed until discharge or death. Criteria for discharge were disappearance of chest in-drawing and persistently normal respiratory rate, and oxygen saturation above 92 percent in air for more than 12 hours. All data was noted on the attached Proforma. The druation of hospital stay in days was recorded.

All the data was entered and analyzed using SPSS 20. Quantitative variables like age, weight and duration of hospitalization was presented by calculating mean and standard deviation. Qualitative variables like sex and discharge or death presented by calculating frequencies and percentages. T-test was applied to compare mean hospital stay in both groups. A p value of <0.05 was considered significant. The data was stratified for age, gestational age (term/preterm) and weight (normal or under weight) to deal with effect modifiers. Post stratification length of hosptial stay was compared in both groups. P value ≤0.05 was considered as significant.

RESULTS:

A total of 200 (100 case in each group) fulfilling the inclusion/exclusion criteria were enrolled to compare the mean length of hospital stay in children 2- 24 months of age with severe pneumonia, treated with antibiotics with and without zinc supplementation. Age distribution of the children was done showing that 38%(n=38) in Zinc Group and 32%(n=32) without Zinc group were between 2-12 months of age while 62%(n=62) in Zinc and 68%(n=68) in without Zinc were between 13-24 months of age, mean±sd was calcualted as 13.90±6.02 and 15.27±5.97 months respectively. (Table No. 1). Gender distribution of the children was done showing that 54%(n=54) in Zinc Group and 58%(n=58) without Zinc group were male while 46%(n=46) in Zinc and 42%(n=42) in without Zinc were females. (Table No. 2).

Mean weight of the children was recorded as 8.11±2.31 in Zinc Group while 8.54±2.09 in without Zinc group. (Table No. 3). Frequency of discharge or death of the children was recorded as 97%(n=97) in Zinc and 91%(n=91) in without Zinc group were discharged while 3%(n=3) in Zinc and 9%(n=9) in without Zinc group were died. (Table No. 4).

Comparison of mean length of hospital stay in children in both groups was recorded as 3.69±0.98 in Zinc and 4.7±1.09 days in without Zinc group, p value was calculated as 0.0001 showing a significant difference. (Table No. 5)

Stratification for age with regards to hospital stay shows 3.63±1.05 in Zinc and 4.41±1.10 days in without Zinc group were between 2-12 months, p value was calculated as 0.003 showing a significant difference, while 3.73±0.94 in Zinc and 4.84±1.06 days in without Zinc group were between 13-24 months, p value was calculated as 0.001 showing a significant difference. (Table No. 6) Stratification for gestational age with regards to hospital stay shows 3.27±0.87 in Zinc and 4.52±1.30 days in without Zinc group were preterm cases, p value was calculated as 0.00 showing a significant difference, while 3.52±0.88 in Zinc and 4.23±1.15 days in without Zinc group were term children, p value was calculated as 0.00 showing a significant difference. (Table No. 7)

Stratification for weight of the children with regards to hospital stay shows 3.20±1.04 in Zinc and 4.43±1.24 days in without Zinc group had normal weight, p value was calculated as 0.00 showing a significant difference, while 3.44±1.12 in Zinc and 4.38±1.20 days in without Zinc group had under weight children, p value was calculated as 0.00 showing a significant difference. (Table No. 8).

Table No.1 Age Distribution (n=200)

Age (in months)	Antibiotics with zinc supplementation (n=100)		Antibiotics without zinc supplementation (n=100)	
	No. of patients	%	No. of patients	%
2-12	38	38	32	32
13-24	62	62	68	68
Total	**100**	**100**	**100**	**100**
Mean±SD	**13.90±6.02**		**15.27±5.97**	

Table No.2 Gender Distribution (n=200)

Age (in months)	Antibiotics with zinc supplementation (n=100)		Antibiotics without zinc supplementation (n=100)	
	No. of patients	%	No. of patients	%
Male	54	54	58	58
Female	46	46	42	42
Total	**100**	**100**	**100**	**100**

Table No.3 Mean Weight of the Patients (n=200)

Mean weight of the children (in kgs)	Antibiotics with zinc supplementation (n=100)		Antibiotics without zinc supplementation (n=100)	
	Mean	SD	Mean	SD
	8.11	2.31	8.54	2.09

Table No.4 Frequency of Discharge or Death of the Children (n=200)

Discharge/ death	Antibiotics with zinc supplementation (n=100)		Antibiotics without zinc supplementation (n=100)	
	No. of patients	%	No. of patients	%
Discharge	97	97	91	91
Death	3	3	9	9
Total	**100**	**100**	**100**	**100**

Table No.5 Comparison of Mean Length of Hospital Stay in Children in Both Groups (n=200)

Mean Length of hospital stay (in days)	Antibiotics with zinc supplementation (n=100)		Antibiotics without zinc supplementation (n=100)	
	Mean	SD	Mean	SD
	3.69	0.98	4.7	1.09

P value=0.0001

Table No.6 Stratification for Age with Regards to Hospital Stay (n=200)

Age (in months)	Antibiotics with zinc supplementation (n=100)		Antibiotics without zinc supplementation (n=100)		P value
	Mean	SD	Mean	SD	
2-12	3.63	1.05	4.41	1.10	0.003
13-24	3.73	0.94	4.84	1.06	0.001

Table No.7 Stratification for Gestational Age (n=200)

Gestational Age	Antibiotics with zinc supplementation (n=100)		Antibiotics without zinc supplementation (n=100)		P value
	Mean	SD	Mean	SD	
Preterm	3.27	0.87	4.52	1.30	0.00
Term	3.52	0.88	4.23	1.15	0.00

Table No.8 Stratification for Weight of the Children (n=200)

Weight of the children	Antibiotics with zinc supplementation (n=100)		Antibiotics without zinc supplementation (n=100)		P value
	Mean	SD	Mean	SD	
Normal weight	3.20	1.04	4.43	1.24	0.00
Under weight	3.44	1.12	4.38	1.20	0.00

DISCUSSION:

Pneumonia is an illness usually caused by infection in which lung parenchyma become inflamed and congested reducing oxygen exchange and leading to cough and breathlessness. Zinc is an important trace element in body [17]. Meat, shellfish, legumes, cheese and whole grains are sources of zinc. Zinc plays an important role in maintaining normal immune function. Mild to moderate zinc deficiency impairs the function of immune response thus reduces the resistance to infection and reduces the t lymphocyte effectiveness [18].

This study was carried out with the view that in our country very few studies are conducted and the data is scanty, however, we planned to determine the effect of zinc on speeding up recovery of severe pneumonia in 2 to 24 months old children and reducing their duration of illness and stay in hospital. In our study, out of 200 cases(100 in each group), 38%(n=38) in Zinc Group and 32%(n=32) without Zinc group were between 2-12 months of age while 62%(n=62) in Zinc and 68%(n=68) in without Zinc were between 13-24 months of age [19], Mean±SD was calcualted as 13.90±6.02 and 15.27±5.97 months respectively, 54%(n=54) in Zinc Group and 58%(n=58) without Zinc group were male while 46%(n=46) in Zinc and 42%(n=42) in without Zinc were females, comparison of mean length of hospital stay in children in both groups was recorded as 3.69±0.98 in Zinc and 4.7±1.09 days in without Zinc group, p value was calculated as 0.0001 showing a significant difference [20,21]. Our findings are in agreement with a study conducted in Multan showed mean duration of 4.6(±0.125) against 6.84(±0.269) days with zinc supplementation in pneumonia in children, as we recorded significant lower hospital stay in Zinc group as compared to without zinc group [22]. Arun Kumar Singh and colleagues[77] studied the effect of zinc supplementation on duration of hospital stay in children (6 months to 5 years) with pneumonia, mean duration of hospital stay was significantly reduced in treatment group (p value < 0.05) [23,24].

Sudha Basnet and others measured the efficacy of zinc when given to children hospitalized and treated with antibiotics for severe pneumonia, they recorded that zinc recipients recovered marginally faster, but this difference was not statistically significant (hazard ratio = 1.10, 95% CI 0.94–1.30) [25,26]. Similarly, the risk of treatment failure was slightly but not significantly lower in those who received zinc (risk ratio = 0.88 95% CI 0.71–1.10). They concluded that adjunct treatment with zinc reduced the time to cessation of severe pneumonia and the risk of treatment failure only marginally, if at all, in hospitalized children [27]. Khan et al have shown that zinc supplementation increases the efficacy of antibiotic against the lethal microorganisms which causes pneumonia in children because Zn salt increases activity of an antibiotic at a concentration ranging from 9-15 ug per antibiotic disc. In this way low dose of antibiotics helps the children in recovery from severe pneumonia [28]. Sazawal has shown that zinc supplementation reduces the incidence of acute lower respiratory tract infections in infants and preschool children [29]. However, in light of the findings of the current study in accordance with other studies, the hypothesis of the study that "there is a difference in mean duration of hospitalization in children with severe pneumonia under 2 years of age supplemented with zinc (10mg/kg) and those not supplemented with zinc in addition to antibiotic therapy" is justified [30], it also clarifies that zinc is effective for speeding up recovery of severe pneumonia in 2 to 24 months old children and reducing their duration of illness and stay in hospital.

CONCLUSION:

We concluded that the mean length of hospital stays in children 2- 24 months of age with severe pneumonia, treated with antibiotics with zinc supplementation is significnatly lower when compared without zinc supplementation.

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