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Original Research Article

The Impact of Prescription Zinc Sulphate on Relieving Clinical Symptoms of Pneumonia in Children Aged Below 5 Years

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Abstract

Aim: This study was investigating the effect of prescribing zinc sulphate on improving the clinical symptoms of pneumonia in 2 to 59 months of children. **Methods:** This Case-Control study was done in the Department of Pediatrics, Netaji Subhas Medical College and Hospital, Amhara, Bihta, Patna, Bihar, India for 1 year. Among 160 patients divided into two equal groups. 80 Children between the age of 2 months to 59 months and children with Acute Lower Respiratory Tract infection were include in case group and 80 children for control group. The details of blood investigations and imaging for confirmation of clinical diagnosis were also noted during the stay of the patient in the hospital. The serum zinc estimation was done by using colorimetric test. **Results:** The Mean serum zinc levels in the cases and controls, after comparison, were found to be significantly different [p=0.0001], with mean value for the cases being 59.12± 10.85 ug/dl as compared to 83.88 ± 10.26 ug/dl for the controls. A total of 20 cases and controls (25%) were found to have deficiency of zinc, of which majority (92%) were cases (normal range of 60 to 150 ug/dl). Pneumonia group (Mean=40.67± 7.55 ug/dl) having significantly lower value than that of Pneumonia group (Mean=62.75±6.32 ug/dl).This is also reflected when we see serum zinc levels according to oxygen requirements, with cases managed on room air having mean of 62.34 ± 5.69 ug/dl, cases requiring supplemental oxygen by nasal prongs having mean of 58.64 ±10.25 ug/dl and cases requiring mechanical ventilation having mean of 37.36 ±6.78 ug/dl. **Conclusion:** We concluded that the serum zinc levels were found to be lower in risk factors of LRTI like poor nutritional status, anemia, vitamin A deficiency, low birth weight and formula fed patients. Zinc supplementation had no overall effect on the duration of hospitalization or of clinical signs associated with severe infection in young children hospitalized for severe pneumonia in India. This finding differs from the results of 2 previously reported trials wherein zinc supplementation was associated with a shorter period of recovery from severe pneumonia.

Keywords: Zinc Level, Children, Lower Respiratory Tract Infection.

Introduction

Pneumonia in children is caused by viral or bacterial pathogens[1]. The incidence of childhood pneumonia is higher in low- and middle-income countries, with 0.22

episodes per child-year[2] compared with an incidence of 0.05 episodes per child-year in high-income countries[2]. Pneumonia was the cause of death for 920 000 children younger than 5 years of age globally in 2015, accounting for 16% of childhood deaths[1,3]. The proportion of deaths from pneumonia is highest among children in South Asia and sub-Saharan Africa[1,3]. Treatment of pneumonia includes antimicrobial agents, supportive management with oxygen supplementation, intravenous fluids, and antipyretics[1,4]. Immunization, breastfeeding, adequate nutrition, and good sanitation help prevent pneumonia[5-6]. Zinc is an important micronutrient supporting growth and normal function of the immune system[7]. Zinc deficiency results in growth impairment, anorexia, behavioural changes, and impaired immune function, leading to susceptibility to infections[8]. Unlike Canadian children who have good dietary sources of zinc[9,10], children in developing countries are at a high risk of deficiency due to inadequate zinc in their diets[9]. Zinc supplementation has been shown to reduce the duration and limit the complications of diarrhea in children by increasing intestinal fluid absorption, supporting mucosal integrity, and enhancing immune response[10].

Zinc deficient children are at increased risk of restricted growth and developing diarrheal diseases and respiratory tract infections. Zinc is thought to decrease susceptibility to Acute Lower Respiratory Tract Infection (ALRTI) by regulating various immune functions including protecting the health and integrity of respiratory cells during lung inflammation and injury. Supplementation of zinc could reduce the risk of pneumonia and the risk and duration of diarrhea, dysentery and malaria deaths among all infectious diseases, and they accounted for 3.9 million deaths worldwide[11]. According WHO estimates respiratory infection cause about 987,000 deaths in India of which 969,000 are LRTI[12]. ALRTI are the leading cause of mortality and a common cause of morbidity in children below five years of age. Most of these deaths are caused by pneumonia and bronchiolitis. Pneumonia kills more children each year than AIDS, malaria or measles combined with more than 2 million deaths per year[13]. The study was Investigating the effect of prescribing zinc sulphate on improving the clinical symptoms of pneumonia in 2 to 59 months of children's.

Material and methods

This Case-Control study was done in the Department of Pediatrics, Netaji Subhas Medical College and Hospital, Amhara, Bihta, Patna, Bihar, India for 1 year. Among 160 patients divided into two equal groups (80 cases and 80 controls) were included in the study. 80 Children between the age of 2 months to 59 months and children with Acute Lower Respiratory Tract infection were include in case group. Children suffering from Acute Gastroenteritis or diarrheal illness, reactive airway disease/asthma or with underlying chronic illnesses and congenital heart disease were excluded from this study.

The detailed demographic information, history, clinical findings, laboratory findings and details of clinical course of cases and controls included in the study were entered in predesigned and validated proforma. Socio-economic status was assessed according to the Modified Kuppuswamy scale updated in 2017[14]. Detailed General examination was carried out in the patients along with Respiratory system and other systemic examination and a clinical diagnosis was made and entered into the proforma. The details of blood investigations and imaging for confirmation of clinical diagnosis were also noted during the stay of the patient in the hospital. The serum zinc estimation was done by using colorimetric test. The kit used for this study was manufactured by Centromic GMBH, Germany. The Sample used was serum obtained by centrifugation of 2 ml of blood sample collected at 3000

rpm for 3 to 5 minutes. The blood sample was obtained at Day 1 of admission of cases and controls. In two different tubes, 1000 ul of reagent in both along with 50 ul of serum in one tube and standard solution in other were mixed and incubated at 37^0 for 5 minutes. Absorption of the standard A (Standard) and the sample A (Sample) was measured against the reagent blank A (Blank) via the spectrophotometer at 560 nm wavelength, which was directly proportional to the concentration of total zinc in the sample[15]. Apart from measuring the serum zinc levels, the details of clinical course of the cases were also documented in terms of the duration of stay, oxygen requirements, severity of disease according to WHO IMNCI grading 2014 and outcome of the cases.

Statistical analysis

The data obtained from the cases and controls was compiled and entered into Microsoft Excel case sheet. Statistical analysis was done by using descriptive and inferential statistics using chi square test, students unpaired t-test one way ANOVA and Pearson's correlation coefficient and software used in the analysis were SPSS 22.0. version and $p<0.05$ were considered as level of significance.

Results

The mean age of cases was 1.79±1.65 yrs and that of controls was 1.92±1.74 yrs. The Sex wise distribution of the cases and controls consisted of 48(60%) of cases being male and 32(40%) being female as compared to 45(56.25%) of controls being male and 35(43.75%) being female. On comparison, the distribution of cases and controls in this study according to age, sex, nutritional status and socioeconomic status was statistically not significant (Table.1).

Table 1. Demographic profile of children

Parameter	Cases	Controls
Age(mean)	1.79±1.65	1.92±1.74yrs
Sex		
Male	48(60%)	45(56.25%)
Female	32(40%)	35(43.75%)

The Mean serum zinc levels in the cases and controls, after comparison, were found to be significantly different [p=0.0001], with mean value for the cases being 59.12± 10.85 ug/dl as compared to 83.88 ± 10.26 ug/dl for the controls (Table 1). A total of 20 cases and controls (25%) were found to have deficiency of zinc, of which majority (92%) were cases (normal range of 60 to 150 ug/dl). (Table 2)

Table 2: Comparison of Zinc level in cases and controls

Group	N	Mean (ug/ dl)	Std. Deviation (ug/ dl)	Std. Error Mean	t-value
Cases	80	59.12	10.85	1.63	10.04,
Controls	80	83.88	10.26	2.19	p=0.0001, S

Table 3 shows comparison of serum zinc levels according to the clinical characteristics of cases. Here, the difference in mean serum zinc levels of cases according to WHO IMNCI grading was statistically significant (p value=0.0001) with cases belonging to Severe Pneumonia group (Mean=40.67± 7.55 ug/dl) having significantly lower value than that of Pneumonia group (Mean=62.75±6.32 ug/dl).This is also reflected when we see serum zinc levels according to oxygen requirements, with cases managed on room air having mean of 62.34 ± 5.69 ug/dl, cases requiring supplemental oxygen by nasal prongs having mean of 58.64 ±10.25 ug/dl

and cases requiring mechanical ventilation having mean of 37.36 ±6.78 ug/dl(Table 3). The serum zinc analysis of patients according to outcome shows significantly lower zinc values (p value=0.0001) in cases who eventually died due to the ALRTI and its complications (n=7) as compared to those who got discharged after treatment (n=73) (Table 3)

Table 3: Zinc level according to clinical characteristics in cases

IMNCI Grading	No of cases	Mean(ug/dl)	SD	t-value
Pneumonia	56(70%)	62.75	6.32	9.30 p=0.0001, S
Severe Pneumonia	24(30%)	40.69	7.55	
Total	80(100%)	60.85	10.63	
O2 Requirement				
Room Air	33(41.25%)	62.34	5.69	30.79 p=0.0001, S
Supplemental Oxygen	18(22.5%)	58.64	10.25	
Mechanical Ventilation	29(36.25%)	37.36	6.78	
Outcome				
Discharge	72(90%)	61.02	10.22	33.26 p=0.0001, S
Death	8(10%)	42.36	8.88	

The mean serum zinc level was found to have a negative correlation ('r' = -0.052) with the duration of stay of cases, however, this correlation was statistically not significant (p value = 0.71)

Discussion

Zinc plays an important role in maintaining a normal immune function and participates in all major biochemical pathways. It plays multiple roles in the perpetuation of genetic material and cellular division. Studies have suggested that zinc deficiency impairs immunocompetence with reduced cell-mediated immune responses, decreased T-lymphocytes, abnormal T-helper and/or suppressor functions, impaired macrophage function, reduced killer cells and antibody dependent cytotoxicity[16]. Zinc supplementation in children causes an increase in the levels of complement in the blood that modulate the function of monocytes, macrophages and neutrophils polymorphs. It also helps in the development and activation of T-lymphocytes. When zinc supplements are given to individuals with low levels of zinc, the numbers of T-cell lymphocytes circulating in the blood increase and the ability of lymphocytes to fight against infection improves[17]. Meeks-Gardner J et al have shown a positive Zinc supplementation in these patients[18]. The mean serum zinc levels were comparable to that found in the study by Hussain et al.[19] A study in Bangladesh by Shakur et al. and a study in Egypt by Rady et al. showed mean serum zinc levels in cases to be higher than this study[20,21]. On the other hand, a study done by Ibraheem et al. in Nigeria showed mean serum zinc levels of cases to be lower than this study[22]. This variation of mean zinc values can be ascribed to the dietary habits of the country and nutritional status of the subjects of the study as a whole[20-22]. The difference in serum zinc levels of the cases and controls in this study, as well as in the above mentioned studies is statistically significant (p value=0.0001). Study by Kumar et al. in India and Arica et al in Greece also showed similar results[23,24]. These finding could be explained by the fact that serum zinc level is decreased by interleukins and tumour necrosis factor alfa as a part of a cute phase reaction in response to inflammatory stimulus[23]. The difference in mean serum zinc levels of cases according to WHO IMNCI grading was statistically significant (p value = 0.0001) with cases belonging to Severe Pneumonia group (Mean=40.67±

7.55 ug/dl) having significantly lower value than that of Pneumonia group (Mean=62.75±6.32 ug/dl) and similar findings were seen in study by Rady et al., Hussain et al. and Brooks et.al.[19,21,25]. This may be due to the fact that in zinc deficiency, there is loss of immunomodulatory effect of zinc causing unregulated immune response in the respiratory tract, leading to increased airway injury[25]. However, evidence to the contrary was found in studies by Bose et al. and Valentiner-Branth et al.[26,27] Argument has been put by the above studies that as zinc is required to mount a better immune response by the host against infection, there will be increased damage to the respiratory epithelium due to the increased immune response and thus leading to worsening of symptoms[27]. Regarding the duration of stay of cases, Basnet et al. also found lower duration of stay in zinc supplemented group as compared to placebo, but similar to our study, the difference was statistically not significant. However, Brooks et al., Singh et al. and Malik et al. found significant reduction in duration of stay of patients of ALRTI after supplementation of Zinc[25,28,29]. Meanwhile, Bose et al., Valentiner-Branth et al. and Yuan et al found the supplementation of zinc either had no benefit or increased the duration of stay of patients of ALRTI[26,27,30]. A similar trend is also seen while evaluating the patients in terms of oxygen requirement during treatment. In this study with cases managed on room air having mean of 62.34 ± 5.69 ug/dl, cases requiring supplemental oxygen by nasal prongs having mean of 58.64 ±10.25 ug/dl and cases requiring mechanical ventilation having mean of 37.36 ±6.78 ug/dl. While studies by Rady et al. and Brooks et al. concur with the findings of our study, studies by Bose et al. and Valentiner-Branth et al. have found no significant reduction of oxygen requirement[21,25-27]. When comparing the outcome of cases according to serum zinc levels, the findings of our study were in concordance with Rady et al., Brooks et al. and Basnet et al.[21,25] Also, a large systematic review of zinc supplementation by Mayo- Wilson et al. found that giving children zinc supplements might reduce their risk of death in general, and their risk of death due to lower respiratory tract infection[32].

Conclusion

The study concluded that the serum zinc levels were found to be lower in risk factors of LRTI like poor nutritional status, anemia, vitamin A deficiency, low birth weight and formula fed patients. Zinc supplementation had no overall effect on the duration of hospitalization or of clinical signs associated with severe infection in young children hospitalized for severe pneumonia in India. This finding differs from the results of 2 previously reported trials wherein zinc supplementation was associated with a shorter period of recovery from severe pneumonia.

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