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Original Research Article

Evaluating the Effect of Prescribing Zinc Sulfate on Improving the Clinical Symptoms of Pneumonia in 2-59-Month-Old Children: A Hospital Based Study

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Conflict of interest: Nil

Abstract:

Aim: The aim of the present study was to investigate the effect of zinc sulfate on improving the clinical symptoms of pneumonia in 2-59- month-old children.

Methods: This double-blind clinical trial study was performed on 100, 2-59-month-old children with diagnosis of pneumonia referring to the pediatric ward . The children with pneumonia were randomly assigned into intervention (n=50), and control (n=50) groups.

Results: The gender distribution of the tested patients was 52% boys and 48% girls. There was no significant difference between the two groups in terms of age, gender, and weight. The mean age in the intervention group was 13.56+0.736 and in the control it was 11.97+0.712 ($p>0.05$). The mean age of hospitalization in the case and control groups was 12.58+0.732 and 10.92+0.720 months, respectively, which was not statistically significant ($p=0.540$). The mean duration of hospitalization cases and control groups was 5.4+0.314 and 5.10+0.302 days respectively; based on the Mann-Whitney test, there was no significant difference between the two groups ($p=0.180$). The serum level of zinc was calculated at the beginning of hospitalization and at the time of discharge for both intervention and control groups. The mean serum level of zinc in the intervention group (receiving zinc sulfate syrup) was 71.68+12.6 and 91.9+10.6 mcg/dl at the baseline and at the end of hospitalization respectively ($p<0.001$); while the mean serum level of zinc in the control group (receiving placebo) was 72.8+11.8 and 74.6+8.6 mcg/dl at the beginning and end of hospitalization respectively ($p=0.55$). According to Chi-square test, there was no significant difference between the two groups when comparing the presence or absence of tachypnea during hospitalization, as well as 12 and 24 hours post-hospitalization. However, at 36 hours post-hospitalization, there was a significant difference ($p=0.03$).

Conclusion: Based on this study, it is suggested that prescription of oral zinc sulfate supplement be considered for pediatric patients hospitalized due to pneumonia, in addition to the standard and conventional pharmacotherapy of pneumonia.

Keywords: Children, Cyanosis-Tachypnea, Pneumonia, Zinc sulfate.

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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 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] 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]

Pneumonia is caused by a number of infectious agents, including viruses, bacteria and fungi. The most common are Streptococcus pneumonia, Haemophilus influenzae type B. In infants infected with HIV, Pneumocystis jiroveci is one of the most common causes of pneumonia, responsible for at least one quarter of all pneumonia deaths in HIV-infected infants. In children under 5 years of age, 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 in drawing where their chest moves in or retracts during inhalation (in a healthy person, the chest expands during inhalation). [11] According to WHO, clinically, pneumonia involves acute cough attacks with or without fever associated with respiratory problems or tachypnea. [12] Zinc is an essential trace element required for maintaining intestinal cells, bone growth, and immune function.

Children who are living in low-income settings are often undernourished and zinc deficient. [13] Deficiencies may arise from the insufficient intake of foods containing zinc or insufficient absorption. Most foods high in zinc are of animal origin, such as meats, fish and dairy products. These foods may be more difficult to access for low-income populations. Zinc deficient children are at increased risk of restricted growth and developing diarrheal diseases, as well as respiratory tract infections such as acute lower respiratory tract infections. [14,15] Under-nutrition is considered the underlying cause of approximately half of these fatal acute lower respiratory tract infections. [15]

The aim of the present study was to investigate the effect of zinc sulfate on improving the clinical symptoms of pneumonia in 2-59- month-old children.

Materials and Methods

This double-blind clinical trial study was performed on 100, 2-59-month-old children with diagnosis of pneumonia referring to the pediatric ward of Darbhanga Medical College and Hospital, Darbhanga, Bihar, India.

Intervention

Any child with the symptoms of cough and fever as well as tachypnea plus respiratory distress and pulmonary infiltration as pneumonia was included. Then, based on clinical examination by a pediatrician and the chest x-ray pattern which was reticular, lobar, or bronchoalveolar, they were categorized as viral and bacterial pneumonia. The children with pneumonia were randomly assigned into intervention (n=50), and control (n=50) groups. This research was performed as double-blind clinical trial, and only the physician was aware of the contents of the two drugs. The control group received placebo. On the other hand, the intervention group received zinc sulfate as 10 mg/day in children younger than six months, and 20 mg/day in children above six months . (during hospitalization). The rest of the standard and conventional treatments of pneumonia were performed according to the protocol and routine in the pediatric wards of Darbhanga Medical College and Hospital, Darbhanga, Bihar, India for both groups.

The severity of disease of both groups was assessed based on clinical and para-clinical symptoms according to the pediatrician as well as response to treatment with improvement of clinical symptoms such as resolution of fever and overall well-being, increased appetite alongside resolution or mitigation of coughs and wheezing as well as normalization of the number of breaths and elimination of respiratory distress. During hospitalization, every 12 hours the clinical symptoms of both groups including tachypnea (number of breaths), coughs, fever, intercostal retraction, hypoxia, crackles, wheezing, lethargy, and duration of hospitalization were evaluated by a pediatric resident. In both groups, at the beginning and end of hospitalization, one blood sample was taken by an experienced nurse for the necessary tests and for determining the serum level of zinc through the brachial vein and sent to laboratory. The inclusion criteria were children 2-59-months-old with a diagnosis of pneumonia based on history and clinical examination, and if necessary, chest x-ray by a pediatrician.

Exclusion Criteria

Children with chronic diseases such as immunodeficiency, cystic fibrosis, renal diseases, chronic pulmonary diseases, malnutrition and chronic diarrhea, acute severe infection, history of hospitalization over the past three months, use of immunosuppressive drugs, and history of taking zinc supplements over the past two weeks were excluded. Chronic diarrhea was defined as diarrhea for more than 14 days. Malnutrition was characterized based on clinical symptoms of kwashiorkor or marasmus or FTT. Severe infection meant severe sepsis. Further, the patients suspected of foreign bodies and gastroesophageal reflux was also excluded.

Data Analysis

After coding, the data were analyzed by SPSS software version 16.0. In descriptive statistics, central indices (mean, standard deviation, frequency, and percentage) were used. Normality of distribution of quantitative variables was determined based on Kolmogorov-Smirnov test. To analyze and compare the quantitative and normal variables, t-test, and for qualitative and abnormal

variables, Mann-Whitney test were used. For the qualitative and ranked variables, Mann-Whitney test, and for qualitative and nominal variables, Chi-square wereapplied; $p<0.05$ was considered statistically significant.

Results

Table 1: Baseline characteristics

Gender	Intervention	Control
Male	51	53
Female	49	47
Mean age	12.58+0.732	10.92+0.720
Mean duration of hospitalization	5.4+0.314	5.10+0.302

The gender distribution of the tested patients was 52% boys and 48% girls. There was no significant difference between the two groups in terms of age, gender, and weight. The mean age in the intervention group was 13.56+0.736 and in the control it was 11.97+0.712 ($p>0.05$). The mean age of hospitalization in the case and control groups was 12.58+0.732 and 10.92+0.720 months, respectively, which was not statistically significant ($p=0.540$). The mean duration of hospitalization cases and control groups was 5.4+0.314 and 5.10+0.302 days respectively; based on the Mann-Whitney test, there was no significant difference between the two groups ($p=0.180$).

Table 2: Comparison of serum zinc levels in two groups of intervention and control before hospitalization and during discharge

Group	Zinc level duringhospitalization	Zinc level duringdischarge	P-value
	Mean (SD)	Mean (SD)	
Intervention	71.68(12.6)	91.9(10.6)	<0.001
Control	72.8(11.8)	74.6(8.6)	0.55

The serum level of zinc was calculated at the beginning of hospitalization and at the time of discharge for both intervention and control groups. The mean serum level of zinc in the intervention group (receiving zinc sulfate syrup) was 71.68+12.6 and 91.9+10.6 mcg/dl at the baseline and at the end of hospitalization respectively ($p<0.001$); while the mean serum level of zinc in the control group (receiving placebo) was 72.8+11.8 and 74.6+8.6 mcg/dl at the beginning and end of hospitalization respectively ($p=0.55$).

Table 3: Comparison of tachypnea in two groups based on measurement time

Time	Sub-group	Group		Total	P-value
		Intervention	Control		
During hospital-ization	Yes	40	45	85(85)	0.220
	No	8	6	15(15)	
12 hours after hospitalization	Yes	38	37	75(75)	0.914
	No	13	12	25(25)	
24 hours after hospitalization	Yes	35	30	65(65)	0.132
	No	17	18	35(35)	
36 hours after hospitalization	Yes	17	8	25(25)	0.03
	No	30	45	75(75)	
48 hours after hospitalization	Yes	6	4	10(10)	0.7
	No	44	46	90(90)	

The number of breaths of all patients (control and intervention) was registered from the beginning of hospitalization and every 12 hours until the end of hospitalization. According to Chi-square test, there was no significant difference between the two groups when comparing the presence or absence of tachypnea during hospitalization, as well as 12 and 24 hours post-hospitalization. However, at 36 hours post-hospitalization, there was a significant difference ($p=0.03$).

Discussion

According to WHO, annually 4.1 million deaths occur worldwide due to acute respiratory infections (ARIs), with 90% being due to acute pneumonia. Specifically, 1.9 million of them are children younger than five years old [16], mostly related to developing countries because of malnutrition. [17] Meanwhile, lower respiratory tract infections and especially pneumonia constitute around 20% of the causes of pediatric mortality; per every 1000 live children born in developing countries, 12-20

children die before the age of five because of pneumonia. [16,18] By definition, lung inflammation is called pneumonitis, and if the cause of this inflammation is a microbial agent, it is called pneumonia. Microbial agents can include bacterial, viral, or parasitic. According to WHO, clinically, pneumonia involves acute cough attacks with or without fever associated with respiratory problems or tachypnea. [19] 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. [20]

The gender distribution of the tested patients was 52% boys and 48% girls. There was no significant difference between the two groups in terms of age, gender, and weight. The mean age in the intervention group was 13.56+0.736 and in the control it was 11.97+0.712 ($p>0.05$). The mean age of hospitalization in the case and control groups was 12.58+0.732 and 10.92+0.720 months, respectively, which was not statistically significant ($p=0.540$). The results of this study are in line with the study by Habibian et al [21], reported that prescription of zinc supplement had no effect on number of breaths and duration of hospitalization, but it could reduce the fever. Brooks et al [22] in their study on 270 2-23-month-old children with severe pneumonia concluded that addition of zinc by 20 ml/day resulted in facilitation of pneumonia improvement in the children and reduced the pneumonia complications. In another study, the effect of zinc was examined on treating severe pneumonia in children younger than two. The researchers did not report any considerable impact on improving the pneumonia symptoms in children. [23] In our study, a significant decrease was found in the duration of hospitalization and recovery from pneumonia symptoms in zinc-receiving children compared to the comparison group. This indicates the effect of zinc therapy and a change in the clinical course of pneumonia among the children under investigation. This finding is consistent with the results of most studies in this field. [22,24]

The mean duration of hospitalization cases and control groups was 5.4+0.314 and 5.10+0.302 days respectively; based on the Mann-Whitney test, there was no significant difference between the two groups ($p=0.180$). The serum level of zinc was calculated at the beginning of hospitalization and at the time of discharge for both intervention and control groups. The mean serum level of zinc in the intervention group (receiving zinc sulfate syrup) was 71.68+12.6 and 91.9+10.6 mcg/dl at the baseline and at the end of hospitalization respectively ($p<0.001$); while the mean serum level of zinc in the control group (receiving placebo) was 72.8+11.8 and 74.6+8.6 mcg/dl at the beginning and end of hospitalization respectively ($p=0.55$). The number of breaths of all patients (control and intervention) was registered from the beginning of hospitalization and every 12 hours until the end of hospitalization. According to Chi-square test, there was no significant difference between the two groups when comparing the presence or absence of tachypnea during hospitalization, as well as 12 and 24 hours post-hospitalization. However, at 36 hours post-hospitalization, there was a significant difference ($p=0.03$). Possibly, the effect of zinc on reducing the duration of fever in children in the present study has been due to the fact that we eliminated the severe cases of infection. The results of another study showed that children with malnutrition who received zinc supplement for 60 days reported lower incidence of coughs, fever, and upper respiratory infections compared to the control group. [25] Research findings in Zahedan showed that zinc deficiency is associated with increased susceptibility to pneumonia and gastroenteritis in children younger than five. Investigation of the effect of prescribing zinc compounds or fortifying the food with zinc in regions with zinc deficiency have been recommended for reducing incidence of pneumonia and gastroenteritis in this age group in future studies. [26]

Conclusion

Oral prescription of zinc sulfate in children referring with pneumonia symptoms had a useful effect on reducing the duration of fever and improving the respiratory status (tachypnea) in 2 to 59-month-old children. Based on this study, it is suggested that prescription of oral zinc sulfate supplement be considered for pediatric patients hospitalized due to pneumonia, in addition to the standard and conventional pharmacotherapy of pneumonia.

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