Original Research Article

Study of Effect of Zinc Sulphate On Improving The Clinical Symptoms of Pneumonia In Paediatric Population

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Abstract

Background: Pneumonia is one of the common mortality causes in young children. Some studies have shown beneficial effect of zinc supplements on treatment of pneumonia. The aim of the present study was to examine the effect of zinc sulphate on improving the clinical symptoms of pneumonia in 2-59- month-old children. **Materials and methods:** A clinical study was conducted in the Department of Paediatrics VIMS, Pawapuri, Nalanda, Bihar, India fromOctober 2019 to February 2020. The children with pneumonia were randomly assigned into intervention (n=50), and control (n=50) groups. The control group received placebo. The intervention group received zinc sulphate as 10 mg/day in children younger than one, and 20 mg/day in children above one year-old every 12 hours (during hospitalization). 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. In both groups, at the beginning and end of hospitalization, Blood sample was taken for the necessary tests and for determining the serum level of zinc through the brachial vein and sent to laboratory. **Results:** In this study 100 patients were include. Out of 100, 50 patients were included to the intervention and 50 to the control groups. 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 of the hospitalized patients was13.25+0.685, with the minimum andmaximum of 2 and 59 months-old, respectively. The mean age in the intervention group was 14.36+0.784 and in the control it was 12.12+0.685 ($p>0.05$). The mean age of hospitalization in the case and control groups was 14.31+0.765 and 12.55+0.841 months, respectively, which was not statistically significant ($p=0.498$). The mean duration of hospitalization was 5.66+0.545, with the minimum and maximum of 2 and 12 days respectively. The mean duration of hospitalization cases and control groups was 5.8+0.284 and 5.14+0.294 days respectively; based on the Mann-Whitney test, there was no significant difference between the two groups ($p=0.165$). 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 sulphate syrup) was 69.89(11.8) and 94.8(12.3) 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 71.3(10.3)and 71.9(10.2)mcg/dl at the beginning and end of hospitalization respectively ($p=0.47$).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 ($p=0.01$). **Conclusion:** Zinc sulphate supplement be considered for pediatric patients hospitalized due to pneumonia, in addition to the standard and conventional pharmacotherapy of pneumonia.

Keywords: Pneumonia, zinc, supplementation, treatment.

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Introduction

Worldwide, pneumonia is the leading cause of pediatric morbidity and mortality. It is estimated that pneumonia is responsible for 2 million deaths each year in children below 5 yrs of age, which represents 19% of the annual deaths in this age group.[1]

Approximately 95% of the pneumonia-related deaths occur in developing countries, and the youngest age groups have the highest risk of death.[2] India has the highest number of deaths of children below 5 yrsof age in the world—an estimated 2402 000, or 3 times the number in China.[3] Pneumonia case management, which relies on early diagnosis and prompt empiric antibiotic therapy, has been effective in reducing pneumonia-related deaths by 47%.[4] However, the efficacy of this strategy may be diminished by poor nutritional status.[5] Under nutrition is known to be associated with greater severity of pneumonia, a higher frequency of complications, longer episodes of infection, and greater case fatality rates.[6] Malnutrition plays a significant role in its increased prevalence, severity, and prognosis of pneumonia, especially among children. Zinc and iron deficiency is one of the most common nutritional problems in Iran and many developed countries. According to statistics, about 50% of the common nutritional problems are due to a combined deficiency of the two elements, though the beneficial role of zinc compared to iron has been forgotten in Iran.[7]

Zinc is an essential trace element required for maintaining the integrity of intestinal endothelial cells, bone growth, and immune function. Children who are living in low-income settings are often under-nourished and zinc deficient .This element plays an important and vital role in the physical development of digestive and immune systems. Zinc deficiency in children can cause stunted growth and increased incidence of infections (pneumonia, gastroenteritis) through weakening the immune system and changing neural and behavioral actions.[8,9] Severe zinc deficiency has been associated with stunting of growth, impaired immunity, skin disorders, learning disabilities and anorexia.3 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. Dietary fibre and compounds called phytates, which are often found in foods such as cereals, nuts and legumes, bind to zinc and result in poor absorption.[10] Frequent diarrhoea, that is also associated with chronic under nutrition, may further deplete body stores of zinc.[11,12]

Zinc deficient children are at increased risk of restricted growth and development together with developing diarrhoeal diseases as well as respiratory tract infections such as acute lower respiratory tract infections.[13] Hence the present study was conducted with the aim to evaluate the effect of zinc sulfate on improving the clinical symptoms of pneumonia in 2-59- month-old children.

Materials and Methods

A clinical study was conducted in the Department of Paediatrics VIMS, Pawapuri, Nalanda, Bihar, India from October 2019 to Feb 2020.

Method: 100 childrens with the symptoms of cough, cold, fever as well as tachypnea with respiratory distress and pulmonary infiltrations as pneumonia were included. Thenbased on clinical examinations and the chest x-ray patterns which were central, peripheral, perihilar, reticular, lobaror 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 sulphate as 10 mg/day in children under one yr of age and 20 mg/day in children above one year of age every 12 hours (during hospitalization). During hospitalization, every 12 hours the clinical symptoms of both groups including tachypnea (number of breaths), coughs, cold, fever, intercostal retraction, subcostal recession, hypoxia, crackles, wheezing, lethargy, and duration of hospitalization were evaluated. In both groups, at the beginning and at the end of hospitalization, one blood sample each time was taken from brachial vein for the necessary tests to be performed in laboratory for determining the serum level of zinc. The children 2-59-months-old with a diagnosis of pneumonia based on history and clinical examination and diagnostic tools were include in this study. 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 from the study.

Statistical Analysis: Data was 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 analyse and to 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 were applied; $p < 0.05$ was considered statistically significant.

Results

In this study 100 patients were include. Out of 100, 50 patients were included to the intervention and 50 to the control groups. 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 of the hospitalized patients was 13.25+0.685, with the minimum and maximum of 2 and 59 months-old, respectively. The mean age in the intervention group was 14.36+0.784 and in the control it was 12.12+0.685 ($p>0.05$). The mean age of hospitalization in the case and control groups was 14.31+0.765 and 12.55+0.841 months, respectively, which was not statistically significant ($p=0.498$). The mean duration of hospitalization was 5.66+0.545, with the minimum and maximum of 2 and 12 days respectively. The mean duration of hospitalization cases and control groups was 5.8+0.284 and 5.14+0.294 days respectively; based on the Mann-Whitney test, there was no significant difference between the two groups ($p=0.165$).

Table 1: Gender distribution of children's

Gender	N=100	%
Male	52	52%
Female	48	48%

Table 2: Basic character

Group	Intervention	Control	P-value
	Mean (SD)	Mean (SD)	
Age	14.36+0.784	12.12+0.685	p>0.05
Hospitalization age	14.31+0.765	12.55+0.841	(p=0.498).
duration of hospitalization	5.8+0.284	5.14+0.294	(p=0.165).

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 sulphate syrup) was 69.89(11.8) and 94.8(12.3) 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 71.3(10.3)and 71.9(10.2)mcg/dl at the beginning and end of hospitalization respectively ($p=0.47$) (**Table.3**).

Table-3: Comparison of serum zinc levels in two groups of intervention and control before hospitalization and during discharge

Group	Zinc level during hospitalization	Zinc level during discharge	P-value
	Mean (SD)	Mean (SD)	
Intervention	69.89(11.8) mcg/dl	94.8(12.3) mcg/dl	<0.001
Control	71.3(10.3) mcg/dl	71.9(10.2) mcg/dl	0.47

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. As observed in **Table.4**, 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 ($p=0.01$). The peripheral capillary blood oxygen saturation was calculated andrecorded from the beginning of hospitalization every 12 hours until discharge for both control and intervention groups. According to Chi-square and Fisher exact test, there was no significant difference between the two groups regarding presence or absence of cyanosis during hospitalization and some hours post-hospitalization. Presence or absence of coughs in the study patients was recorded from the hospitalization every 12 hours. Regarding cough and cold improvement in the intervention and control groups in terms of age, no significant improvement was observed in the study

groups. In all of the patients studied (both intervention and control), from the beginning of hospitalizationand every 12 hours thereafter until complete recovery, presence or absence of intercostal and subcostal retraction wasrecorded. According to Chi-square and Fisher exact test, there was no significant difference between the two groups regarding presence or absence of retraction at the time of hospitalization and hours after hospitalization. The severity of wheezing was calculated and recorded in both intervention and control groups at the beginning of hospitalization and thereafter every 12 hours. According to Chi-square and Fisher exact test, there was no significant difference between the two groups regarding presence or absence of wheezing during hospitalization and hours post-hospitalization. The findings also indicated that based on Chi-square and Fisher exact test, there was no significant difference between the intervention and control groups when comparing presence or absence of lethargy during hospitalization as well as 12 and 24 hours post-hospitalization.

Table 4: Comparison of tachypnea in two groups based on measurement time

Time	Sub-group	Group		Total	P-value
		Intervention	Control		
During hospitalization	Yes	42(84)	46(92)	88(88)	0.234
	No	8(16)	4(8)	12(12)	
12 hours after hospitalization	Yes	39(78)	39(78)	78(78)	0.878
	No	11(22)	11(22)	22(22)	
24 hours after hospitalization	Yes	35(70)	30(60)	65(65)	0.114
	No	15(30)	20(40)	35(35)	
36 hours after hospitalization	Yes	16(32)	9(18)	25(25)	0.01
	No	34(68)	41(82)	75(75)	
48 hours after hospitalization	Yes	4(8)	3(6)	7(7)	0.6
	No	46(92)	47(94)	93(93)	

Discussion

The high prevalence of respiratory infections in children which is one of the major causes of morbidity, mortality and occupation of hospital beds.Regarding the staggering costs these infections incur to the healthcare system of the country. Reduction of child mortality is one of the top priorities of the Ministry of Health. So that prescription of supplements and drugs capable of reducing the duration of hospitalization as well as severity of symptoms and eventually mortality and morbidity can significantly help the healthcare system of the country. The aim of the present study was to examine the effect of zinc sulphate on improving the clinical symptoms of pneumonia in 2-59- month-old children. The results showed that Zink supplement in patients with pneumonia had a useful effect in reducing the duration of fever and number of breaths, but it had no significant effect on the cough and duration of hospitalization. The results of this study was similar by Habibian et al., reported that prescription of zinc supplement had no effect on number of breaths and duration of hospitalization, but it could reduce the fever[14]. Brooks et al. 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[15]. In another study, the effect of zinc was examined on treating severe pneumonia in children younger than two yrs. The researchers did not report any considerable impact on improving the pneumonia symptoms in children[16]. Ina study, Mahalanabis et al. used zinc supplement in the treatment regimen of children with pneumonia and concluded that the treatment group showed diminished fever, but it had no effect on tachypnea[17]. In the study by Sandstead in India, it was found that zinc supplement had no useful effect on measles-associated pneumonia[18]. Some studies have found that zinc supplement is effective in preventing acute respiratory infection[19],and pneumonia complications would diminish following proper nutrition for children[20]. Meanwhile, the results of a study indicated that zinc supplement does not have any effect in severe and very severe pneumonia[21]. 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[22]. Also, the results of other studies indicated that incidence of respiratory infections was lower in the children receiving zinc supplements[23,24]

In other studies, it was found that zinc supplement had no effect on reducing the duration of pneumonia symptoms in children below five[25].In our study, no side effect of supplement was observed in patients. In some studies, digestive side effects have been reported[26].The most important finding in the present study was the relationship between zinc supplement and reduction of fever duration in both study groups. Possibly, reduction of inflammatory cytokines in the group receiving the zinc supplement is one of the reasons for this reduction in fever duration[27]. It is suggested that this study be conducted with a larger sample size and on a wider scale with different doses and treatment duration and the results then be compared to each other. In another study, performed as double-blind in Nepal on 122 children with severe pneumonia, no change was observed in the duration of hospitalization in the case and control groups who had received zinc and placebo. In our study, variables including the number of breaths, chest wall retraction, cyanosis, nasal flaring, fever, wheezing, alteration of antibiotic, and duration of hospitalization were recorded in both caseand control groups and no significant difference was found. In another study performed in Australia, prescription of zinc supplement or vitamins had no effect on children with lower respiratory tract infection in hospitalized patients[17].

Research findings in Zahedan showed that zinc deficiency is associated with increased susceptibility to pneumonia andgastroenteritis in children younger thanfive yrs of age. Investigation of the effect of prescribing zinc compounds or fortifying the food with zinc in regions with zinc deficiency have been recommended forreducing incidence of pneumonia and gastroenteritis in this age group in future studies.[28] In this study, no significant change was observed in the duration of hospitalization, but the mean zinc level in both intervention and control groups was at the minimum level against the normal value. It is possible that the patients with a higher zinc level become less ill and even if they do get sick, they do not need to be hospitalized, although this requires a wider and more comprehensivestudy.

Conclusion

Oral prescription of zinc sulfate in children suffering 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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