Original Article

The Efficacy of Zinc Supplementation in Treatment of Severe Pneumonia in Hospitalized Children

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Abstract

Background: *Zinc affects many elements of the immune device, from the skin barrier to gene regulation inside lymphocytes. The function of macrophage is adversely affected by zinc deficiency. Zinc plays a crucial role in the development of acquired immunity, immunoglobulin G production, intracellular killing, cytokine production, and phagocytosis, thus regulating the defense mechanism in children with acute infection.* ***Objective:*** *This study was done to observe the efficacy of zinc as adjuvant therapy for severe pneumonia in hospitalized children.* ***Study Design:*** *This randomized double blind controlled trial was conducted in the Department of Paediatrics, Sylhet MAG Osmani Medical College Hospital, Sylhet during the period from 1st July 2013 to 30th June 2015.* ***Methodology:*** *A total 133 hospitalized children with severe pneumonia fulfilling inclusion and exclusion criteria were enrolled by systematic random sampling in this research. Group-A and Group-B allocation was done by lottery method, each of which consisting of 67 and 66 patients. Identical small packet that contained 10mg zinc sulphate powder or 10 mg placebo powder were coded as A and B by guide.* ***Results:*** *Adverse effect of treatment was vomiting in 5 (7.5%) patients in placebo group and in 7 (10.6%) patients in zinc group. The difference was not statistically significant ($p>0.05$) between two groups. Mean length of hospital stay was found 6.63±0.49 days in placebo group and 5.67±0.71 days in zinc group. Mean length of hospital stay was significantly longer in placebo group than zinc group ($p<0.05$).* ***Conclusion:*** *Adjuvant zinc therapy in severe pneumonia children causes fewer needs of second line medication, early clinical recovery and shorter length of hospital stay.*

Key words: Zinc supplementation, Severe pneumonia, Adjuvant therapy

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Introduction

Zinc is an important micronutrient in humans. Globally, pneumonia represents 18% of mortality in children under five years of age and the main infectious purpose of early life mortality[1]. There is a higher pneumonia risk in a population with zinc deficiency[2]. Zinc affects many elements of the immune system, from the skin barrier to gene regulation inside lymphocytes. The function of macrophage is adversely affected by zinc deficiency[3]. Zinc plays a crucial role in the development of the acquired immunity, immunoglobulin G production, intracellular killing, cytokine production and phagocytosis, thus regulating the defense mechanism in children with acute infection[4].

Pneumonia is one of acute lower respiratory tract infections that involve the airways and parenchyma with a consolidation of alveolar spaces (infection of the lung alveoli)[5]. The World Health Organization and the United Nations Children's Fund recommend that children in developing countries should intake zinc supplements for 10 to 12 days as follows: 10 mg daily for infants younger than six months and 20 mg daily for infants older than six months to hasten recovery from severe pneumonia in developing countries[6]. This can be linked to boost immunity in response to the zinc supplementation[4,7]. Zinc strengthens the immune system via its role in the maintenance of epithelial and tissue structure by promoting cell growth and reducing apoptosis[8]. It also has antioxidant properties which protect against free radical damage sustained during inflammatory responses[5,9]. Studies of zinc supplementation for the treatment or improved management of acute lower respiratory tract infections, including pneumonia have had mixed results[10,11].

This clinical trial is done to assess the efficacy of zinc as adjuvant therapy to standard antibiotic treatment in reducing the time to cure and to reduce the risk of treatment failure in patients with severe pneumonia episode.

Materials and Methods

This randomized double-blind placebo-controlled trial was conducted in the Department of Paediatrics, Sylhet MAG Osmani Medical College

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Hospital, Sylhet, Bangladesh during the period from 1st July 2013 to 30th June 2015 with a view to explore the role of zinc as adjuvant therapy for severe pneumonia in under-5 years children. A total 133 severe pneumonia hospitalized children fulfilling inclusion and exclusion criteria were enrolled by systematic random sampling. Group allocation of Group-A and Group-B was done by lottery method and each consisting 67 and 66 patients. Identical small packet that contained 10 mg zinc sulphate powder or 10 mg placebo powder were coded as A and B by guide. The patients of group-A and group-B were treated with coded A packet and coded B packet for total of 7 days.

Antibiotic and supportive treatment was administered according to WHO guideline[12]. The primary outcome was recovery from severe pneumonia. 67 patients of Group A and 66 patients of Group B completed the schedule treatment protocol. Decoding was done by the guide after the completion of the study, coded A blister was placebo and coded B blister was zinc. The patients of group-A were treated with code-A packet and those of group-B were treated with code-B packet. Children aged less than 12 months received one packet of code-A or one packet of code-B, while those aged 12 months or more received two packet of code-A or two packet of code-B daily for 7 days. Children received code-A or code-B powder was mixed with breast milk or water and were taken by mouth at the time of enrollment. From day 2, they received one or two packets of their assigned treatment by mouth twice a day for total of 7 days. The standard treatments of severe pneumonia (antibiotic, oxygen therapy, fluid and nutrition) were given to both groups accordingly.

Results

Mean age was found 11.37±10.52 months in placebo group and 11.33±8.75 months in zinc group. More than three fourth (76.1%) patents were male in placebo group and 45 (68.2%) in zinc group. The mean weight was found 7.31±2.67 kg in placebo group and 6.98±1.66 kg in zinc group. The difference was not statistically significant (p>0.05) between two groups (Table-I). Time for normalization of chest indrawing was 112.36±15.06 hours in placebo group and 95.58±27.15 hours in zinc group. Time for normalization of temperature was 34.34±15.30 hours in placebo group and 24.36±4.69 hours in zinc group. Time for normalization of SPO_2 was 31.64±16.71 hours in placebo group and 23.21±10.08 hours in zinc group.

Table-I: Baseline characteristics of the study participants

Characteristics	Placebo group (n=67)	Zinc group (n=66)	p value
Age			
2-6 months	18 (26.9%)	13 (19.7%)	0.981[ns]
6 months-2 years	40 (59.7%)	44 (66.7%)	
>2 years	9 (13.4%)	9 (13.4%)	
Mean age (months)	11.37 ± 10.52	11.33 ± 8.75	
Sex			
Male	51 (76.1%)	45 (68.2%)	0.307[ns]
Female	16 (23.9%)	21 (31.8%)	
Body weight (kg)			
Mean weight (kg)	7.31 ± 2.67	6.98 ± 1.66	0.386[ns]

ns= not significant

Table-II: Time for normalization of the study participants

Time for normalization (hours)	Placebo group (n=67) Mean ± SD, n (%)	Zinc group (n=66) Mean ± SD, n (%)	p value
Respiratory rate	116.15 ± 17.16	111.24 ± 24.33	0.108[ns]
Chest indrawing	112.36 ± 15.06	95.58 ± 27.15	0.001[s]
Nasal flare	29.14 ± 6.41	26.40 ± 5.37	0.454[ns]
Temperature	34.34 ± 15.30	24.36 ± 4.69	0.001[s]
SPO_2	31.64 ± 16.71	23.21 ± 10.08	0.001[s]
Crepitation	99.01 ± 53.40	80.91± 46.94	0.040[s]
Time for normalization of all parameter (hours)	125.52 ± 27.87	108.00 ± 37.25	0.003[s]
Second line medication	26 (38.8%)	7 (10.6%)	0.001[s]
Adverse effects	5 (7.5%)	7 (10.6%)	0.527[ns]
Length of hospital stay (day)	6.63 ± 0.49	5.67 ± 0.71	0.001[s]

s= significant, ns= not significant

Time for normalization of all parameters (clinical recovery) in placebo group and zinc group was 125.52±27.87 hours and 108.00±37.25 hours respectively, which were statistically significant ($p<0.05$) but others parameter was not statistically significant ($p>0.05$) between two groups. The need of second line medication was 26 (38.8%) in placebo group and 7 (10.6%) in the zinc group. The difference was statistically significant ($p<0.05$) between two groups. Adverse effect of treatment was vomiting in 5 (7.5%) patients in placebo group and in 7 (10.6%) in zinc group. The difference was not statistically significant ($p>0.05$) between two groups. All patients were discharged in both groups. Mean length of hospital stay was found 6.63±0.49 days in placebo group and 5.67±0.71 days in zinc group. Mean length of hospital stay was significantly longer in placebo group than zinc group ($p<0.05$) [Table-II].

Discussion

In this study the mean age of study participants was found 11.37±10.52 months in placebo group and 11.33±8.75 months in zinc group. 51 (76.1%) patients were male in placebo group and 45 (68.2%) in zinc group. The mean weight was found 7.31±2.67 kg in placebo group and 6.98±1.66 kg in zinc group. The difference was not statistically significant ($p>0.05$) between two groups.

Study by Laghari et al.[13] reported that the mean age of the entire sample was 29±7 months. The zinc group had 60% (n = 30) male children and the non-zinc group had 66% (n = 33) male children. This result correlated with the study of Basnet et al. where the mean age of the patients in placebo group was 7.1±5.6 months and that of zinc group was 7.8±6.0 months[14]. Sempértegui et al.[15] also found that the mean age of the patients in placebo group was 12.99±11.24 months and that of zinc group was 13.06±10.32 months. In this regards Srinivasan et al. found that the age of their patients ranged from 6 to 59 months with a mean of 17.9±12.2 months in the zinc group and 18.1±11.7 months for the placebo group[16].

This study also showed that maximum patients were in the age group of 6 months to 2 years in both placebo and zinc group (43.2% versus 54.2%) and there was no significant difference between placebo and zinc group ($p=0.118$). This result was supported by Shah et al. in which 43 (67%) patients were male and 21 (32.8%) patients were female in zinc group; while 33 (62.3%) patients were male and 20 (37.7%) patients were female in placebo[17]. The sex of the patients in zinc group and placebo group did not show any statistically significant difference ($p=0.578$). Qasemzadeh et al. reported that there was no statistically significant difference between the two groups in terms of the age and sex variables[18]. Howie et al. also reported in their study that median age at enrolment in both arms was 13 months[19].

In current study observed time for normalization of chest indrawing was 112.36±15.06 hours in placebo group and 95.58±27.15 hours in zinc group. Time for normalization of temperature was 34.34±15.30 hours in placebo group and 24.36±4.69 hours in zinc group. Time for normalization of SPO_2 was 31.64±16.71 hours in placebo group and 23.21±10.08 hours in zinc group. Time for normalization of all parameters (clinical recovery) in placebo group and zinc group was 125.52±27.87 hours and 108.00±37.25 hours respectively. Which were statistically significant ($p<0.05$) but others parameter was not statistically significant ($p>0.05$) between two groups.

Howie et al.[19] reported that the time for resolution for all respiratory symptoms of severity was not significantly different between placebo and zinc arms (42.3 vs 30.9 hours respectively; $p = 0.242$). This result was correlated with the study done by Wadhwa et al.[20], which revealed that time for normalization of the chest indrawing in placebo group and zinc group did not differ significantly (RR=0.92; 95% CI=0.70-1.22).

Conversely Brooks et al.[21] found early recovery of chest indrawing in zinc group (RR=0.68; 95% CI=0.48-0.96). This result correlated with the study of Mahalanbis et al.[9] which found time for normalization of fever was earlier in zinc group. But Srinivasan et al.[16] found that time for normalization of temperature (hours) did not differ significantly between zinc group and placebo group (18.0 and 18.0 h; RR=1.016; 95% CI: 0.79, 1.30; $p=0.897$). This result was correlated with the study done by Wadhwa et al.[20], where they found that there was no significant difference in the time of recovery from severe pneumonia between the zinc and placebo groups. By study of Brooks et al.[21], overall duration of pneumonia was found shorter in zinc group.

Present study showed that the need of second line medication was 26 (38.8%) in placebo group and 7 (10.6%) in the zinc group. The difference was statistically significant ($p<0.05$) between two groups. Brook et al.[21], Mahalanabis et al.[9] and Grant CC et al.[22] showed that zinc administration decreased the risk for treatment failure with RR=0.30; [95% CI: 0.08, 1.07] and RR=0.74 [95% CI: 0.13, 4.24], respectively. However, these results were not statistically significant.

In this study, it was observed that the adverse effect of the treatment was vomiting in 5 (7.5%) patients of the placebo group and in 7 (10.6%) patients of the zinc group. The difference found was not statistically significant ($p>0.05$) between the two

groups. Basnet et al.[14], in their study, found that the proportion of children who vomited after the first dose of supplement was higher (14%) in the zinc group than the children in the placebo group (9%) but this finding did not reach the level of significance (p=0.052). Srinivasan et al.[17] in their study found that two children developed vomiting immediately after receiving the first dose of the intervention, one in the zinc group and one in the placebo group. Subsequent doses were tolerated well by the both groups.

Conclusion

Findings of the present study of zinc adjuvant therapy in severe pneumonia showed that the time for clinical recovery was significantly earlier, the need of second line medication was significantly fewer and the length of hospital stay was significantly shorter in zinc group than that of placebo group. The outcome of treatment was similar and adverse effect did not differ significantly between zinc group and placebo group. So, it can be concluded that oral zinc is effective and safe as adjuvant treatment in severe pneumonia to prevent morbidity in children.

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