

The Role of Zinc in Acute Bronchiolitis in children less than 2 years old

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Abstract

Background: Bronchiolitis is an acute respiratory illness which is the leading cause of respiratory distress in infancy and early childhood with its greatest morbidity in infants. Although zinc supplementation is effective in both preventing and treating pneumonia but its role in acute bronchiolitis has rarely been examined.

Objective: To assess the effect of zinc sulfate to improve the clinical manifestations of acute bronchiolitis (Severe cases) in children less than 2 years of age.

Materials and Methods: This was a double blind randomized clinical trial on 70 patients aged 2 to 23 months admitted in the Pediatric ward of Khwaja Yunus Ali Medical College and Hospital from September 2019 to September 2020 with the diagnosis of acute bronchiolitis. Patients were randomly divided equally into 2 groups: a case group was assigned oral zinc sulfate and the control group received placebo.

Results: Mean age of case group was 174.63 ± 98.7 days and control group 176.86 ± 97.43 days ($p=0.924$) with male predominance in both groups. Symptoms and signs of acute bronchiolitis (Severe cases) were compared between the 2 groups during admission and then at 24, 48 and 72 hours after initiation of treatment.

No statistically significant differences were observed between the 2 groups in improvement of symptoms and signs including fever, fast breathing, chest indrawing and wheezing on 48 and 72 hours after treatment with zinc sulfate ($p > 0.05$). The duration of hospitalization was 4.2 ± 2.6 days in the case group and 4.4 ± 2.2 days in the control group and this difference was not significant.

Conclusion: The present study showed that zinc sulfate has no benefit in improving the clinical manifestations of acute bronchiolitis.

Keywords: acute Bronchiolitis, zinc sulfate.

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Introduction

Acute bronchiolitis is the most common acute viral infection of the lower respiratory tract in infants and children less than 2 years of age and is the leading cause for their hospitalization.¹ The primary cause of bronchiolitis is Respiratory Syncytial Virus (RSV) and infrequently other viruses and Mycoplasma which cause inflammation and obstruction of the small bronchioles resulting in first-time wheezing among infants.² Some of the infants hospitalized with acute bronchiolitis can develop subsequent episodes of wheezing.³ Thus bronchiolitis poses a significant public health problem.⁴ Children with bronchiolitis often receive unnecessary antibiotics and often require hospitalization.⁵ Although various treatment options have been proposed no

specific treatment is currently available. Treatment of acute bronchiolitis remains supportive care including respiratory monitoring, control of fever, adequate hydration, nasal suctioning and supplemental oxygen.⁶ Zinc sulfate has been evaluated in cases of pneumonia and shown to be effective in both preventing and treating pneumonia.^{7,8} However, only rarely have studies particularly examined the role of zinc sulfate in acute bronchiolitis in patients aged 2 to 23 months.⁹ Therefore, this study was conducted to assess whether there is a role of zinc sulfate in the treatment of acute bronchiolitis in children under 2 years of age in reducing the symptoms.

Materials and Methods

The Study design was a double blind randomized clinical trial conducted on 70 children aged 2 to

23 months hospitalized with the diagnosis of severe illness of acute bronchiolitis during admission.

Inclusion criteria:

- (i) Age - 2 months to 23 months
- (ii) Symptoms and signs of severe bronchiolitis: e.g, fever, fast breathing, chest indrawing, dyspnoea, rhinorrhoea and nasal flaring
- (iii) first-time wheezing episode in previously healthy children
- (iv) chest x-ray findings of bronchiolitis during admission or hospital stay: including hyperinflation and increased translucency

Exclusion criteria:

- (i) History of-previous episodes of wheezing or bronchodilator therapy
- (ii) congenital heart disease
- (iii) suspected TB, sepsis, meningitis, active measles,
- (iv) chest x-ray showing pneumonia,
- (v) and gestational age at birth <34 weeks

The patients were admitted in the Pediatric ward of Khwaja Yunus Ali Medical College and Hospital, Enayetpur, Chauhali, Sirajganj-6751 from September 2019 to September 2020. Patients were enrolled into this study according to the above-mentioned inclusion criteria. Then randomly divided into 2 equal groups: a Case group received oral zinc sulfate and the Control group received placebo. Written consent was obtained from parents before including the children into the study and they were not aware of the type of drug being administered.

Zinc Sulfate was given in the dose of 10mg/day for children aged 2 months to less than 6 months and 20mg/day for children aged 6 months to less than 24 months. Bottles of drug and placebo were similar in size and shape as well as in taste. Data was collected by written questionnaires.

Operational definition:

- (1) **rhinorrhoea:** runny nose or free discharge of thin nasal secretions
- (2) **fever:** defined as axillary temperature above 37.5°C or 99.5°F
- (3) **nasal flaring:** defined as nasal openings enlargement during inspiration
- (4) **Dyspnoea:** difficulty breathing or shortness of breath
- (5) **fast breathing:** respiratory rate of 50 breaths per minute or more at rest in infants below 1 year old and respiratory rate of 40 breaths per minute or more at rest in children above 1 year old,
- (6) **chest indrawing:** the continuous visible inward movement of the lower chest wall during inspiration,
- (7) **wheezing:** clinically as a musical sound heard during expiration.

All these features were evaluated at admission, and at 24, 48 and 72 hours after starting treatment with zinc sulfate.

Management of severe bronchiolitis in hospital for both case group and control group was supportive care including respiratory monitoring, control of fever, adequate hydration, nasal suctioning, nebulization with normal saline and supplemental oxygen.

Recovery from acute bronchiolitis was considered when fast breathing, chest indrawing, wheezing or fever were completely improved. These important clinical manifestations were compared between both case and control groups during hospitalization.

Descriptive statistical methods were used to analyze data after completing checklists for all patients. Data was analysed with SPSS version 23.0. For quantitative variables t-test and for qualitative variables Chi-square were used. $p < 0.05$ was considered significant. This study was approved by the local ethical committee of the hospital.

Results

There were no significant differences between the 2 groups, case and control, in terms of age, sex, feeding status and clinical features such as, rhinorrhoea, fever, nasal flaring, dyspnoea, fast breathing, chest indrawing and wheezing before starting therapy ($p > 0.05$).

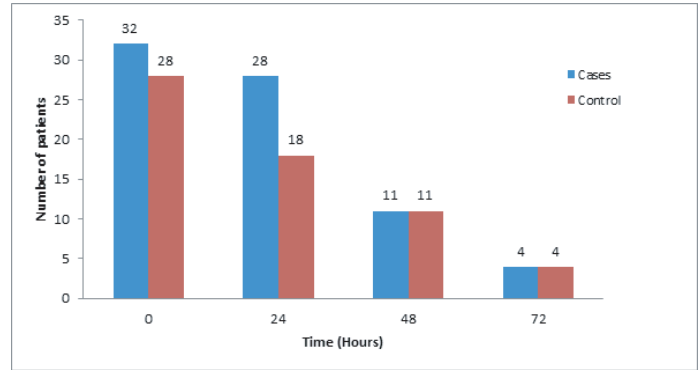
The Mean age in case group was 174.63±98.7 days and in control group 176.86±97.43 days ($P=0.924$). Case group consisted of 25 (71.4%) males and 10 (28.6%) females and control group had 21 (60%) males and 14 (40%) females ($P=0.313$). In case group 28 (80%) patients were fed with breast milk and 7 (20%) patients fed mixed feeding with breast milk and formula milk or other feedings. In control group it was 24 (68.6%) and 8 (31.4%) patients respectively ($p=0.274$). All baseline data has shown in Table I.

Table I : Baseline data of Case and Control groups

	Case group N=35	Control group N=35	P value
Mean age (day)	174.63±98.7	176.86±97.43	0.924 ^{ns}
	n (%)	n (%)	
Sex			
Male	25 (71.4%)	21 (60.0%)	0.313 ^{ns}
Female	10 (28.6%)	14 (40.0%)	
Feeding Status			
Breast Feeding	28 (80.0%)	24 (68.6%)	0.274 ^{ns}
Mixed Feeding with Breast Milk plus formula Milk or food	07 (20.0%)	11 (31.4%)	

In our study most of the patients of both groups had similar sign and symptoms during admission and statistically it was not significant. Clinical findings after initiation of supportive treatment along with zinc and placebo we recorded their condition at 24, 48, 72 hours. We found no significant difference in both Case and Control group (Table II).

Table II : Comparison of clinical manifestations between the two groups at admission and after starting therapy (n=70)



Clinical Sign	At admission			24 hours after admission			48 hours after admission			72 hours after admission		
	Case	Control	<i>P</i>	Case	Control	<i>P</i>	Case	Control	<i>P</i>	Case	Control	<i>P</i>
Rhinorrhea	29	24	0.163 ^{ns}	24	15	0.030 ^s	11	7	0.274 ^{ns}	1	3	0.303 ^{ns}
Fever	22	22	1.000 ^{ns}	11	13	0.614 ^{ns}	3	3	1.000 ^{ns}	0	0	-
Fast Breathing	32	28	0.171 ^{ns}	24	17	0.089 ^{ns}	10	11	0.794 ^{ns}	4	1	0.163 ^{ns}
Dyspnea	29	25	0.254 ^{ns}	13	14	0.806 ^{ns}	6	4	0.494 ^{ns}	3	1	0.303 ^{ns}
Nasal flaring	13	14	0.806 ^{ns}	6	8	0.550 ^{ns}	0	0	-	0	0	-
Chest Indrawing	21	24	0.454 ^{ns}	11	10	0.794 ^{ns}	4	1	0.163 ^{ns}	3	0	0.076 ^{ns}
Wheezing	27	23	0.289 ^{ns}	24	18	0.143 ^{ns}	10	11	0.794 ^{ns}	4	4	1.000 ^{ns}

s= significant; ns=not significant;

P value reached from Chi square test

Clinical response of rhinorrhoea, fast breathing, wheezing and chest indrawing in the 2 groups observed and recorded at the initiation of treatment and during follow up at 24, 48, 72 hours (Clinical response was considered good when the above features improved clinically) In this study patients in control group showed some improvement or recovery from rhinorrhoea, fast breathing, chest indrawing after 24 hours of treatment and wheezing in contrary to patients of case group ($p < 0.05$). But there were no statistically significant differences in recovery from clinical features in 48 and 72 in the two groups ($p > 0.05$). The case group receiving zinc did not differ from the control group receiving placebo regarding rhinorrhoea, fast breathing, chest indrawing and wheezing on 48 hours and 72 hours after treatment (Figure I).

Duration of hospitalization in the case group receiving zinc and in control group were 4.2 ± 2.6 and 4.4 ± 2.2 days respectively and this difference was also not significant.

Discussion

Although zinc supplementation decreases the morbidity of pneumonia in paediatric patients we sought to determine if zinc supplementation mediates a specific effect on the process of healing of acute bronchiolitis in young children. The findings of the present study shows that treatment with zinc sulfate is not favourable in improving the clinical manifestations of acute bronchiolitis in children below 2 years of age. In a double-blind pilot trial Heydarian evaluated the role of zinc sulfate in acute bronchiolitis in children younger than 2 years and concluded that it has no benefit on improvement of the disease.⁹ Another study was conducted by Khoshnevisasl to assess the effect of zinc and vitamin-D on treatment of infants with acute bronchiolitis. They demonstrated that vitamin-D or zinc administration was

ineffective in decreasing tachypnoea and wheezing in children with bronchiolitis.¹⁰

However a double blind placebo controlled trial Abolfazl and Parvis et al showed that administration of zinc sulfate accelerates improvement from clinical signs and symptoms of acute bronchiolitis and recommended the use of zinc sulfate for the treatment of acute bronchiolitis.¹¹ Another study by Ahadi, Mirzarahimi and Barak showed that the use of zinc gluconate as a zinc supplement in infants with acute bronchiolitis could improve tachypnoea, dyspnoea and fever in children aged 2 to 23 months with acute bronchiolitis and decrease the duration of hospitalization.¹²

The findings of some of the above studies are somewhat contradictory. If zinc can be successfully used in the treatment of acute bronchiolitis, then it may not only help to reduce morbidity but also reduce future episodes of wheezing in children. However, we did not find a role of micronutrients such as zinc supplementation in the prevention of wheezing or shorten the symptoms of acute viral bronchiolitis in our study. Despite attempts to identify pharmacologic strategies to improve the clinical course and outcomes of this infection the most effective management of acute bronchiolitis remains limited to supportive care measures mentioned before. There is no solid scientific evidence supporting use of any pharmacologic agents currently available.¹³

Zinc enhances host resistance to infection and plays a critical role in homeostasis of the immune system.¹⁴ Studies that examine the role of zinc deficiency and infant zinc supplementation on RSV bronchiolitis may be important especially among populations with zinc deficiency.¹⁵ Unfortunately, due to economic burden of the parents, serum zinc level of the patients was not evaluated at admission before starting treatment with zinc sulfate. This can be seen as a limitation of our study. However, it is suggested that zinc may have a pharmacologic effect during acute phase of illness to increase the strength of the immune system. This may be seen even in patients with normal level of serum zinc.¹⁶ However we did not observe this possible effect of zinc supplement in our study.

Conclusion

Administration of zinc sulfate during acute bronchiolitis had no benefit on the progression of the disease or its improvement which may be due to the short-term nature of the disease.

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