

## The Role of Zinc Sulfate in Acute Bronchiolitis in Patients Aged 2 to 23 Months

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### Abstract

**Objective:** Evaluating the effect of zinc sulfate in improving the clinical manifestations of acute bronchiolitis in children younger than 2 years.

**Methods:** This was a double blind pilot trial on 50 patients aged 2 to 23 months at Ghaem and Dr. Sheikh Hospitals in Mashhad from January 2008 to March 2009. Patients were randomly divided into two groups: a case group received oral zinc sulfate and to the control group was given placebo.

**Findings:** Mean age of case group was  $168.0 \pm 108.6$  days and control group  $169.2 \pm 90.4$  days ( $P=0.98$ ) with male predominance in both groups. At first there was no statistically significant difference between the two groups in reducing the symptoms. But 24 hours after treating, improvement of some important manifestations including tachypnea, subcostal and intercostal retraction, wheezing and cyanosis revealed statistically significant difference in control group in comparison with case group ( $P=0.04$ ).

**Conclusion:** Zinc sulfate has no benefit in improving clinical manifestations of acute bronchiolitis.

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**Key Words:** Zinc Sulfate; Acute Bronchiolitis; Cyanosis; Tachypnea; Infants

### Introduction

Acute bronchiolitis occurs most commonly in infants and may lead to hospital staying with some morbidity and mortality<sup>[1-6]</sup>. Some infants who suffer from acute bronchiolitis may develop asthma later in their life<sup>[7]</sup>. Finding agents that reduce severity of symptoms and hospitalization

can cause decrement of morbidity. Zinc sulfate is evaluated in cases of pneumonia. There are reports indicating its effectiveness in improving pneumonia<sup>[8,9]</sup>. Other studies did not find efficacy of zinc sulfate in recovering pneumonia<sup>[10,11]</sup>.

To elucidate the effect of zinc sulfate in acute lower respiratory tract infection, we arranged this study.

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## Subjects and Methods

This was a double-blind pilot study on 50 patients aged 2 to 23 months. Acute bronchiolitis was diagnosed clinically and radiologically as first episode of wheezing in previously healthy infant. Patients were randomly divided into two groups: case group took oral zinc sulfate 1% at a rate of 1cc per kg for infants under one year old and 10cc (20 mg of elemental zinc) for patients older than one year old. Control group received placebo. Bottles of drug and placebo were similar in size and shape.

Inclusion criteria were: age 2 months to 23 months and first episode of wheezing attack. Exclusion criteria were: previous episodes of wheezing, congenital heart disease, severe malnutrition, taking zinc sulfate in the last month prior to admission and pneumonia.

Data was collected by written questionnaires. Clinical manifestations including tachypnea defined as respiratory rate above 50 per minute at rest in infants below 1 year old and respiratory rate above 40 per minute at rest in children above 1 year old, wheezing defined clinically as high pitched, musical inspiratory lung sound, cyanosis defined as blue color of mucous membranes and skin, subcostal and intercostal retraction defined as skin inward movement between or below ribs during inspiration, nasal flaring defined as nasal openings enlargement during inspiration, and fever defined as axillary temperature above 37°C, were evaluated at admission, 24, 48 and 72 hours after begin of treatment.

Recovery from acute bronchiolitis was considered when tachypnea, subcostal and intercostal retractions, wheezing or cyanosis were completely improved. These important clinical manifestations were compared between both groups during hospitalization.

Data was analyzed with SPSS version 16.0. For quantitative variables t-test and for qualitative variables Chi-square were used.  $P < 0.05$  was considered significant.

This study was approved by ethics committee of Mashhad University of Medical Sciences. Written consents were obtained from parents before including into the study.

## Findings

There were no significant differences in clinical features regarding cyanosis, tachypnea, intercostal and subcostal retractions, and wheezing in the 2 groups before starting therapy ( $P > 0.05$ ).

Mean age in case group was  $168.3 \pm 108.6$  days and in control group  $169.16 \pm 90.39$  days ( $P = 0.9$ ). Case group consisted of 18 males and 7 females and control group had 15 males and 10 females ( $P = 0.5$ ). Baseline data is shown in Table 1. In case group 20 patients were fed with breast milk and 5 patients with breast milk and formula or other feedings. In control group it was 17 and 8 patients respectively ( $P = 0.4$ ).

Clinical findings before treating and 24, 48, 72 hours after treating is shown in Table 2. Fig 1 shows that 24 hours after treating patients in control group showed complete recovery of tachypnea, cyanosis, intercostal and subcostal retractions and wheezing in contrary to patients of case group ( $P = 0.04$ ). But there was no statistically significant differences in recovery of respiratory distress in days 2 and 3 in the two groups ( $P = 0.9$  for each one).

## Discussion

This study showed that zinc sulfate had no effect in improving clinical manifestations of acute bronchiolitis. Other studies mainly focused on zinc sulfate effects on pneumonia.

Table1: Baseline data of Case and Control groups

	Case group	Control group	P value
Mean age (day)	$168.3 \pm 108.6$	$169.16 \pm 90.39$	0.98
Male/Female	18/7	15/10	0.55
Breast Feeding/Breast feeding plus formula or food	20/5	17/8	0.42

Table 2: Comparison of clinical manifestations between the two groups at admission and after starting therapy

Clinical Sign	At admission			24 hours after admission			48 hours after admission			72 hours after admission		
	Case	Control	P	Case	Control	P	Case	Control	P	Case	Control	P
Rhinorrhea	21	17	0.2	17	11	0.1	8	5	0.5	1	2	0.6
Fever	16	16	1	8	9	0.8	2	2	1	0	0	1
Tachypnea	23	20	0.4	17	12	0.2	7	8	0.8	3	1	0.6
Dyspnea	21	18	0.5	9	10	0.8	4	3	0.7	2	1	0.6
Nasal flaring	9	10	0.9	4	6	0.7	0	0	1	0	0	1
Sub costal retraction	15	17	0.8	8	7	0.8	3	1	0.6	2	0	0.4
Intercostals' retraction	13	9	0.4	1	5	0.2	0	1	0.5	0	1	0.5
Cyanosis	4	6	0.7	1	2	0.5	2	0	0.5	2	0	0.5
Wheezing	19	25	0.01	17	13	0.4	7	8	0.9	3	3	1

Brooks et al studied effect of zinc on children less than 2 years old who suffered from pneumonia. Patients were divided into 2 groups: case group took 20 mg of elemental zinc and control group received placebo during hospitalization. In case group improvement of severity of disease including tachypnea, chest retraction, and hypoxia was accelerated. Also hospital stay was shorter than in control group<sup>[8]</sup>.

Mahalanabis and co-workers reported that severity of disease was decreased in those patients who took zinc<sup>[9]</sup>. This may be attributed to the role of zinc in reducing inflammation of lower respiratory tract resulting in improvement of respiratory distress. Zinc deficiency may damage

mucosal integrity; zinc helps revitalize mucus membranes<sup>[12-15]</sup>. Another mechanism may be immune regulatory role of the zinc<sup>[8]</sup>. It is suggested that zinc through its antioxidant effect may improve symptoms of respiratory tract infection<sup>[16]</sup>.

In another study by Bose et al on patients aged 2 months to 23 months with severe pneumonia, case group took zinc at a rate of 20 mg daily and control group received placebo during hospital stay. It was detected that no significant differences were shown in severity of disease including respiratory rate, chest retractions, feeding disturbances and also in duration of hospital stay<sup>[10]</sup>.

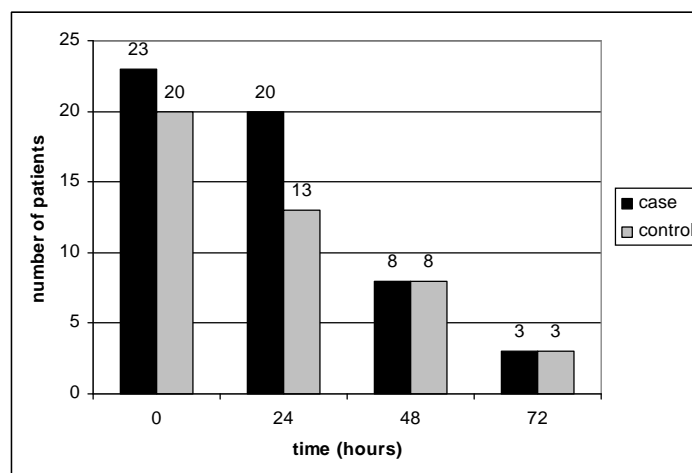


Fig. 1: Clinical response of tachypnea, cyanosis, wheezing, intercostal and subcostal retractions in the 2 groups after starting treatment (Clinical response was considered when all of above clinical features were disappeared)

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Also according to Chang et al zinc had no significant benefit in clinical recovery with regard to decrement of fever duration, respiratory rate or hospital stay in cases aged less than 11 years with acute lower respiratory tract infection<sup>[11]</sup>.

These findings may be due to serum zinc level of both groups. If the rate of serum zinc is within normal range before treating, it is possible that zinc administration does not improve clinical manifestations and hospitalization. Unfortunately-ly we had not evaluated serum zinc level of patients at admission, so that the initial serum zinc level of our case group might have been normal. We do not have any explanation why respiratory distress symptoms were improved significantly 24 hours after therapy in the control group.

The lack of evaluation of serum zinc level in both groups before starting treatment can be seen as a limitation of our study.

## Conclusion

Zinc sulfate administration during acute bronchitis has no benefit on improvement of the disease.

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**Conflict of Interest:** None

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