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

Farhad Heydarian*1, MD; Fatemeh Behmanesh1, MD; Mohammadkhaje Daluee2, MD; Hamidreza Kianifar1, MD, and Mohammadnasir Hematian1, MD

1. Department of Pediatrics, Mashhad University of Medical Sciences, Mashhad, Iran
2. Department of Social Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Received: May 10, 2010; Final Revision: Nov 02, 2010; Accepted: Dec 22, 2010

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±108.6 days and control group 169.2±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.

key Words: Zinc Sulfate; Acute Bronchiolitis; Cyanosis; Tachypnea; Infants
**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 1 cc per kg for infants under one year old and 10 cc (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.

| Table 1: Baseline data of Case and Control groups |
|-----------------|-----------------|--------|
| **Mean age (day)** | **Case group**  | **Control group** | **P value** |
| 168.3±108.6      | 169.16±90.39    | 0.98   |
| **Male/Female**   |                 |        |
| 18/7             | 15/10           | 0.55   |
| **Breast Feeding/Breast feeding plus formula or food** | **Case group** | **Control group** | **P value** |
| 20/5             | 17/8            | 0.42   |
Table 2: Comparison of clinical manifestations between the two groups at admission and after starting therapy

<table>
<thead>
<tr>
<th>Clinical Sign</th>
<th>At admission</th>
<th>24 hours after admission</th>
<th>48 hours after admission</th>
<th>72 hours after admission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case</td>
<td>Control</td>
<td>P</td>
<td>Case</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>21</td>
<td>17</td>
<td>0.2</td>
<td>17</td>
</tr>
<tr>
<td>Fever</td>
<td>16</td>
<td>16</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>23</td>
<td>20</td>
<td>0.4</td>
<td>17</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>21</td>
<td>18</td>
<td>0.5</td>
<td>9</td>
</tr>
<tr>
<td>Nasal flaring</td>
<td>9</td>
<td>10</td>
<td>0.9</td>
<td>4</td>
</tr>
<tr>
<td>Subcostal retraction</td>
<td>15</td>
<td>17</td>
<td>0.8</td>
<td>8</td>
</tr>
<tr>
<td>Intercostals’ retraction</td>
<td>13</td>
<td>9</td>
<td>0.4</td>
<td>1</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>4</td>
<td>6</td>
<td>0.7</td>
<td>1</td>
</tr>
<tr>
<td>Wheezing</td>
<td>19</td>
<td>25</td>
<td>0.01</td>
<td>17</td>
</tr>
</tbody>
</table>

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[8].

Mahalanabis and co-workers reported that severity of disease was decreased in those patients who took zinc[9]. 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[12-15]. Another mechanism may be immune regulatory role of the zinc[8]. It is suggested that zinc through its antioxidant effect may improve symptoms of respiratory tract infection[16].

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 [10].

![Fig. 1](image-url) 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)
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[11].

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 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 bronchiolitis has no benefit on improvement of the disease.

Acknowledgment

This study was supported financially by Vice-Chancel for Research of Mashhad University of Medical Sciences. Also, we thank pediatric residents and nursing staff for special cooperation during this study. The registered No. in IRCT is: IRCT 201011065114 N1

Conflict of Interest: None

References