

Zinc in Acute Bronchiolitis: Is It Really Ineffective?

Rashmi Ranjan Das, MD

Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India

Received: Jul 03, 2011; Accepted: Jul 17, 2011

Dear Editor

I read with great interest the article by Heydarian et al [1]. The authors had conducted a clinical trial and found that zinc supplementation did not benefit clinical manifestations of acute bronchiolitis. The study is well described, but there are few points that need comment.

The authors described that bottles of drug and placebo were similar in size and shape. However, it is well known that, the most important factor in zinc trials have been problem in blinding due to bad taste of zinc salts. There is also no description of the adverse events in the study (even in the zinc group), which is really surprising[2]. So, author's description of double-blinding might have been compromised, with resultant affection of the findings of the study. The authors also excluded children with pneumonia. But, how did they exclude children with viral pneumonia (as both are difficult to distinguish clinically and radiologically)? This is an important question, as it has been found that zinc might not be effective in viral pneumonia[3]. It is also not clear, whether the person responsible for the administration of the intervention and evaluation of clinical signs of bronchiolitis is same or different. Because, if both have been done by the same person, then it might have also affected blinding and resultant data collection. These factors question the validity of the result.

The authors also described that, as studies using zinc have found conflicting results in pneumonia, they conducted this trial to find if zinc benefits another acute lower respiratory tract infection (ALRTI), namely acute bronchiolitis. But

they also did not find any beneficial effect. This can be explained as follows. It is known that, benefit from zinc administration seems to increase after 100 hours of illness, and might be inherent in the mechanism of the zinc effect [4]. So, in an acute illness such as ALRTI, there probably is insufficient time for mounting an immune response to favorably modify the acute illness besides favorably modifying the acute phase response. Secondly, early in an infection zinc is also shifted into the liver due to the acute phase response, whereby it is sequestered for purposes of removing it from pathogen access as well as for reviving up the immune response[5]. This adds weight to the assessment that zinc may work by different mechanisms in ALRTI and acute diarrhea.

Though the authors do not have any explanation why respiratory distress symptoms were improved significantly 24 hours after therapy in the control group, the same has not been shown in the Table 2 (I could not find any result to be significant between the two groups in the table, even after 48 or 72 hrs).

Lastly, the authors describe that, zinc administration does not improve clinical manifestations and hospitalization, in subjects with normal serum zinc level before treatment. However, this is not true if we consider the following points. First, plasma zinc levels are not the most reliable indicators of zinc status in the body[6]. In children with acute infection, zinc level decreases as part of an acute phase response and increases during recovery[6]. Second, plasma zinc level rises even in non zinc supplemented children when they recover from ALRTI, a finding supported by the increase in plasma zinc at discharge among children who did not receive zinc in many of the zinc-pneumonia trials [3,7,8].

To conclude, more research is needed in this area before any firm conclusion can be made. For the result to be meaningful, above factors must be taken care of.

Conflicts of interest: None

* **Corresponding Author; Address:** Department of Pediatrics
All India Institute of Medical Sciences, New Delhi-110029, India
E-mail: dr_rashmipgi@yahoo.com

Key words: Zinc Sulfate; Acute Bronchiolitis; Acute Lower Respiratory Tract Infection

References

1. Heydarian F, Behmanesh F, Daluee M, et al. The role of zinc sulfate in acute bronchiolitis in patients aged 2 to 23 months. *Iran J Pediatr* 2011; 21(2):231-4.
2. Das RR, Singh M. Zinc lozenges for the common cold: Should we ignore the side-effects? *Med Hypotheses* 2011; 77(2):308-9.
3. Brooks WA, Yunus M, Santosham M, et al. Zinc for severe pneumonia in very young children: double-blind placebo-controlled trial. *Lancet* 2004; 363(9422):1683-8.
4. Sazawal S, Black RE, Bhan MK, et al. Zinc supplementation in young children with acute diarrhea in India. *N Engl J Med* 1995; 333(13): 839- 44.
5. Ramadori G, Christ B. Cytokines and the hepatic acute-phase response. *Semin Liver Dis* 1999; 19(2):141-55.
6. Brown KH. Effect of infections on plasma zinc concentration and implications for zinc status assessment in low-income countries. *Am J Clin Nutr* 1998; 68(2 suppl):S425-9.
7. Mahalanabis D, Lahiri M, Paul D, et al. Randomized, double-blind, placebo-controlled clinical trial of the efficacy of treatment with zinc or vitamin A in infants and young children with severe acute lower respiratory infection. *Am J Clin Nutr* 2004; 79(3):430-6.
8. Bose A, Coles CL, Gunavathi, et al. Efficacy of zinc in the treatment of severe pneumonia in hospitalized children <2 y old. *Am J Clin Nutr* 2006; 83(5):1089-96.

Author's Reply

Farhad Heydarian*, MD; Department of Pediatrics, Mashhad University of Medical Sciences, Mashhad, Iran

I thank Dr. Das for his comment on our article. I like to state that in our study^[1] bottles of drugs and placebo were similar in size and shape as well as in taste. This study was performed in two separate hospitals simultaneously and data was collected by different pediatric residents. No significant drug reaction was detected during study.

Since pneumonia is diagnosed radiologically, those patients who had any signs of pneumonia in chest x-ray, were excluded from the study.

It is demonstrated that zinc may improve acute illness. It prevents premature cell destruction and promotes activity of enzymes that affect production of prostaglandin from essential fatty acids, and as a result, leads to decrement of inflammation in airways [2,3]. It also can activate natural killer cells, macrophages and lymphocytes[4]. Zinc administration has also been demonstrated to improve tachypnea in 22 (4-69) hours during acute phase of ALRTI in hospitalized children [5].

It is suggested that zinc may have a pharmacologic effect during acute phase of illness to increase the strength of immune system. This may be seen even in patients with normal level of serum zinc [6]. But I did not observe this possible effect of zinc supplements in our study [1].

Clinical response of tachypnea, cyanosis, wheezing, intercostal and subcostal retractions in the 2 groups after initiation of therapy was illustrated in Fig. 1 of the article [1].

References

1. Heydarian F, Behmanesh F, Daluee M, et al, The role of zinc sulfate in acute bronchiolitis in patients aged 2 to 23 months. *Iran J Pediatrics* 2011;21(2):231-4.
2. Truong-Tran AQ, Grosser D, Ruffin RE, et al. Apoptosis in the normal and inflamed airway epithelium: role of zinc in epithelial protection and procaspase-3 regulation. *Biochem Pharmacol* 2003;66(8):1459-68.
3. Devereux G. Early life events in asthma-diet. *Pediatr Pulmonol* 2007;42(8):663-73.
4. Cousins RJ. Absorption, transport, and hepatic metabolism of copper and zinc: special reference to metallothionein and ceruloplasmin. *Physiol Rev* 1985;65(2):238-309.
5. Chang AB, Torzillo PJ, Boyce NC, et al. Zinc and vitamin A supplementation in Indigenous Australian children. *Med J Aust* 2006;184(3): 107-12.
6. Brooks WA, Yunus M, Santosham M, et al. Zinc for severe pneumonia in very young children: double-blind placebo-controlled trial. *Lancet* 2004; 363(9422):1683-8.

* **Corresponding Author; Address:** Pediatrics Ward, Ghaem Hospital, Ahmad Abad St, Mashhad, Iran

E-mail: heydarianf@mums.ac.ir