



ACUTE LOWER RESPIRATORY TRACT INFECTION; THERAPEUTIC ROLE OF ZINC IN PATIENTS

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Article received on:

04/09/2015

Accepted for publication:

20/11/2015

Received after proof reading:

13/01/2016

ABSTRACT... Zinc is an essential micronutrient with catalytic role in over a hundred specific metabolic enzymes in human metabolism regulates the expression of the metallothionein gene, apoptosis and synaptic signaling and needed for many aspects of immune system. Thus the zinc supplementation in patients with acute lower respiratory tract infections might have potential benefits. **Objectives:** To evaluate the efficacy of zinc supplementation in patients with acute lower respiratory tract infections. **Study design:** Quasi experimental study. **Setting:** Study was conducted in the pediatrics department Independent hospital Faisalabad; the indoor patients meeting the inclusion criteria from 26th January to 25th July 2013 were included in study. **Material and methods:** 100 children meeting the inclusion criteria were included in the study which were divided into two groups with random allocation i.e. Group A (Odd number) & Group B (Even number). Group A was given zinc supplementation 20mg of elemental zinc for 14 days. Along with antimicrobials, oxygen and antipyretics for fever while 50 children in Group B were given with antimicrobials. Oxygen and antipyretics for fever without zinc. **Results:** Baseline clinical parameters were comparable in both groups at admission. Outcome measures considered were duration of fever, tachypnoea, chest indrawings and total duration of hospital admission. Effect of zinc supplementation is significant with p-value of less than 0.05 for duration of tachypnoea and chest indrawings and total duration of hospital admission while result showed p-value equal to 0.05 that is just significant for duration of fever.

Key words: Zinc, lower respiratory tract infections

Article Citation: Bahawal S, Manzoor F, Siddiqui MA, Ahmad S, Sarwar I. Acute lower respiratory tract infection; therapeutic role of zinc in patients. Professional Med J 2016;23(1):065-070. DOI: 10.17957/TPMJ/16.2992

INTRODUCTION

Acute respiratory infections (ARI) are the, leading cause of child mortality in the developing world.¹ Globally at least 4 million children die annually of ARI with acute lower respiratory infections (ALRI) i.e. bronchiolitis and pneumonia accounting for the most of deaths.² In Pakistan 15 million ARI episodes occur in children annually causing at least 100,000 child deaths.³

In Pakistan children less than 5 years of age suffer an average of 6 episodes per year of cough with fever.⁴ Risk factors for ALRI include age less than one year malnutrition. Vitamin A deficiency, low birth weight, lack of immunization, lack of exclusive breast feeding, crowding, exposure to indoor pollutants from combustion of wood or cow dung or smoking.⁵ Etiology of ALRI includes certain pathogens including viruses and bacteria

most commonly. Etiology varies with age of patient.¹² Group B streptococci and E.coli. In Neonates and Streptococcus pneumonia in younger children. Mortality can be prevented with immunization, exclusive breast feeding, vitamin A and zinc supplementation, improved nutrition, improve personal and domestic hygiene and antimicrobial therapy after culture and sensitivity.⁶ Among the different new treatment options for diarrhea zinc supplementation is being studied world widely.⁷ Zinc is an essential micronutrient for catalytic role in over a 100 specific enzymes in human metabolism including oxidoreductases, transferases, hydrolases, lyases. isomerases and ligases.⁸ Zinc also regulates the expression of metallothionein gene, apoptosis and synaptic signaling. Lack of zinc is associated with atrophy of thymus and impaired function of T lymphocytes.⁹ The potential benefits of on immune system can

be mediated via stabilization of the epithelial barrier and function of neutrophils, natural killer cells, monocytes and macrophages.¹⁰ Zinc deficiency increases the risk of mortality from diarrhea pneumonia and malaria by 13-21% its supplementation plays an important role in prevention and treatment of ALRI.¹¹ Thus zinc supplementation in patients with ALRI might have potential benefits. The rationale of this study is to evaluate the therapeutic effects of such a cost effective measure in controlling such a prevailing disease that is putting burden over health services and economy.

PURPOSE OF STUDY

Acute lower respiratory tract infections are the common infectious disease prevailing in our country. In the recent year's education and application of national ARI Programme as designed by WHO for early detection and proper referral of cases of pneumonia has decreased the deaths from the disease. However the morbidity rate for ALRI still remains high, placing an enormous burden on health care system and increasing the misery of parents. Morbidity and hospitalization rate might substantially be reduced by improved case management and emphasis on education of parents and primary health care providers. The new treatment modalities like the introduction of zinc may help us reducing the disease burden and removing the problem like antimicrobial resistance and opportunistic, infections.

MATERIAL AND METHODS

Study Design

Quasi experimental study.

Setting & Duration

This hospital based study was conducted in the pediatric department of Independent hospital Faisalabad affiliated with Independent medical college during period of six months starting from 26th January to 25th July after approval from ethical committee. Only indoor patients with acute lower respiratory tract infection were included in the study.

Sample Size & Sampling Technique

100 children meeting the inclusion criteria were included in the study which were divided into two groups with random allocation i.e. Group A (Odd number) & Group B (Even number). Group A was given zinc supplementation along with antimicrobials, oxygen and antipyretics for fever while 50 children in Group B were given with antimicrobials, oxygen and antipyretics for fever without zinc.

Inclusion Criteria

Children admitted for ALRI of age between 6 months to 5 years of both sexes.

Exclusion Criteria

1. Children with other serious illnesses like septicemia, meningitis, liver or renal failure
2. Children with bronchiolitis syndrome (wheezing and coryza) or established chronic lung disease (bronchiectasis or any chronic cough for over 2 months).

DATA COLLECTION PROCEDURE

100 patients of ALRI meeting the inclusion criteria were selected after explaining purpose, Procedure & risk benefit ratio, addressing the ethical issues & taking informed consent from the parents of the children. Patients were admitted through outpatient department and emergency, diagnosed on the basis of history, examination and investigation.

Exclusion criteria were, strictly followed to control the confounding variables. Patients included in the Study were thoroughly evaluated by taking detailed history including presenting complaints (fever, cough, chest indrawings, level of consciousness, fits or any other complaint) feeding history, vaccination history & examination including general physical examination & systemic examination. These patients were divided in two groups each containing 50 patients by random allocation into two groups, Group A (Odd number) & Group B (Even number). Patients in Group A received zinc sulphate at a daily dose of 20mg (infants under 12 months) or 40mg. Both groups also received appropriate nutrition,

antibiotics, antipyretics and IV fluids according to the requirement. Patients were evaluated daily for parameters like fever, tachypnoea & chest indrawings during the hospital stay. Outcome measures considered were duration of resolution of fever, tachypnoea and chest indrawings and duration of hospital stay. Data collected through an especially designed proforma attached hereby.

DATA ANALYSIS

At the end of the study, results were analysed with the help of SPSS version 12. Study variables were age, gender, symptoms and signs. Simple descriptive statistics were used to analyze the data. Mean and standard deviation were calculated for age, frequency % for gender, symptoms and signs. The variables in examination and investigations were presented as frequency distribution table. Outcome measures were duration of resolution of tachypnoea, fever & chest indrawings & duration of hospital stay and mean & standard deviation were calculated & standard error is calculated to compare both groups. P-value ≤ 0.05 will be considered as level of significance.

RESULTS

In my study outcome measures were duration of fever, tachypnoea and chest in drawings and also the total duration of hospital stay of patient with pneumonia. There was a mark difference noted in all the outcome measures. As far as fever was considered mean duration was 3.34 days for Group A and it was 3.66 days for Group B with Standard Deviation of 1.002 and 0.917 respectively. Statistically this was just significant with P-value = 0.05 as shown in table 1. When tachypnoea was considered as the outcome measure we found out that there was Mean duration of 5.2 day for Group A as compared with 5.92 days for Group B with Standard Deviation of 0.639 and 0.778 respectively. Statistically this was very significant with P-value < 0.05 as shown in table-II.

For duration of 'chest in drawings there was Mean duration of 3.68 days for Group A as compared with 4.50 days for Group B with Standard Deviation of 0.741 and 0.886 respectively. Statistically this was very significant with P-value < 0.05 as shown

in table.³ When total duration of hospital was compared among both groups there was an averagereduction of 0.76 days i.e. 18 hours among Group A children than Group B. There was Mean duration of 8.1 days for Group A as compared with 8.86 day's for Group B with Standard Deviation of 0.735 and 1.05 respectively. Statistically this was very significant with P-value < 0.05 as shown in table.⁴ Above results showed that there was earlier improvement of symptoms in children with zinc supplementation as far as fever, tachypnoea and chest in drawings were considered. Total Hospital stay was also reduced in children having zinc supplementation.

Compliance in our study was acceptable because of regular follow up for six months duration. In our study no systemic side effects of zinc were observed. A few studies have reported vomiting as a side effect of zinc supplementation but we could not evaluate that as vomiting was also as a result of illness itself. The long term follow up was not possible for all the patients as only a few patients returned for weekly follow up for next month after discharge from the hospital, that's why we could not analyze the effect of zinc on prevention of further episodes of ALRI. Other factors influencing the outcome measures like age, socioeconomic status, and use of drugs and nutritional status of the patients were addressed by randomizing the subjects and thus reducing the chance of confounding by the above mentioned and other unknown factors. However: Element of bias cannot be ruled out in a non-blinded study like ours although every effort was made to minimize it.

DISCUSSION

Zinc has significant anti-oxidant and anti-inflammatory activity; children having zinc deficiency are at risk of poor growth diarrhoeal and respiratory tract infections.¹³

Micro nutrients like zinc is essential for childhood health and survival particularly in developing countries.¹⁴ Zinc has heterogeneous effects in different diseases like diarrhea and respiratory tract infections.

| | | Duration of fever (days) | | | | Total |
|-------|-----------------------------|--------------------------|----|----|----|-------|
| | | 2 | 3 | 4 | 5 | 2 |
| Group | A (Zn Supplementation) | 12 | 16 | 15 | 07 | 50 |
| | B (Without Supplementation) | 04 | 20 | 15 | 11 | 50 |
| Total | | 16 | 36 | 30 | 18 | 100 |

Table-I. Duration of fever

| | | Duration of tachypnea (days) | | | | Total |
|-------|-----------------------------|------------------------------|----|----|----|-------|
| | | 4 | 5 | 6 | 7 | 4 |
| Group | A (Zn Supplementation) | 06 | 28 | 16 | - | 50 |
| | B (Without Supplementation) | 01 | 14 | 23 | 12 | 50 |
| Total | | 07 | 42 | 39 | 12 | 100 |

Table-II. Duration of tachypnea

| | | Duration of chest indrawings in days | | | | | Total | |
|-------|-----------------------------|--------------------------------------|----|----|----|----|-------|----|
| | | 2 | 3 | 4 | 5 | 6 | 7 | 2 |
| Group | A (Zn Supplementation) | 02 | 18 | 24 | 06 | - | - | |
| | B (Without Supplementation) | 02 | 02 | 19 | 24 | 02 | 01 | |
| Total | | 04 | 20 | 43 | 30 | 02 | 01 | 01 |

Table-III. Duration of chest indrawings

Group* Duration of chest indrawings in days Crosstabulation

| | | Duration of hospitalization in days | | | | | Total | |
|-------|-----------------------------|-------------------------------------|----|----|----|----|-------|----|
| | | 7 | 8 | 9 | 10 | 11 | 12 | 7 |
| Group | A (Zn Supplementation) | 10 | 26 | 13 | 01 | - | - | |
| | B (Without Supplementation) | 05 | 12 | 21 | 10 | 01 | 01 | |
| Total | | 15 | 38 | 34 | 11 | 01 | 01 | 01 |

Table-IV. Duration of chest indrawings

We can compare our study with other international studies because of the difference in doses, population and study design and outcome measures. We can interpret the results of these studies in relation to our study.¹⁵

As far as our Study is concerned, there is significant reduction in the duration of fever, tachypnoea and chest in drawings in zinc supplemented group. In our study twice daily recommended dose is used for supplementation to avoid the impairment in absorption due to worm infestation or infection.¹⁶ Comparing the results with a study done in India and Johns Hopkins University seventy children aged 2-36 months were randomized to receive 30 mg elemental zinc (as zinc acetate syrup) or placebo daily. The zinc group had reduced duration of severe pneumonia including duration of lower chest in drawing, respiratory rate >40/min, oxygen saturation <90% and' duration of

hospitalization.¹⁷

Results in our study also showed that there was rapid improvement of symptoms in children with zinc supplementation as far as fever, tachypnoea and chest in drawings were considered. Zinc supplementation in children leads to reduction in total hospital stay.

Beck FW et.al determine that 30mg/day zinc reduce the number of days of oral antibiotic in patients in pneumonia higher doses of zinc needed to decrease infections.¹⁸

Mazumdars et.al shows 45% reductions in incidence of acute lower respiratory tract infection in zinc supplemented children 20mg of zinc daily for 120 days.

Dilip Mahalanabis et al randomized children

shows use of zinc > than 2 month for children < 6 year age has a beneficial effect on number episodes of respiratory illness. Days of illness, respiratory tract infections (rate ratio 0.86) and significantly fewer attacks of infections rate ratio (0.70) than those who received placebo.¹⁹

AMJ Clin Nutr et.al showed that plasma zinc concentration > 8.4 micro mol/L had a beneficial role in morbidities due to respiratory infections.

Study done in Bangladesh reports that decline in morbidity infants 1-12 month of age who were small for gestational age received zinc suggests benefits in this age group.

Peter Carter propose that zinc has protective role for airways epithelium due to its antioxidant properties airways epithelium shows more concentration of zinc as compare to alveolar epithelium. Zinc supplemented children had 0.17 episodes / child / year compare with 0.35 episode in control children.

Study done by sentz J, Miller et al shows that zinc supplementation reduce the number of episodes and days of hospital stay, severity of bronchiolitis and pneumonia up to 50%.

Bose A et al in a study suggested that there were no clinical or statistically significant differences in the duration of tachypnoea, hypoxia, chest in drawings, inability to feed, lethargy, severe illness, or hospitalization. Zinc supplementation was associated with a significantly longer duration of pneumonia in the hot season (P = 0.015).²⁰

Study done by RR Das et.al shows that zinc not only have a preventive role, find a therapeutic role of zinc in children < 5year of age hospitalized for sever acute lower respiratory tract infection.

Meta-analysis of studies in South East Asia shows those children who were given 70 milligrams of zinc per week have less episode of bronchiolitis and pneumonia but this review was not able to determine whether zinc less effective if lower doses were given.

CONCLUSION

On the basis of our study. We conclude that the use of zinc is very much beneficial in reducing the duration of fever, tachypnoea and chest indrawings and also the total duration of hospital stay in children admitted with the diagnosis of ALRI. This study of zinc supplementation may help us reducing the disease burden and removing the problem like drug resistance and opportunistic infections.

However like any good study, it has raised further questions, which should be addressed by larger drug trials and its interaction with other drugs and possible adverse effect by using the therapeutic doses. Our study also could not address the role of zinc in prevention of repeated ALRI but this is an area which definitely requires further research.

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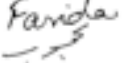



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“Creativity is thinking up new things.
Innovation is doing new things.”

Theodore Levitt 1925-2006

AUTHORSHIP AND CONTRIBUTION DECLARATION

| Sr. # | Author-s Full Name | Contribution to the paper | Author=s Signature |
|-------|---------------------------|--|---|
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| 2 | Dr. Farida Manzoor | Data collection |  |
| 3 | Dr. Mehboob Alam Siddiqui | Data collection and analysis |  |
| 4 | Dr. Shakil Ahmad | Data collection and & supervision |  |
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