

Role of Zinc Supplementation in Treatment of Pneumonia

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ABSTRACT

Aim: To compare the mean duration of treatment with and without zinc supplementation as adjunct to antibiotic treatment for pneumonia in children 2 to 59 months of age.

Method: This present study was Randomized Controlled Trial conducted at Department of Pediatrics, Fatima Memorial Hospital, and Lahore. In this study non probability purposive sampling technique was used. After taking approval from ethical committee of hospital, 100 children fulfilling the selection criteria were enrolled. Informed consent from parents was taken. Demographic information (name, age, sex, address) were obtained. Children were randomly divided into two groups by using lottery method. Group A was get standard antimicrobial (ceftriaxone) treatment only. Group Z got zinc as adjunct therapy and standard antibiotics (ceftriaxone). Oral zinc was given in dosage of 10mg once daily in <1 year children and 10mg twice daily to children >1year old. Duration of recovery was noted from start of treatment till resolution of symptoms. Both groups were compared for mean duration of recovery by using independent sample $t < 0.05$ was considered as significant. **Results:** Total 100 cases were enrolled in this study. The mean age of the children was noted as 28.94 ± 17.58 month with minimum and maximum age of 2 & 59 days respectively. The study results showed 43% patients were males while 57% patients were females. In this study 50(50%) patients were appeared with resolution of temperature and 50(50%) appeared with no resolution of temperature. Resolution of Tachypnea was observed in 61% patients whereas it was not observed in 39% patients. **Conclusion:** Addition of zinc as adjunct to standard treatment for pneumonia is beneficial in reducing the course of treatment. Moreover, helpful in reducing duration of disease symptoms.

Keywords: Children, duration of treatment, pneumonia, standard antibiotic, Zinc Supplementation

INTRODUCTION

Pneumonia continues to be the biggest single cause of childhood death, accounting for approximately 20% of the 10 million annual deaths globally¹. The pneumonia is responsible for more than 2 million deaths each year in children below 5 year of age and contributes for 20% of annual deaths in this age group in under developed countries². The estimated incidence of clinical pneumonia in children aged below 5 years is 0.29 episodes per child per year³.

Pneumonia represents an inflammatory, usually infectious process involving the alveoli and airway structures of the lungs. The treatment is empirical antibiotics and adjunctive therapy (oxygen, intravenous fluids, nebulization) according to requirement. The role of zinc as an adjunct in treatment of pneumonia is controversial. Srinivasan has proved in a study that zinc adjunct therapy reduces case fatality rate in severe childhood pneumonia^{4,5}.

Another study in Multan, Pakistan demonstrated that recovery time in children supplemented with zinc along with conventional treatment was 4.6 ± 0.125 days while without zinc supplementation

was 6.84 ± 0.269 days (p -value= <0.05)⁶. On contrary a randomized controlled trial, yielded a small but statistically insignificant efficacy for zinc in hospitalized 2-35 months old children. The median time to recovery with zinc supplementation group was 49 days and without zinc supplementation was 49 days (p -value=0.22)^{3,7}.

Recently a study from Nepal also demonstrated that adjuvant zinc neither reduced the risk of treatment failure nor hasten recovery from non-severe or severe pneumonia².

Rationale of this study is that only two studies are published in Pakistan, one show there is good results with zinc supplementation⁶ but other one show no effect of zinc on pneumonia duration⁸. So to resolve this confusion this study was conducted.

Diagnosis was done according to WHO criteria i.e., Fever (Temperature >98.6 °F), cough, chest in drawing, nasal flaring, cyanosis and tachypnea (RR >50 /min in children <1 year and >40 /min in children from 1 to 5 year). Symptom of tachypnea was mandatory along with any 2 or more symptoms. Duration of treatment was measured in days starting from the day of admission till the resolution of pneumonia i.e., when there was resolution of fever (temp= 98.6 °F) and resolution of tachypnea for at least 24 hours of duration.

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MATERIALS AND METHOD

This randomized controlled trial was conducted in the Department of Pediatrics, Fatima Memorial Hospital, Lahore. Sample size of 100 cases; 50 cases in each group is calculated with 95% confidence interval, 90% power of test and taking magnitude of duration of treatment i.e. 4.6 ± 0.125 days with zinc and 6.84 ± 0.269 days without zinc supplementation as adjunct to antibiotic treatment for pneumonia in children 2 to 59 months of age. Sampling Technique used was non probability, purposive sampling. Both male and female children of age 2-59 months of admitted with diagnosis of pneumonia were included in the study. After taking approval from ethical committee of hospital, 100 children fulfilling the selection criteria were enrolled from indoor ward of Department of Pediatrics, Fatima Memorial Hospital, and Lahore, Informed consent from parents was taken. Demographic information (name, age, sex, address) was obtained. Children were divided into two groups by using lottery method. Group A got standard antimicrobial (ceftriaxone) treatment only.

Group Z got zinc as adjunct therapy and standard antibiotics (ceftriaxone). Oral zinc was given in dosage of 10mg once daily in <1 year children and 10mg twice daily to children >1 year old. Duration of recovery was noted from start of treatment till resolution of symptoms (as per operational definition). All the information was recorded on a predefined Proforma.

All the collected information was entered and analyzed through SPSS version 16. Quantitative data like age, duration of recovery was presented as mean, standard deviation. Qualitative data like gender was presented as frequency and percentage. Both groups were compared for mean duration of recovery by using independent sample t-test. p-value <0.05 was considered as significant. Stratification with respect to age and gender was done.

RESULTS

Total 100 cases were enrolled in this study. The mean age of the children was noted as 28.94 ± 17.58 month with minimum and maximum age of 2 & 59 days respectively. The study results showed 43% patients were males while 57% patients were females. In this study 50(50%) patients were appeared with resolution of temperature and 50(50%) appeared with no resolution of temperature. Resolution of Tachypnea was observed in 61% patients whereas it was not observed in 39% patients. The mean duration of time of the patients was noted as 5.14 ± 1.38 days with minimum and maximum values of 3 & 8 days respectively.

In this study the mean duration time of the patients in with zinc group was noted as 4.34 ± 1.06 days and the mean duration time in without zinc group was noted as 5.94 ± 1.20 days. Statistically there is highly significant difference was found between the study group. The study results showed that 50 patients were appeared with zinc group in which 22 were females and 28 were males, similarly 50 patients appeared with without zinc group in which 21 were males and 29 were females. Statistically there is insignificant difference was found. In this study the mean age of the with zinc group patients was noted as 29.08 ± 17.55 days where in without zinc group study groups. i.e., p-value=0.93

Table

	Study group with zinc	Study group A Without zinc
n	50	50
Mean	4.34	5.94
SD	1.06	1.20

DISCUSSION

This present study was conducted at Department of Pediatrics, Fatima Memorial Hospital Lahore to determine the mean duration of treatment with and without zinc supplementation as adjunct to antibiotic treatment for pneumonia in children 2 to 59 months of age. Acute respiratory infections (ARIs), especially pneumonia and diarrhoeal disorders are the two most common causes of death in low-income countries. Zinc supplementation as an adjunct to antibiotics failed to show any significant effect on time clinical recovery from pneumonia in children. Children with zinc deficiency have increased susceptibility to bacterial disease and are more likely to die.^(9,10) The annual estimated incidence of pneumonia is 151 million new cases per year (Rudan 2004), of which two million die annually. It is the largest killer, accounting for 19% of all child deaths in low-income countries (Bryce 2005; Rudan 2008), and with the inclusion of neonatal pneumonia, recent estimates indicate that it accounts for 28% to 34% of deaths globally in children below five years of age.⁽¹¹⁾ Our study results showed that duration of time reduces in patients who were treated with zinc supplements as compared to without zinc supplements. In our study highly significant difference was found between the study groups and duration of time of the patients. Some studies support the results of our study but some are in controversy. As Brooks 2004 evaluated the effect of 20 mg of daily zinc supplementation on clinical recovery in children treated for severe pneumonia with intravenous antibiotic therapy. They did not find any impact of zinc on recovery from severe pneumonia¹². The Bose

2006 trial also evaluated the effect of daily 20mg zinc supplementation in children with severe pneumonia treated with intravenous benzyl penicillin and gentamicin and found no overall effect of zinc supplementation on clinical recovery or duration of hospitalization¹³.

Palle Valentiner-Branth, et al concluded in their study that adjuvant treatment with zinc neither reduced the risk of treatment failure nor accelerated recovery in episodes of nonsevere or severe pneumonia. There was no difference in time to recovery between zinc and placebo group for non severe (median: 2 d; hazard ratio: 1.0; 95% CI: 0.96, 1.1) or severe (median: 4 d; hazard ratio: 1.1; 95% CI: 0.79, 1.5) pneumonia. However a study conducted in Bangladesh demonstrated a significant difference in time to normalization of respiratory rate (40 to 48 hours in the zinc and placebo group.

In our study the mean duration time of symptoms at the time of enrollment the patients was noted as 5.4±1.38 days.

The mean duration of illness at enrollment in the Vellore trial was 5.8±11.0 days in the zinc-treated group and 4.7±6.2days in the placebo group. This is nearly 3 days longer than the average duration of illness in the Bangladesh trial. It has been suggested that the longer duration of illness at enrollment may indicate that the children in the Vellore trial suffered from milder illnesses or were in recovery at admission. However, with the five times greater rate of treatment failure. Vellore, it seems unlikely that the illnesses were milder in that study than in the Bangladesh trial¹⁴.

CONCLUSION

Thus it has been concluded that additional of zinc as adjunct to standard treatment for pneumonia is beneficial in reducing the course of treatment moreover, helpful in reducing duration of disease symptoms. Now in future we are able to implement the use of zinc supplementation for early recovery of pneumonia in children <6 years of age.

REFERENCES

1. Ngom PT, Howie S, Ota MO, Prentice AM, Watanabe H, Sato S, et al. The potential role and possible immunological mechanisms of zinc adjunctive therapy for severe pneumonia in children. *The Open Immunology Journal*.2011;4:1-10
2. Shah GS, Dutta AK, Shah D, Mishra OP. Role of zinc in severe pneumonia: a randomized double blind placebo controlled study. *Ital J Pediatr*. 2012;38:36
3. Basnet S, Shrestha PS, Sharma A, Mathisen M, Prasai R, Bhandari N, et al. A randomized controlled trial of zinc as adjuvant therapy for severe pneumonia in young children. *Pediatrics*. 2012;129(4):701-8
4. Rudan I, Boschi-Pinto C, Biloglav Z, Mulholland K, Campbell H. Epidemiology and etiology of childhood pneumonia. *Bulletin of the World Health Organization* 2008;86(5):408-16B
5. Srinivasan MG, Ndeezi G, Mboijana CK, Kiguli S, Bimenya GS, Nankabirwa V, et al. Zinc adjunct therapy reduces case fatality in severe childhood pneumonia: a randomized double blind placebo-controlled trial. *BMC medicine*. 2012;10(1):14
6. Iqbal I, Mahmood S, Tariq A. Effect of oral zinc supplementation on duration of illness and mortality in children in conventional treatment for pneumonia. *Nistar Med J*. 2010;2(2):51-5
7. Valentiner-Branth P, Shrestha PS, Chandyo RK, Mathisen M, Basnet S, Bhandari N, et al. A randomized controlled trial of the effect of zinc as adjuvant therapy in children 2-35 mo of age with severe or nonsevere pneumonia in Bhaktapur, Nepal. *Am J Clin Nutr* 2010;91(6):1667-74.
8. Haider BA, Lassi ZS, Ahmed A, Bhutta ZA. Zinc supplementation as an adjunct to antibiotics in the treatment of pneumonia in children 2 to 59 months of age *CochraneDatabaseSystRev*.2011(10):CD007368
9. Bryce J, Boschi-Pinto C, Shibuya K, Black RE. WHO estimates of the causes of death in children. *The Lancet*. 2005;365(9465):11475-52
10. Rudan I, Tomaskovic L, Boschi-Pinto C, Campbell H. Global estimate of the incidence of clinical pneumonia among children under five years of age. *Bulletin of the World Health Organization*. 2004;82(12):895-903.
11. Wardlaw T, Salama P, Johansson EW, Mason E. Pneumonia: the leading killer of children. *The Lancet*. 2006;368(9541):1048-50
12. BrooksWA, Yunus M, Santosham M, Wahed M, Nahar K, Yeasmin S, et al. Zinc for severe pneumonia in very young children: double-blind placebo-controlled trial. *The Lancet*. 2004;363(9422):1683-8.
13. Bose A, Coles C, Gunavathi JH, Moses P, Raghupathy P. Efficacy of zinc in the treatment of severe pneumonia in hospitalized children < 2 y old.[see comment]. *American Journal of Clinical Nutrition*. 2006;83(5):1089-96.
14. Bhatnagar S, Wadhwa N, Aneja S, Lodha R, Kabra SK, Natchu UCM, et al. Zinc as adjunct treatment in infants aged between 7 and 120 days with probable serious bacterial infection: a randomised, double-blind, placebo-controlled trial *TheLancet*. 2012; 379(9831): 2072-8.