A prospective study of effect of zinc as adjuvant therapy in acute pneumonia in children under 5 year of age

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Abstract

Introduction: It is has been observed from the work of various author that zinc deficiency is associated impaired growth and immune function. Trail for evaluation of efficacy of zinc as an adjuvant to therapy in children with mild to moderate zinc deficiency has been conducted. Some study has suggested that it is associated with accelerated recovery and reduced duration of hospital stay, but so many trail in India have found no effect. The present study was undertaken to study the effect of zinc as on adjuvant therapy in acute pneumonia beside standard anti-microbial agent in children below 5 year of age.

Materials and Methods: About 116 children under five years of age were enrolled for this study based on inclusion and exclusion criteria. They were grouped in to two study groups by stratified randomisation. Each group consists of 55 children and 6 children were, dropped from the study.

Result: The mean time of resolution of distress was higher in group B than group A that is 60.48 VS 48.42 having P value 0.2840 which is not significant statistically. The mean duration of oxygen use was 20.42 hr in group A and 36.42hrs in group B with P value 0.4326 which is not significant. Patients in group A has taken less time to become asymptomatic that is (64.27 hrs versus 52.73 hrs) but this difference is not significant (P=0.138006). The duration of stay of group B patients were significantly higher than group A (8.13 hrs vs 7.2hr) with P value 0.021274.

Discussion and Conclusion: From our study we would like to conclude from our result that adjuvant treatment with 20 mg zinc per day along with antibiotic is associated with accelerated achievement of saturation above 90% and reduced duration of stay in hospital.

Keywords: Zinc, Adjuvant therapy, Paediatric pneumonia.

Introduction

As per the fact sheets on pneumonia published on 7 November 2016, pneumonia accounts for 10% of all deaths of children under 5yrs old. It remains the leading cause of under five children death globally killing approximately 2400 children per day.[1,2] As per the report of sample registration system (2010-2013), pneumonia (17.1%) is the second most common cause of death, after prematurity and low birth weight.[3] A healthy child with natural defences can fight with infection. But child with compromised immune system are at higher risk of developing pneumonia. Reason for compromised immune system may be malnutrition and under nutrition, in addition to other causes which is less common.

It is has been observed from the work of various author that zinc deficiency is associated impaired growth and immune function.[4] Bahl et al has reported that among all the children the prevalence of acute lower respiratory tract infection was about 3 fold higher in zinc deficient and duration of ALRI was also prolonged[5]. Shankar and Prasad et al[6] has summarised his observation by stating that zinc deficiency has greater effect on infections requiring T-lymphocyte- dependent antibody responses and where IgG required for protection. Infections for which Thl cytokines like IFN-Y is required are more effected. He has also stated that development of immunological cells is most sensitive to zinc deficiency indicating it to be critical area for intervention.

As per the report of WHO, in total 1.4% (0.8 million) of deaths worldwide were attributable to zinc deficiency 1.4% in males, and 1.5% in females. Zinc deficiency is responsible for lower respiratory tract infection. Trail for evaluation of efficacy of zinc as an adjuvant to therapy in children with mild to moderate zinc deficiency has been conducted. Some study has suggested that it is associated with accelerated recovery and reduced duration of hospital stay, Ehsan Valavi et al,[8] but so many trail in India have found no effect.[9]

The present study was undertaken to study the effect of zinc as on adjuvant therapy in acute pneumonia beside standard anti-microbial agent in children below 5 year of age.

Materials and Methods

Present study is a prospective randomised trail conducted in the department of paediatric Konaseema institute of medical science from February 2016 to September 2018.

This study is approved by institutional ethics committee and a written informed consent was obtained from parent or guardian of patient before enrolment for study. Patients were enrolled as per exclusion and inclusion criteria.

Inclusion Criteria

1. Age below 5yrs
2. Full filling WHO/IMCI guideline of pneumonia
3. Both sex

Exclusion Criteria

1. Congenital heart disease
2. Developmental delay
3. Congenital lung deformities

4. Pneumonia other than community acquired pneumonia

Sample Size: Based on previous studies and considering power of study to be 80% and 5% significant level sample size was calculated to be 54, by using n master version 2.0 soft were.[10,11]

About 116 children under five years of age were enrolled for this study based on inclusion and exclusion criteria. They were grouped in to two study groups by stratified randomisation. Each group consists of 55 children and 6 children were, dropped from the study.

At the time of admission various parameters, like respiratory rate, chest in drawing was observed. The oxygen saturation (by pulse oximeter), auscultator finding like, bronchial breath sounds, wheeze, crept, and danger signs like cyanosis, inability to feed, lethargy, convulsion, unconsciousness, and stridor was noted. Patient who full fill the WHO/IMCI guideline of pneumonia were enrolled, Severe Pneumonia is defined as a respiratory rate >50/min, which was accompanied with crepitation on auscultation and the presence of >1 of the following danger signs: lethargy, inability to feed, chest in drawing, or central cyanosis.

Group A = Along with standard treatment of pneumonia, received 20mg of elemental zinc.

Group B= they were given standard treatment of pneumonia without zinc.

All the children were given standard treatment for the pneumonia in the form of oxygen, intravenous fluids, bronchodilators, and parental antibiotics was prescribe and care was taken about its interaction with zinc so that those antibiotic can be avoided, once respiratory distress get settled intravenous fluid stopped and patient were shifted to oral feeding.

Observation were noted interns of time of disappearance of danger signs, time taken to reach saturation more than 90%, time for resolution of tachypnoea and retraction, time to become asymptomatic, which can be defined as resolution of distress and disappearance of danger signs with saturation above 90% in room air.

Statistical Analysis

Data were collected and analysed by using SPSS version 19.0 .paired t- test and chi-square test was used for calculation of P value. P values less than 0.05 was taken to be significant.

Estimation of Zinc: Two millilitre of blood was collected from all children enrolled for this study, was centrifuged and zinc estimation was made by systronic spectrophotometer. Reference range of normal zinc level was set as 65-150ug/dl.

Result

In present study a total of 116 patients were enrolled. This out of that 6 patients were dropped, remaining 110 patients were equally divided in to two groups.

Table 1: Demography of the patients and control (n=10)

variables		Group A	Group B	P value
Age	< 1yrs	24	23	0.8471
	1-5yrs	31	32	chi square statistic 0.0371
Sex	male	40	38	0.8486
	female	15	17	chi square statistic 0.0364
Region	Rural	32	34	0.6970
	Urban	23	21	chi square statistic 0.1515

As per tables 1 number of patients below one year in group A was 24and in group B it was 23. Numbers of patient between 2 to 5 yrs were 31 in group A and 32 in group. The P value was 0.8471 which was not significant. There was 40 male and 75 female in group A and 38 male and 17 female children in group B. There was no statistical difference between two group regarding age of patients. 32 patients were from rural area and 23 patients were form urban area in group A. similarly in Group B 34 patients were from rural area and 21 patients were form urban area P value 0.6970.

Table 2: Clinical profile of the patient in two groups

Variables		Group A	Group B	P value
Chief complains	fever	55	55	0.970678 chi. Square statistic 0.0595
	Tachypnoea	53	50	
	cough	55	55	
Respiratory rates	1<yrs			P value 0.871 chi. Square statistic 0.0264
	50-60	11	10	
	>60	13	13	
	>1yrs			0.6744 chi. Square statistic 0.1765
	40-50	20	19	
	>50	11	13	
Oxygen saturation	<90	27	28	P=0.0364 chi. Square statistic 0.848
	>90	28	27	

As per table 2 regarding clinical profile of the patients,

All the patients were presented with fever in both groups; tachypnoea was present in 53 patients in group A and 50 patients in group B. In Group A, 11 below one year patients were having respiratory rates 50-60 /min. In Group B, same was present in 10 patients. 13 patients in both groups have respiratory rate more than 60/mins. In above one year old patients, 20 patients in group A having respiratory rate between 40-50 /min and in group B, 19 patients respiratory rate was between 40 to 50/min.

Among more than one year old patients in Group A, 11 patients have respiratory rate more than 50/min, 13 patients in group B have respiratory rate more than 50/min. Both the groups were not significantly different from each other. 27 patients in group A have oxygen saturation less than 90 and 28 patients in group B have oxygen saturation less than 90. More than 90 oxygen saturation was present among 28 patients in group A and 27 patients in group B the P value was 0.848 which is not significant.

Table 3: Danger signs of pneumonia

Variables	Group A	Group B	P value
absent	9	8	0.6786
present	46	47	0.1717

As per table -3 in group A danger signs were present in 36 patients and absent in 18 patients. In group B danger signs were present in 38 patients and absent in 18 patients. There is no difference between two groups, having P value 0.6786.

Table 4: Chest refraction, and severity of pneumonia

Variables		Group A	Group B	P value
Chest retraction	Present	8	9	0.791955 chi Square statistic 0.696
	Absent	47	46	
Chest findings	Crepts	46	45	0.704807 chi Square statistic 0.6997
	Wheeze	24	18	
	Bronchial breath sound	6	7	
Severity of Pneumonia	Pneumonia	12 (21.8%)	16(29.9%)	0.381286 Square statistic 0.>664
	Severe pneumonia	43(28.2%)	39(70.1%)	

Regarding various clinical finding in chest, in Group A chest retraction was found in 8 patients and absent in 47 patients, In group B, chest retraction was present in 9 patients and absorption 46 patients having p value 0.791955.Regarding auscultatory finding in chest, in group A 46 patients present with crepts, wheeze was present in 24 patients and 6 patients have bronchial breath sounds. Similarly in group B crepts was present in 45 patients, 18 patients presented with wheeze and bronchial breath sound was present in 8 patients the P value was 0.704807.43 patients in group A were presented with severe pneumonia and 12 patients having pneumonia, similarly in group B 39 patients were presented with severe Pneumonia and 16 patients presented with pneumonia. P value was 0.381286.

Table 5: Relation between levels of zinc inμg/ dl in two groups

Variables	Group A	Group B	P value
<60 (μg/ dl)	15(27.27)	14(25.45)	Chi Square statistic 0.2314 P=0.890
60-150 (μg/ dl)	36(65.45)	38(69.09)	
>150 (μg/ dl)	4(7.2%)	3(5.45%)	

In Group A zinc level in blood was below 60 μg /dl in 15 patients, in 36 patients it was between 60-150 μg/ dl, and in 4 patients it was more than150 μg/dl similarly in group B, 14 patients have zinc level below 60μg /dl, 38 patients have zinc level between 60μg /dl to 150 μg /dl and 3 patients have zinc level above 150μg /dl. The P value was 0.890.

Table 6: Companion of study variables in two groups

Variables	group	<24	24-48	48-72	>72	P value
Time for disappearance of danger sign	GP A	12	38	10	5	0.6155
	GP B	10	26	10	9	
Time to reach saturation 90%	GP A	14	32	8	1	0.0066
	GP B	8	24	15	10	
Time for resolution of distress	GP A	10	34	11	1	0.4024
	GP B	6	30	18	1	
Time to be asymptomatic	GP A	8	22	20	5	0.2936
	GP B	4	16	20	10	
Duration of 02 use	GP A	40	13	1	0	0.19406
	GP B	30	20	4	0	

As per table-6 regarding comparison of various variables in group A danger sign was disappear within 24hr in 12 patients, between 24hr to 48hr in 38 patients, 48hr to 72hr in 10 patients and after 72hr in 5 patients. In group B, danger signs of pneumonia disappear within 24hr in 10 patients, between 24to 48hr in 26 patients between 48 to72hrs in 10 patients and more than 72 hr, in 9 patients the P value was 0.6155.

In group A 14 patients have reached saturation more than 90% in 24hours, 32 patients reached saturation 90% in 24-48hrs.8 patients took 72 hour and 1 patients took more than 72hour to reach saturation 90%.

In group B eight patient reached saturation in 24hour, 24 patients achieved saturation in 48hour, 15 patients has taken 74hour to achieve saturation 90% 10 patients has reached saturation after 72hr. This finding was significant statistically with P value 0.0066.

In ten patients of Gr A distress get resolved in 24hr, in 34 patients it has taken 24to 48hr. Distress resolution has taken 48 to 72hr in 11 patients, but in 1 patient it has taken more than 72hr.

Similar in group B time taken for resolution of distress was less than 24hr in 6 patients, in 30 patients it was between 24 to 48hours, In 18 patients time taken for regulation of distress was 48-72hr, in one, patient time taken for resolution of distress was more than 72hr. This was significant statistically having P value 0.4024.

In group A 8 patients become asymptomatic in 24hr, 22 patients become asymptomatic in 24to 48hr. 20 patients has taken48 to 24hr to become asymptomatic 5 patients has taken more than 72hr to become asymptomatic. Similarly in group B, 4 patients become asymptomatic in 24hr, in 16 patients it has taken 24-48hr, 20 patients become asymptomatic in 48 to 72hrs 10 patients has taken more than 72 hrs to become asymptomatic. Both groups are not different statistically as P value is 0.2936.

In group A 40 patients required 02 for less than 24hr, 13 pts required for 24to 48hr, 1 patient required for 48to 72hr, and 1patient required for more than 72hr. In group B, 30 patients required 02 for 24hr, 20 patients required for 24 to 48hr, 4 patients require 02 for 48 to 72hrs and 1 patient required for more than 72hr. The P value was 0.1940.

Table 7: Duration of stayin hospital

Group	7days	7 to 15days	>10days	P value
GP A	44	10	1	0.003365
GP B	28	20	7	

Regarding duration of stay in hospital, in group A 44 patient's duration of stay in hospital was less than 7days. For 10 patients duration of stay was between 7 to 10days. One patient stayed for more than 10days. In group B, duration of stay less than 7 days was in 28 patients between 7 to 10 days was in 20 patients and more than 10days was in 7 patients. This difference in group was statistically significant with P value 0.0003365.

Table 8: Comparison of outcome of treatment in two groups

variables	GP A zinc mean +SD	GP B zinc mean +SD B	P value
Time for disappearance of danger sign(hr.)	42.3±9.86	48.6±11.033	0.79117
Time for reach saturation above 90%	36.42±12.79	44.42±15.09	0.037407
Time for resolution of distress.	48.42±22.34	50.48±23.42	0.2840
Duration of oxygen use	20.42±28.40	36.42±33.4	0.4326
Time to become asymptomatic	52.73±11.72	64.27±9.24	0.138006
Duration of stay in hospital	7.2±1.6	8.13±1.58	0.021274

As per table 8 mean time for disappearance of danger sign were 42.3±9.86 hr in group A and 48.06± 11.033 hrs in group B having P value 0.79117. This is not significant. Mean time to reach saturation above 90% was 36.42± 12.79 hrs in group A and 44.42± 15.09 hrs in group B the P value was 0.037407 which is statistically significant.

The mean time of resolution of distress was higher in group B than group A that is 60.48 VS 48.42 having P value 0.2840 which is not significant statistically. The mean duration of oxygen use was 20.42 hr in group A and 36.42hrs in group B with P value 0.4326 which is not significant. Patients in group A has taken less time to become asymptomatic that is (64.27 hrs versus 52.73 hrs) but this difference is not significant (P=0.138006). The duration of stay of group B patients were significantly higher than group A (8.13hrs vs 7.2hr) with P value 0.021274.

Discussion

The present study has been conducted to evaluate the efficacy of zinc supplementation as an adjuvant therapy to acute pneumonia in paediatric patients. A total 110 patients were enrolled and divided in to two groups. Overall basic characteristics, clinical profile and findings were comparable between two groups.

In our study we have included patients below 5yrs of age, and divided in two groups that is less than 1yr and between 1-5yrs and is comparable to each other which corroborates with the study of Valentiner Branth et al.[8] There was male predominance in both group and patients

were mostly from rural then urban area. Both the groups were statistically comparable to each other with P value more than 0.05 which is supported by the work of shah GS et al,[9] and Tejesh Malla et al.[12]

Regarding clinical profile of patients there was no significant difference between two groups with respect to chief complains, respiratory rates and oxygen saturation which corroborates with the finding of Vasudev Komapally et al.[13]

We have observed that among all the patients enrolled for study percentage of severe pneumonia (78% in Gr A and 70% in group B) was higher than pneumonia, which is supported by the work of Sudha Banet et al.[14]

In present study serum zinc level below 60microgm/dl was present in 27.27%pts in Group A, and 25.95% in group B and above 150 microgm/dl in 7.2% patient in group A vs 5.45% in group B. This observation is comparable to each other, which is supported by the work of Panneerselam R et al.[15]

Regarding comparison of study variables and outcome of treatment between zinc and non-zinc groups, we have observed that the time of disappearance of danger sign is more in non-zinc group than zinc group (48.3± 11.033 vs 41.3± 9.86) but is not significant statistically (P=0.79117). This finding is supported by the work of Sudha Basnet et al[16] and Aruradha Bose et al.[9] But our study is not supported by the study of brooks et al and Snehzadn et al.[17,18]

In our study we have observed that time to reach saturation above 90% was significantly early in zinc group this finding is supported by the study of Brooks WA et al but not supported by the work of Das RR et al.[17,19]

The time required for the resolution of distress was longer in non-zinc group than the zinc group but this difference is not significant statistically (P=0.28). This finding is supported by the work of Bose A et al and Das RR et al.[9,19]

The mean duration of oxygen requirement was less in zinc group than non-zinc group (20.42 hrs vs 36.42hrs) but was not significant statically (P=0.4320). This is supported by the work of Palle Valentiner-Branthet al, Bose A et al, and change et al.[8,9,20]

We have observed that there is no significant difference between the time required to become a symptomatic in both groups (P= 0.138006). This is supported by the work of Das RR et al and Chang AB et al.[19,20]

But the duration of stay in the hospital was significantly lower in zinc (7.2± 1.6 vs 8.13±1.58hr) with P value 0.021274. This finding is supported by the work of Basnet et al, Brooks et al and valve et al.[16,17,22] But not supported by the work of Bose A et al, Chang AB et al and Das RR et al.[9,19,20]

Conclusion

From our study we would like to conclude from our result that adjuvant treatment with 20 mg zinc per day along with antibiotic is associated with accelerated achievement of saturation above 90% and reduced duration of stay in hospital. It has no effect on time for disappearance of danger sign, time for resolution of distress, duration of oxygen use and time to become asymptomatic.

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