Original Article

ROLE OF ZINC SUPPLEMENTATION IN GROWTH AND NEURO-DEVELOPMENT OF PREMATURE AND SMALL FOR GESTATIONAL AGE (SGA) BABIES

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Financial Support: None Declared

Conflict of interest: None Declared

How to cite this article:
Parakh M, Gupta BD, Bhansali S, Parakh P, Sharma P, Gurjar M: Role of zinc supplementation in growth and neuro-development of premature and small for gestational age (SGA) babies. Natl J Community Med. 2012; 3(4):736-9.

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Date of Submission: 1-11-12

Date of Acceptance: 25-12-12

Date of Publication: 30-12-12

ABSTRACT

Objectives: A negative Zinc balance exists in preterm and small for gestational age infants. The current study evaluates the role of zinc supplementation on growth and neurodevelopmental outcome of these infants.

Methods: One hundred and twenty eight infants who were born either premature and/or small for gestational age were followed for six months. A detailed assessment of anthropometry, neurodevelopment and morbidity patterns due to Diarrhea and Acute Respiratory Infection were recorded during each visit.

Results: At birth and at six months the mean serum Zinc level in the study and control group was 0.87±0.398, 1.03±0.567, 0.88±0.248, 0.83±0.355mg/L respectively. The SZnR 6/B is significantly higher in study group as compared to controls (1.153 ± 0.55 Vs 0.913±0.438, $p<0.01$) suggesting better maintained serum zinc levels in zinc supplemented infants. Zinc supplemented exclusively breast fed infants had significantly higher SZnR 6/B as compared to non supplemented exclusively breast fed infants (1.555±0.654 vs 0.850±0.406,$p<0.01$). Further Zinc supplemented exclusively breast fed infants had significantly higher SZnR 6/B as compared both Zinc supplemented mixed and top fed infants. No effect of zinc supplementation was observed on growth, neurodevelopmental out come and morbidity pattern due to Diarrhea and ARI.

Conclusion: It can be concluded from the present study that zinc supplementation and exclusive breast feeding in premature and/or SGA infants results in better serum Zinc ratio. However Zinc supplementation has no role in the growth or neurodevelopmental outcome or morbidity patterns due to acute diarrhea and respiratory infections of premature and/or small for gestational age infants. But the breast milk has a definite value to improve morbidity patterns due to diarrhea in these infants

Key words: Zinc Supplementation, Small for Gestational Age (SGA), Premature infants

GLOSSARY:
SGA: Small for Gestational Age
ARI: Acute Respiratory Infection
SZN R 6/B: Ratio of serum zinc level at birth and at 6 months of age
CDS: Corrected Development Score

INTRODUCTION

Zinc, an essential trace nutrient, has important function to play in growth, reproduction, tissue repair and cellular immunity. Many studies have indicated that a negative Zinc balance exists in preterm and small for gestational age infants until approximately 36 weeks of gestation.[1,2]Several workers have recorded an improved Zinc status, good weight gain and better linear growth velocities in preterm infants supplemented with Zinc.[3,4,5,6] Whether the effect of Zinc is a direct consequence of improved supply of this nutrient for growth and metabolism or is mediated through stimulation of appetite and /or less diarrhoeal episodes is unclear.

The current study was planned to evaluate the importance of Zinc supplementation in growth, development and morbidity pattern of preterm and SGA babies with the objectives to determine the serum Zinc levels at birth and compare the values at six months of age. The study also attempted to find out correlation, if any, between babies supplemented with Zinc compared with a control group for neuro-developmental outcome, number of episodes of diarrhea, acute respiratory infections (ARI) and other morbidity. Role of exclusive breast feeding in prevention of Zinc deficiency was also studied.

METHODS

A total of 176 consecutively born preterm and SGA babies were enrolled in the study and followed up for a period of one year. Babies with congenital malformations, asphyxia, congenital infections and babies whose mothers had diabetes or pre-eclampsia were excluded. An informed verbal consent was obtained from the parents. The babies were alternately assigned to group A and B with infants in Group A receiving 0.8mg/kg of elemental Zinc per day from birth to 6 months of age and infants in Group B supplemented with a multivitamin solution not containing Zinc. Parents were counselled to exclusively breast feed their babies till 6 months of age. All episodes of diarrhoea, acute respiratory infections and other morbidity were recorded in the proforma during their monthly follow up visits. Zinc levels were assessed in the serum within 3 days of birth and again at 6 months of age. The estimation was done using atomic absorption spectrophotometry.[7]

Babies were followed up monthly in well baby clinics for their anthropometry, morbidity pattern and compliance of supplemental Zinc or multi-vitamin syrup. Development of these infants was assessed using the Woodside scale of development.[8] Statistical analysis was done using the Student's t test and the Z test to assess the significance of difference in mean between the two variables.

OBSERVATIONS

The study cohort consisted of 75 babies in the study group (Group A) and 74 babies in the control group (Group B) who could complete the study period. Two babies died during the study period of 6 months and a total of 25 babies from both groups (14 and 11 respectively) dropped out of the study for various reasons. Babies were further categorised into three groups based on their feeding pattern-exclusively breast fed, top fed or mixed feeding groups. Maximum babies in both the groups (A and B) were exclusively breast fed (Table 1).

Table 1: Distribution of infants according to gestational age, feeding pattern and Serum Zn Ratio

Parameters	Study Group (%)	Control Group (%)
Gestational Age		
<34 weeks	7 (9.33)	12(16.2)
34-37 weeks	53(70.67)	53(71.62)
>37 weeks	15(20.0)	9(12.16)
Feeding Pattern		
Exclusive Breast Fed	37(48)	37(50)
Mixed Fed	29(38.6)	27(36.4)
Top Fed	10(13.4)	10(13.5)
SZnR6/B		
<0.90	28(37.3)	39(52.7)
0.90-1.10	13(17.3)	9(12.1)
>1.10	34(45.3)	26(35.1)

Mean gestational age in the study and the control group was 35.75 ± 1.98 weeks and 35.14± 2.33 weeks respectively and the difference was not statistically significant. Mean serum Zinc level at birth was significantly higher in control as compared to study group ($p<0.05$), however the mean serum Zinc level at six months was not significantly different in both the groups (Table No.2). The mean serum Zinc level was higher at 6 months of age in the babies who were exclusively breast fed. A ratio of serum Zinc level at birth and at 6 months of age (SZN R 6/B) was calculated in order to know that how much Zinc has been retained in the body of the supplemented group. Physical growth, morbidity and neuro-development of infants in the study group were assessed using this index as the reflector of change in the serum status.

The ratio was significantly higher in the study group compared to the control group (p<0.01) (Table No.2). The mean SZN R 6/B amongst the exclusively breast fed infants in the study group (1.55±0.654) was significantly higher as compared to the mixed fed (1.157±0.424;p<0.01) and top fed groups(1.134±0.489; p<0.02) respectively.

The mean weight at birth of both the groups was comparable (p>0.05). At six months of age the mean weight in group A was higher as compared to group B, but the difference was not statistically significant (Table No.2). No effect of Zinc supplementation was observed on mean head circumference, length and mid arm circumference in the current study (Table No.2). However mean increment in weight in the study group was better in exclusively breast fed infants compared to mixed fed (p<0.001) or top fed babies (p<0.001).

Table 2: Serum Zinc level and its effect on growth

Parameters	At Birth		At 6months	
	Group A	Group B	Group A	Group B
Mean Serum Zinc (mg/L)	0.87±0.398	1.03±0.567	0.88±0.248	0.83±0.355
Mean SZnR6/B	-----	-----	1.153 ±0.55	0.913± 0.438
Mean Weight (Kg)	1.79±0.20	1.72±0.32	4.962±0.75	4.77±0.75
Mean Head Circumference(cms)	30.37±1.65	29.88±1.52	41.13±1.53	41.15±1.42
Mean Length(cms)	44.49±2.15	43.97±2.40	62.27±1.73	61.95±2.23
Mid Arm Circumference (cms)	7.51±1.13	7.26±0.58	11.78±0.71	11.65±1.54

All value in mean±SD format

Average frequency and duration of episodes of diarrhoea and total morbidity days in the two groups were not significantly different (p >0.05) (Table No.3). But it was seen that the infants in control group who were exclusively breast fed had statistically significant lower episodes of diarrhoea (p<0.01) and duration of total morbidity days (p<0.05) as compared to those who were only top fed (Table No.3). There was no statistically significant difference in the morbidity patterns due to ARI among infants in both the groups and among the infants who had different patterns of feeding in either study or control group(Table No.3).

Table 3: Effect of zinc and feeding pattern on morbidity due to diarrhea, ARI and neurodevelopmental outcome

Parameters	Group A	Group B	Exclusively breast feeding		Mixed Feeding		Top Feeding	
			Group A	Group B	Group A	Group B	Group A	Group B
Avg. Freq. of Diarrhoea*	0.83±0.89	0.70±0.78	0.80±0.94	0.51±0.60	0.86±0.90	0.78±0.99	0.78±0.74	1.20±0.60
Avg. Duration of Diarrhea#	2.79±2.97	2.81±2.99	2.01±2.53	2.53±3.10	3.62±3.50	2.58±2.88	2.78±2.56	4.25±2.29
Total morbidity days#	4.04±4.84	3.69±4.41	3.33±4.23	2.84±3.46	4.86±5.16	4.29±5.65	3.89±3.93	5.20±2.67
Avg. Frequency of ARI*	0.87±0.85	1.00±0.94	1.00±0.88	0.83±0.90	0.78±0.80	1.18±0.95	0.78±0.74	1.10±0.94
Avg. Duration of ARI#	3.12±3.221	3.63±2.97	3.144±2.78	3.35±3.23	3.12±3.77	4.22±2.70	3.17±2.79	3.03±2.33
Total Morbidity Days#	5.06±6.04	5.57±5.96	5.37±5.25	4.89±5.41	4.68±7.10	6.74±6.703	2.43±4.351	4.89±5.23
Corrected Developmental Scores	1.35±0.79	1.38±0.33	1.17±0.50	1.135±0.747	1.379±0.89	1.370±0.87	1.67±0.77	2.300±1.10

All value indicate mean±SD; *No. of episodes, #No. of Days

The corrected development score (CDS) of the study group differed non significantly from control group (Table No.3), but it was significantly better (p < 0.001) in the breast fed control group babies compared to the babies who received only top milk (Table No.3).

DISCUSSION

Mild subclinical Zinc deficiency is frequent in infants and its role in growth and neurodevelopment has been much talked about. Increasing values of mean serum Zinc levels at birth were noted in our study with increasing gestational age. This is in accordance with the observations made in earlier studies.[9, 10] Zinc binding capacity reduces in expectant mothers as the gestational age increases and increasing transfer of Zinc occurs from mother to the foetus with advancing pregnancy. The change in the level of Zinc from birth to 6 months was expressed as a ratio and babies were grouped into 3 groups according to this ratio (< 0.9, 0.9-1.1 and > 1.1 respectively) representing a decrease, no / minimal change and increase in serum Zinc levels from birth to 6 months of age. In our study 37.3 % babies in the supplemental group and 52.7 % babies in group B had the ratio < 0.9, but supplementation of Zinc did show a favourable effect on the Zinc balance in the body. Human breast milk contains a special Zinc binding ligand which increases the bioavailability of Zinc to the infant. Mothers of preterm babies have higher levels of Zinc throughout lactation to meet the increased requirement of these infants.[11]

In the current study we observed that serum Zinc ratio (SZN R 6/B) in the supplemented group was better compared to the control (Table No. 2). Castillo Duran et al[4] in their pioneer study had similar observations. Similarly, mean serum Zinc ratio (SZN R 6/B) was significantly higher in the Zinc supplemented exclusively breast fed infants.

We tried to study the effect of Zinc supplementation on physical growth but did not note statistically significant difference (Table No.3). This was in contrast to the observations of Castillo Duran et al[4] and Islam et al[6] who demonstrated significantly higher increments in the supplemented groups. This was probably because of non existence of subclinical deficiency in our infants as the serum Zinc levels were normal at birth and better maintained throughout the first eight months of life. But we could establish that exclusive breastfeeding is a more crucial factor determining increments in weight during the first 6 months of life.

The observations that Zinc supplementation has no effect on reducing the frequency and duration of acute diarrhea in the current study was in contrast to those made by Islam et al[6], Osendarp et al[12] and Sur et al[13]. They demonstrated that Zinc supplementation was effective in reducing diarrhea incidence.

CONCLUSION

Thus it can be concluded from the present study that Zinc supplementation in premature and/or small for gestational age infants results in better serum Zinc ratio. Further, it has been clearly demonstrated in the current study that breast milk has an additive effect on maintenance of higher serum Zinc levels at six months of age among Zinc supplemented premature and/or small for gestational age infants. However Zinc supplementation neither improves the growth or neurodevelopment of premature and/or small for gestational age infants, nor it affects the morbidity patterns due to acute diarrhea and respiratory infections in infants who were born premature and/or small for gestational age. We also conclude that breast milk has a definite value to improve morbidity patterns due to diarrhea in these infants

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