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A Study of Role of Zinc in the Treatment of Low Birth Weight Neonates

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Abstract

Background: *Low Birth Weight (LBW) is one of the main causes of neonatal mortality and morbidity in developing countries. There is evidence of the positive effect of zinc supplementation on growth in children with low birth weight. Aim: we in this study tried to measure the effect of zinc supplementation on LBW neonates during the first month of life and to observe the growth pattern of supplemented (Zn) with the non-supplemented group.* ***Materials and Methods:*** *It is a randomized, double-blind placebo-controlled (RCT) study of the effect of zinc on weight gain in low birth weight neonates. The study was carried on LBW neonates who were admitted to NICU, Prathima Institute of Medical Sciences, Karimnagar. BW babies' 1501-2499 gms with a gestation period between 30 – 42 weeks were selected.* ***Results:*** *In our study, 52% were male and 48% were female. And 56% were pre-terms and 44% were term IUGR babies. The mean (±SD) birth weight was 1850.4± 302.59 gm, 1813± 271.25gm for zinc and placebo groups respectively. Weight gain was more in the zinc group than the placebo group when observed after 7 days of birth. Highly significant weight gain was noted after 21 days (2236.4 ± 407.25 gms) in zinc group than the placebo group (2089 ± 394.57gm) and by 28 days it was 2595 ± 503.32 gms in zinc group and in the placebo group it was 2322.4 ± 472.12 gm. It was found that the increment of effectiveness in the Zinc group was higher than that of the placebo group. Problems like infection, jaundice were less in the zinc group compared to the placebo group.* ***Conclusions:*** *One of the important causes of neonatal mortality in our country is LBW. Zinc supplementation in low birth weight babies produced greater weight and length gain and fewer problems like sepsis, duration of hospital stay, and jaundice, when compared to non-zinc, supplemented group. Therefore, we conclude that zinc supplementation in LBW neonates is found to be beneficial and is a cost-effective measure to enhance growth.*

Keywords*: Low Birth weight, Zinc supplementation, Neonates*

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Introduction

Zinc is one of the most critical trace elements for the body it plays a major role in various aspects of physiology, immunity, and skeletal growth. Its many roles include participation in basic metabolic functions such as cellular respiration, synthesis of several proteins and enzymes, DNA and RNA replication, carbohydrate metabolism, cell division and growth, pituitary and adrenal gland functions, the integrity of biological membranes including bone metabolism [1]. The problem of zinc deficiency in LBW infants has been a subject of investigation for over a decade. During the first weeks of life, there is a progressive decrease in the serum levels of zinc, accentuated in the small-for-gestational-age (SGA) group [2]. In SGA and LBW infants, there occurs postnatal zinc deficiency due to several factors, including higher zinc nutritional requirements to support catch-up growth inadequate intake, impaired zinc absorption, increased endogenous losses associated with organ immaturity, especially the

gastrointestinal tract, increased losses associated with infections and impaired zinc status at birth [3, 4]. The exchangeable zinc pool is smaller in SGA infants and they have smaller liver size, the magnitude of difference being 35–40% [5]. Low concentrations of zinc in the cord blood of low-birth-weight infants have been noted in several settings and are correlated with birth weight and gestation [6]. Furthermore, a significant reduction in zinc concentrations during lactation is reported, and it has been postulated that the amount of zinc provided by breast milk may be lower than the Recommended Dietary Allowance (RDA) of zinc [6]. Zinc supplementation accelerated weight gain by increases circulating insulin-like growth factor (IGF-I) [7-9], appetite [10,11] improved ingestion of energy and protein. [12, 13] IGF-I is the mediator of the growth-promoting action of growth hormone. The positive effect of zinc supplementation circulating IGF-1 was reported by some studies. [12] Zinc may promote growth through changes in protein synthesis and cell replication, contributing to the accumulation of lean tissue. Zinc, which has important immunology and the growth-promoting role is among micronutrients. Zinc supplementation significantly reduces the incidence of low birth weight. Taking the above points into consideration, we conducted this study to evaluate the efficacy of oral zinc on growth in LBW neonates.

Materials and Methods

This study was a double-blinded randomized trial conducted on LBW neonates who were admitted in NICU, PIMS, Karimnagar. The study was approved by the Ethical Committee of Institution. Written consent was obtained from the parents of the neonates included in the study.

Inclusion criteria

a. Birth weight between 1501-2499 gm with the gestation period between 30 – 42 weeks.
b. Neonates who were admitted on the first day of life.

Exclusion criteria

a. Neonates admitted with respiratory distress syndrome, severe birth asphyxia, etc.
b. The parents did not consent to participate in the study.
c. Neonates with congenital heart disease and other life-threatening congenital anomalies.

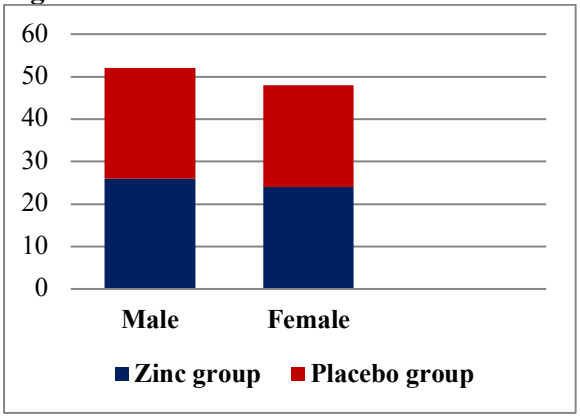
A total of n=146 LBW babies were selected for screening who were admitted in NICU on day one of life. Among these n=20 subjects were not eligible due to non-residents (n=15), malformations (n=5). Among the remaining n=126 subjects, n=10 subjects' parents did not give consent to participate in the study, so they were not randomized. Hence remaining n=116 subjects were randomized into two groups. Group A includes n=58 subjects and Group B includes n=58 subjects. Immediately on the admission of the patient, a detailed history was taken from mother or relative and physical examination was done. Written consent (or thumb imprints for those who could not write) was obtained from caregivers of enrolled neonates, and a copy of the consent form was secured with the family. Gestational age was determined by maternal records and by the New Ballard Score System. [14] Before the intervention, weight was measured by an electronic weighing scale which was accurate to 10gm and was calibrated before each measurement. The weighing was carried out with the baby nude and before feeding. In the first 28 days of life group A was supplemented with X drops, given in a dosage of 10mg (0.5ml), and group B was supplemented with Y drops, given in dosage of 0.5ml/day. During NICU stay, the researcher administered X drops to group A and Y drops to group B every morning at 10 am. At the time of discharge, parents or caregiver were instructed to feed drops every morning at 10 am to their neonates up to 28 days. Mothers were advised to attend follow up clinics according to schedule which was given to them. Weight of all neonates was measured without cloth before feeding at 9 am after 3 days, 7 days, 14 days, 21 days, and 28 days and recorded in record form. The length of all neonates was measured on D1 and D 28 and recorded in record form. At the end of the trial 100 subjects completed their trial. In each group, 8 subjects were unable to complete the trial due to loss of follow up. At the end of the study, it revealed that group A was a zinc supplemented group, and group B was the placebo group. X drops contained zinc in dry powder form which was made into a 15ml solution by adding sterile water. This

preparation contains 20mg/ml of zinc sulfate. Y drops contain multivitamins. The overall supervision was maintained by the researcher. Data were analyzed by using statistical software SPSS version 19 on windows format.

Results

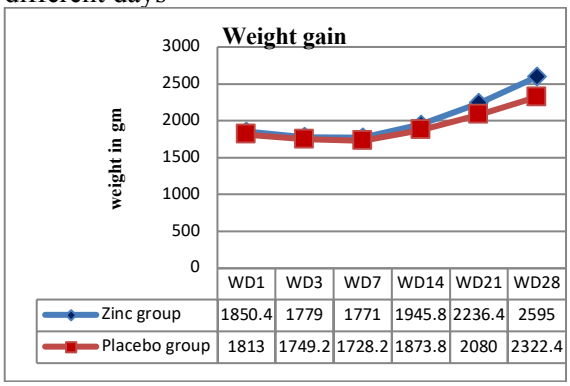
In our study, sex distribution was equal in both groups, which contained 52% males and 48% females (figure 1). In our study, 2 types of LBW babies were considered those who were pre-term and term IUGR babies. Out of n=50 cases in the zinc group n=28 were preterm, n=22 term IUGR. In the placebo group out of n=50 cases, n=32 were preterm, and n=18 were term IUGR.

Figure 1: Sex wise distribution



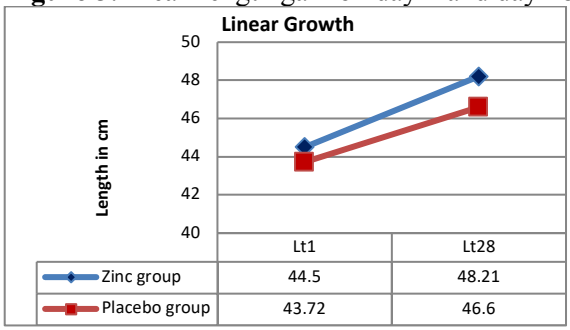
Measurement of weight on Days D1, D3, D7, D14, D21, and D28 among both zinc group and placebo group. On observation, there was an initial loss of weight up to 7 days in both groups. After the 7th day there was an increase in weight, but between D7 to D14, although the difference in gain was not significant in both groups. Maximum weight gain was noted after 21 days that was 358.6 gm in the zinc group and 242.4 gm in the placebo group. D1 average weight in the zinc group was 1850.4±302.6 gm and in the placebo group was 1813±271.25gm, which is not significant variation (p>0.05). On the 28th day, the average weight in the zinc group was 2595 ± 503.31gm and in placebo group 2322.4±472.12 gm, which is a significant variation (p<0.05). The overall weight gain during the neonatal period in the zinc group was 727.8±308.50gm and in the placebo group was 512.4±262.62gm, which showed significant weight gain (<0.001). Mean weight gain 25.99 ±11.01 gm/day of zinc group was significantly higher (P<0.001) than the mean weight gain 18.3±9.37gm/day of the placebo group (figure 2).

Figure 2: Mean weight gain in grams on different days



The length was measured with an infantometer on day 1 and day 28. In the zinc group, the average length observed was 44.5±2.27cm and in the placebo group was 43.72 ± 2.49cm, which is not significant variation (p>0.05; 0.105). On the 28th day, the average length in the zinc group was 48.21 ± 2.75cm and in the placebo group was 46.6±3.22cm, which is significant (p<0.05; 0.009). The mean average length gain in the zinc group was 3.71±1.01cm and in the placebo group was 2.88±1.14, which was significant (<0.001). Mean length gain 0.92±0.25 cm/wk of zinc group was significantly higher (p<0.001) than the mean length gain 0.72±0.28cm/wk of the placebo group. So zinc supplementation helps in linear growth among LBW babies (figure 3).

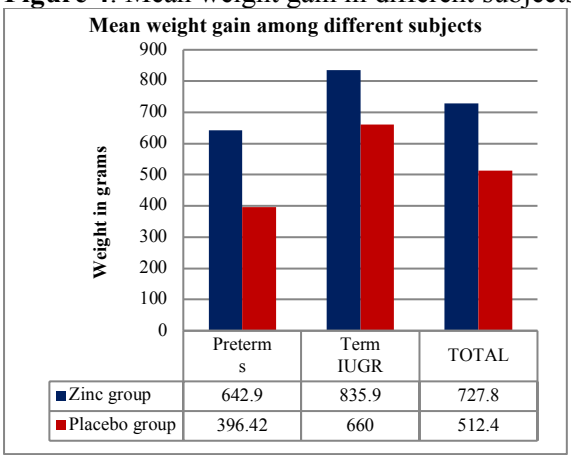
Figure 3: Mean length gain on day 1 and day 28



The overall weight gain in Term IUGR babies during the neonatal period in the zinc group was 835.90 ± 350.62 gm and in the placebo group was 660.0 ± 219.21gm, which is insignificant weight gain (>0.05; 0.053). So in our study, during the neonatal period there was significant weight gain among preterms babies but in the

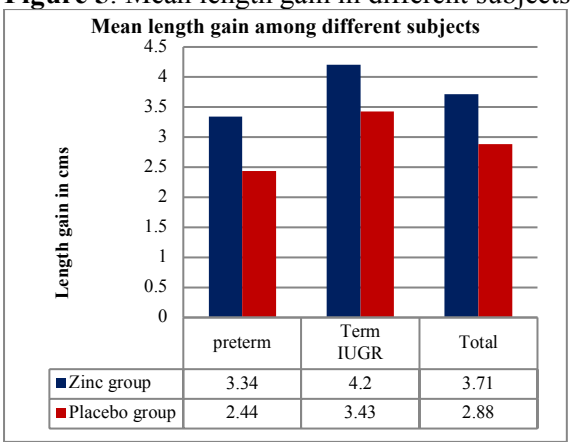
case of Term IUGR babies' weight gain was not significant (figure 4).

Figure 4: Mean weight gain in different subjects



Mean length gain during the neonatal period among preterm babies was 3.34±0.91cm for zinc group and 2.44 ± 1.13cm for the placebo group, which is significant (<0.05; 0.002) length gain. Mean length gain 0.835± 0.227 cm/wk of zinc group was significantly higher ($p<0.001$) than the mean length gain 0.61± 0.28cm/wk of the placebo group (figure 5).

Figure 5: Mean length gain in different subjects



In our study, the overall hospitalization was 8.32 days for the zinc group and 12.50 days for the placebo group. Preterm babies who stayed for > 2wks were n=9 babies in the zinc group and n=19 babies in the placebo group. In the case of the zinc group, the lowest hospital stay was 2 days (n=5), and among the placebo group, it was 3d (n=1) and 5d (n=3). Hence the average duration of hospitalization in the zinc group was significantly lower ($p<0.001$) than the placebo group. In our study, we observed that 54% of babies developed sepsis. Among these, 48% belong to the zinc group and 60% belong to the placebo group. The incidence of sepsis was much higher in the placebo group than in the zinc group. Therefore, it can be inferred that zinc supplementation can provide immunity to LBW babies and reduce the incidence of sepsis.

Discussion

It is supported by literature that zinc has an effective role in the growth and development of children. But insufficient data available on the effect of zinc on growth in LBW neonates, Primary outcome is to measure the effectiveness of zinc on weight gain and linear growth in LBW babies in the neonatal period. The secondary outcome is to compare the study group with the control group given sepsis, jaundice, duration of hospital stay, and tolerance of zinc. The zinc supplemented group gained more weight and length when compared to the control group. Zinc supplementation accelerated weight gain and linear growth. Our findings, however, agree with those trials performed in LBW babies in developing countries like in India, Bangladesh where zinc supplementation accelerated gain in weight and height.[11,12] In our study, mean weight gain (25.99 ± 11.012 gm/day ($p<0.001$)) in the zinc group was higher than the mean weight gain (18.3 ± 9.37 gm/day) in the placebo group. And mean length gain (0.92 ± 0.258 cm/wk ($p<0.001$)) in zinc group was higher than the mean length gain (0.72 ± 0.28 cm/wk) in placebo group. It is highly likely that zinc supplements need to be given every day along with an appropriate balanced diet because there may be no adequate stores of zinc and other nutrients and zinc turnover is also rapid. The accelerated weight gain in LBW neonates showed 728 gm in the zinc group and 510 gm in the placebo group. The average daily weight gain in the zinc group was 26 gm and in the placebo group was 18 gm.

The results of the present study were similar to those reported by C.C Duran et al;[15] in a randomized controlled trial of zinc supplementation (3 mg/day) among n=68 term SGA neonates who received mixed feeding of breast milk and enriched supplemented cow's milk formula over 6 months. The zinc supplemented groups were observed to have significantly higher weight and length at 6 months of age. The weight change in these infants was, however, reported to be influenced

by sex and enriched formula also and not zinc alone. The study had also observed that the effect of zinc on linear growth was noted as early as 30 days after initiation of zinc supplementation; an observation which is noted in the present study. Two other studies in VLBW infants by Friel et al; [16] and Gomez et al; [17] reported significant improvement in linear growth among zinc supplemented infants, but not for weight and head circumference. The lack of effect on weight and head circumference in these studies may have been due to a lower dosage of zinc supplementation compared to the higher (therapeutic) dose used in the present study. In contrast, a community-based randomized double-blind trial by Lira et al; [18] which enrolled full-term LBW infants between 1500 and 2499 gms, observed only a significant difference in weight gain (mean birth weight 2337±152 g) among the zinc supplemented group at 26 weeks of age. The authors postulated that the lack of effect of zinc on linear growth in their study could be due to the low number (about 27%) of stunted infants (less than±2 SD of length for age), which was about 27%. In India, Sazawal et al; [19] concluded that there was a significant gain in weight and length but no effect on occipitofrontal Circumference (OFC) in SGA babies with 6 months supplementation of zinc. These results were similar to the study conducted by Islam et al; [20] but the duration of supplementation was only for 6 weeks. Taneja et al; [21] conducted a study on Indian term LBW babies for one year and Ravi Kumar et al; [22] on Indian VLBW infants for 60 days and found that there was no effect of zinc supplementation on growth. The results of the present study were similar to those reported by Hoque et al; [23] in a randomized controlled trial of zinc supplementation (5mg/day) for 28 days in Bangladesh LBW neonates, that significant weight gain was observed in zinc group, but in our study dosage of zinc used was 10mg/day.

Conclusion

LBW neonates are zinc deficient and that might adversely affect postnatal growth. The study revealed that zinc supplementation in low birth weight enhanced more weight and length gain and experienced fewer problems like infection, less duration of hospital stay. There were no adverse effects noted in the zinc supplementation group. Therefore, we conclude that zinc supplementation to LBW neonates is a beneficial and cost-effective measure to enhance growth and decrease neonatal morbidity and mortality.

Conflict of Interest: *None declared*
Source of Support: *Nil*
Ethical Permission: *Obtained*

References

1. Prasad AS. Clinical, biochemical, and pharmacological role of zinc. Ann Rev Pharmacol Toxicol 1979;19: 393–426.
2. Domenech E, Dı´az-Go´ Mez NM, Barroso F, Cortabarria C. Zinc, and perinatal growth. Early Hum Dev 2001;65:S111–17.
3. Hambidge M. Human zinc deficiency. J Nutr 2000;130: 1344s–9s.
4. Higashi A, Matsuda I, Masumoto T, et al. Serum zinc and copper concentrations in low birth weight infants during first three months of life: correlation to birth weight and different feedings. Tohuku J Exp Med 1985;146:253–63.
5. Krebs N, Westcott J, Rodden D, et al. Exchangeable zinc pool size at birth is smaller in small-for-gestation age than in appropriate-for-gestational age preterm infants. Am J Clin Nutr 2006;84:1340–43.
6. Lamounier JA, Danelluzzi JC, Vannucchi H. Zinc concentrations in human milk during lactation: a 6-month longitudinal study in southern Brazil. J Trop Pediatr 1989;35:31–4.
7. Hiltz RL, Suskind R, Amatayakul K. Thanankul O, Olson. Plasma somatomedin and growth hormone values in children with protein caloric malnutrition. J Pediatr 1978;92;153-56
8. Maiter D, Flieren T, underwood LE, et al. Dietary protein restriction decreases insulin-like growth factor 1 independent of insulin and liver growth hormone binding. Endocrinology 1989: 124: 2604-11.
9. Thissen JP. Ketelslegers JM. underwood LE. The nutritional regulation of the insulin-like growth factor. Endocr Rev 1994; 15: 80-101.
10. Hambidge KM, Hambidge C, Jacobs M. Baum JD. Low levels of zinc in hair, anorexia, poor growth, and hypogeusia in children. Pediatr Res 1972; 6: 868-74.

11. Cum CX, AnYT, Sheng HJ, Yan MQ, Min HZ, Xiarg LL. Low levels of zinc in hair and blood, pica, anorexia, and poor growth in Chinese preschool children. Am J Clin Nutr 1985; 42: 694-700.
12. Simmer K, Khanum S, Carlsson L, Thomson RPH. Nutritional rehabilitation in Bangladesh the importance of zinc. Amj Clin Nutr 1988; 47: 1036-40.
13. Payne-Robinson HM, Golden MHN, Golden BE, Simeon DT, The zinc sandwich, and growth. Lancet 1991; 337: 925-6.
14. Ballard JL, Khoury JC, Wedig K, et al: New Ballard Score, expanded to include extremely premature infants. The Journal of Pediatrics 1991;119 (3):417–23.
15. Carlos Castillo-Duran. Zinc supplementation and growth of the Fetus and Low birth weight Infant. J. Nutr 2003: 1494-97.
16. Friel, J. K., Andrews, W. L., Matthew, J. D., Long, D. R., Cornel, A. M., Cox, M., McKim, E. & Zerbe, G. O. Zinc supplementation in very low birth- weight infants. J. Pediatr. Gastroenterol. Nutr 1993; 17: 97–104.
17. Diaz Gomez, Domenech E, Barroso F, Castell S. The effect of zinc supplementation on linear growth, body composition, and growth factors in preterm infants. AAP J 2003; 111: 1002-09.
18. Lira, P. I., Ashworth, A. & Morris, S. S. Effect of zinc supplementation on the morbidity, immune function, and growth of low-birth-weight, full-term infants in Northeast Brazil. Am. J. Clin. Nutr 1998; 68 (suppl. 2): 418S–423S.
19. Sazawal, S., Black, R. E., Menon, V. P., Dhingra, P., Caulfield, L. E., Dhingera, U. & Bagati, A. Zinc supplementation in infants born small for gestational age reduces mortality: a prospective, randomized, controlled trial. Pediatrics 2001;108: 1280–86.
20. Islam MN, Chowdhury M, Siddika M, Quraishi SB, Bhuiyan MK, Hoque MM, et al. Effect of oral zinc supplementation on the growth of preterm infants. Indian Pediatr 2010; 47: 845-849.
21. Taneja S, Bhandari N, Rongsen-Chandola T, Mahalanabis D, Fontaine O, Bhan MK. Effect of zinc supplementation on morbidity and growth in hospital-born, low-birth-weight infants. Am J Clin Nutr 2009; 90: 385-391
22. T.V.Ravi Kumar, Siddarth Ramji. Effect of Zinc supplementation on growth in VLBW infants. J Trop Pediatr 2012;58(1):50-54.
23. Hoque A, Ali SMK. Role of zinc in LBW Neonates. Bangladesh Med J 2009;24-30.