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Effect of zinc supplementation on growth of preterm infants

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Abstract

Background and objectives: Nutritional deficits are almost universal in low-birth weight babies. This study aimed to show the effect of zinc supplementation on growth and certain hematological parameters in preterm infants.

Methods: The current case-control study was carried out on 80 healthy preterm infants below 37 weeks of age divided into two groups. The first group was a zinc-supplemented group fed with breast milk exclusively and supplemented with zinc (2 mg/kg/day) since the first day of life. The second group was a non-zinc-supplemented group fed with breast milk exclusively (without zinc supplementation). Both groups were followed up at the age of 4 months for monitoring growth and determining serum zinc and hemoglobin levels.

Results: With the beginning of the study; there was no significant statistical difference between the zinc supplemented & non zinc supplemented groups in weight (2.4±0.2 kg vs 2.5±0.4kg), length (45.0±1.6 cm vs 45.2±1.5 cm) and occipitofrontal circumference (31.5±1.2 cm vs 31.5±1.1cm) respectively, but there was statistical significant difference at 4 months follow up with regard to weight (6.2±0.3 kg vs 6.0±0.2 kg) and length (63.2±2.1 cm vs 61.1±2.0 cm). Also, there was a highly significant increase in serum hemoglobin levels (11.7±1.6 gm/dl vs 10.6±1.5 gm/dl) and serum zinc level (101.2±8.1 µg/dl vs 84.1±7.0 µg/dl) in the zinc-supplemented group compared to the non-zinc-supplemented group at 4 months follow up.

Conclusion: Zinc supplementation was found to be effective to enhance the growth as well as increasing serum zinc and hemoglobin levels in early months of life of preterm infants.

Key words: Hemoglobin; Length; Occipitofrontal circumference; Weight; Zinc.

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Introduction

Failure to thrive (FTT) is an inappropriate growth rate in early childhood in comparison with standards of the same age and sex (weight and/or height below the 5th percentile)[1]. Prolonged malnutrition or under nutrition of babies with FTT adversely affects future growth and cognitive development. It is mainly related to non-organic causes; whereas underlying organic diseases are found in only 10% of children with FTT[2].During the third trimester of pregnancy, an increase of protein, glycogen, fat-soluble vitamins, minerals, and trace elements occurs[3, 4]. Preterm is a major problem in the developing world, and is accompanied by high perinatal morbidity and mortality rate. Out of 22 million preterm babies, 21 million are born every year in the developing countries; of theses 16 million are small for gestational age babies[5].Preterm infants suffer from significant energy and nutrient deficit due to inadequate nutritional intake together with associated disease, incomplete digestion and absorption in the gastrointestinal tract, and limited storages of trace elements. Hence, FTT and nutritional deficits are very common in preterm infants[6]. Zinc is contributed in many aspects of cellular metabolism [7], it is an essential nutrient and important supplement to many enzymes that regulate cellular growth and hormonal levels. Its deficiency is associated with underdevelopment, decreased appetite, delayed wound healing, and impaired immunity. Preterm infants have lower stores of zinc than term infants because of immaturity[8]. Preterm infants are particularly vulnerable to zinc deficiency because of low body stores, limited capacity to absorb and maintain micronutrients. As well as increased internal losses associated with immaturity of organ, rising nutrient demand for supporting growth, and insufficient intake due to exclusive breastfeeding[9].Unlike iron deficiency, zinc being one of the most hidden health problems in children, since it's something which was not routinely screened by the pediatricians. Several studies in children with FTT reported positive effects of zinc supplementation on weight gain and/or linear growth[10, 11]. Similarly, improved weight gain and linear growth was noted after zinc supplementation in short children with mild to moderate zinc deficiency[12]. Zinc supplementation has been shown to reduce the rates of diarrhea and pneumonia, and to enhance physical growth of young infants[13]. This study aimed to display zinc supplementation effects on growth of

preterm infants in the first four months of life.

Subjects and methods

This case-control study was carried out on 80 apparently healthy preterm infants below 37 weeks (male and female with weight between 1800 and 2700 g) admitted in the Neonatal Care Unit (NCU) at Maternity and Raparin Teaching Hospitals, Erbil Governorate. It was conducted from 01/09/2018 to 30/04/2019. The infants were divided into two groups; first group included 40 exclusively breastfed preterm infants from birth to the age of 4 months; they received zinc supplementation of 2 mg/kg/day orally for 4 months. The second group (the control group), included 40 exclusively breastfed preterm infants who did not receive zinc supplementation. Both groups fulfilled the same inclusion and exclusion criteria. The inclusion criteria were preterm with gestational age (GA) between 32 and 36 weeks, birth weight (BW) between 1800 - 2700 g, with no clinical evidence of diseases that are likely to influence their growth. The exclusion criteria were term neonates (≥37 weeks of gestation), intrauterine growth restriction, infants with major birth defect or congenital deformities, unstable vital signs, and infants with parents unwilling to participate. The study protocol was approved by Ethical Committee of Kurdistan Board for Medical Specialties. Informed written consent was obtained from the parents before enrollment of the preterm infant in the study. Anthropometric measurements (weight, length, and occipitofrontal circumference) were recorded during the study. Blood samples were drawn in the first few days of life for the serum hemoglobin (Hb gm/dl) and zinc levels (µg/dl) determination (Normal value for hemoglobin is 13-20 gm/dl, and for the zinc is 65-137µg/dl). At the age of 4 months, the above mentioned anthropometric measurements for all infants were recorded again. Blood samples were drawn again for serum zinc level (µg/dl) and (Hb gm/dl) level determination at the age of 4 months. Statistical analyses were done by statistical package for social sciences (SPSS) version 25. Two types of statistical analyses were carried out: descriptive statistics (frequency, percentage, mean, and standard deviation), and analytic statistics (Independent samples t-test) were used to evaluate the significance of differences between the groups. A p-value ≤ 0.05 was considered statistically significant.

Results

This study recruited 80 healthy exclusively breast-fed preterm infants, which were divided equally into two groups; 40 infants of zinc- supplementation and 40 infants of non-zinc- supplementation. General characteristics of infants and their mean gestational ages are shown in table (1).

Table (1): General characteristics of studied groups with their gestational ages:

	Zinc supplemented (n=40)		Non zinc‑supplemented (n=40)	
Sex	14 (Male)	26 (Female)	22 (Male)	18 (Female)
Gestational age in weeks (Mean±SD)	35.1 (0.8)		34.8 (0.9)	

On comparison between both groups for anthropometry, it was observed that the zinc-supplemented group had a highly significant (p-value <0.001) increase in weight and length at 4 months of age. While there was a non-significant increase in occipitofrontal circumference at 4 months compared with the non-zinc-supplemented group, indicating a significant effect of zinc supplementation on the growth of preterm infants as shown in table(2).

Table (2): Comparison between studied groups in regards of (weight gain, length, and occipitofrontal circumference):

	Zinc supplemented (n=40)		Non zinc‑supplemented (n=40)		t-test	p-value
	Mean	SD	Mean	SD		
Weight at birth (kg)	2.4	0.2	2.5	0.4	- 1.41	0.1613
Weight at 4 months (kg)	6.2	0.3	6.0	0.2	3.50	0.0008
length at birth (cm)	45.0	1.6	45.2	1.5	- 0.58	0.5658
length at 4 months (cm)	63.2	2.1	61.1	2.0	4.58	0.0001
OFC at birth (cm)	31.5	1.2	31.5	1.1	0.0	1.0000
OFC at 4 months (cm)	40.2	1.0	40.0	0.8	0.99	0.3263

OFC: Occipito-Frontal Circumference. We also found that the zinc-supplemented group had a highly significant (p-value $\leq$ 0.001) increase in the levels of serum zinc (µg/dl) and a significant (p-value $\leq$ 0.05) increase in the levels of hemoglobin (gm/dl) at 4 months compared with the non-zinc-supplemented group as illustrated below in table(3).

Table (3): Serum zinc and hemoglobin levels of the studied groups at enrollment and after supplementation:

	Zinc supplemented (n=40)		Non zinc‑supplemented (n=40)		t-test	p-value
	Mean	SD	Mean	SD		
Hb at birth (gm/dl)	15.3	1.7	15.8	2.1	- 1.17	0.2454
Hb at 4 months (gm/dl)	11.7	1.6	10.6	1.5	3.17	0.0022
Zinc at birth (µg/dl)	65.1	5.6	63.7	6.5	1.03	0.3053
Zinc at 4 months (µg/dl)	101.2	8.1	84.1	7.0	10.10	0.0001

Discussion

Adequate nutrition during early life in infancy is essential to enhance growth catch-up and neurodevelopment. If catch-up growth does occur early in life, the possibility that it will occur later in life is low[14, 15]. In infants, this critical period comprises the first year of life with regards to development of occipitofrontal circumference, and the first three years of life with regards to height[16, 17]. During this critical period, the quickly developing brain is in particular vulnerable to nutrient deficiency[18]. Therefore, nutritional management of FTT includes sufficient energy and protein provision, beside specific micronutrient supplementation like iron, zinc, trace elements, and vitamins according to the deficiency situation. Principally in preterm infants, nutritional deficits are quite common. Preterm infants with weight or length below the 10th percentile of the reference curve at post conception age of (35-36) weeks are at high-risk for long-term growth impairment, neurodevelopmental deficit, and behavioral problems[19, 20]. Hence, early "vigorous" nutrition that provides a high in energy diet and protein, in addition to micronutrient supplements to promote early growth catch-up are recommended in preterm infants[21, 22]. In this study, weight, length, and occipitofrontal circumference were similar in both groups at the beginning of the study. Significant differences in weight gain and increase in length were found at the age of fourth months between the two groups, but did not find a similar significant effect on occipitofrontal circumference. This demonstrates the high bioavailability of oral zinc on raising serum zinc levels, with subsequent positive effects on weight and length. In agreement with our study, studies done by Islam[24] and El Sadek[25] have also found that zinc supplementation for preterm low birth weight infants is highly effective in enhancing the growth in early months of

life. This is also in agreement with another study conducted by Sonawane[26] which showed that zinc supplementation at 2 mg/kg/day for 8 weeks in low birth weight infants have significantly higher weight gain, length, linear growth velocity and head circumference at 8 weeks. This was reasonable, since zinc plays a deep role on cellular growth and reproduction and accomplishes various metabolic functions[27]. Several studies on preterm infants with zinc supplementation (in various doses and for different periods), have reported improved growth and weight gain. Conversely, another randomized clinical trial conducted on preterm Indian infants did not yield any valuable effect of zinc supplementation given for a period of one year on length and weight gain, despite the fact that it had a positive effect on plasma zinc concentration[28]. Another study that had conducted by Díaz-Gómez[29] among preterm infants showed positive effect on plasma zinc concentrations and linear growth, and a study by Bueno[30] on preterm infants showed no effect. However, no significant effect on weight gain was seen in any of them. Some of the incompatible data regarding effect of zinc on growth in preterm infants may be attributed to mixing low birth weight and preterm births. Almost all the studies in low birth weight infants in developing countries that had assessed the effect of zinc supplementation have not reported gestational age because of the difficulty in obtaining it, and thus had included a mixture of preterm and small for gestational age infants. In our study, there was a highly significant increase ($p<0.001$) in serum levels of zinc values in the zinc-supplemented group, but not in non-zinc-supplemented group. This indicates that supplementation of zinc was successful in improving serum zinc status of these infants. This is in agreement with other studies that showed significant improvements in serum zinc values in the zinc-supplemented compared to non-zinc-supplemented group[29, 31]. In our study, we also found that there was a significant increase in the serum levels of hemoglobin in response to increased serum zinc, indicating the role of zinc supplementation in improving hemoglobin level in preterm infants. This comes in compatible with other studies which found that hemoglobin levels were significantly higher ($p<0.05$) in zinc-supplemented group than non-zinc-supplemented group after supplementation of zinc[32, 33]. Limitations of the study were: no long term follow up was done because of time restriction.

Conclusions

Oral zinc supplementation is effective to promote growth of preterm infants in early months of life and has a positive effect on serum zinc and hemoglobin level.We recommend Zinc supplementation along with other vitamins and minerals to preterm infants for their growth. Measurement of serum zinc level at the start and after zinc supplement to correlate it to growth parameters will be of significance.

Conflicts of interest

There were no conflicts of interest.

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