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## Effects of Dietary Zinc Supplement During Lactation on Longitudinal Changes in Plasma and Milk Zinc Concentration

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**Abstract:** Effects of dietary zinc supplement during lactation on maternal zinc plasma and milk zinc concentration through 5 months of lactation were examined. One hundred and thirty eight healthy lactating mothers received a weekly 100 mg elemental zinc supplement (ZS, n = 67) or placebo (PG, n = 71) starting one week postpartum in a double blind, randomized design. Milk and plasma zinc concentrations were determined by atomic absorption spectrophotometer. During the course of study, there was not a significantly difference between ZG and PG groups in dietary zinc and energy intake. The mean plasma zinc concentration at 1st week and 5th month were  $134 \pm 49.1$  and  $115.6 \pm 23 \mu\text{g dL}^{-1}$  (PV = 0.005) for PG group, respectively; that of the ZG group these figures were  $124.9 \pm 52.8$  and  $121 \pm 27.1 \mu\text{g dL}^{-1}$  (PV = 0.38), respectively. The mean serum alkaline phosphatase concentration at 1st week and 5th month were  $94.8 \pm 37$  and  $92.6 \pm 29.9 \text{ iu L}^{-1}$  for PG group, respectively; that of the ZG group these fissures were  $90.5 \pm 36$  and  $90 \pm 29 \text{ iu L}^{-1}$  (PV = 0.21), respectively. Milk zinc concentration declined significantly over the course of study for two groups, with the sharpest decline occurring during the first 2 months. The mean monthly zinc concentration of ZG group declined from  $310 \pm 138$  at 1st week to  $118 \pm 64 \mu\text{g dL}^{-1}$  at 5th month (declined by 52%). Corresponding means for PG group were  $322 \pm 161$  and  $109 \pm 70 \mu\text{g dL}^{-1}$  (declined by 60%), respectively. Milk zinc concentration significantly different between two groups at 3 and 4 months. A similar study, however, with different zinc dose and administration manner, in zinc marginal deficient lactating mothers is needed to assess the impact of zinc supplementation on milk zinc concentrations.

**Key words:** Zinc, marginal zinc deficiency, plasma zinc, milk zinc, zinc supplementation, dietary zinc intake

### INTRODUCTION

Mother's milk has long been regarded as the ideal food for infants, against which all other types of feeding are compared. As such, it is important to have accurate data on the composition of human milk. Several reports concluded that milk zinc concentration not influenced by maternal dietary intake (Moser-Veillon and Reynods, 1990; Moore *et al.*, 1984; Kirksey *et al.*, 1979; Krebs *et al.*, 1995). Many reports, however, showed a significantly slower rate of decline in the zinc concentrations of milk over 9 months of lactation in a group of women who received a supplement of zinc compared with non-supplemented control subjects (Krebs *et al.*, 1985). The clinical entity of zinc deficiency in human was first described in young males in Iran and Egypt (Prasad *et al.*, 1963) and in recent years, many studies have showed zinc deficiency in many areas of Iran (Sohrabi, 1993; Montazeri *et al.*, 1999; Mahmudi *et al.*, 1999; Golestan *et al.*, 2004). Hence, Iran can be one of the

countries where is frequently observed marginal zinc deficiency. Over the last 20 years various studies have been performed on the zinc supplementation effect zinc status of breast milk; however, as yet the relation of zinc supplementation to breast milk zinc concentrations, specially in marginal zinc deficiency areas is not sufficiently elucidated.

The objective of the present study was to determine the effect of maternal zinc supplement on zinc concentration of plasma and milk the healthy lactating women during the first 5 months of lactation.

### MATERIALS AND METHODS

The study was designed as a double blind randomized clinical trial conducted in Yazd-Iran from 2003 to 2005. One hundred and thirty eight healthy lactating mothers, first week after delivery, were randomly assigned to supplemented group (ZG, n = 67) and placebo group (PG, n = 71). The ZG group received 2 zinc sulphate

capsules weekly each containing 50 mg elemental zinc. The PG group received 2 of the same capsules containing starch which were indistinguishable from the zinc sulphate capsules. The lactating mothers were instructed to take the capsules 0.5 h before or 3 h after the evening meal. Compliance monitored by counting the remaining capsules each month, averaged  $92.9 \pm 2.1\%$ . All mothers were health had unremarkably obstetric histories, delivered at term, had healthy infants and which were nursed with exclusively with breast feeding during the study. Mothers did not smoke, were used no alcohol, nor using contraceptive pills. All women gave informed consent to participate in the study. The ages (mean $\pm$ SD) of the ZG and PG groups were  $25.4 \pm 5.8$  and  $24.7 \pm 6.2$ , respectively. Mean parities were  $4 \pm 1.4$  and  $3.9 \pm 1.5$  for the ZG and PG groups, respectively. For determination of plasma zinc and serum alkaline phosphatase, a 5 mL, blood sample was collected by peripheral venipuncture using disposal plastic syringes and stainless steel needles during the first week and until 5th month of lactation. The samples were collected between 9.00 am and 12.00 noons while they were no fasting. 2.5 mL of each sample of blood was transferred to plastic tubes containing 500 units of heparin. The syringes, heparin and tubes were free of detectable zinc. After centrifuging, plasma was separated using glass capillary pipettes that had been washed in HCL and deionized water and was stored at  $-20^{\circ}\text{C}$  in plastic tubes. The remaining 2.5 mL of the blood sample was transferred to plastic tubes and the serum was separated. Alkaline phosphatase concentration was determined by calorimetry with Zist Shimi kit. For determination of milk zinc concentrations, milk samples of

5-10 mL were hand expressed after mothers cleaned the areola with deionized water at the first week and then once in a month. Zinc free vials were provided to subjects, who were given instructions for avoiding zinc contamination of the mother's milk. Samples were frozen and stored at  $-20^{\circ}\text{C}$  until the day analysis. Milk and plasma zinc concentrations were determined on each sample by atomic absorption spectrophotometer in the laboratory of the health faculty of Shaheed Sadoughi Medical Sciences and Health Services University of Yazd.

Twenty four hours dietary recall was recorded in each visit and was reviewed for accuracy and completeness by the nutritionist at the time of sample collection. Nutrient intakes were computer calculated using NIII software.

Data was processed by SPSS win software. The differences between plasma zinc concentration before and after were compared by paired t-test. Milk zinc concentrations were compared by student t-test. Data are presented as mean $\pm$ SD and 0.95% confidence interval. A value of  $p \leq 0.05$  was considered statistically significant.

## RESULTS

Mean calculated dietary zinc and energy intake at each visit are shown in Table 1 and 2. Over the course of study, there was no significant difference between ZG and PG groups in dietary zinc and energy intake.

The mean plasma zinc concentration at 1st week and 5th month were  $134 \pm 49.1$  and  $115.6 \pm 23 \mu\text{g dL}^{-1}$  ( $PV = 0.005$ ) for placebo group and of the zinc supplemented group these figures were  $124.9 \pm 52.8$  and  $121 \pm 27.1 \mu\text{g dL}^{-1}$  ( $PV = 0.38$ ), respectively.

Table 1: Daily intakes of zinc (mg) by two groups during the study period

| Time of lactation | Zinc supplemented group |                         |           | Placebo group |                         |           |         |
|-------------------|-------------------------|-------------------------|-----------|---------------|-------------------------|-----------|---------|
|                   | N                       | $\bar{X} \pm \text{SD}$ | 95% CI**  | N             | $\bar{X} \pm \text{SD}$ | 95% CI    | p-value |
| 1st week          | 65                      | $10.27 \pm 1.9$         | 9.7-10.7  | 70            | $10.48 \pm 2.5$         | 9.8-11.1  | 0.59    |
| 1st month         | 56                      | $11.25 \pm 2.5$         | 10.5-11.9 | 65            | $10.7 \pm 2.4$          | 10.1-11.3 | 0.23    |
| 2nd month         | 97                      | $10.33 \pm 1.5$         | 9.8-10.7  | 58            | $9.9 \pm 1.9$           | 9.4-10.4  | 0.25    |
| 3rd month         | 46                      | $10.16 \pm 1.9$         | 9.5-10.7  | 55            | $9.8 \pm 1.9$           | 9.3-10.2  | 0.31    |
| 4th month         | 42                      | $11.34 \pm 3.4$         | 10.2-12.4 | 55            | $10.8 \pm 2.5$          | 10.1-11.5 | 0.47    |
| 5th month         | 42                      | $11.33 \pm 3.4$         | 10.2-12.3 | 53            | $10.3 \pm 2.0$          | 9.7-10.8  | 0.07    |

\*Student t-test, \*\*95% confidence interval

Table 2: Daily intakes of energy (kcal) by two groups during the study period

| Time of lactation | Zinc supplemented group |                         |           | Placebo group |                         |           |         |
|-------------------|-------------------------|-------------------------|-----------|---------------|-------------------------|-----------|---------|
|                   | N                       | $\bar{X} \pm \text{SD}$ | 95% CI**  | N             | $\bar{X} \pm \text{SD}$ | 95% CI    | p-value |
| 1st week          | 65                      | $234 \pm 606$           | 2173-2474 | 70            | $2361 \pm 543$          | 2231-2490 | 0.7     |
| 1st month         | 56                      | $2371 \pm 617$          | 2206-2537 | 65            | $2453 \pm 819$          | 2250-2656 | 0.5     |
| 2nd month         | 47                      | $2460 \pm 537$          | 2303-2618 | 57            | $2547 \pm 676$          | 2367-2727 | 0.4     |
| 3rd month         | 46                      | $2502 \pm 552$          | 2338-2665 | 55            | $2585 \pm 762$          | 2379-2791 | 0.5     |
| 4th month         | 42                      | $2502 \pm 684$          | 2289-2716 | 55            | $2543 \pm 574$          | 2387-2698 | 0.7     |
| 5th month         | 42                      | $2482 \pm 566$          | 2305-2659 | 53            | $2460 \pm 561$          | 230-2615  | 0.8     |

Table 3: The milk zinc concentration ( $\mu\text{g dL}^{-1}$ ) by two groups during the study period

| Time of lactation | Zinc supplemented group |                         |          | Placebo group |                         |         | p-value |
|-------------------|-------------------------|-------------------------|----------|---------------|-------------------------|---------|---------|
|                   | N                       | $\bar{X} \pm \text{SD}$ | 95% CI** | N             | $\bar{X} \pm \text{SD}$ | 95% CI  |         |
| 1st week          | 68                      | 310 $\pm$ 138           | 277-344  | 71            | 322 $\pm$ 161           | 284-360 | 0.32    |
| 1st month         | 56                      | 226 $\pm$ 84            | 203-249  | 64            | 212 $\pm$ 90            | 189-234 | 0.17    |
| 2nd month         | 49                      | 182 $\pm$ 79            | 159-205  | 59            | 152 $\pm$ 69            | 134-170 | 0.02    |
| 3rd month         | 48                      | 159 $\pm$ 73            | 138-181  | 58            | 129 $\pm$ 57            | 113-144 | 0.005   |
| 4th month         | 45                      | 111 $\pm$ 54            | 94-127   | 56            | 103 $\pm$ 66            | 85-121  | 0.26    |
| 5th month         | 43                      | 118 $\pm$ 64            | 98-137   | 56            | 109 $\pm$ 70            | 90-128  | 0.26    |

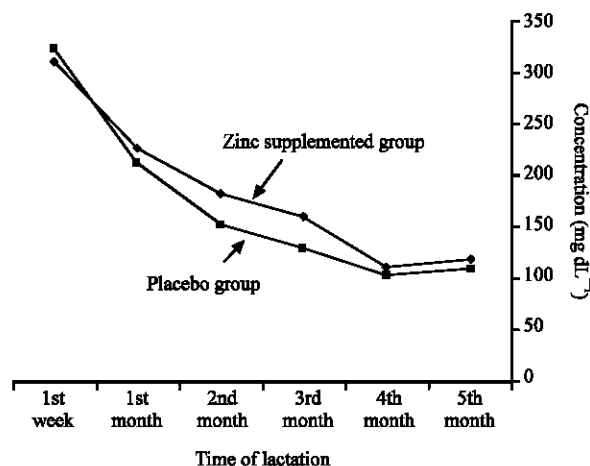


Fig. 1: Trend of milk zinc concentrations by lactation progress

The mean serum alkaline phosphatase concentration at 1st week and 5th month were  $94.8 \pm 37$  and  $92.6 \pm 29.9$   $\text{iu L}^{-1}$  for placebo group, respectively; that of the zinc supplemented group these figures were  $90.5 \pm 36$  and  $90 \pm 29$   $\text{iu L}^{-1}$  ( $PV = 0.21$ ), respectively.

Milk zinc concentration declined significantly over the course of study for two groups, with the sharpest decline occurring during the first 2 months (Fig. 1, Table 3). The mean monthly zinc concentration of ZG group declined from  $310 \pm 138$  at 1st week to  $118 \pm 64$   $\mu\text{g dL}^{-1}$  at 5th month (declined by 52%). Corresponding means for PG group were  $322 \pm 161$  and  $109 \pm 70$   $\mu\text{g dL}^{-1}$  (declined by 60%), respectively. As showed Table 3, Milk zinc concentration was significantly different between two groups at 3 and 4 months.

## DISCUSSION

According to the results, the overall calculated mean daily dietary zinc, energy and other nutrients intake in two groups were similar and were higher than 75% of related RDA. These results were approximately in agreement with the other studies (Moser-Veillon *et al.*, 1984; Krebs *et al.*, 1995; Krebs *et al.*, 1985; Vuori *et al.*, 1980; Moser *et al.*, 1983). Also, other confounded variables (parity, weight variation, age, education level and body mass index) were not statistically different in two groups throughout the

study. Hence, the results indicated appropriate randomization and could not be as confounded variables on Plasma and milk zinc concentration results.

The overall mean of plasma zinc at 1st week and 5th month of lactation were  $128 \pm 50$  and  $117.9 \pm 24.6$   $\mu\text{g dL}^{-1}$ , respectively. Also, plasma zinc differences during at 1st week and 5th month of lactation for ZG and PG were 3 and 19  $\mu\text{g dL}^{-1}$  ( $PV = 0.005$ ), respectively. This decline may be due to physiological factors in early postpartum and lactation. Elevation of plasma zinc concentration in the early postpartum period can be attributed to physiological changes associated with delivery, including restoration of normal non-pregnant blood volume, hormonal changes and an increase in serum albumin. In contrast to pregnancy, there were no recognized physiological factors operating during lactation that depress plasma zinc concentrations. Thus, the slow decline of rate of plasma zinc level may be due to the effects of zinc supplementation.

The plasma zinc level in lactating women has been reported higher than present study (Vaughan *et al.*, 1979). While in many studies it has been less than present study (Moser-Veillon *et al.*, 1984; Krebs *et al.*, 1995; Krebs *et al.*, 1985; Moser *et al.*, 1983; Karra *et al.*, 1988).

This difference may be attributable to the significant variation in dietary zinc intake, method of study, type of supplementation (daily or weekly, dose of zinc administration, technique of zinc determination and so on).

Milk zinc concentration decreased as lactation progressed in both groups. The mean for the PG group was declined by 52% between first week and the subsequent 2 months. The corresponding figure for ZG was 41%. Comparable figures from other studies ranged from 40-60% (Krebs *et al.*, 1985; Moser *et al.*, 1983; Lamounier *et al.*, 1989; Dorea *et al.*, 2002). The similarities between different studies at comparable stages of lactation suggest that these figures may to a large extent be accepted as part of a normal physiological pattern of decline in zinc concentrations of human milk as lactation progresses. However, in contrast with resent study (Krebs *et al.*, 1995) there was significant difference in the rate of decline in milk zinc concentrations throughout lactation (especially 2-3 months) between the zinc supplemented and placebo groups.

In summary, the present study showed relatively slow decline of milk zinc between supplemented and non-supplemented lactating mothers. Hence, for the better clarification of the process, we believe the other randomized control studies with different zinc doses should be conducted on marginal zinc deficient lactating mothers.

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