SHORT REPORT

Oral zinc supplementation in pregnant women and its effect on birth weight: a randomised controlled trial

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Pakistan lies in a zinc deficient area where oral zinc supplementation has been advocated for various reasons. A double blind, randomised case-control study was carried out on pregnant women to evaluate the effects of oral zinc supplementation on the weights of newborns. No significant difference was found in the birth weights between the cases supplemented with 20 mg elemental zinc and controls receiving oral placebos (p = 0.57).

Zinc plays a very important and critical role in various functions of the human body including protein synthesis and nucleic acid metabolism.[1] The effects of zinc deficiency are prominent even in intrauterine life.[2] Trials of zinc supplementation performed previously in populations have produced conflicting results on various pregnancy outcomes.[3 4] Pakistan lies in an area extending from western India to eastern Iran where soil is deficient in zinc.[5] A few studies carried out on zinc status of women and children living in this region have shown an alarming prevalence of zinc deficiency.[6] Oral zinc supplementation is a potential measure to prevent the birth of low birthweight babies and thus eventually avert the morbidity and mortality of the newborns associated with this condition. However, ample evidence to support routine zinc supplementation is still not available. The aim of this study was to evaluate the effects of oral zinc supplementation on the birth weight of newborns.

MATERIAL AND METHODS

The double blind, randomised, controlled trial was conducted over a period of one year (April 2003 to April 2004) at two large urban hospitals and one rural community. All pregnant women at 10–16 weeks gestation were offered the opportunity to enter the study at the booking visit. Women with known systemic disease were excluded. Informed consent was obtained from all subjects, and an effort was made to obtain patients equally from rural and urban settings.

The patients were randomised into test and control groups by simple random sampling, and each patient was allotted a preassigned code on first contact. Both the patient and health worker were blinded to the content of the medication (20 mg elemental zinc in the form of zinc sulphate powder capsule and a similar capsule as placebo), filled with glucose given from booking till the end of gestation. This supplementation was in addition to routine supplements of folic acid and iron. The dietary zinc intake was also taken into account by maintaining a food diary. Various food items were assigned a score, and the mean ''dietary zinc score'' was estimated for every study participant. The patients were followed up at monthly intervals by trained staff, and compliance was ensured by recruiting health visitors who carried out home visits where necessary. Pills were counted out every month before the issue of a new supply, to double check the consumption of the medicine. Blood samples were collected at enrolment into containers free of trace elements, and serum zinc was determined on an atomic absorption spectrophotometer using standard methodology. Newborns were weighed on electronic scales by the health visitor or doctor within 24 hours of birth.

A sample size of 250 (half as cases and the rest as controls) was calculated to give a true difference of at least 250 g in the birth weights of two groups. The level of significance was taken as 99%, and the power of the study was 95%. Computer software SPSS10 was used for analysis. Student's *t* test and regression analysis were applied where required.

Table 1 Basic characteristics of mothers receiving zinc supplement and those receiving placebo

Variable	Zinc group	Placebo group	p Value
Age of mother (years)	26.07 (4.7)	25.33 (4.8)	0.23
Weight of mother (kg)	54.84 (10.6)	55.17 (11.2)	0.81
Height of mother (cm)	155.67 (5.8)	155.50 (5.9)	0.91
BMI of mother	17.58 (3.3)	17.71 (3.5)	0.77
Hb at enrolment (g/l)	108.6 (14)	110.1 (12)	0.45
Serum zinc at enrolment (μg/dl)	71.51 (21)	74.09 (23.2)	0.39
Dietary zinc score	74.94 (21)	72.42 (27.3)	0.83
Systolic BP at enrolment (mmHg)	110.40 (9.03)	109.76 (8.7)	0.63
Diastolic BP at enrolment (mmHg)	70.98 (7.46)	69.98 (6.7)	0.36
Gestation at enrolment (weeks)	12.95 (2.9)	13.22 (3.2)	0.51
Household income <5000 (%)	48	48	1.00
Mothers having schooling of <5 years (%)	34	42	0.30
Husbands having schooling of <5 years (%)	18	17	1.00
Addiction (%)	1	1	1.00
Ethnic Punjabi (%)	83	89	0.11
Primigravida mothers (%)	39	38	0.91

Values are mean (SD) or percentage.
BMI, Body mass index; Hb, haemoglobin; BP, blood pressure.

Table 2 Birth weight and other pregnancy outcomes

Variable	Zinc group	Placebo group	Mean of diff	95% CI of diff	p Value
Birth weight (g)	3023 (456)	3061 (444)	37	−17 to 95	0.57
Length (cm)	48.89 (3.0)	48.80 (3.1)	0.09	−0.9 to 1.15	0.86
OFC (cm)	34.96 (2.1)	34.99 (2.0)	0.23	−0.9 to 0.5	0.52
Premature labour (<37 weeks) (%)	17.8	8.1			0.07
LBW (<2.5 kg) (%)	12.0	9.1			0.63
Abortion/IUD (%)	3.2	2.5			0.55

Values are mean (SD) or percentage.
OFC, Occipitofrontal circumference; LBW, low birth weight; IUD, intrauterine device; diff, difference.

RESULTS

A total of 242 subjects were enrolled till the end of the study period. The mean (SD) age of the study participants was 25.7 (4.8) years (range 16–40). Table 1 shows the basic characteristics of the subjects randomised to the zinc supplement (n = 121) and placebo (n = 121) group. About 15% patients were lost to follow up in the two groups which was non-differential. About 65% of the subjects had good to excellent compliance, which was similar in both the groups. Fifty three percent of the babies were male, and the two groups had similar distributions of sex (p = 0.29), place of delivery (p = 0.99), and birth attendants (p = 0.74).

There was no significant difference in the birth weights (and other anthropometric data) of the zinc supplemented group compared with the placebo group (table 2). The effect of various potential confounders on birth weight was assessed by linear regression analysis including age, sex, serum zinc concentration, haemoglobin status, gestation at delivery, height, weight, and body mass index of mother, and education, dietary intake, and socioeconomic status of parents. Low body mass index and prematurity were significantly associated with birth weight when all other factors were taken into account (p = 0.01), and low maternal education was associated but did not reach statistical significance (p = 0.07).

DISCUSSION

We show that supplementing pregnant women with a daily oral dose of 20 mg elemental zinc throughout their pregnancies beginning at 12 weeks gestation did not result in a significant change in the birth weight. Previous trials of zinc supplementation in populations with various zinc concentrations have produced conflicting results on various pregnancy outcomes,[3 4] including birth weight. However, some previous studies have shown a positive effect on the birth weight and pregnancy outcomes. A possible reason for not picking up a true effect in this study is the small sample size, which was meant to pick up a real difference of 250 g between the two groups. However, one can argue that, birth weight is only a proxy assessment of the morbidity and mortality associated with low birthweight babies, and we should actually be looking for the appropriate outcome. No significant previous study has looked adequately into this aspect. If only a very small gain is achieved in the birth weight of newborns by zinc supplementation (less than 250 g), then it is not a worthwhile public health measure, as the ultimate gain would not be cost effective.

The daily intake from the diet, which is predominantly cereal based, is about 13 mg/day (unpublished research data) in the Rawalpindi Islamabad area. Keeping this low intake in mind, we considered 20 mg elemental zinc to be a safe dose for supplementation. The study showed a very impressive follow up rate and excellent compliance. The place of delivery, haemoglobin concentrations, and other confounding variables were equally distributed in the populations. The maturity of the baby, body mass index of mother, and maternal education had a positive effect on the birth weight. Similar trends have been shown in previous studies.[7]

In conclusion, oral supplementation of pregnant women with 20 mg elemental zinc did not bring about a significant increase in the birth weight of our population. We suggest that supplementation trials with larger dose of zinc should be carried out, and studies should be planned to directly look at the effects of zinc on neonatal morbidity and mortality rather than seeking indirect evidence.

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REFERENCES

1 **Valee BL**, Flachuk KH. The biochemical basis of zinc physiology. *Physiol Rev* 1993;**73**:79–118.
2 **Roungsi pragarn R**, Bornug S, Herabutya I. Plasma zinc level and intrauterine growth retardation study of pregnant women in Ramathibodi Hospital. *J Med Assoc Thai*, 1999 Feb, **82**:178–81.
3 **Kynast G**, Saling E. Effect of oral zinc application during pregnancy. *Gynecol Obstet Invest* 1986;**21**:117–23.
4 **Tamura T**, Golden berg RL, Johnston KE, *et al*. Maternal plasma zinc concentration and pregnancy outcome. *Am J Clin Nutr* 2000;**71**:109–13.
5 Soil status and scope of micro nutrients in Pakistan agriculture. Islamabad: PARC, 1986.
6 **Government of Pakistan**. *National nutritional survey of Pakistan, 2001–2*. Islamabad: Government of Pakistan.
7 **Najmi RS**. Distribution of birth weights of hospital born Pakistani infants. *J Pak Med Assoc* 2000;**50**:121–4.