Plasma and Erythrocyte Zinc in Pre-eclampsia and its Correlation with Foetal Outcome


Abstract

Objectives: To determine the plasma and erythrocyte zinc levels in women with preeclampsia and eclampsia after 28 weeks of gestation and compare with normal pregnancy and to correlate with the foetal outcome.

Material and Methods: 150 antenatal women were divided into Study group A (75 women with pre-eclampsia or eclampsia); Control group B (75 women with normal pregnancy). Plasma and erythrocyte zinc levels were estimated in both the groups and correlated with the foetal outcome.

Results: The plasma zinc levels were significantly low (p < 0.01) in women with severe pre-eclampsia (9.28 ± 1.63 µmol/l) and eclampsia (9.28 ± 2.61 µmol/l) as compared to controls (10.63 ± 1.82 µmol/l). The difference in the erythrocyte zinc levels was not statistically significant in the two groups. There were 4 (5.33%) stillbirths and 8 (10.66%) neonatal deaths in the study group as compared to 2 (2.6%) neonatal deaths in the control group. There was no statistically significant difference in the plasma and erythrocyte zinc levels in infants weighing less than 2500 gm in both the groups. The maternal mortality rate was 1.33% and the overall perinatal mortality rate in the study group was 17.3% as compared to 2.6% in the control group.

Conclusions: Plasma zinc levels were significantly lowered in severe preeclampsia and eclampsia while the erythrocyte zinc levels did not show any significant change. There was no correlation between plasma or erythrocyte zinc levels and intrauterine growth restriction in pre-eclampsia.

Introduction

Pre-eclampsia is a pregnancy-specific condition that increases maternal and infant mortality and morbidity. It is diagnosed by new-onset increased blood pressure and proteinuria during gestation; for many years these markers were the sole targets for study. More recently, increased attention to the multisystemic nature of the syndrome with involvement of almost all organs, activation of coagulation and increased sensitivity to pressor agents has expanded understanding of the disorder. The epidemiology of pre-eclampsia, being more common in poor women, long ago suggested that nutrients might be involved in the disorder. Numerous conflicting hypotheses were advanced but the testing of these hypotheses has either been done poorly or not at all.1

Zinc is considered crucial for maternal and foetal metabolism during pregnancy.2 It plays a role in the stabilisation of bio membranes. It also has a role in the antimicrobial and antiviral activity. Towards the end of normal pregnancy, maternal serum zinc level declines on account of foetal demands, haemodilution, decrease in serum albumin levels and hormonal changes,3 as well as zinc shift from plasma to red blood corpuscle can be the possible cause of serum zinc decrease in pregnant women.4 In serum, 95 to 98% of zinc is bound to protein, mainly albumin and alpha 2 macro globulin and its level fluctuates widely with stress and plasma zinc represents less than 1% of total
body pool. So a single estimate of total plasma zinc can not be used to predict the zinc status of tissues.

Erythrocyte zinc can be determined easily, but it may be relatively stable even in severe zinc depletion, while changes may occur in metabolic diseases such as hyperthyroidism. Erythrocyte zinc is largely found in enzyme carbonic anhydrase, the concentrations of which increase with gestation probably due to effect of progesteron.

It is also suggested that the supply of readily mobilisable zinc is limited and that dietary zinc is important for the maintenance of plasma concentrations. Consequently, if the zinc intake of mother is marginal, the decline in plasma zinc concentration should be exaggerated.5

Changes in the serum trace metal concentration especially copper and zinc have been documented during normal pregnancy and a low maternal serum zinc concentration has been reported in pregnancies complicated by pre-eclampsia6 and it has been suggested that its incidence may be reduced by zinc supplementation.7

Zinc deficiency, as a possible risk factor for pre-eclampsia, is questionable and the results of latest studies showed that lack of zinc causes increased lipid level and peroxidation, which suggest the possibility of the role of zinc deficiency in incidence of pre-eclampsia by increasing lipid peroxidation.8 Besides, the importance of micronutrients in pre-eclampsia was related to their biological roles, as cofactors of antioxidant enzymes.9

This study was conducted to determine and compare maternal plasma and erythrocyte zinc levels in the normal antenatal women and in women with pre-eclampsia or eclampsia after 28 weeks of gestation and find the correlation between them and with the neonatal outcome.

**Material and Methods**

This was an analytical case control study. The study population included 150 antenatal women attending the OPD or emergency or from the in patient department of Obstetrics and Gynaecology of Dayanand Medical College and Hospital, Ludhiana who were divided into two groups.

75 cases in study group A with pre-eclampsia or eclampsia

75 cases in control group B with normal pregnancy

Women with any other medical disorder were excluded from the study.

A detailed history was taken, complete examination done.

Routine investigations like Haemoglobin, TLC, ABORH, Urine routine especially for proteins were done. Special investigation for pre-eclampsia like blood urea, serum uric acid, serum creatinine, ophthalmic fundus examination were done.

Pre-eclampsia was defined as a pregnancy-specific syndrome observed after the 20th week of pregnancy with systolic blood pressure of ≥ 140 mm Hg or diastolic blood pressure of ≥ 90 mm Hg accompanied by significant proteinuria (i.e., urinary excretion of ≥ 0.3 g protein in a 24 hour specimen). Eclampsia was the occurrence, in a woman with pre-eclampsia, of seizures that cannot be attributed to other causes.10,11

**Tests**

10 ml of non fasting random blood samples were taken in a heparinised tube for the estimation of plasma and erythrocyte zinc.

Evaluation of Zinc in plasma: Plasma was separated and stored at -20°C. To know the known volume of plasma, equal volume of trichloroacetic acid (25% w/v) was added for protein precipitation. It was mixed well and kept in ice for half an hour. The solution was then centrifuged for 10 minutes and the supernatant was directly aspirated to the atomic absorption spectrometer for estimation of plasma zinc.

Evaluation of Zinc in erythrocyte: Cells were washed three times with 20 volume of cold isotonic magnesium chloride (osmolality = 290 osm/kg). The haemosylate was prepared by adding 0.2 ml washed red cells to 5 ml of cesium chloride (1.5 mmol/l). Haemosylate zinc concentration was assayed as plasma zinc. Haemosylate haemoglobin (Hb) concentration was determined by a modified cyanomethaemoglobin method on a centrifugal analyser.

Erythrocyte Zinc was calculated according to the following equation:

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\text{Erythrocyte Zn (µmol/l of RBC) = } \frac{10 \times \text{MCHC (g Hb/100 ml of RBC)} \times \text{Haemolysate Zn (µmol/l)}}{\text{Haemosylate Haemoglobin (g/l)}}
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It was expressed in µmol/l of red cells to eliminate the effect of pregnancy haemodilution. The factor 10 was used for unit conversion.

Pregnancy outcome was observed, birth weight was recorded, Apgar scores at 1 and 5 minutes was noted. Zinc levels were compared with foetal outcome using the students’ ‘t’ test.

**Observations**

Of the 75 patients in group A; 47 (62.66 %) patients had mild pre-eclampsia (Blood pressure ≥ 140/90 mm Hg but less than 160/100 mm Hg), 18 (24 %) patients had severe pre-eclampsia (Blood pressure ≥ 160/100 mm Hg) and 10 (13.33 %) patients had eclampsia.
No significant difference was observed in age, diet, period of amenorrhoea, gravidity, parity and socioeconomic status in the two groups. In the control group, 65 (86.66%) patients were from urban area as compared to 55 (73.33%) in the study group. 20 (26.6%) women in the study group complained of headache and pedal oedema; whereas 16 (21.3%) had only pedal oedema. In the study group, 69 (92%) patients had fundal height corresponding to the period of amenorrhoea (AGA) and 6 (8%) had less than period of amenorrhoea (SGA), thereby indicating intrauterine growth restriction.

In the study group, 18 (24%) women showed retinal changes on fundoscopy (Table 1).

There was a significant increase in the blood urea (p < 0.001) in the women with eclampsia than controls (Table 2). There was a significant increase (p < 0.001) in the serum uric acid in the study group than controls (Table 3).

The plasma zinc levels were significantly low (p < 0.01) in women with severe pre-eclampsia (9.28 ± 1.63 µmol/l) and eclampsia (9.28 ± 2.61 µmol/l) than controls (10.63 ± 1.82 µmol/l) (Table 4). The difference in the erythrocyte zinc levels was not significant in both the groups (Table 5).

53 (70.66%) patients in the study group had vaginal delivery and 22 (29.33%) delivered by LSCS. Of the 53 patients who delivered vaginally, 4 (5.33%) had forceps delivery. In the control group, 46 (61.33%) patients delivered vaginally of whom 3 (4%) had forceps delivery and 29 (38.66%) patients delivered by LSCS.

The mean birth weight of the neonate was 2.35 kg in the study group and 2.8 kg in the control group (Table 6). The Apgar score at 5 minutes was seven or more in the majority of neonates born to the mothers in the study group 64 (85.33%) and control group 76 (98.70%) (Table 7).

There were 4 (5.33%) stillbirths and 8 (10.66%) neonatal deaths in the study group than 4 (5.2%) neonatal deaths in the control group. There was one maternal death in the study group (uncontrollable eclampsia) thereby giving group maternal mortality rate of 13.3 per 1000 live births (1.33%).

**Discussion**

Pre-eclampsia is the most common medical complication of pregnancy associated with increased
maternal and infant mortality and morbidity. In many studies, nutritional data (questionnaires or biomarkers) are obtained on women with pre-eclampsia. Many times it is impossible to decipher the cause from effect. Nonetheless, current concepts of the genetics of pre-eclampsia that include endothelial dysfunction, inflammatory activation, oxidative stress and predisposing maternal factors provide targets for well-designed nutritional investigation.

The results of our study showed that the difference in the mean plasma zinc levels between the controls (10.63 ± 1.82 µmol/l) and mild pre-eclampsia (10.46 ± 2.05 µmol/l) was not significant but that between controls and severe pre-eclampsia (9.28 ± 1.63 µmol/l) and eclampsia (9.28 ± 1.63 µmol/l) was statistically significant. This finding is supported by many authors. They observed a low level of zinc in women with pre-eclampsia but the values were not statistically significant. The difference may be because they did not divide the pre-eclamptic women into groups based on severity. We too did not observe a significant difference in the women with mild pre-eclampsia but found so in severe pre-eclampsia and eclampsia. These studies did not include women with eclampsia in whom the affection of disease would have been more. Bahadoran et al observed an association between serum zinc concentration and the severity of pre-eclampsia and recommended assessment of serum zinc concentrations as an index for predicting the severity of pre-eclampsia.

Jain et al also observed a low level of plasma zinc in pre-eclamptic women and suggested that supplementation of calcium, magnesium and zinc in diet may be of value to prevent pre-eclampsia.

Various authors have not found an association between zinc levels and pre-eclampsia. Tamura concluded that plasma zinc concentrations during the late first trimester to the early third trimester do not predict pregnancy outcomes in women of a low socio-economic background.

Lao et al measured plasma and erythrocyte zinc levels in pre-eclamptic women and suggested that zinc deficiency is unlikely to play a significant role in pre-eclampsia and that measurement of plasma and erythrocyte zinc concentrations is of doubtful clinical value in the management of pre-eclampsia. In our study, the difference in the erythrocyte zinc was not significant in any of the groups.

On the contrary, some authors have observed a rise in the zinc levels in pre-eclamptic women. Geographical differences and different nutrition and food may be reasons for this variation.

There was a statistically significant (p < 0.001) difference between birthweight of the neonates in the control group (2805 ± 481 gm) and the study group (2348 ± 527 gm). The difference between the birthweights of the control group and the mild pre-eclampsia (2665 ± 470 gm) was not statistically significant but with severe pre-eclampsia (2032 ± 584 gm) was highly significant (p < 0.001). Higher incidence of intrauterine growth restriction and low birth weight has been associated with pre-eclampsia and it increases with the severity of pre-eclampsia.

The difference in the mean plasma Zinc in women (9.3 ± 2.49 µmol/l) who delivered babies weighing less than 2500 gm and in women (9.9 ± 2.18 µmol/l) who delivered babies weighing more than 2500 gm was statistically not significant. This finding has been supported by Tamura et al who concluded that plasma zinc concentrations were not significantly associated with any measure of pregnancy outcome or neonatal condition.

**Conclusion**

Our results suggest that plasma zinc levels are significantly lower in severe pre-eclampsia and eclampsia while the erythrocyte zinc levels do not show any significant change. There is no correlation between plasma or erythrocyte zinc levels and intrauterine growth restriction in pre-eclampsia. There is an association between serum zinc concentration and the severity of pre-eclampsia and we recommend assessment of serum zinc concentrations as an index for predicting the severity of pre-eclampsia.

**References**

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