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**Effect of Zinc Supplementation on Red Blood Cell Osmotic Fragility
in hemodialysis Patients.**

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Abstract:

Introduction: Zinc deficiency may aggravate the effect of oxidative stress on RBC (Red Blood Cell) of chronic uremia. In this study, there is an attempt to show the relationship between the plasma zinc level and RBC osmotic fragility in hemodialysis patients.

Patients and Methods: Thirty five patients with low level of serum zinc (serum zinc level < 70) participated in the trial. RBC osmotic fragility, Hb (hemoglobin) and BUN (blood urea nitrogen) were checked. The patients received zinc supplement (zinc sulfate) (250 mg/day). Plasma level of zinc, Hb, BUN and osmotic fragility rechecked after 6 weeks.

Results: The mean serum zinc concentration among the participants increased and it was statistically significant ($p < 0.05$). Erythrocytes at day 0 (59 ± 3.5) were significantly ($P < 0.05$) more fragile in hypotonic saline than those at day 43 (38 ± 2.9), (at NaCl 40%). No significant changes were noted in the level of Hb.

Discussion: In this trial, oral zinc supplementation caused a significant rise in the plasma zinc level after 6 weeks. Although Hb concentration was not changed during the trial the level of osmotic fragility in red cells reduced significantly.

Keywords: osmotic fragility, hemodialysis, zinc

Introduction:

Zinc is an essential trace element.⁽¹⁾ Zinc deficiency leads to pathological signs that are related to impaired function of plasma membrane proteins.⁽²⁾ Zinc deficiency in rats increases the osmotic fragility of erythrocytes, due to structural defect in the plasma membrane.⁽³⁾

Both anemia and zinc deficiency are commonly observed in patients with chronic uremia.^(3,4) Oxidative stress of the RBCs has been suggested to participate in the development of anemia in the patients with chronic uremia due to reduced life span of RBC ⁽⁴⁾

Zinc deficiency may aggravate the effect of oxidative stress on RBC in chronic uremia.

Furthermore Peroxidation of the membrane structure of red blood cell leads to anemia in haemodialysis patients.⁽⁵⁾ In this study, we try to show the relation between the plasma zinc level and RBC osmotic fragility in hemodialysis patients.

Patients and Methods:

A prospective study was designed to assess the effects of oral zinc sulfate supplementation on the red blood cells osmotic fragility level in hemodialysis patients.

One hundred thirty patients with ESRD (End Stage Renal Disease) on HD (hemodialysis) from the outpatient HD unit of Shiraz University Hospitals, southern Iran, were included in the study.

All the participants gave informed consent to be included in the study. At the time of data collection, formal ethical application was received from the patients who want to cooperate in the study.

Zinc plasma level was assessed with fasting plasma level samples which were obtained in acid washed tubes, in all patients. It was measured with atomic absorption method in gastrointestinal research centre in Nemazee hospital Shiraz Iran. We also checked the plasma level of Hb and level of serum iron too. The plasma level of BUN was checked for detecting any stage of uremia. Thirty five patients with low level of serum zinc (serum zinc level <70) were included in the trial. Then, we checked the red blood cell osmotic fragility with blood samples which were obtained in heparinized syringes. Osmotic fragility test was done with serial dilution method.

The patients received zinc supplement (zinc sulfate) (250 mg/day) for 6 weeks. The zinc sulfate capsules were obtained from Alhavi pharmacy, Iran.

The plasma level of zinc, Hb, serum Iron, BUN and osmotic fragility rechecked after 6 weeks.

An analysis of variables with repeated measure design was used to determine the changes in the serum parameters over time after 6 weeks in all the patients. Parametric data are presented as mean (standard deviation (SD)). The

variables were analyzed with SPSS 15. Level of signifancy was $P > 0.05$.

Results:

Thirty two patients completed the study. Two of them were unable to complete the study because of hospitalization and one of them expired before completion of the study. A total of 3 subjects were eliminated from the analyses. The mean age of the patients was 54 (SD: 18) (range 24–83) years. The Mean duration of dialysis in the patients was 12 months (range: 3- 48 months). The initial mean serum zinc concentration for the subjects before zinc supplement administration was $55.67 \mu\text{g/ml}$. (SD: 15.51) after 42 days, the mean serum zinc concentration among the participants increased up to

$79.40 \mu\text{g/ml}$ (SD: 21.92) which was statistically significant ($p < 0.05$).

No significant changes were noted in the level of Hb from day 0 (9.8 mg/ml) (SD: 1.64) to day 43 (10 mg/ml) (SD: 1.56).

Also, no significant changes were noted in the serum level of Iron from day 0 ($108. \text{ mg/ml}$) (SD: 53.22) to day 43 (102 mg/ml) (SD: 45.62).

Erythrocytes at day 0 (59 ± 3.5) were significantly ($P < 0.05$) more fragile in hypotonic saline than those at day 43 (38 ± 2.9), (at NaCl 40%) Mean level of plasma BUN did not change significantly from day 0; $56.7(23.84)$ to day 43; $61.7(22.41)$. Table 1

Table 1: Zinc and the plasma levels of Iron and BUN, Hb concentration and osmotic fragility (at NaCl 40%) before and after administration of zinc supplementation.

	Before intervention	After intervention	P.Value
Osmotic fragility (hemolysis in NaCl 40%)	59 ± 3.5	38 ± 2.9	< 0.05
Level of Hb (g/ml)	9.8 (SD: 1.64)	10 (SD: 1.56)	> 0.05
Plasma level of BUN	$56.7(23.84)$	$61.7(22.41)$	> 0.05
serum level of Iron	$108.$ SD: 53.22)	102 (SD: 45.62).	> 0.05
Zinc level $\mu\text{g/ml}$	55.67 (SD: 15.51)	79.40 (SD: 21.92)	< 0.05

Discussion:

Zinc is an essential trace element. This trace element required for the action of more than 200 metallo enzymes and plays an important role in polymeric organization of macromolecules (like DNA and RNA), protein synthesis and cell division. Zinc plays many significant roles in metabolism ⁽¹⁾

Zinc deficiency is a common problem around the world.⁽⁷⁾ Its rate in Middle East and Iran is estimated to be about

31% in otherwise healthy persons. It is more common in many disease states such as ESRD patients undertaking HD.⁽⁸⁾ The rate of zinc deficiency in patients with HD is about 40-78%.^(9, 10)

Zinc deficiency leads to pathological signs that are related to impaired function of plasma membrane proteins.⁽²⁾

Low-zinc status lowers the plasma membrane sulfhydryl concentration, and the decreased reducing potential is inversely related to osmotic fragility, and pre-

sumably, with impaired volume recovery of erythrocytes.⁽²⁾ This condition and peroxidation of the membrane structure of red blood cell leads to anemia in the HD patients.⁽⁵⁾

Dietary zinc deficiency in rats causes increased osmotic fragility of their erythrocytes.⁽⁶⁾ O'Dell BL et al. suggested that the osmotic fragility induced by zinc deficiency was prevented by high sulfur amino acid intake and was readily reversed by dietary zinc.⁽¹¹⁾

In this trial oral zinc supplement caused a significant rises in the plasma zinc level after 6 weeks.

Anemia and hemoglobin variability are associated with mortality in hemodialysis patients moreover the treatment of anemia in dialysis patients improves patient well-being and reduces the need for transfusions.⁽¹²⁾

Although Hb concentration was not changed during this trial, the level of osmotic fragility in red blood cells reduced significantly. Finally we suggest that zinc supplementation can improve osmotic fragility in red blood cells in HD patients and may improve the related anemia in long term.

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