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CLINICAL STUDY

# Impact of oral zinc therapy on the level of sex hormones in male patients on hemodialysis

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#### ABSTRACT

Background: Sexual dysfunction in chronic renal failure patients undergoing hemodialysis is common. It is demonstrated that the zinc level is significantly lower in the hemodialysis patients. Objective: In this clinical trial, we investigate the effect of zinc supplement therapy on the serum levels of sexual hormones in hemodialysis male patients. Patients and methods: We carried out a clinical trial study including 100 of our male patients with end-stage renal disease on hemodialysis. Testosterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, and zinc plasma level were measured in all of the patients. The patients received zinc supplement (zinc sulfate, 250 mg/day) for 6 weeks, and sex hormones and zinc plasma level were checked again. Results: Serum level of FSH and prolactin did not have any significant changes before and after intervention, but serum level of testosterone, LH, and zinc increased significantly. Discussion: These results suggest that although zinc administration did not have a definite effect on hemodialysis patients with sexual dysfunction, it can cause increase in the serum level of sex hormones which may improve the sexual function of the patients in some aspects.

Keywords: oral zinc therapy; sex hormones; hemodialysis; male patients; chronic renal failure

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## INTRODUCTION

Sexual dysfunction in chronic renal failure patients undergoing hemodialysis is common<sup>1,2</sup>; it impairs their quality of life and has a complex pathogenesis. The exact pathophysiology underlying this problem is not still understood. It has been shown that several factors could be important in this pathology: abnormal hormonal balance, hypotestosteronemia, low basal luteinizing hormone (LH) levels, hyper-prolactinemia, iron overload, and underlying diabetes.

Renal failure because of diabetes associated with atherosclerosis and renal failure-associated hypoxia changes of the contractile components of the erectile tissue could be important factors.<sup>3–9</sup> Psychiatric factors could be other related factors.<sup>9</sup>

It is demonstrated that the zinc level is significantly lower in the hemodialysis patients.<sup>10</sup> Zinc is an essential trace element. This trace element required for the action of many metallo-enzymes and plays an important role in biological functions such as protein synthesis, growth and development, and gonadal functions.<sup>11</sup> Zinc deficiency may account for the persistence of gonadal dysfunction in a majority of uratemic men despite adequate dialysis.<sup>11</sup> In this clinical trial, we investigate the effect of zinc supplement therapy on the serum levels of sexual hormones in hemodialysis male patients.

### PATIENTS AND METHODS

We carried out a clinical trial study including 100 of our male patients (age >18 years) who had advanced chronic kidney disease (CKD) or end-stage renal disease (ESRD) on hemodialysis. No exclusion criteria were applied. The patients' previous exposure to systemic corticosteroids (particularly relevant to the transplant population) was carefully noted, and other clinical parameters, such as age, primary renal disease, and the total duration of dialysis treatment, were recorded. All the patients gave informed consent to be included in the study. At the time of data collection, formal ethical application was received from the patients. Gonadal status was assessed by obtaining fasting early morning plasma samples. Testosterone, follicle-stimulating hormone (FSH), LH, and prolactin were measured in all of them. All the sex hormone levels were measured with radioimmunoassay method program in Endocrine Research Centre at Nemazi Hospital, Shiraz, Iran.

Serum/plasma zinc level was measured with atomic absorption method in Gastrointestinal Research Centre at Nemazi Hospital. The patients received zinc supplement (zinc sulfate, 250 mg/day) for 6 weeks. The zinc sulfate capsules were obtained from Alhavi Pharmacy, Tehran, Iran. An analysis of variables with repeated measure design was used to determine changes in serum parameters over time after 6 weeks in all the patients. An independent *t*-test was used to determine the possible differences in various serum parameters at days 0 and 43. Pearson correlation coefficient was used to determine the strength of the relationship that existed among various parameters. The data were analyzed using the statistical pack for social science series (SPSS 15.0) and  $p \le 0.05$  was considered significant for all the statistical test results.

### RESULTS

Ninety-five patients completed the study. Two of them were unable to complete the study because of hospitalization, two of them did not complete the study because of noncompliance with prescribed behavior, and one of them unfortunately died before completion of the study. A total of five patients were eliminated from the analyses.

The mean age of the patients was 54 (SD=18; range 24–83) years. Overall, 43% of the patients were diabetic, 28% had hypertension, 12% had polycystic

kidney disease, and 17% had obstruction were other causes of ESRD. The mean duration of dialysis in the patients was 12 months (range 3–48 months).

The initial mean serum zinc concentration for the patients before zinc supplement administration was 55.67  $\mu$ g/dL (SD = 15.51). After 42 days, the mean serum zinc concentration among the participants increased up to 79.40  $\mu$ g/dL (SD = 21.92), which was statistically significant (p < 0.05). At day 43, there was a significant elevation in the serum level of testosterone (2.94 nm/dL; SD = 2.13) compared with the beginning of the study (1.55 nm/dL; SD = 1.24; p < 0.05). No significant changes were noted in the serum level of prolactin from day 0 (308.66 mg/mL; SD = 277.23) to day 43 (405.3 mg/mL; SD = 372.5). Moreover, there was a significant increase in the mean serum level of LH in the patients from day 0 (4.85 mg/ dL; SD = 4.66) to day 43 (15.77 mg/dL; SD = 14.92). Serum level of FSH did not have any significant changes before and after intervention. Serum zinc and the plasma levels of the sex hormones and prolactin before and after the intervention are summarized in Table 1.

#### DISCUSSION

Zinc is an essential 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.<sup>11</sup> Zinc plays an important role in prostate, epididymal, and testicular functions.<sup>12</sup> Hypozincemia leads to gonad dysfunction, decreased testicular weight, atrophy of seminiferous tubules, and complete cessation of spermatogenesis.<sup>13</sup>

As mentioned earlier it was demonstrated that the zinc level was significantly lower in the hemodialysis patients compared to healthy individuals.<sup>10</sup> Zinc deficiency may account for the persistence of gonadal dysfunction in a majority of uremic men despite adequate dialysis. Some studies suggest that zinc deficiency is a reversible cause of gonadal dysfunction in patients

TABLE 1. Zinc and the plasma levels of the sex hormones and prolactin before and after administration of zinc supplement.

	Before intervention	After intervention	<i>p</i> -Value
Testosterone level (nm/dL)	1.55 (1.24)	2.94 (2.13)	0.03
Prolactin level (nm/dL)	308.66 (277.23)	405.3 (372.5)	0.25
LH level (nm/dL)	4.85 (4.66)	15.77 (14.92)	0.01
FSH level (nm/dL)	6.62 (5.71)	10.7 (9.23)	0.36
Zinc level (µg/dL)	55.67 (15.51)	79.40 (21.92)	0.02

Note: The values in the parentheses represent SD.

having regular hemodialysis.<sup>10,14</sup> Zinc deficiency impairs angiotensin-converting enzyme (ACE) activity, and this in turn leads to depletion of testosterone and inhibition of spermatogenesis.<sup>15</sup>

On the other hand, defects in spermatozoa are frequently observed in the zinc-deficient rat. Zinc is thought to help extend the functional life span of the ejaculated spermatozoa.<sup>15</sup> Moreover, zinc deficiency in the females can lead to impaired synthesis/secretion of FSH and LH too.<sup>14,15</sup>

In this study, after oral zinc supplement administration, plasma testosterone concentrations and basal serum LH level were raised. Zinc administration had no significant effect on the FSH level and serum prolactin level. These results suggest that although zinc administration did not have a definite effect on hemodialysis patients with sexual dysfunction it can cause increase in the serum level of sex hormones which may improve the sexual function of the patients in some aspects.

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