

# Erkek Hemodiyaliz Hastalarında Serum Çinko Seviyesi, Hormonal Profil ve Seksüel Disfonksiyon Arasındaki İlişki

## *Relationship Between Serum Zinc Levels, Hormonal Profiles and Sexual Dysfunctions in Male Hemodialysis Patients*

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### ÖZET

**Amaç:** Erkek hemodiyaliz hastalarında seksüel bozuklukların sıklığı ile serum çinko seviyesi, hormonal profil ve seksüel disfonksiyon arasındaki ilişkinin değerlendirilmesi.

**Materyal ve Metot:** En az altı aydır haftada 15 saat konvansiyonel bikarbonat tedavisi gören 41 erkek hasta değerlendirildi. Serum PRL, FSH, LH, progesteron, testosteron, TSH, serbest T<sub>4</sub> ve çinko düzeyleri ölçüldü. Seksüel disfonksiyon kişisel anketle değerlendirildi.

**Bulgular:** Üç hastada düşük serum çinko düzeyi tespit edildi. 33 (%80.5) hastada PRL yüksekti. Hastaların 17'sinde (%41.5) prematür ejakülasyon, 10'unda (%24.4) erektil disfonksiyon, 7'sinde (%17) impotans ve 7'sinde (%17) azalmış libido saptandı. Yaş ile impotans arasında ( $r=0.594$ ,  $p=0.000$ ) ve hipozinkemi ile prematür ejakülasyon arasında ( $r=0.334$ ,  $p=0.033$ ) pozitif korelasyon bulundu. Hemodiyaliz süresi ile PRL düzeyi arasında negatif bir korelasyon saptandı ( $r=-0.363$ ,  $p=0.020$ ). Hipozinkemi ile hiperprolaktinemi arasında anlamlı korelasyon bulunmadı ( $r=0.084$ ,  $p=0.456$ ).

**Sonuç:** Hipozinkemi ve hiperprolaktinemi hemodiyaliz hastalarında yaygındır. Hipozinkemi ile hiperprolaktinemi arasında ilişki bulunmadı.

PRL düzeyi, hemodiyaliz süresine bağlı azalmış bulundu. Serum çinko düzeyi ile prematür ejakülasyon arasında pozitif korelasyon saptandı.

**Anahtar sözcükler:** hipozinkemi, seksüel disfonksiyon, hiperprolaktinemi, HD patients

### ABSTRACT

**Objectives:** To investigate the frequency of sexual disorders and the relationship between serum zinc levels, hormonal profiles and sexual dysfunctions in male HD patients.

**Materials and Methods:** Forty-one male patients who were on chronic HD programme for at least six months, and treated by conventional bicarbonated HD 15 hours/week were evaluated. The serum levels of PRL, FSH, LH, progesterone, testosterone, TSH, free thyroxine and zinc were measured. A personal questionnaire was used to evaluate the sexual dysfunctions.

**Results:** Three of the 41 patients had low serum zinc levels. Thirty-three (80.5%) of patients had elevated PRL levels. 17 (41.5%) of the patients had premature ejaculation, 10 (24.4%) had erectile dysfunction, 7 (17%) had impotence, and 7(17%) had decreased libido. A positive correlation was found between age and impotence ( $r=0.594$ ,  $p=0.000$ ) and between hypozincemia and premature ejaculation ( $r=0.334$ ,  $p=0.033$ ). A negative correlation was found between HD duration and PRL levels ( $r=-0.363$ ,  $p=0.020$ ). There was not any significant correlation between hypozincemia and hyperprolactinemia ( $r=0.084$ ,  $p=0.456$ ).

**Conclusion:** Hypozincemia and hyperprolactinemia were prevalent among HD patients. No correlation was found between hypozincemia and hyperprolactinemia. PRL levels decreased due to HD duration. A correlation was found between serum Zn levels and premature ejaculation.

**Keywords:** hypozincemia, sexual dysfunction, hyperprolactinemia, HD patients

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## Introduction

Endocrine disturbances frequently occur in patients with end stage renal disease (ESRD). These disturbances are primarily organic in nature including marked hypothalamo-pituitary-gonadal dysfunction and are related to uremia as well as the other comorbid conditions such as hypozincemia and renal anemia. As a result of this disturbances the sexual dysfunction is occurred which is a common finding in both men and women with ESRD. The common sexual dysfunctions are impotence, premature ejaculation and erectile dysfunction (ED) in men, the menstrual abnormalities such as amenorrhea, oligomenorrhea, in women, and decreased libido and fertility in both sexes (1). The other abnormalities such as uremic toxins, renal anemia and zinc (Zn) deficiency are also reported to be the causative factors of sexual dysfunction (2).

The aim of this study was to investigate the frequency of sexual disorders and the relationship between serum zinc levels, hormonal profiles and sexual dysfunctions in male hemodialysis (HD) patients.

## Materials and Methods

Forty-one uremic male patients who were on maintenance HD programme for at least six months were evaluated. All the patients were treated by conventional bicarbonated HD for 15 hours/week by polysulfone hallow fiber dialysers. The demographic features and weekly requiring dose of rHuEPO of the patients were recorded at the beginning of the study. Kt/V of all the patients was established by urea kinetic modelling formula that modified by Daugirdas (3). The blood samples were collected after a 12-hour fasting period and before the hemodialysis sessions in the morning. The serum levels of prolactin (PRL), follicle stimulating hormone (FSH), luteinizing hormone (LH), and progesterone (P), testosterone (T), thyroid stimulating hormone (TSH), and free thyroxine (FT<sub>4</sub>) were measured with Roche elecsys kit by electrochemiluminescence immunoassay and the serum level of zinc is assessed through spectrophotometric assay. Hyperprolactinemia is defined as serum PRL level greater than 18.4 ng/ml.

ED was defined as could not have adequate erection for a satisfying sexual performance and

the sexual dysfunctions of the patients were evaluated by a personal questionnaire on their sexual activity (Sexual Health Inventory For Men: IIEF-5) and a score  $\leq 21$  was accepted as ED. The statistical analysis were evaluated on SPSS 11.0 PC program. Datas were defined as mean  $\pm$  SD. The chi-square test was used at the analysis of the categorical variables. The independent sample t-test and chi-square tests were used for analysis of the continue variables. The Pearson correlation test was used to analyse of correlation. The  $p < 0.05$  was accepted as statistically significant.

## Results

The results of demographic features, hematocrit (Hct) levels, weekly requiring dose of the rHuEPO and Kt/V values of the patients were shown in Table I. We did not find any significant relationship between hypozincemia and those parameters ( $r=0.149$ ,  $p=0.188$ ,  $r=0.157$ ,  $p=0.164$ , and  $r=0.059$ ,  $p=0.601$ , respectively).

Three of the 40 (7.5%) patients had low serum zinc levels. The mean serum zinc level was  $0.64 \pm 0.12$  ppm. In all patients, 8 (19.5%) had normal serum PRL levels, 5 (12.2%) had serum PRL levels higher than 100 ng/ml, and the levels of the remaining took place between 18.4 and 100 ng/ml ( $p=0.100$ ). The results of serum Zn levels and hormonal profiles of the study patients were shown in Table II. There was not any significant correlation between hypozincemia and hyperprolactinemia ( $r=0.084$ ,  $p=0.456$ ).

In evaluating sexual dysfunction, 17 (41.5%) of the patients had premature ejaculation which was the most frequent form of dysfunction among our patients, 10 (24.4%) erectile dysfunction, 7 (17%) impotence, and 7 (17%) had decreased libido.

**Table I. Demographic and hematologic parameters of patients and Kt/V values**

Characteristics	Values (n=41)
Age (years)	40.5 $\pm$ 16.1
Duration of HD (months)	21.3 $\pm$ 22.5
Hct (%)	33.2 $\pm$ 4.5
rHuEPO (U/wk)	2800.0 $\pm$ 1800.0
Kt/V	1.24 $\pm$ 0.18

<b>Table II. Serum zinc levels and hormonal profiles of the patients</b>	
<b>Parameters</b>	<b>Levels (n=41)</b>
Level of serum Zn (ppm)	0.64 ±0.12
PRL (ng/ml)	46.1±57.2
LH (mIU/ml)	12.7±20.8
FSH (mIU/ml)	8.8±16.6
Progesteron (mIU/ml)	4.5±6.2
Testosteron (ng/dl)	4.9±2.1
TSH (mIU/ml)	1.6±1.0
FT4 (ng/dl)	1.0±0.3

<b>Table III. Findings of sexual dysfunctions in patients</b>		
<b>Parameters</b>	<b>Patients (n=41)</b>	<b>Rate (%)</b>
Premature ejaculation	17	41.5
Erectile dysfunction	10	24.4
Impotence	7	17
Decreased libido	7	17

Among patients, a positive correlation was found between age and frequency of impotence ( $r=0.594$ ,  $p=0.000$ ) and between hypozincemia and frequency of premature ejaculation ( $r=0.334$ ,  $p=0.033$ ). In addition there was a negative correlation between serum T levels and frequency of impotence ( $r=-0.319$ ,  $p=0.042$ ), and between serum progesteron levels and impotence ( $r=-0.335$ ,  $p=0.032$ ). According to the duration of HD elevated serum PRL levels were found in 23 of the 25 (92%) patients who were undergoing HD less than one year and this ratio was 10/16 (62.5%) in patients receiving HD therapy more than one year ( $p=0.020$ ). A negative correlation was found between HD duration and PRL levels ( $r=-0.363$ ,  $p=0.020$ ) among patients.

### Discussion

It has been reported for many years that there was an association between uremia and sexual dysfunction in HD patients that was based on hyperprolactinemia and/or deficiency of trace ele-

ments such as hypozincemia. Weizman et al suggested that there was an association between sexual dysfunction and hyperprolactinemia in uremic patients. They reported that the male and female patients who report disturbance of sexual function had significantly higher prolactin level than those with normal sexual function which accounts half of the patients (4). It is well established that elevated serum PRL levels and decreased T levels are known to cause impotence in patients with normal renal function and have also been reported in uremia. Gura et al suggested that elevated serum PRL levels may be an important cause of impotence among HD patients (5). In the present study, the frequency of impotence was 17% among the male patients. Although, we did not find any association between PRL levels and impotence, and between PRL and serum T levels, we found a negative correlation between serum T levels and impotence, in addition a positive correlation between age and impotence. Thus, it may be said that in addition to the elevated serum PRL levels, age may be more important effect than it is thought.

For the hormonal profiles of the male HD patients it has been commonly reported that these patients had low T levels, increased LH and sometimes FSH levels (6). We established that although the serum T levels of the study patients were in normal range, the gonadotropins were high just like as the literature. Thus the normal range of the serum T levels is due to the hematocrit levels and young age of the male patients. However, little is known about the effect of hyperprolactinemia and age on hypogonadism, Mastrogiacono et al emphasized that a positive correlation was found between LH and FSH, a negative correlation between PRL and both T and LH (6). Like these results we found a positive correlation between LH and FSH, but no correlation between serum PRL levels both T and LH. In our study although serum PRL levels were higher than normal in our patients, the T levels were in normal ranges and this might be due to the factors such as younger age, having target Hct levels and racial specialities.

Decreased libido, erectile dysfunction and premature ejaculation are widely prevalent among the male HD patients. In this issue Zamd M et al addressed that the male subjects had erection disorders (44.9%), decreased libido (44.9%), and ejaculation problems (26.8%) among the patients in the-

ir study (7). In another study Zhang WD et al suggested that the prevalence of sexual dysfunction was wider in patients with chronic renal insufficiency than in those without. The main manifestations in male patients were decreased libido, erectile dysfunction and premature ejaculation (8). We observed that the premature ejaculation was the most frequent disorder with a percentage of 41.5 and followed by erectile dysfunction (24.4%), impotence (17%) and decreased libido (17%) respectively among our patients. Also we found a negative correlation between hypozincemia and premature ejaculation ( $r=0.334$ ,  $p=0.033$ ). In the treatment of sexual dysfunction some authors reported that recombinant human erythropoietin (rHuEpo) may resolve these problems. Kinugasa et al reported that uremic toxins, renal anemia, hyperparathyroidism, zinc deficiency, vascular and neurologic abnormalities are the causative factors of sexual dysfunction. Among these parameters correction of anemia with rHuEpo sometimes results in the amelioration of sexual potency, probably due to improvement of erectile performance by increased blood viscosity (9). Moreover, Schaefer RM et al suggested that treatment of anemia in end-stage renal disease by rHuEpo may improve sexual function by lowering elevated serum prolactin concentrations (10).

Another groups of authors have been reported that the sexual dysfunctions of the male patients still go on despite rHuEpo therapy. Lawrence et al reported that many male dialysis patients receiving rHuEpo continue to complain of sexual dysfunction. Male dialysis patients complaining of sexual dysfunction after correction of anaemia with rHuEpo are characterized by higher levels of serum T and sex hormone binding globulin (SHBG), but not suppression of hyperprolactinaemia or hyperoestrogenism (11). In the present study, although Hct levels of male patients were in target range, serum PRL levels were higher than normal limits among these patients. But in contrast serum testosterone levels were in normal range. In spite of having target Hct values, normal T levels, the male patients had various complaining of sexual dysfunction, as found in the study of Lawrence et al. Thus correcting anemia with rHuEpo may not be enough to correct male sexual dysfunction.

In a cross-sectional study, the serum PRL levels gradually decreased with longer duration of dialy-

sis (12). We found a negative correlation between HD duration and PRL levels among patients ( $r=-0.363$ ,  $p=0.020$ ).

Some authors have been reported that there was a coexistence of hypozincemia and hyperprolactinemia among the both male and female HD patients. But this subject remains controversial. Because it is unclear whether hypozincemia and hyperprolactinemia affects each other or it is only a coincidental situation that was seen in both gender in HD patients. Castro et al presented that Zn supplementation did not correct hyperprolactinemia in uremic patients, although the coexistence of hypozincemia and hyperprolactinemia had shown in the previous studies (13). In another study of Castro et al reported that there were no correlation between blood concentrations of  $Zn^{2+}$  and PRL, PTH, LH, and FSH in dialysis patients (14). As in these studies we did not find any correlation between these parameters.

In conclusion, the main manifestations of sexual dysfunction were premature ejaculation, erectile dysfunction, impotence and decreased libido among male HD patients. Hypozincemia and hyperprolactinemia were prevalent among HD patients. No correlation was found between hypozincemia and hyperprolactinemia. PRL levels decreased due to HD duration. A correlation was found between serum Zn levels and premature ejaculation.

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