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The Relationship Between Oxidative Stress and Osteoporosis in Chronic Dialysis Patients

Kronik Diyaliz Hastalarında Oksidatif Stres ile Osteoporoz Arasındaki İlişki

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Abstract

Aim: End Stage Renal Disease (ESRD) patients are subjected to enhanced oxidative stress (OS), and osteoporosis (OP) is an important cause of morbidity in patients with ESRD. Although it is controversial, in many studies made in population without renal disease, OS is related to increased OP risk. In recent study we aimed to investigate the association between OS and OP in dialysis patients.

Materials and methods: Sixty two patients on maintenance dialysis programme were included into the study. Total oxidant status (TOS), lipid hydroperoxides (LOOH), and total antioxidant capacity (TAC) and bone mineral density was measured. Demographic and biochemical parameters were recorded. Patients were divided as group 1: Hemodialysis and group 2: Peritoneal Dialysis and compared.

Results: Twentynine of 62 patients were on HD and 33 were on PD. In Bone mineral density BMD T–scores while there was no statistically significant difference between two groups at femur neck, according to lumbar spine among HD patients T score was better then PD patients. Mean serum concentration of LOOH was 6.07±2.91 and 5.82±2.20 µmolH_2O_2Eq/L, TOS was 8.89±5.89 and 7.62±3.99 µmol H_2O_2Eq/L, and the TAC was 1.01±0.20 and 0.93±0.16 mmolTroloxEq/L in group 1 and in group 2 respectively. Among all patients there was a positive correlation between TAC and T score in FN. There was no correlation between TOS and T-scores.

Conclusion: Although enhanced OS and reduced antioxidant capacity in dialysis patients we did not find any effect of OS on OP. This result may be due to low OP rate in our patients and this novel topic needs further large scale studies in dialysis population.

Key words: End stage renal disease; Oxidative stress; Osteoporosis; Dialysis.

Özet

Amaç: Son dönem böbrek yetmezliği hastaları, artmış morbiditeye yol açan oksidatif stres (OS) ve osteoporoz (OP) ile karşı karşıyadırlar. Tartışmalı olmakla birlikte, böbrek hastalığı olmayan popülasyonda yapılan birçok çalışmada OS, artmış OP riski ile ilişkilidir. Bu çalışmada, kronik diyaliz hastalarında OS ve OP arasındaki ilişkiyi araştırmayı amaçladık.

Materyal ve metod: Kronik diyaliz programında olan 62 hasta çalışmaya dahil edildi. Total oksidan durum (TOS), lipid hidroperoksid (LOOH), total antioksidan kapasite (TAC) ve kemik mineral yoğunluğu ölçüldü. Demografik ve biyokimyasal veriler kaydedildi. Hastalar Grup1: Hemodiyaliz ve Grup2: Periton Diyalizi olarak 2 gruba ayrılarak bulgular karşılaştırıldı.

Bulgular: Altmış iki hastanın 29'u HD ve 33'ü PD hastası idi. Kemik mineral yoğunluğu ölçümlerinde T-skorları femur boynunda iki grup arasında istatistiksel olarak anlamlı bir fark göstermezken, lomber omurga ölçümlerinde sonuçlar HD hastalarında PD hastalarına göre daha iyiydi. Grup 1 ve 2'de sırasıyla ortalama serum LOOH konsantrasyonu 6,07±2,91 ve 5,82±2,20 µmolH2O2Eq/L, TOS 8,89±5,89 ve 7,62±3,99 µmol H2O2Eq/L ve TAC 1,01±0,20 ve 0,93±0,16 mmol TroloxEq/L idi. Tüm hastalarda TAC ile femur boynu T-skor arasında pozitif bir korelasyon bulunurken, TOS ve T-skor arasında ilişki bulunmadı.

Sonuç: Yapmış olduğumuz bu çalışmada kronik diyaliz hastalarında OS artmış, antioksidan kapasite azalmış olmasına rağmen, OS'in OP üzerinde herhangi bir etkisini gösterememiş olmakla birlikte, bu sonucun hastalarımızdaki düşük OP oranına bağlı olabileceğini düşünmekteyiz. Diyaliz popülasyonunda OS ile OP ilişkisini irdeleyen daha geniş ölçekli çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Son dönem böbrek yetmezliği; Oksidatif stres; Osteoporoz; Diyaliz.

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INTRODUCTION

End Stage Renal Disease (ESRD) patients are subjected to enhanced oxidative stress, as a result of reduced anti-oxidant systems, and increased pro-oxidant activity (1). On the other hand osteoporosis (OP) is an important cause of morbidity in patients with ESRD (2,3). Although it is controversial, in many studies made in population without renal disease, oxidative stress found as related to increased osteoporosis risk (4-7).

There are many studies that evaluate the relationship between OP and oxidative stress, but there is no study about association of oxidative stress and osteoporosis in patients receiving dialysis treatment. In recent study we aimed to investigate the association between oxidative stress parameters and osteoporosis in dialysis patients.

MATERIALS AND METHODS

Sixty two adult uremic patients on maintenance dialysis programme for at least 6 months in Dialysis Centre in Medicine Faculty of Dicle University were included into the study. Obese (Body Mass Index >30 kg/m^2) and diabetic patients were excluded. Total oxidant status (TOS), lipid hydroperoxides (LOOH), and total antioxidant capacity (TAC) were measured to evaluate oxidative status. Serum levels of TOS and TAC of were determined using a novel automated colorimetric measurement method, developed by Erel (8). Serum LOOH levels were measured by the ferrous ion oxidation-xylenol orange (FOX–2) method.

Bone mineral density (BMD) was measured using dual energy X–ray absorptiometry (DEXA) in L1–L4 segments of lumbar spine (LS) and femoral neck (FN). BMD was classified due to World Health Organization (WHO) criteria based on T–scores within 1 SD (+1 or – 1) of the young adult mean accepted as normal, 1 to 2.5 SD below the young adult mean (–1 to –2.5 SD) as osteopenia, 2.5 SD or more below the young adult mean (<–2.5 SD) as osteoporosis. The body mass index (BMI) of all patients was calculated by the formula of kg/m^2.

Age, gender, and dialysis duration of patients were recorded. Serum levels of albumin, calcium (Ca), Phosphorus (P), and hemoglobine (Hb) levels were measured by using routine biochemical, and hematological procedures. Intact parathormone (iPTH) was detected with two–site chemiluminescent enzyme–labeled immunometric method. Patients were divided into two groups according to dialysis modality, group 1: HD, group 2: PD.

Statistical analysis were done by student-t test, pearson's correlation and chi-square tests on SPSS–11 PC programme, data were shown as ± SD, and $P<0.05$ was considered as satistically significant.

RESULTS

Twentynine (46.8%) of 62 patients were on hemodialysis (HD) programme and 33 (53.2%) were on peritoneal dialysis (PD) programme. The mean age of patients was 43.3 ± 15.7 and 39.2 ± 13.1 years, the mean BMI was 21.7 ± 5.1 and 22.5 ± 4.0 kg/m^2 in group 1 and 2 respectively. In these parameters statistically there were no differences between two groups (p=0.270 and p=0.486 respectively). The demographic features, biochemical and hematological parameters of groups are shown in Table 1.

According to T–scores, at FN, 2 patients (6.9%) in group1 and 2 (6.1%) in group 2, at LS, 15 (51.7%) of patients in group 1 and 9 (27.3%) in group 2 were osteoporotic. In the measurement of oxidative parameters mean serum concentration of LOOH was 6.07 ± 2.91 and 5.82 ± 2.20 $\mu molH_2O_2Eq/L$ (p=0.695), TOS was 8.89 ± 5.89 and 7.62 ± 3.99 $\mu mol\ H_2O_2Eq/L$ (p=0.321) and the TAC was 1.01 ± 0.20 and 0.93 ± 0.16 mmolTroloxEq/L (p=0.083) in group 1 and in group 2 respectively. In BMD T–scores while there was no statistically significant difference between two groups at FN [–1.20 ± 0.76 vs –0.75 ± 1.04 (p=0.059)], at LS among HD patients T score was better then PD patients [2.15 ± 1.48 vs –1.48 ± 1.77 (p<0.001)]. The oxidative parameters and BMD T-scores of patients are shown in Table 2.

Table 1. The demographic features, biochemical and hematological parameters of groups

Characteristics	***Group 1 (n = 29)***	***Group 2 (n = 33)***	***P***
Age *(years)*	43.3 ± 15.7	39.2 ± 13.1	0.270
Gender*(male/female)*	15 / 14	14 / 19	0.317
Dialysis duration *(months)*	33.1 ± 23.7	54.4 ± 54.2	0.055
BMI *(kg/m^2)*	21.7 ± 5.1	22.5 ± 4.0	0.486
Hb *(g/dl)*	10.3 ± 1.7	10.6 ± 1.9	0.596
Albumin *(g/dl)*	3.6 ± 0.4	3.1 ± 0.5	***0.003***
Ca x P *(mg^2 /ml^2)*	63.4 ± 16.9	51.2 ± 20.0	***0.012***
iPTH *(pg/ml)*	405.0 ± 275.4	363.6 ± 489.3	0.688
ALP *(mg/dl)*	116.2 ± 68.0	129.4 ± 70.3	0,460

BMI: Body Mass Index, **Hb:** Hemoglobine, **Ca:** Calcium, **P:**Phosphorus, **iPTH:** Intact parathormone, **ALP:** Alkaline phosphatase

Table 2. The oxidative parameters and BMD T-scores of patients.

Parameters	***Group 1 (n = 29)***	***Group 2 (n = 33)***	***p***
LOOH *(μmolH_2O_2Eq/L)*	6.07±2.91	5.82 ± 2.20	0.695
TOS *(μmolH_2O_2Eq/L)*	8.89±5.89	7.62 ± 3.99	0.321
TAC *(mmolTroloxEq/L)*	1.01±0.20	0.93 ± 0.16	0.083
T- Score in FN	- 1.20±0.76	- 0.75 ± 1.04	0.059
T- Score in LS	2.15±1.48	- 1.48 ± 1.77	***< 0.001***

LOOH: lipid hydroperoxides, **TOS:** total oxidant status, **TAC:** total antioxidant capacity, **FN:** femur neck , **LS:** lumbar spine

Among all patients there was a positive correlation between TAC and T score in FN (r=0.257, p=0.044). No significant correlation was found between both TOS and T-scores of both region like as between LOOH and T scores at FN and LS (p=0.792, p=0.265 and p=0.068, p=0.095 respectively).

DISCUSSION

ESRD patients are exposed to enhanced oxidative stress, as a result of reduced anti-oxidant systems such as deficiency of vitamins (vitamin C, reduced intracellular levels of vitamin E), and elements (defficiency of selenium), reduced activity of the glutathione system, and increased pro-oxidant activity such as, uremic syndrome, incompatible dialysis membranes and solutions, chronic inflammatory state, advanced age, high frequency of diabetes (9). Oxidative stress and inflammation are deeply interrelated, as different oxidant free radicals are generated by phagocytic cells in response to inflammatory stimuli: both are related to many cellular dysfunctions in tissues such as endothelium, bone, and the others (10). There is growing evidence, from experimental and clinical studies, that oxidative stress may be implicated in the pathogenesis of many complications of ESRD and in this circumstance interventions to excess oxidative state gain more importance to decrease morbidity and mortality (10–15).

Decrease in bone mineral density is common in patients with ESRD, and it is also a risk factor for fractures, and may cause permanent disability in this population (2,3). In this population phosphate excretions, impaired vitamin D_3 metabolism, hypocalcemia, increased parathyroid hormone, chronic acidozis, advanced age, high frequency of

diabetes as etiologic cause, poor nutrition are accused as causes of bone disease (16,17). On the other hand in the studies made among subjects without ESRD suggest that oxidative stress is associated with high incidence of OP (18). Although the patients with ESRD are exposed to enhanced oxidative stress, and have higher incidence of OP, there is no study investigating the relationship of these two conditions. Recent study is the first study that investigate the relationship between oxidative stress and OP in patients with ESRD.

Among patients we studied this relationship, we found no statistically difference in the oxidative state between dialysis modality, hemodialysis and peritoneal dialysis. The mean serum concentration of LOOH was 6.07 ± 2.91 and 5.82 ± 2.20 μmolH_2O_2Eq/L (p = 0.695), TOS was 8.89 ± 5.89 and 7.62 ± 3.99 μmolH_2O_2Eq/L (p = 0.321) and TAC was 11.01±0.20 and 0.93 ± 0.16 mmol TroloxEq/L (p=0.083) in group 1 and in group 2 respectively. Although there was no statistically significant difference in oxidative state between HD and PD patients, a difference was found in LS T-score between two groups [2.15 ± 1.48 vs-1.48 ± 1.77 (p<0.001)], it was better among HD patients than PD patients. We released that alhough the modality of dialysis did not affect the net oxidative status in among patirnts, OP had higher incidence in PD patients, and these results supported our thought of no affect of excess oxidative state on OP among ESRD patients receiving HD or PD.

Yalin et al (19) suggested that oxidative stress plays an important role in the pathophysiology of primary male osteoporosis, and like this, in another study Ozgocmen et al (20) showed that postmenopausal osteporotic women had significantly higher SOD enzyme activity and higher MDA (lipid peroxidation end–product) levels than normal controls. Although these results were in non–uremic population, we did not find any correlation between LOOH, TAC and BMD T–scores in both region. But only a positive corralation was found between TAC and T–score at FN. The other findings did not support this positive correlation, thus these results are necessitate further large scale studies to achieve a net conclusion.

In conclusion, although enhanced oxidative stress and reduced antioxidant capacity in dialysis patients we did not find any effect of oxidative stress on osteoporosis. This result may be due to low osteoporosis rate in our patients thus this novel topic needs further large scale studies in dialysis population.

Conflict of Interest

None

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Authors Contributions

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Check: HK, MEY
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Analysis: HK, DŞ, AKK
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