



The Evaluation of the Effect of the Treatments on Oxidative Stress and Inflammation in Patients Receiving Different Dialysis Modalities

Farklı Diyaliz Yöntemleri Alan Hastalarda Tedavilerin Oksidatif Stres ve İnflamasyon Üzerindeki Etkisinin Değerlendirilmesi

¹Sumeyra Koyuncu¹, ¹Hilal Sipahioglu¹, ¹Ismail Kocayigit², ¹Oktay Oymak², ¹Bulent Tokgoz²,
¹Murat Hayri Sipahioğlu²

¹Health Sciences University, Kayseri Medical Faculty, Department of Internal Medicine

²Department of Nephrology, Erciyes Medical Faculty, Kayseri, Turkey

Abstract

Aim: To evaluate the effects of different dialysis methods on oxidative stress and inflammation in patients with end-stage renal disease (ESRD) who are newly enrolled in a routine dialysis program.

Material and Method: In this prospective study, 138 ESRD patients and 30 healthy volunteers were evaluated. Fifty-four of 73 hemodialysis (HD) patients and 51 of 65 periton dialysis (PD) patients completed the study. Other patients were excluded from the study. The levels of superoxide dismutase (SOD) and total antioxidant capacity (TAC) were measured to determine the oxidative stress status, and IL-6, IL-10, and F2 isoprostane levels were measured to determine the inflammation status, just before the start of dialysis treatment and at 6 months.

Results: At the beginning of the study, hs-CRP and IL-6 levels were significantly higher in the patient group compared to the control group ($p<0.001$, $p<0.001$, respectively), and IL-10 levels were significantly lower ($p=0.008$). The hs-CRP and IL-10 levels in the HD group were found to be similar at the beginning of the study and in the 6th month. On the other hand, IL-6 levels decreased significantly compared to baseline values at 6 months ($p=0.016$). In the PD group, no difference was observed in terms of hs-CRP and IL-10 levels at the beginning and the 6th month ($p>0.05$), but IL-6 levels were found to be decreased compared to baseline at the 6th month ($p<0.001$). When HD and PD patient groups were compared with each other, no difference was found between the groups in terms of hs-CRP and IL-10 levels in the 6th month of dialysis treatment. IL-6 levels were found to be significantly higher in the HD group ($p<0.001$). At the beginning of the study, the F2 isoprostane level was significantly higher in the patient group than the control group ($p<0.001$), whereas the SOD and TAC levels were significantly lower ($p=0.001$, $p=0.024$, respectively). In the HD group, the F2 isoprostane level was found to be significantly higher at 6 months compared to baseline ($p=0.019$). There was no significant change in SOD and TAC levels. There was no significant difference in F2 isoprostane and TAC levels at 6 months from baseline in the PD group, whereas SOD levels were found to be significantly lower ($p=0.015$).

Conclusion: The oxidative status found in ESRD patients increases with dialysis treatments. Oxidative stress increase is more prominent in HD patients. Therefore, we think that giving antioxidant treatment in patient groups undergoing dialysis treatment may benefit complications related to oxidative stress.

Keywords: Hemodialysis, peritoneal dialysis, oxidative stress

Öz

Amaç: Rutin diyaliz programına yeni başlayan son dönem böbrek yetmezliği (ESRD) olan hastalarda farklı diyaliz yöntemlerinin oksidatif stres ve inflamasyon üzerine etkilerini değerlendirmek.

Gereç ve Yöntem: Bu prospektif çalışmada 138 SDBY hastası ve 30 sağlıklı gönüllü değerlendirildi. 73 hemodiyaliz (HD) hastasının 54'ü ve 65 periton diyalizi (PD) hastasının 51'i çalışmayı tamamladı. Diğer hastalar çalışma dışı bırakıldı. Oksidatif stres durumunu belirlemek için süperoksit dismutaz (SOD) ve toplam antioksidan kapasite (TAC) seviyeleri, inflamasyon durumunu belirlemek için IL-6, IL-10 ve F2 izoprostan seviyeleri, diyaliz tedavisi başlamadan hemen önce ölçüldü ve 6. ayda ölçüldü.

Bulgular: Çalışmanın başında hasta grubunda kontrol grubuna göre hs-CRP ve IL-6 düzeyleri anlamlı olarak yüksek (sırasıyla $p<0.001$, $p<0.001$), IL-10 düzeyleri anlamlı olarak düşüktü ($p=0.008$). HD grubunda hs-CRP ve IL-10 düzeyleri çalışmanın başında ve 6. ayda benzer bulundu. IL-6 seviyeleri ise 6. ayda başlangıç değerlerine göre anlamlı olarak azaldı ($p=0.016$). PD grubunda başlangıç ve 6. ay hs-CRP ve IL-10 düzeyleri açısından fark izlenmezken ($p>0.05$), ancak 6. ayda IL-6 düzeylerinin başlangıca göre düştüğü saptandı. ($p<0.001$). HD ve PD hasta grupları kendi aralarında karşılaştırıldığında diyaliz tedavisinin 6. ayında hs-CRP ve IL-10 düzeyleri açısından gruplar arasında fark saptanmadı. IL-6 düzeyleri HD grubunda anlamlı olarak yüksek bulundu ($p<0.001$). Çalışmanın başında F2 izoprostan düzeyi hasta grubunda kontrol grubuna göre anlamlı olarak yüksek ($p<0.001$), SOD ve TAC düzeyleri anlamlı olarak düşüktü (sırasıyla, $p=0.001$, $p=0.024$). HD grubunda 6. ayda F2 izoprostan düzeyi başlangıca göre anlamlı olarak yüksek bulundu ($p=0.019$). SOD ve TAC düzeylerinde anlamlı bir değişiklik olmadı. PD grubunda 6. ayda F2 izoprostan ve TAC düzeylerinde başlangıca göre anlamlı fark bulunmazken, SOD düzeyleri anlamlı olarak düşük bulundu ($p=0.015$).

Sonuç: SDBY hastalarında bulunan oksidatif durum diyaliz tedavileri ile artmaktadır. Oksidatif stres artışı HD hastalarında daha belirgindir. Bu nedenle diyaliz tedavisi gören hasta gruplarında antioksidan tedavi verilmesinin oksidatif strese bağlı komplikasyonlara fayda sağlayabileceğini düşünüyoruz.

Anahtar Kelimeler: Hemodiyaliz, periton diyalizi, oksidatif stres



INTRODUCTION

Cardiovascular events are the most common cause of morbidity and mortality in patients with chronic renal failure (CRF).^[1] These events include inflammation, oxidative stress, hyperhomocysteinemia, defects in bone-mineral metabolism, retention of uremic toxins, anemia, and high troponin levels.^[2]

CRF is a chronic inflammatory disease. It is known that patients with end-stage renal disease (ESRD) have 10-fold higher serum proinflammatory cytokine levels compared to the normal population. Several factors are responsible for the occurrence of inflammation; the usage of catheters, the increase in adipose tissue, and impaired adipokine balance cause inflammation due to reasons such as the decrease in the clearance of proinflammatory cytokines, aggregation of uremic toxins, fluid overload, increased level of endotoxins, especially in peritoneal dialysis (PD) patients.^[3]

In ESRD patients, an increase in the formation of oxygen free radicals (OFR) and a chronic decrease in major antioxidant systems was observed with dialysis. The reason for this is different in hemodialysis (HD) and PD patients. The reasons that are responsible for the increase in oxidative stress products are the type of dialysis membrane, the use of heparin, intravenous iron intake, activation of thrombocytes and leukocytes in HD patients, and the low pH of the solution, high lactate concentration, and increased osmolarity in patients with dialysis.^[4]

Several studies have shown that proinflammatory cytokines (TNF- α , IL-1, IL-6, and others) and CRP levels are higher than the normal population in these patients during the predialysis period and after dialysis treatment.^[5-7]

In this study, we aimed to investigate the difference between the effects of different renal replacement methods on oxidative stress and inflammation through various parameters in patients with ESRD.

MATERIAL AND METHOD

This study was carried out in University Faculty of Medicine, Department of Nephrology. Ethical approval was obtained from the Ethics Committee of University (2011/36, 04.01.2011) before the study and informed consent was obtained from all patients and healthy volunteers that were included in the study. Patients aged between 18 and 70 years with stage 5 renal failure were included in the study. Diabetic patients, patients with malignancy, active infection, severe heart failure, respiratory failure, patients that have hepatitis or that are the carriers, patients with a rheumatic disease using anti-inflammatory drugs were all excluded from the study. A total of 73 HD and 65 PD patients participated in the study. Thirteen of the HD patients died before the second evaluation, 4 patients were excluded from the study because they did not need dialysis anymore, and 2 patients could not be reached. Ten of the PD patients died before the second control, 3 of them underwent renal transplantation, and 1 of them was

excluded from the study because they did not require dialysis. As a result, 54 HD and 51 PD patients completed the study. 30 healthy volunteers were taken as the control group. Socio-demographic characteristics of the patients such as age and gender were recorded.

Blood urea nitrogen (BUN) and serum creatinine, glucose, triglyceride, total cholesterol, LDL and HDL cholesterol, uric acid, alkaline phosphatase (ALP), total protein, albumin, calcium (Ca), phosphorus (P), parathyroid hormone (PTH), hemoglobin concentration, hematocrit, transferrin saturation, and ferritin levels were measured from blood samples taken from the patients.

Interleukin 6 (IL-6), interleukin 10 (IL-10), and high sensitivity C-reactive protein (hs-CRP) measurements were used in the evaluation of inflammation, whereas F2 isoprostane, Superoxide Dismutase (SOD), Total Antioxidant Capacity (TAC) measurements were used in the evaluation of the oxidative stress-antioxidant system. These measurements were performed twice, firstly when the patient was admitted to the service for renal replacement and secondly 6 months after being included in the renal replacement treatment program. Blood samples in HD patients were taken in the period right before dialysis, whereas in PD patients and healthy volunteers, they were taken on an empty stomach at 8 am. SOD level was studied in plasma, other parameters were studied in serum. The collected blood samples were stored at -80°C after centrifugation until the day of the study.

Statistical Analysis

SPSS 15.0 software was used for statistical analysis of the data. Percentages were calculated for categorical variables and the chi-square test was used for comparison. Kolmogorov-Smirnov test was used to determine the distribution of the data. Normally distributed data were expressed as mean value \pm standard deviation, and data not distributing normally were expressed as median (minimum-maximum). In the comparison of HD, PD, and control groups, the Anova test was used when the group distribution was equal, and the Kruskal-Wallis test was used when the group distribution was not equal. In the one-to-one comparison of the groups; Student's t-test was used when group distribution was equal, and the Mann-Whitney U test was used when group distribution was not equal. In comparison of the baseline and 6th-month values; the paired samples test was used when group distribution was equal, and Wilson signed ranks test was used when group distribution was not equal. The relationship between inflammation and oxidant-antioxidant parameters was evaluated by Spearman correlation analysis. The statistical significance level was accepted as $p < 0.05$.

RESULTS

138 patients with ESRD who were included in this study but 105 of them completed the study. Fifty-four patients were on the HD and 51 patients were on the PD program. As a

control group, 30 healthy volunteers participated in the study. All study participants were evaluated according to demographical parameters and shown in **Table 1**. While 15 were females (50 %) in the control group, 29 were females (53%) in the HD group, and 24 were females (47%) in the PD group. Additionally, the average age of the control group was 42.6±5.0 years, it was 59.22±11.2 years HD group, and the PD group was 43.96±15.62. The inflammation parameters of all groups are shown in **Table 2** at the beginning of the study.

Table 1: Demographical characteristics of the patients in this study.

Parameters	HD group n (%)	PD group n (%)
Age (year)	59.2±11.2	43.9±15.2
Gender (female)	24 (47.1)	29 (53.7)
Etiology		
Hypertension	33 (61.1)	14 (27.4)
Cystic disease	4 (7.3)	8 (15.7)
Obstructive Uropathy	2 (3.7)	3 (5.9)
Glomerulonephritis	1 (1.9)	2 (3.9)
Amyloidosis	0 (0)	3 (5.9)
ATN*	1 (1.9)	2 (3.9)
Interstitial nephritis/ Pyelonephritis	0 (0)	3 (5.9)
Unknown	13 (24.1)	16 (31.4)

*Acute tubular necrosis

Table 2: The relationship between the control group and the patient groups in terms of inflammation and oxidant/antioxidant parameters

Parameters	Control	HD	PD	p
Hs-CRP (mg/dl)	3.2 ^{a,b} (3-9.3)	7.3 (3-98)	4.6 (3-203)	<0.001
IL-6 (pg/ml)	12.7 ^{c,d} (3.6-260)	41.8 (8.2-1824.6)	33.6 (8.2-1476.4)	<0.001
IL-10 (pg/ml)	20.9 ^{e,f} (2.7-137.3)	7.7 (4.6- 91.8)	7.27 (4.6-123.6)	0.028
F2 isoprostane (pg/ml)	86 ^{g,y} (76-149)	108 (72-4152)	109 (81-3254)	<0.001
SOD* (units/ml)	0.1 ^{z,t} (0.02-0.2)	0.1 (0.03-0.6)	0.1 (0.02-0.8)	0.004
TAC** (mM)	1.7 ^{p,r} (0.3-3.6)	2.1 (0.01-10.6)	3.4 (0.03-13)	0.012

a: Control group and HD group p<0.001, b: Control group and PD group p<0.001 c: Control group and HD group p<0.001, d: Control group and PD group p<0.001

e: Control group and HD group p=0.015, f: Control group and PD group p=0.017

x: Control group and HD group p<0.001, y: Control group and PD group p<0.001

z: Control group and HD group p=0.007, t: Control group and PD group p=0.001

p: Control group and HD group p=0.004

IL: Interleukin

* Superoxide Dismutase

**Total Antioxidant Capacity

At the beginning of the study, hs-CRP and IL-6 levels were found to be significantly higher in the patient group compared to the control group, and the IL-10 level was found to be significantly lower. In HD and PD groups, hs-CRP levels were found to be significantly higher than the control group (p<0.001, p<0.001 respectively), IL-6 levels were significantly higher (p<0.001, p<0.001 respectively), and IL-10 levels were significantly lower (p=0.015, p=0.017, respectively). There was no significant difference between PD and HD groups in terms of hs-CRP, IL-6, and IL-10 levels (p=0.236, p=0.090, p=0.584 respectively). The hs-CRP values were found to be similar at the baseline and in the 6th month. IL-6 levels were found to be significantly decreased after 6 months compared to baseline. There was no significant difference in IL-10 levels. There was

no significant difference in terms of hs-CRP values. IL-6 levels were found to be decreased after 6 months compared to baseline. There was no significant difference in terms of IL-10 levels. There was no significant difference between the two groups in terms of hs-CRP values. In the 6th month of the study, IL-6 levels were found to be significantly higher in the HD group. There was no significant difference in terms of IL-10 levels. The comparison of inflammation parameters between dialysis groups in the 6th month of the study is shown in **Table 3**.

Table 3: Comparison of baseline and 6th month inflammation parameters of patients between HD and PD groups

	Parameters	Baseline	6 th month	p
HD Group	hs-CRP (mg/dl)	7.3 (3-186)	11.9 (3-98)	0.224
	IL-6 (pg/ml)	41.8 (8.2-1824.5)	27.3 (8.2-1480.9)	0.016
	IL-10 (pg/ml)	7.7 (5.6-91.8)	8.2 (2.7-209.1)	0.064
PD Group	hs-CRP (mg/dl)	4.61 (3-203)	11.4 (3-102)	0.300
	IL-6 (pg/ml)	33.6 (8.2-1476.4)	16.4 (2.7-129.1)	<0.001
	IL-10 (pg/ml)	7.3 (4.6-123.6)	7.27 (4.6-180.9)	0.765

HD: Hemodialysis, PD: Periton dialysis, IL: Interleukin

Table 4: Comparison of baseline and 6th month oxidant-antioxidant parameters of patients in HD and PD groups

	Parameters	Baseline	6 th month	P
HD Group	F2 isoprostane (pg/ml)	108 (72-4152)	162 (79-4866)	0.019
	SOD (units/ml)	0.1 (0.003-0.573)	0.1 (0.003-0.670)	0.476
	TAC (mM)	2.1 (0.01-10.59)	2.3 (0.01-13.0)	0.533
PD Group	F2 isoprostane (pg/ml)	109 (81-3524)	101 (75-5040)	0.099
	SOD (units/ml)	0.1 (0.02-0.8)	0.1 (0.02-0.5)	0.015
	TAC (mM)	3.4 (0.03-13)	3.4 (0.1-8.8)	0.183

SOD: Superoxide Dismutase, TAC: Total Antioxidant Capacity

The oxidant-antioxidant system parameters of all groups at the beginning of the study are shown in Tables 4. At the beginning of the study, the levels of F2 isoprostane, SOD, and TAC in the patient group were found to be significantly higher than the control group. F2 isoprostane level was higher in HD and PD groups (p<0.001, p<0.001 respectively). SOD level was found to be significantly higher in HD and PD groups compared to the control group (p=0.007, p=0.001 respectively). In the control group, the TAC level was found to be similar to the HD group (p=0.198), but lower than the PD group (p=0.004). No significant difference was found between the HD and the PD groups in terms of F2 isoprostane and SOD levels (p=0.491, p=0.274 respectively). Although the TAC level was higher in the PD group compared to the HD group, no statistically significant difference was found (p=0.059). F2 isoprostane was significantly higher in the HD group after 6 months compared to baseline. There was no significant

difference in SOD and TAC levels. There was no significant difference in terms of the F2 isoprostane level in the 6th month in the PD group compared to the baseline. SOD levels were found to be significantly lower. There was no significant difference in terms of the TAC level.

When the patient groups (54 HD patients and 51 PD patients) were evaluated and correlation analysis was made between inflammation and oxidant-antioxidant parameters at the beginning of the study; there was a directly proportional and statistically significant relationship between hs-CRP and IL-6 ($r=0.224$, $p=0.023$), between IL-6 and F2 isoprostane ($r=0.233$, $p=0.019$), between IL-10 and TAC ($r=0.199$, $p=0.043$) SOD and uric acid ($r=0.252$, $p=0.012$) levels. Besides, there was an inversely proportional but not statistically significant relationship between hs-CRP and TAC levels ($r=0.192$, $p=0.051$). No significant relationship was found between inflammation and oxidant-antioxidant parameters. In the 6th month of the study, when the patient groups (54 HD patients and 51 PD patients) were evaluated and correlation analysis was made between inflammation and oxidant-antioxidant parameters; a directly proportional and statistically significant correlation was found between IL-6 and F2 isoprostane ($r=0.309$, $p=0.002$) and between IL-10 and TAC ($r=0.234$, $p=0.016$) levels. No significant relationship was found between inflammation and oxidant-antioxidant parameters.

DISCUSSION

In our study, oxidative stress parameters F2 isoprostane, SOD, and TAC were found to be higher in patients who just started dialysis compared to the healthy control group. At the sixth month, an increase in the F2 isoprostane level was detected in HD patients, while the SOD level in PD patients increased. Considering the values in the sixth month, the F2 isoprostane level was higher in HD patients compared to PD patients.

When the inflammatory parameters were evaluated, it was observed that CRP and pro-inflammatory cytokine IL-6 was higher in dialysis patients compared to the control group, and anti-inflammatory cytokine IL-10 level was lower in dialysis patients. It was observed that IL-6 levels decreased in both HD and PD groups compared to the baseline after the six months. This decrease was more in the PD group, and the 6th-month IL-6 level was lower in the PD group compared to the HD group ($p<0.001$).

Inflammation is common in ESRD patients. Serological markers of acute-phase response have been found in 30-50% of them.^[8] It has been known that inflammation status is increased in patients who receive renal replacement treatment. In a study by Borazan et al. comparing the inflammation status in patients who underwent HD and PD, the CRP, TNF- α , IL-6, and IL-10 levels of the patients were compared at the beginning of dialysis and after 3 months and also they were compared with the healthy control group. No significant difference was found in cytokine levels between

the PD and HD groups at the beginning of the treatment and after 3 months, however, the levels of the PD and HD groups were found to be significantly higher than the control group.^[9]

In this study, hs-CRP and IL-6 levels were found to be higher, and IL-10 levels were found to be significantly lower in patients with renal failure compared to the control group. The increases in CRP and IL-6 supported the general literature data showing the increase in inflammation in CRF patients. On the other hand, the low level of IL-10 in patients may indicate that the anti-inflammatory system is not effective enough in CRF patients or that there is a continuous inflammatory stimulus in such patients that requires suppression of the anti-inflammatory system. IL-6 levels measured at the 6th month of replacement treatment were found to be lower in HD and PD groups than the baseline levels. The decrease in cytokine level was more in the PD group and 6th-month values showed a significant difference in HD and PD groups. These data obtained in this study show that initiation of dialysis treatment in patients with ESRD leads to a significant improvement in inflammatory status. This improvement was more pronounced in PD patients. Removal of small and medium molecular weight toxins, which play a role in the inflammatory process, from the body along with dialysis may have played a role in the partial recovery of the inflammatory process. The higher improvement in PD patients can be partially explained by the better protection of residual renal functions and the absence of extracorporeal circulation that may cause leukocyte activation as in HD.

CRP is a strong predictor of important cardiovascular events and all-cause mortality in the dialysis population. This situation has been demonstrated in many studies.^[10,11]

Even plasma IL-6 level is an independent indicator of cardiovascular events, the progression of atherosclerosis, and all-cause deaths in dialysis patients.^[12-15]

The levels of CRP and IL-6 were studied in a study evaluating ESRD (stage 3-5) patients. Similarly, high levels of CRP and IL-6 were found in patients with renal failure.^[16]

It is known that inflammation status is increased in patients who receive renal replacement treatment. In the study by Sundl et al. CRP and IL-6 levels were found to be significantly higher than the control group ($n: 37$) in PD patients ($n: 37$).^[17]

Similarly, in another study, higher CRP and IL-6 levels were found in HD patients compared to the control group.^[18]

In the study by Kim et al., TNF- α , IL-1, IL-6, IL-8, IL-10, and IL-12 levels were found higher in HD patients than in the control group.^[19]

Oxidative stress increases from the early stages of renal failure. Low molecular weight toxins with prooxidant activity may accumulate in CRF and cause an increase in oxidative stress.^[20]

Dialysis modalities (HD, PD) also exacerbate oxidative stress. In HD, the loss of hydrophilic free small molecular

weight substances such as vitamin C, trace elements, and regulatory enzyme compounds, thermal damage resulting from the temperature difference between dialysate and body temperature, the cytotoxic effect of chloramine in the dialysate, activation of the neutrophil and complement system from the HD membrane, the activation of the lipoprotein lipase enzyme and the increase in free fatty acids by heparin used for anticoagulation, cause lipid peroxidation and oxidant stress. Dialyzer interactions, microbial contamination or dialysate containing pyrogen substances, and the probable pro-oxidant effect of metabolites in high concentrations in the patient's plasma are seen as the major 3 causes of oxidative stress. In peritoneal dialysis, the formation of acute gastroenteritis due to heat sterilization stimulates the oxidative stress response.^[4,21]

In this study, F2 isoprostane levels, which are a lipid peroxidation product and indicate the presence of oxidative stress, were found to be significantly higher in patients with ESRD. It was similar between the groups that chose HD or PD at the beginning of the study whereas, in the 6th month, it was found to be higher in the HD group compared to PD. In this study, the data we obtained with F2 isoprostane levels supported the presence of oxidative stress in patients with CRF. We showed that HD has more aspects that can activate oxidative stress than PD.

Oberg et al. examined protein carbonyl (protein oxidation product) and F2 isoprostane levels in patients with CRF (stage 3-5) and compared them with healthy subjects. The level of oxidative stress parameters was found to be higher in patients with CRF.^[16]

In the study conducted by Montesa et al. with stage 4 predialysis patients (n: 32), F2 isoprostane and CRP levels were found to be significantly higher in the predialysis group than the control group. In this study, it was concluded that there is a negative correlation between F2 isoprostane and GFR.^[22,23]

In the study conducted by Ramos et al., stage 3-4 CRF patients (n: 184) and healthy control group (n: 43) were compared, and F2 isoprostane and CRP levels were found to be significantly higher in CRF patients.

In our study, a directly proportional and significant relationship was found between F2 isoprostane and IL-6 levels. There appears to be a synergism between systemic inflammatory response and oxidative stress. Oxidative stress metabolites (hydrogen peroxide) can activate the NFκB pathway, which enables the synthesis of proinflammatory cytokines, resulting in amplification of the inflammatory cascade. Also, acute phase reactants can regulate the production of oxidative agents. For example, CRP has been shown to increase intracellular OFR production from IgG stimulated phagocytic cells. In these ways, events associated with increased oxidative stress may perpetuate the chronic inflammatory state.

In this study, TAC and SOD levels were found to be higher in the patient group compared to the control group. There was

no significant difference between HD and PD groups at the beginning of the study and 6 months. There was a significant decrease in the PD group at 6 months compared to the beginning of the study. There are studies in the literature that have

CONCLUSION

As a result, as proved in this study, increased levels of inflammation and oxidative stress are observed in ESRD patients compared to healthy people. The initiation of dialysis treatment probably improves the level of inflammation by increasing cytokine clearance. It has been shown in this study that PD treatment provides more improvement in inflammation in the early period. Also, while HD treatment caused an increase in oxidative stress in the early period, this increase was not observed in PD treatment. The use of the peritoneal membrane as a dialysis membrane seems to be a more appropriate treatment modality in renal replacement treatments. However, we think that it would be beneficial to provide antioxidant supplements to reduce the complications that may be caused by increased oxidative stress in both patients with chronic renal failure and receiving dialysis treatment.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethical approval was obtained from the Ethics Committee of Erciyes University, Date: 04.01.2011, Decision No: 2011/36

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Acknowledgment: We respectfully commemorate Dr Havva Cilan who collected the data of the study.

REFERENCES

1. Himmelfarb J, Hakim RM. Oxidative stress in uremia. *Curr Opin Nephrol Hypertens* 2003;12 Suppl 6:593-8.
2. Himmelfarb J. Linking oxidative stress and inflammation in kidney disease: which is the chicken and which is the egg? *Semin Dial* 2004;17:449-54.
3. Li PK, Ng JK, McIntyre CW. Inflammation and Peritoneal Dialysis. *Semin Nephrol*. 2017;37(1):54-65
4. Roumeliotis S, Eleftheriadis T, Liakopoulos V. Is oxidative stress an issue in peritoneal dialysis? *Semin Dial*. 2019;32(5):463-66
5. Calò LA, Naso A, Carraro G, et al. Effect of haemodiafiltration with online regeneration of ultrafiltrate on oxidative stress in dialysis patients. *Nephrol Dial Transplant*. 2007;22:1413-9.

6. Coombes JS, Fasset RG. Antioxidant therapy in hemodialysis patients: a systematic review. *Kidney Int.* 2012;81(3):233-46
7. Kamimura MA, Draibe SA, Dalboni MA, et al. Serum and cellular interleukin-6 in haemodialysis patients: relationship with energy expenditure. *Nephrol Dial Transplant.* 2007;22(3):839-44.
8. Borazan A, Üstün H, Üstündag Y, et al. The effects of peritoneal dialysis and hemodialysis on serum tumor necros factör- alpha, interleukin-6, interleukin- 10 and C-reactive protein levels. *Mediators Inflamm* 2004;13Suppl 3:201- 14.
9. Arici M, Walls J. End-stage renal disease, atherosclerosis, and cardiovascular mortality: is C-reactive protein the missing link? *Kidney Int* 2001;59:407-14.
10. Stenvinkel P, Heimbürger O, Paultre F, et al. Strong association between malnutrition, inflammation, and atherosclerosis in chronic renal failure. *Kidney Int.* 1999;55 Suppl 5:1899-911.
11. Kato A, Odamaki M, Takita T, Maruyama Y, Kumagai H, Hishida A. Association between interleukin-6 and carotid atherosclerosis in hemodialysis patients. *Kidney Int.* 2002;61 Suppl 3:1143-52.
12. Memoli B, Minutolo R, Bisesti V, et al. Collaborative Study Group on SMC Membrane. Changes of serum albumin and C-reactive protein are related to changes of interleukin-6 release by peripheral blood mononuclear cells in hemodialysis patients treated with different membranes. *Am J Kidney Dis.* 2002;39 Suppl 2:266-73.
13. Pecoits-Filho R, Bárány P, Lindholm B, Heimbürger O, Stenvinkel P. Interleukin-6 is an independent predictor of mortality in patients starting dialysis treatment. *Nephrol Dial Transplant.* 2002;17 Suppl 9:1684-8.
14. Zhang W, He J, Zhang F, et al. Prognostic role of C-reactive protein and interleukin-6 in dialysis patients: a systematic review and meta-analysis. *J Nephrol.* 2013;26:243-53.
15. Oberg BP, McMenamin E, Lucas FL, et al. Increased prevalence of oxidant stress and inflammation in patients with moderate to severe chronic kidney disease. *Kidney Int.* 2004;65 Suppl 3:1009-16.
16. Sundl I, Roob JM, Meinitzer A, et al. Antioxidant status of patients on peritoneal dialysis: associations with inflammation and glycoxidative stress. *Perit Dial Int.* 2009;29 Suppl 1:89-101.
17. Danielski M, Ikizler TA, McMonagle E, et al. Linkage of hypoalbuminemia, inflammation, and oxidative stress in patients receiving maintenance hemodialysis therapy. *Am J Kidney Dis.* 2003;42:286-94.
18. Kim HW, Woo YS, Yang HN, et al. Primed monocytes: putative culprits of chronic low-grade inflammation and impaired innate immune responses in patients on hemodialysis. *Clin Exp Nephrol.* 2011;15 Suppl 2:258-63.
19. Hasselwander O, Young IS. Oxidative stres in chronic renal failure. *Free Radic Res* 1998;29:1-11.
20. Mekki K, Taleb W, Bouzidi N, et al. Effect of hemodialysis and peritoneal dialysis on redox status in chronic renal failure patients: a comparative study. *Lipids Health Dis.* 2010;9:93.
21. Puchades Montesa MJ, González Rico MA, Solís Salguero MA, et al. Study of oxidative stress in advanced kidney disease. *Nefrologia.* 2009;29 Suppl 5:464-73.
22. Liakopoulos V, Roumeliotis S, Gorny X, Eleftheriadis T, Mertens PR. Oxidative stress in patients undergoing peritoneal dialysis: a current review of the literature. *Oxid Med Cell Longev.* 2017;2017:3494867