

# Comparison of Different Dialysis Modalities in End-Stage Renal Disease Patients with Acute Dialysis Requirement

## *Acil Diyaliz Gereksinimi Olan Son Dönem Böbrek Yetmezlikli Hastalarda Farklı Diyaliz Yöntemlerinin Karşılaştırılması*

### ABSTRACT

**OBJECTIVE:** There is little knowledge on the differences between PD or HD initiation in terms of early and late morbidity and other complications. We aimed to compare the effect of different dialysis modalities on inflammation and other complications in a one-year prospective follow-up.

**MATERIAL and METHODS:** The patients were divided into three groups depending on their dialysis requirements and compared in terms of inflammation and complications. Group 1: The patients who had acute dialysis indication and started urgent PD (n=23), Group 2: The patients who had acute dialysis indication and started urgent HD (n=21), Group 3: The patients with no acute dialysis indication and started dialysis two weeks after PD catheter insertion (n=20).

**RESULTS:** HD patients had significantly lower urine levels and higher hemoglobin levels after 12 months in comparison with other groups. Complications of catheter-related infections were similar among the three groups, although catheter-related leaks were only found in the urgent PD group. There were no differences in terms of inflammatory markers among the groups.

**CONCLUSION:** Urgent PD could be an alternative modality in end-stage renal disease patients with acute dialysis requirement.

**KEY WORDS:** Chronic kidney disease, Inflammation, Peritoneal dialysis, Hemodialysis

### ÖZ

**AMAÇ:** Farklı diyaliz modalitelerinin erken ve geç dönem morbiditesi ile birlikte inflamasyon, kateter ilişkili komplikasyon ve kalan böbrek işi gibi komplikasyonlar açısından farkları hakkında az miktarda bilgi mevcuttur. Bu yüzden, bir yıllık prospektif takip süresi olan bu çalışmada farklı diyaliz modalitelerinin inflamasyon ve diğer komplikasyonlar açısından farklarını incelemeyi hedefledik.

**GEREÇ ve YÖNTEMLER:** Hastalar diyaliz gerekliliklerine göre üç gruba ayrılmış ve inflamasyon ve komplikasyonlar açısından karşılaştırılmıştır. Grup 1: akut diyaliz endikasyonu olan ve ivedi PD başlanan hastalar (n=23), Grup 2: akut diyaliz endikasyonu olan ve ivedi HD başlanan hastalar (n=21), Grup 3: akut diyaliz endikasyonu olmayan ve planlanmış PD başlanan hastalar (n=20).

**BULGULAR:** HD hastaları 12. ayın sonunda diğer gruplarla karşılaştırıldığında anlamlı ölçüde düşük idrar volumü ve yüksek hemoglobin seviyesine sahipti. Kateter ilişkili enfeksiyon komplikasyonu açısından üç grupta benzerdi, buna rağmen kateter ilişkili kaçak sadece ivedi PD grubunda saptandı. İnflamatuvar göstergeler açısından her üç grup arasında fark yoktu.

**SONUÇ:** İvedi PD'nin akut diyaliz endikasyonu olan hastalarda alternatif bir tedavi olabileceği düşünüldü.

**ANAHTAR SÖZCÜKLER:** Kronik böbrek hastalığı, İnflamasyon, Periton diyalizi, Hemodiyaliz

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Received : 07.12.2016

Accepted : 10.02.2017

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## INTRODUCTION

Chronic kidney disease (CKD) is a worldwide public health problem (1). Patients with end-stage renal disease (ESRD) who do not receive any renal replacement therapy (RRT) are very close to death (2). It has been well established that the best treatment for ESRD patients is kidney transplantation; however transplantation can not reach the target rate due to the number of the insufficient donors. Furthermore, ESRD patients have to continue their treatment with hemodialysis (HD) and/or peritoneal dialysis (PD) (2).

Patients with chronic kidney disease (CKD) may present with acute, unplanned dialysis requirement due to rapid renal function decline or delayed referral to the nephrology centers (3). Acute dialysis is generally performed by HD after placing a central venous catheter throughout the world. It has been reported that effective treatment with PD is possible shortly after peritoneal catheter insertion in patients with ESRD requiring acute dialysis with increased clinical experience in the last 10 years (3).

Dialysis-related inflammation has a pathological role in ESRD patients (4). Recent clinical trials have shown that the pentraxin-3 (PTX-3) level is significantly associated with autoimmune, inflammatory, cardiovascular diseases and kidney failure (5,6). Increased plasma PTX-3 levels are associated with other inflammatory markers [CRP, TNF- $\alpha$ , IL-6] in chronic kidney disease (7). Many studies have reported a negative correlation between plasma PTX-3 level and kidney function (7). It has been shown that elevated PTX-3 levels may lead to endothelial dysfunction, albuminuria, cardiovascular disease (CVD) development and mortality in CKD patients (8).

In this study, CKD patients who were scheduled to undergo renal replacement therapy and admitted to a continuous peritoneal dialysis program without renal transplantation were randomly assigned to with different types of dialysis methods (urgent hemodialysis, urgent peritoneal dialysis, planned peritoneal dialysis). We aimed to investigate the role of inflammation measured by PTX3, interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) levels in patients with CKD on different dialysis modalities. In addition, this study was undertaken to compare short- and long-term complications of three different dialysis modalities and their effects on residual renal function.

## MATERIAL and METHODS

### Study Population

This study was conducted between February 2013 and June 2015 on patients who were followed up at the Nephrology Department of Erciyes University Medical Faculty Hospital. Prior to the study, the local ethics committee of the Erciyes University Faculty of Medicine approved the study (ethics committee approval number: 2014/128) and it was performed according to the Helsinki Declaration. Written informed consent was obtained from all patients. All patients' demographic characteristics were recorded.

Stage 5 CKD patients who had no previous dialysis treatment and who were admitted for dialysis were enrolled to the study. After the clinical and laboratory evaluations (hyperkalemia, vomiting, dyspnea, severe acidosis, pericarditis etc.) of the patients, eligible patients were included and randomized according to the dialysis requirement. There were no infection or inflammatory disease including rheumatoid arthritis, vasculitis, FMF or systemic lupus erythematosus in the enrolled patients.

A total of 26 patients with urgent PD in group 1 were included in the study. Two patients switched to HD during follow-up. Renal transplantation was performed in one patient during follow-up. As a result, 23 patients were evaluated in this group.

Twenty-five patients who received HD in group 2 due to acute dialysis were included in the study. One patient died during follow-up. Two patients' RRTs were continued with HD. One patient was also underwent renal transplantation. A total of 21 patients were evaluated.

Twenty-four PD patients were included in the study at the end of the traditional waiting period for initiating peritoneal dialysis (after two weeks) as group 3. Three patients died. One patient switched to HD during follow-up. A total of 20 patients completed the study in group 3.

Patients were checked every two months in terms of catheter-related infection and mechanical complications and they have been followed-up for one year. Serum samples were taken immediately before dialysis and at the fourth month and first year to evaluate inflammation in all patients.

### Biochemical Parameters

**TNF- $\alpha$ :** Invitro gen-brand ELISA kit (Catalog No. KHC3011) was used to measure TNF- $\alpha$  levels in serum. The principle of the method is formation of antigen-antibody complexes without competition. TNF- $\alpha$  (antigen) present in serum samples is bound to wells coated with TNF- $\alpha$  antibody. All serum components that are not anticoagulated are removed from the medium by washing. "Antibody-antigen-labeled antibody" complexes (sandwich ELISA) generated by the addition of biotinylated antibody are incubated with the enzyme substrate. The intensity of the color produced by the enzymatic reaction in proportion to the concentration of TNF- $\alpha$  is measured at 450 nm.

**IL-6:** LZ brand ELISA kit (Catalog No. YHB1747Hu) was used to measure serum IL-6 levels. The principle of the method is the formation of antigen-antibody complexes without competition. The IL-6 (antigen) present in serum samples binds to wells coated with IL-6 antibody. All serum components that are not anticoagulated are removed from the medium by washing. "Antibody-antigen-labeled antibody" complexes (sandwich ELISA) generated by the addition of biotinylated antibody are incubated with the enzyme substrate. The intensity of the color produced by the enzymatic reaction correctly proportional to the IL-6 concentration is measured at 450 nm.

**Pentraxin-3:** Serum LZ brand ELISA kit (Catalog No. YHB2259Hu) was used for the measurement of Pentraxin-3 levels. The principle of the method is the formation of antigen-antibody complexes without competition. Pentraxin-3 (antigen), found in serum samples, binds to wells coated with Pentraxin-3 antibody. All serum components that are not anticoagulated are removed from the medium by washing. “Antibody-antigen-labeled antibody” complexes (sandwich ELISA) generated by the addition of biotinylated antibody are incubated with the enzyme substrate. The intensity of the color produced by the enzymatic reaction, in direct proportion to the pentraxin-3 concentration, is measured at 450 nm.

**Statistical Analysis**

Statistical analysis of the study was conducted using SPSS 15.0 (Statistical Packages for Social Sciences, SPSS Inc. Chicago, Illinois, USA). The patients were randomly selected. The mean and standard deviation ( $x \pm sd$ ) were given as the mean and the parametric condition. The median distribution (25% -75%) was defined for the measurable and parametric conditions. The normal distribution suitability was assessed by the ‘Kolmogorov-Smirnov’ test. One-way Anova (Tukey test)

was used to assess the differences between the groups. Tukey and Tamhane were used in multiple comparisons. Kruskal-Wallis test was used for nonparametric tests. Pearson correlation analysis was applied for correlation. A p value <0.05 was considered as significant in all statistical analysis.

**RESULTS**

Comparison of urgent peritoneal dialysis (group 1), urgent hemodialysis (group 2) and planned PD (group 3) patients in terms of demographic parameters are summarized in Table I. There were no differences in basal demographic and biochemical parameters among the groups.

HD patients (Group 2) had significantly lower urine levels and higher hemoglobin levels after 12 months in comparison with other groups (Table II). Complications of catheter-related infections were similar among the 3 groups, although catheter-related leaks were only found in the urgent PD group (Table III). Hospital stay duration, was statistically lower in the planned PD group (Group 3) among the three groups. In addition, there were no differences in terms of inflammatory markers (pentraxin-3, IL-6, TNF- $\alpha$  levels) among all the groups (Table IV).

**Table I:** Comparison of urgent peritoneal dialysis (group 1), urgent hemodialysis (group 2) and planned PD (group 3) patients in terms of demographic parameters.

Demographic Features	Group 1 <sup>a</sup> (n=23)	Group 2 <sup>b</sup> (n=21)	Group 3 <sup>c</sup> (n=20)	p value
Age	49.6±3.3	53.3±3.2	55.0±3.6	0.51
Gender				0.27
Male	18 (78.3%)	14 (66.7%)	11 (55%)	
Female	5 (21.7%)	7 (33.3%)	9 (45%)	
Educational Status				0.44
Illiterate	1 (4.3%)	1 (4.8%)	4 (20%)	
Primary school	14 (60.9%)	14 (66.7%)	8 (40%)	
Middle school	2 (8.7%)	0 (0%)	1 (5%)	
High school	3 (13%)	3 (14.3%)	5 (25%)	
University	3 (13%)	3 (14.3%)	2 (10%)	
Etiology				0.59
Diabetes mellitus	11 (47.8%)	9 (42.9%)	5 (25%)	
Hypertension	3 (13%)	4 (19%)	4 (20%)	
Glomerulonephritis	1 (4.1%)	2 (9.5%)	4 (20%)	
Tubulointerstitial nephritis	2 (8.7%)	0 (0%)	0 (0%)	
ADPKD	0 (0%)	2 (9.5%)	2 (10%)	
Obstructive uropathy	1 (4.3%)	0 (0%)	1 (5%)	
Others	1 (4.3%)	2 (9.5%)	1 (5%)	
Unknown	4 (17.4%)	2 (9.5%)	3 (15%)	

**ADPKD:** Autosomal dominant polycystic kidney disease.

**a:** Group 1 consisted of patients who underwent peritoneal dialysis immediately after peritoneal dialysis was performed.

**b:** Group 2 consisted of patients with acute dialysis indication and continuing treatment with peritoneal dialysis after urgent HD has been administered.

**c:** Group 3 consisted of patients who started peritoneal dialysis 2 weeks after the insertion of peritoneal dialysis catheter.

The mean and standard deviation ( $x \pm sd$ ) were given as the mean and the parametric condition.

**DISCUSSION**

When CKD patients have a GFR <30 ml / min / 1.73 m<sup>2</sup>, they should be referred to the nephrologist in order to plan renal replacement therapy at the appropriate time. Early diagnosis allows the initiation of dialysis at the optimal time and the evaluation of family members for renal transplantation before dialysis. When renal replacement therapy requirement develops, the patient should be informed about HD, PD, and kidney transplantation, and their advantages and disadvantages

(9,10). Although peritoneal dialysis is widely used as an alternative to hemodialysis for renal replacement therapy in ESRD patients, catheter-related complications such as leakage around the catheter, catheter outflow failure, hernia, tunnel infection, peritonitis, and catheter exit site infections may limit the use of the PD as one of the major causes of morbidity. According to current guidelines, initiation of peritoneal dialysis is recommended at least 2 weeks after insertion of the peritoneal dialysis catheter (11).

**Table II:** Comparison of biochemical parameters of urgent peritoneal dialysis (group 1), urgent hemodialysis (group 2) and planned PD (group 3) patients.

	<b>Group 1<sup>a</sup></b>	<b>Group 2<sup>b</sup></b>	<b>Group 3<sup>c</sup></b>	<b>p value</b>
Basal GFR (ml/min/1.73 m <sup>2</sup> )	11.9±2.7	13.1±5.1	13.5±3.2	0.348
Urine volume (cc)				
Basal	1413.0±712.3	981.0±810.2	1497.0±670.0	0.07
4 <sup>th</sup> month	1585.7±720.6	1191.7±993.0	1480.0±829.3	0.34
12 <sup>th</sup> month	1592.9±692.7	833.3±486.3	1339.5±647.3	0.001
p value	0.54	0.31	0.15	
Hemoglobin(g/dl)				
Basal	10.1±1.5	9.7±2.1	10.6±1.3	0.39
4 <sup>th</sup> month	11.1±1.8	11.3±1.4	11.6±1.6	0.71
12 <sup>th</sup> month	11.0±1.8	11.3±1.9	11.5±1.4	0.65
p value	0.02	0.004	0.002	
Blood urea nitrogen (BUN mg/dl)				
Basal	95.7±24.1	96.1±36.2	66.1±16.8	0.001
4 <sup>th</sup> month	53.9±14.8	55.8±26.8	44.4±13.5	0.14
12 <sup>th</sup> month	46.5±13.8	47.8±14.6	42.6±12.4	0.48
p value	<0.001	<0.001	<0.001	
Creatinine (Cr- mg/dl)				
Basal	8.1±3.0	7.7±3.9	5.8±2.1	0.06
4 <sup>th</sup> month	5.9±2.5	6.1±2.9	4.9±1.9	0.27
12 <sup>th</sup> month	6.2±2.4	5.7±3.1	5.3±2.7	0.56
p value	<0.001	0.026	0.063	
Albumin (g/dl)				
Basal	3.4±0.5	3.1±0.7	3.4±0.6	0.34
4 <sup>th</sup> month	3.4±0.5	3.1±0.9	3.4±0.5	0.35
12 <sup>th</sup> month	3.7±0.5	3.7±0.4	3.8±0.5	0.76
p value	0.015	0.016	0.002	
Parathormone (pg/ml)				
Basal	289 (156-410)	247 (162-428)	240.5 (99.75-460)	0.877
4 <sup>th</sup> month	243 (94-372.8)	220 (150.3-455)	189 (116-427)	0.722
12 <sup>th</sup> month	233 (119.5-312)	296.5 (158.3-432)	249 (113-363)	0.474
p value	0.035	0.125	0.854	

The mean and standard deviation (x ± sd) were given as the mean and the parametric condition. The median distribution (25% -75%) was defined for the measurable and parametric conditions.

Approximately 50% of patients with CKD present with an indication for urgent dialysis due to an unexpected rapid decline in renal function and/or delayed referral to nephrology (12).

Although these patients may be suitable for PD, they usually start with HD by insertion a central venous catheter (12).

**Table III:** Comparison of complications of urgent peritoneal dialysis (group 1), urgent hemodialysis (group 2), and planned PD (group 3) patients.

Complications	Group 1 <sup>a</sup> (n=23)	Group 2 <sup>b</sup> (n=21)	Group 3 <sup>c</sup> (n=20)	p value
Peritonitis	7 (30.4%)	3 (14.3%)	7 (35.0%)	0.28
Tunnel infection	1 (4.3%)	0 (0%)	0 (0%)	0.40
Catheter exit site infection	0 (0%)	2 (9.5%)	1 (5%)	0.33
Leakage	8 (34.8%)	0 (0%)	0 (0%)	<0.001
Hematoma	0 (0%)	0 (0%)	0 (0%)	
Catheter dysfunction	4 (17.4%)	6 (28.6%)	4 (20%)	0.650
Intestinal perforation	0 (0%)	0 (0%)	0 (0%)	
Hernia	0 (0%)	0 (0%)	4 (20%)	0.009

**a:** Group 1 consisted of patients who started peritoneal dialysis immediately after peritoneal dialysis was performed.

**b:** Group 2 consisted of patients with acute dialysis indication and continuing treatment with peritoneal dialysis after urgent HD has been administered.

**c:** Group 3 consisted of patients who started peritoneal dialysis 2 weeks after the insertion of peritoneal dialysis catheter.

**Table IV:** Comparison of inflammatory markers among peritoneal dialysis (group 1), urgent hemodialysis (group 2) and planned PD (group 3) patients at baseline, fourth month, and 12<sup>th</sup> month of the study period.

	Group 1	Group 2	Group 3	p value
<b>PTX-3 Basal</b>	4.0 (3.3-5.4)	5.7 (3.25-16.22)	8.0 (3.3-14.3)	0.21
<b>PTX-3 4<sup>th</sup> month</b>	4.1 (3.2-10.2)	8.5 (4.0-17.0)	15.5 (6.0-22.7)	0.04
<b>PTX-3 12<sup>th</sup> month</b>	5.6 (3.1-16.4)	12.3 (6.1-20.6)	9.9 (4.3-20.4)	0.34
<b>p value</b>	0.16	0.78	0.13	
<b>IL-6 Basal</b>	80.7 (54.8-103.4)	98.9 (68.2-393.3)	124.9 (75.5-270.6)	0.10
<b>IL-6 4<sup>th</sup> month</b>	81.4 (57.4-202.1)	196.9 (84.9-272.0)	253.8 (129.3-431.5)	0.04
<b>IL-6 12<sup>th</sup> month</b>	101.1 (57.1-331.6)	262.2 (128.9-379.1)	149.1 (73.3-381.9)	0.2
<b>p value</b>	0.94	0.78	0.05	
<b>TNF-α Basal</b>	38.0 (34.7-47.9)	44.8 (36.0-62.5)	78.8 (449-186.1)	<0.001
<b>TNF-α 4<sup>th</sup> month</b>	65.0 (46.1-274.8)	45.5 (33.0-84.1)	66.5 (43.2-137.8)	0,26
<b>TNF-α 12<sup>th</sup> month</b>	125.4 (46.1-182.9)	59.3 (48.1-201.7)	57.6 (45.1-481.8)	0,95
<b>p value</b>	0.03	0.13	0.26	

The median distribution (25%-75%) was defined for the measurable and parametric conditions.

**PTX:** Pentraxin, **IL-6:** Interleukin, **TNF:** Tumor necrosis factor

Banlı et al. performed the first study in the literature regarding the evaluation of complications in the treatment of urgent PD. In this study, peritoneal dialysis was initiated on the sixth day after peritoneal dialysis catheter placement by percutaneous intervention. They reported that early postoperative complications were detected in only two patients (4.8%) around the catheter (11). Povlsen and Ivarsen have shown that catheter-related infection complications were found to be equal in the two groups in patients on urgent PD and planned PD treatment programs. Mechanical complications were found to be significantly higher in patients with urgent PD (12). In a retrospective study performed by Yang et al, 310 patients on PD treatment were analyzed for complications over a six-month period. Urgent PD in 226 patients and planned PD in 84 patients were included in the study. Catheter-related complications were found to be similar between the two groups (13).

In our study, we found similar results in the study by Povlsen and Ivarsen in terms of the complications for one-year. Catheter-related infections were found to be similar in all three groups. Leakage around the catheter was seen in eight patients (34.8%) in the urgent PD group, but there was no leakage complication in the other groups. Unlike this study, hernia was seen in four individuals in the planned PD group, but not in the other two groups. Patients with hernia were found to have higher BMI compared to other patients. The BMI was  $29.9 \pm 2.6$  kg / m<sup>2</sup> in patients with hernia and it was  $27.6 \pm 5.8$  kg / m<sup>2</sup> those without hernia, although the difference was not statistically significant.

Ghaffari et al. also compared 18 urgent PD patients including nine normal onset PD patients in their study. Similarly, in our study, there was no difference in catheter-related infection complications in both groups of patients at 3-month follow-up. In addition, leaks around the catheter in the urgent PD group were found to be significantly higher than the other group (14).

Urgent PD and urgent HD programs were economically evaluated in the United States by Liu et al. In 2014. The initial 90 days estimated amount per urgent PD patient was \$16,398. Dialysis catheterization accounted for 15% of the total cost, dialysis services for 48% and hospitalization for 37%. Urgent HD costs were \$19,352 per patient. 27% of the total cost was dialysis access, 47% dialysis services, and 31% hospitalization. The cost per patient who underwent both urgent HD and PD was \$19,400. Unexpected rapid deterioration of renal function due to late admission in the course of CKD hampers elective dialysis treatment. As a result, urgent PD can provide cost savings in eligible patients who need rapid-onset dialysis (15).

The relationship between inflammation and dialysis in CKD patients is quite extensive in the literature. However, there are a limited number of studies on PTX-3, a new inflammatory marker. The cause of inflammation may be the CKD itself or it may be due to the dialysis treatment. Yiğit et al. assessed the relationship between plasma PTX-3 and inflammatory markers in patients with HD. Thirty patients with tunneled permanent

hemodialysis catheter, 30 patients with arterio-venous fistula and 30 healthy subjects were included in the study. PTX3, CRP, TNF- $\alpha$ , ferritin, hemogram and biochemical parameters were measured in all groups. PTX-3 levels were found to be significantly higher in the group of HD patients with tunneled permanent catheter. PTX-3 level was significantly higher in patients with HD and tunnelled catheter with >8 months than those with  $\leq 7$  months (16). In conclusion, our study did not show a significant difference in terms of inflammation between patients with all PD patients and urgent HD patients. It is thought that HD is closely associated with inflammation due to exposure to long-term non-biologic HD solutions, bacterial infections caused by the tunnelled catheter, and decreased clearance of endotoxins. Thus, our study result may be related to the inadequate number of patients in the urgent HD group.

Boehme et al. investigated the relationship between PTX-3 and dialysis and compared 44 chronic HD patients, 35 PD patients, 39 non-dialysis patients, and 14 healthy age-matched subjects. The PTX-3 level was significantly higher in HD patients than the other groups. They proposed an association between PTX-3 and cardiovascular morbidity due to the study demonstrating that an increase of PTX-3 levels in HD patients was associated with increased cardiovascular morbidity and atherosclerosis (17).

Inflammation has been shown to increase risk of CVD and to be associated with high mortality according to the current literature. Decreased clearance of endotoxins by inadequate dialysis may be responsible for inflammation in CKD. It is well established that inflammation increases in all types of dialysis methods. However, there is no study that shows the relationship between urgent PD and inflammation in the current literature. In this study, urgent HD, urgent PD and planned PD patients were evaluated in terms of inflammation. As a result, no significant difference was found between the dialysis methods. Further studies are needed to clarify the role of different dialysis methods on inflammation due to association of inflammation and mortality.

This study has some limitations including limited number of patients and short duration of follow-up. Thus, further studies are needed to evaluate the results of urgent PD in large population with long duration.

It should be kept in mind that urgent PD is a safe, useful and alternative, modality to HD in patients with ESRD who require urgent dialysis. There is no central venous catheterization and the related complications in PD. Dialysis treatment can be started after PD catheter insertion both in the acute and the chronic period. While there is a need for more extensive work in this area, we suggest that each center should consider urgent PD by developing an algorithm for patients with an urgent dialysis indication. This method can be applied by the nursing and dialysis unit support personnel.

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