



Acute Phase Response During Hemodialysis and Peritoneal Dialysis

Mahboob Lessan-Pezeshki^{1,2}, Seifi S¹, Mahdavi-Mazdeh M^{1,2}, Ali Ghafari^{1,2}, Rahbar M^{3*}

Nephrology Research Center, Tehran University of Medical Sciences. Tehran, Iran¹

Center of Excellence in Nephrology²

Sina Hospital, Tehran University of Medical Sciences. Tehran, Iran³

**Corresponding author: Maryam Rahbar, Assistant Professor of Nephrology, Sina Hospital, Tehran University of Medical Sciences. Tehran, Iran, Email address: rahbar_maryam81@yahoo.com, Mailing address: Sina Hospital, Tehran University of Medical Sciences. Tehran, Iran*

<p>Keywords</p> <p>HCV, Proteinuria-Renal transplantation</p>	<p>Abstract</p> <p>Introduction: Acute phase response was reported in people with hemodialysis (HD) and peritoneal dialysis (PD). However, it is not clear if this response is higher in one method of treatment than other. Herein we investigate the differences in serum levels of C-reactive protein (CRP), albumin (Alb), and high-density lipoprotein (HDL) among individuals on HD and PD.</p> <p>[Continued...]</p> <p>© 2018 Journal of Nephrology and Renal Transplantation. All rights reserved</p>
--	--

1. Introduction

The markers of acute phase response such as cytokines, C-reactive protein (CRP), albumin (Alb), and cholesterol have been identified as the predictive factors for the occurrence of different pathologic conditions and mortality in general population. Pro-inflammatory cytokines and CRP are considered positive acute phase mediators which increase during inflammation. Mounting evidence indicated that elevated serum levels of pro-inflammatory cytokines were correlated with increased risk of various autoimmune, neurological, psychiatric, and cardiovascular diseases (1,2). CRP was also found to be a predictive and prognostic mediator for cardiovascular morbidity and occurrence of different malignancies (3). Alb, high density lipoprotein (HDL) cholesterol, on the other hand, are known as negative acute phase reactants and decrease during inflammatory process. Hypoalbuminaemia due to malnutrition was found to be a strong predictor of death.

Hemodialysis (HD) was reported to induce inflammation and increase the levels of pro-inflammatory mediators. Studies demonstrated that hemodialysis was associated with increased serum levels of cytokines such as interleukin (IL)1 and tumor necrosis factor (TNF)-alpha which may have negative impacts on the health of people on hemodialysis (4). Catabolism, wasting, fatigue, and periarticular

fibrosis are frequent symptoms in people on long-term hemodialysis. Moreover, increased risk of various co-morbid conditions have been reported in this population (5). Inflammation due to hemodialysis has been suggested to be responsible for the occurrence of aforementioned complications and co-morbidities.

Our knowledge about the effects of peritoneal dialysis (PD) on inducing inflammation is limited and few studies with conflicting data investigated the serum or peritoneal levels of the mediators of acute phase response (IL1, IL6, and TNF-alpha) in individuals on PD. One prior study reported high plasma levels of IL1 in people on continuous ambulatory peritoneal dialysis (6). Elevated serum levels of IL6 was also described in another trial (7). However, two studies found no association between PD and increased serum levels of IL1 and IL6 (8,9).

In this study, we evaluate the serum levels of CRP as a positive acute phase mediator as well as Alb and HDL as negative acute phase agents in people on HD and PD to find out if there is any significant difference between these two methods of treatments in inducing inflammation.

[Abstract Continued...]

Methods - This is a cross-sectional study conducted in Imam Khomeini Hospital complex. 59 individuals on HD (33 men and 26 women) and 17 participants on PD (6 men and 11 women) were included in our study. CRP, Alb, and HDL values were measured in these groups and compared to each other.

Results Increased serum levels of CRP were more frequent in PD patients. Furthermore, decreased serum levels of Alb, as a negative acute phase protein, were also detected more common in PD group compared to HD patients. On the other hand, levels of HDL were lower in HD individuals. There was no association between CRP and duration of dialysis, as well as, HDL serum levels. But significant correlation was observed between CRP and Alb serum levels.

Conclusion - People with PD therapy are more prone to increased acute phase response which may increase the risk of different complications and co-morbidities.

© 2018 Journal of Nephrology and Renal Transplantation. All rights reserved

2. Patients and Methods

2.1 Patients

This is a cross-sectional study of people with end stage renal disease undergoing HD or PD who referred to Imam Khomeini Hospital Complex affiliated to Tehran University of Medical Sciences between January 10, 2009 to May 10, 2009. Inclusion criteria were patients with end stage renal disease who had survived at least one month on dialysis. Patients received immunosuppressive treatments or suffered from any pathologic conditions including renal failure with unstable clinical manifestations, malignancy, autoimmune diseases, and congestive heart failure were excluded from our study. All participants gave written consent.

2.2 Methods

Blood samples for CRP levels were taken from our included patients in the morning after 12 hours of fasting and stored at -20°C . Serum levels of CRP were measured using enzyme-linked immunosorbent assay. The assay is based on a sandwich ELISA technique which used an anti-CRP antibody as a catching antibody and an identical biotinylated antibody as the detecting antibody. The tentative normal range of CRP is <6 mg/lit and we divided our cases into two subgroups based on their serum CRP levels (negative: $\text{CRP} < 6$ mg/lit and positive: $\text{CRP} \geq 6$ mg/lit).

Serum levels of Alb and HDL in our participants were also measured. Alb serum levels of less than 3.5 were considered as “low level” while 3.5 and higher was in normal range. We also divided our patients into 2 classifications based on serum levels of HDL (serum $\text{HDL} < 30$ mg/dl: low level and $\text{HDL} \geq 30$ mg/dl in normal range).

2.3 Statistical analysis

Continuous variables were presented as means and standard deviations (SD). Also, for statistical analysis, independent T-test was used. Categorical variables were described using percentage and to compare, Chi-square and ANOVA were used. The obtained data were analyzed by SPSS and the statistical significance was set at P-value of <0.05 .

3. Results

59 individuals on HD (33 men and 26 women) and 17 participants on PD (6 men and 11 women) were included in our study. Patients were on dialysis ranging from 1 month to 17 years with the mean (SD) of 4.4 years (8.35). The duration of dialysis was not significantly different between 2 groups (P-value: 0.15). Positive CRP was observed in 11 patients in HD group (18.6%) and was found in 10 individuals on PD (66.7%). There were statistically significant higher levels of CRP in participants on PD compared to individuals in HD group.

In HD group, 11 patients had low serum levels of Alb (18.6%) while they were observed in 13 individuals of PD group (76.5%). Decreased levels of Alb were observed in PD individuals significantly more frequent than HD patients (P-value:0.00). Regarding HDL cholesterol, its low levels were observed in 22 participants and 1 patient in HD and PD groups, respectively.

Negative association was observed between serum levels of CRP and Alb (P-value: 0.002). Furthermore, a positive correlation was found between serum levels of CRP and duration of dialysis (both HD and PD) (P-value: 0.014). However no significant correlation was observed between CRP and HDL serum levels.

4. Discussion

In this study CRP, Alb, and HDL values were investigated in individuals with chronic renal insufficiency undergoing PD and were compared to values measured in patients on HD. We realized that patients on PD were at greater risk for increased CRP and decreased Alb compared to individuals on HD. However, decreased levels of HDL were more common in participants on HD. In contrast to our study, 2 prior trials reported that people with HD therapy had higher levels of CRP compared to individuals with PD therapy (10,11). *Haubitz et al.* (10) compared CRP values between individuals with chronic renal insufficiency, patients with HD and PD therapy. The authors found out that People on PD had the statistically lower levels of CRP compared to individuals with HD therapy. However, no significant difference was reported comparing to people with ESRD and without dialysis. Of interest, another study reported that PD and HD therapies had no significant effects on serum CRP and cytokines (12). These conflicting results can be due to methodological differences. The design of studies, the method of HD and PD using in patients, and

the way that CRP values were measured were all the possible bias which may considerably affect the results. The small sample sizes of all these trials should not also be discounted.

Many aspects of inflammation are yet unclear. Our knowledge is limited about different pathways beginning inflammation and various inflammatory cascades. However, it is now well-recognized that this immune system dysfunction can bring numerous negative long-term outcomes (13,14). Therefore, trying to understand the impact of dialysis on inflammation can let practitioners choose a better method of treatment in people with end stage renal disease and anticipate the impact of the treatment on health of individuals.

Our study had different limitations. The small sample size was the main one. We used a cross-sectional design for our purpose and we did not estimate the effects of dialysis duration on the markers of inflammation. Furthermore different confounders can be mentioned for the association such as age and sex which were not stratified in our study. Overall, we recommend that future studies with long-term follow-up and large samples of patients should be conducted.

In conclusion, we found out that PD therapy may prone people to inflammation more than HD which may lead to higher prevalence of different complications and co-morbid conditions.

REFERENCES

- [1] Hoge EA, Brandstetter K, Moshier S, et al. Broad spectrum of cytokine abnormalities in panic disorder and posttraumatic stress disorder. *Depress Anxiety*. 2009;26(5):447-55.
- [2] Rosas-Ballina M, Tracey KJ. The neurology of the immune system: neural reflexes regulate immunity. *Neuron*. 2009;64(1):28-32.
- [3] Shimada K, Fujita M, Tanaka A, et al. Elevated serum C-reactive protein levels predict cardiovascular events in the Japanese coronary artery disease (JCAD) study. *Circul J*. 2009;73(1):78-85.
- [4] Wang AY, Lam CW, Chan IH, et al. Long-term mortality and cardiovascular risk stratification of peritoneal dialysis patients using a combination of inflammation and calcification markers. *Nephrol Dial Transplant*. 2009;24(12):3826-33.
- [5] Wanner C, Zimmermann J, Schwedler S, et al. Inflammation and cardiovascular risk in dialysis patients. *Kidney Int*. 2002;61:S99-102.

- [6] Carozzi S, Nasini MG, Schelotto C, et al. Peritoneal macrophage beta-2 microglobulin production and bacterial peritonitis in CAPD patients. *TransAm SocArtif Intern Organs*. 1990; 36:369-71.
- [7] Nakahama H, Tanaka Y, Shirai D, et al. Plasma interleukin-6 levels in continuous ambulatory peritoneal dialysis and hemodialysis patients *Nephron* 1992; 61:132-4.
- [8] Goldman M, Vandenabeele P, Moulart J, et al. Intraperitoneal secretion of interleukin-6 during continuous ambulatory peritoneal dialysis. *Nephron*. 1990; 56:277-80.
- [9] Zemel D, ten Berge RJM, Koomen GCM, et al. Serum interleukin-6 in continuous ambulatory peritoneal dialysis in patients (Letter). *Nephron*. 1993; 64:320-1.
- [10] Haubitz M, Brunkhorst R, Wrenger E, et al. Chronic induction of C-reactive protein by hemodialysis, but not by peritoneal dialysis therapy. *Peritoneal Dialysis International*. 1996 Jan 1;16(2):158-62.
- [11] Sethi D, Muller BR, Brown EA, et al. C-reactive protein in haemodialysis patients with dialysis arthropathy. *Nephrol Dial Transplant* 1988; 3:269-71.
- [12] Borazan A, Ustün H, Ustundag Y, et al. The effects of peritoneal dialysis and hemodialysis on serum tumor necrosis factor-alpha, interleukin-6, interleukin-10 and C-reactive-protein levels. *Mediat Inflamm*. 2004;13(3):201-4.
- [13] Amanat M, Salehi M, Rezaei N. Neurological and psychiatric disorders in psoriasis. *Rev Neurosci*. Published online: 2018 Mar 6. DOI: <https://doi.org/10.1515/revneuro-2017-0108>
- [14] Amanat M, Salehi M, Rezaei N. A Guideline for Early Diagnosis of Autoimmune Epilepsy Based on Clinical Manifestations and Common Para-clinical Tests. *Acta Med Iran*. 2018;56(6):419-20.