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Original Article

The effect of peritoneal dialysis on the development of left ventricular hypertrophy: Is it a risk factor?

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Abstract

Background. Left ventricular hypertrophy (LVH) is the most important factor for the survey of the patients that use continuous ambulatory peritoneal dialysis (CAPD). This group of patients has 80% abnormal echocardiographic signs, and most of them are about LVH. We aimed to find out the risk factors of CAPD patients that affect LVH.

Methods. We studied 57 CAPD patients (29 female, 30 male) randomly selected from the nephrology clinic. Patients were divided into two groups as those with and without left ventricular failure. Echocardiography was performed. Risk factors such as age, hypertension, diabetes mellitus, chronic renal failure duration, and peritoneal dialysis time were noted. Creatinine clearance, weekly Kt/V, and protein catabolism rate (PCR) are studied for all patients. Serum creatinine, albumin, sodium, potassium, cholesterol, triglyceride, uric acid, calcium, phosphorus, CRP, parathyroid levels, and hematocrit were measured. The results were examined for statistical significance by Student's t-test, Mann-Whitney U test. The Fischer exact test and chi-square test were used for categorical variables.

Results. Hypertension was found in 74% of the LVH group patients, in 54% of the other group, which was not statistically significant. Mean parathyroid hormone level tended to be higher in the LVH group. There was no difference in hematocrit levels between these two groups as well as in other parameters such as chronic renal failure duration, peritoneal dialysis time, Kt/V, creatinine clearance, PCR, creatinine, albumin, sodium, potassium, cholesterol, triglyceride, uric acid, calcium, phosphorus, and CRP.

Conclusion. While hypertension, anemia, hyperparathyroidism, and hypoalbuminemia were important factors in LVH progression found in the literature, it was not found to be of significant difference in our patients with and without LVH. It is concluded that much larger patient group and a longer period of observation are needed in order to reach a significant relationship, but also a lot of other local factors remains to be investigated.

Keywords: continuous ambulatory peritoneal dialysis (CAPD); left ventricular hypertrophy (LVH); uremia

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Introduction

Renal transplantation as a treatment of chronic renal failure can be administered to only a small percentage of patients in Turkey. The most commonly utilized method of dialysis in the treatment of chronic renal failure is hemodialysis. However, hemodialysis lowers the quality of life, establishes a dependency on hospitalization thereby disrupting daily activities, and has negative effects on hemodynamics. Additionally, as an expensive method, it is of significant cost on the budgets of the patients and social security institutions.

In the recent years, due to the undesirable effects of hemodialysis, peritoneal dialysis has been applied to an increasing number of patients. Peritoneal dialysis is preferred because it is applicable to patients who are in the risk group for hemodialysis complications preventing their need for prolonged hospitalizations, and because it less costly procedure than hemodialysis itself.

Cardiovascular complications with peritoneal dialysis manifest as hypertension, dyslipidemia, increased atherosclerosis, uremic cardiomyopathy, left ventricular hypertrophy (LVH), and heart failure. LVH may depress contractility of the heart, causing abnormal compliance and heart failure as a result [1]. Additionally, it may exacerbate the clinical manifestations of coronary artery disease, and increase the incidence of sudden death. LVH is shown to be the most important factor determining the survival of the patients under continuous ambulatory peritoneal dialysis (CAPD). Although factors like hypertension, anemia, parathyroid hormone, hyper-volemia, and hypoalbuminemia are accepted as responsible in the formation of LVH amongst CAPD patients, some studies single out uremic toxins as the cause [2].

In this study, we compared the effects of hypertension, parathormone, albumin, calcium, phosphorus, creatinine clearance, uric acid, potassium, and weekly Kt/V on LVH on patients with and without this condition.

Patients and methods

A total of 57 patients were randomly included into the study without any age or sex distinctions, followed up regularly in the Istanbul Training and Research Hospital, Peritoneal Dialysis Unit. Patients who received treatments of CAPD, continuous cyclical peritoneal dialysis (CCPD), and nocturnal intermittent peritoneal dialysis (NIPD), whose dry weight was gained back, and who did not present hypervolemia (Table 1) were recruited to the study and treated for three months. Patients whose dry weight was not gained back due to ultrafiltration deficiency were excluded.

The patients' reports of disappearance of symptoms were taken as the clinical criterion for the efficacy of the dialysis. Anamnesis, physical examination, venous blood samples, 12-lead resting EKGs, and telecardiographies were investigated. In the EKGs, LVH was evaluated according to the Skolow-Lyon criteria. Transthoracic echocardiography was performed with a Vingmed System FiVe Device transducer probe. Interventricular septal dimensions (IVSd) in diastole, and posterior wall dimensions (PWd) and left ventricular dimensions at end diastole were measured. The left ventricular mass was calculated by the cubic method, with the formula LV mass=1.05 x (total volume - intracavitary volume) [4]. Left ventricular mass index was calculated by dividing the left ventricular mass by the body surface area.

Blood pressure values over 140/90 were interpreted as hypertension based on *WHO/ISH* (1999), *JNC-VI*, *BHS* (1999) and *Turkish Society of Cardiology National Hypertension Treatment and Follow-Up Manual* (2000) [5,6,7].

In this cross-sectional study, the patient groups were formed using the biochemical values and echocardiographic evaluations at the time of admission. The patients were divided into two groups as the ones with and without LVH, as indicated by the echocardiographic measurements of IVSd, PWd, and left ventricle mass index (g/m²).

Patients' age, blood pressures, diabetes mellitus condition, duration of chronic renal failure and peritoneal dialysis have been recorded. Weekly Kt/V ratio and creatinine clearance have been charted and investigated. Blood samples were collected intravenously from the antecubital vein for investigating hematocrit, albumin, creatinine, uric acid, parathormone, cholesterol, triglyceride, sodium, potassium, calcium, phosphorus, and CRP.

To analyze the results, the packet statistical program SPSS for Windows release 10.0 (SPSS, Chicago, IL, USA) was used. In the comparisons, Student's t-test, Mann-Whitney U test, chi-square, and Fischer's exact test were used.

Results

A total of 57 (27 females and 30 males) peritoneal dialysis patients were analyzed into the study. The mean age for LVH (+) patients was 44.1±10.9, and 41.8±13.6 for LVH (-) patients, being not significantly different. There was no significant difference with respect to the frequency of hypertension or diabetes mellitus.

Table 1. Comparison of patients with and without LVH based on age, and frequency of hypertension and diabetes mellitus

	LVH (+)		LVH (-)			
	n	%	n	%	Chi-square	P
Female	17	48.6	11	50.0	n.s.	n.s.
Male	18	51.4	11	50.0	0.01	n.s.
Hypertension (+)	24	70.6	12	54.5	n.s.	n.s.
Hypertension (-)	10	29.4	10	45.5	n.s.	n.s.
Diabetes (+)	4	11.8	2	9.1	n.s.	n.s.
Diabetes (-)	30	88.2	20	90.9	n.s.	n.s.

Additionally, no significant difference was identified in the mean duration of chronic renal failure and peritoneal dialysis, neither with regard to the type of dialysis.

Groups have been also compared based on hematocrit, creatinine, albumin, sodium, potassium, total cholesterol, triglyceride, uric acid, CRP, parathormone, calcium, and phosphorus values. No difference was found in these parameters as well.

Discussion

Cardiovascular diseases are the main cause of mortality and are responsible for 40% of the deaths [8]. These diseases are more prevalent amongst dialysis patients [9]. Cardiovascular diseases manifest as coronary artery diseases, hypertension, and LVH. It has been found that more than 80% of the dialysis patients present abnormal echocardiographic findings, mainly LVH [10]. In a study conducted with 433 patients, echocardiographic evaluations revealed LVH in 75% of the subjects. LVH in these patients was the main determinant of survival [11]. In uremic patients, cardiac functions are affected by a variety of factors. Some experimental studies show that uremic toxins have a depressing effect on myocardial functions [12].

In dialysis patients, risk factors for LVH are advanced age, hypertension, chronic anemia, hypoalbuminemia, hypervolemia, and the duration of dialysis. In the long term, LVH may depress contractility of the heart, and cause abnormal compliance and heart failure. Additio-

nally, it may increase the clinical manifestations of coronary artery disease and the incidence of sudden death. An increase in the frequency of asymptomatic ventricular arrhythmia and abnormal vasodilator reserve microcirculation are responsible for sudden death [13]. There are various reasons for LVH in CAPD patients. Theoretically, CAPD is hemodynamically advantageous compared to hemodialysis: I) AV fistula does not lead to hypercirculation in CAPD patients; II) CAPD does not cause sudden change in intravenous volume and has no adverse effects on the heart; and III) CAPD results in better blood volume and pressure control.

Hypertension is the main cause of LVH in the general population [13]. The recession of LVH with antihypertensive use has been documented in multiple studies [14,15]. Hence, it could lead us to a conclusion that a sufficient treatment, hypertensive heart disease can be reduced. Leenen *et al.*, in a study including 18 patients with hypertension and LVH, found that LVH worsened only in 1 patient, whereas it showed recession in 15 patients 6-12 months into CAPD treatment [16]. This was associated with the normalization of blood pressure and volume as a result of CAPD. Although this conclusion is supported by other studies, different causes for hypertrophy are investigated.

Eisenberg *et al.* [17] worked with 27 LVH patients, and the echocardiographic findings showed an increase in hypertrophy from the initial 52% to 76% in 18 months. Diastolic blood pressures taken at the onset and the end of the study revealed no difference; however, systolic pressure was greater in the group with severe LVH. No correlation was found between LVH and renal failure, duration of dialysis, anemia, or creatinine levels. Rambaussek *et al.* observed an increase in the left ventricular mass in uremic animals submitted to subtotal nephrectomy. This finding has not changed after I) the animals reached a normotensive state with ACE inhibitors, II) sympathetic activity was eliminated with alpha and beta blockers, and III) the preload was decreased by administering high doses of furosemide to the uremic animals [18]. Mall *et al.* report that in uremic rats with normal blood pressure, interstitial tissue in the myocardium has increased [19]. These studies indicate that not only hypertension, but uremia as well, plays an important role in the formation of LVH.

Our patient group includes subjects who, without hypervolemia, have gained back their dry weight. Hypertension frequency was 70% in the group with LVH, and 54% in the group without hypertrophy. No difference between the groups in hypertension frequency was found. Activated interstitial cells may cause collagen accumulation in the left ventricular myocardium. Changes in mechanical activity due to cardiac contractions, and circulating growth factor levels may play a role in interstitial lesion formation. The changes in the cardiac contractions are connected to a rise in the afterload and shifts in electrolytes. Additionally, prorenin secretion is shown to influence on the coronary flow. Circulating and locally secreted renin may play a role in hypertrophy, alongside with growth factors. Moreover, increase in the reticuloendothelial system activation and sympathetic hyperactivity should be considered as well. All these factors may cause LVH. Tumor necrosis factor-alpha (TNF-alpha) is usually discharged through the kidneys. In uremic patients, a rise in TNF-alpha levels due to a residual renal function loss has been observed. It is thought that TNF-alpha plays a role in peripheral neuropathy, malnutrition, erythropoietin sensitivity and LVH pathogenesis [20]. In peritoneal dialysis patients, a correlation between TNF-alpha levels and severity of LVH was found.

Then the question why do these factors affect only the interstitial cells is raised and why there is an increase in the number of interstitial cells and the fibrosis is limited to the heart, not showing up in the other organs? These questions might be answered mainly through the strong local factors responsible for hypertrophy found in the heart.

Parathormone is thought to be a strong uremic toxin [21]. The heart is sensitive to parathormone. Cardiac cAMP concentration, cardiac velocity, and contractile performance are shown as increased after in-vitro addition of parathormone. However, the increase in myocardial calcium has not been studied in humans. On the other hand, LVH progression has not been improved after rats subjected to parathyroidectomy have been rendered normocalcemic via injection of calcium. Even though parathormone levels were higher in the LVH group in our study, statistically significant difference has not been found. We could not find a significant difference in calcium or phosphorus levels in either group as well.

It has been shown that anemia can cause LVH in dialysis patients, and with anemia treatment LVH could have been reduced. Hüting *et al.* [22], in a study with 55 CAPD patients, observed a direct correlation between LVH regression and mean arterial pressure. They found no correlation among diastolic blood pressure, hemoglobin, parathyroid hormone in serum, and CAPD duration. In our study, we did not find any connection between LVH and hemoglobin concentration as well. Wang *et al.*, after investigating the relationship between residual renal function and left ventricular function in 158 CAPD patients, have reported uremic levels and the residual renal function as key indicators. It has been reported that the decrease in erythropoietin secretion with a loss in residual renal function is one of the reasons causing LVH [23]. In our study, it was shown that patients with further loss of renal residual function had a higher degree of anemia, needed a higher dose of erythropoietin, and presented with more advanced LVH. It was reported in other studies that anemia can cause LVH in dialysis patients, which can only partially respond to anemia treatment [24]. In contrast, Rambaussed *et al.* showed even though hematocrit levels raised up to 40% via blood transfusion, myocardial hypertrophy could not have been prevented. Though we found lower levels of hematocrit level in our patient group with LVH, this has not been found to be significant.

One of the most critical complications in CAPD patients is malnutrition. Patients treated with peritoneal dialysis lose significant amounts of protein. The level of albumin

loss composes 50-79% of the total protein loss [25]. In a cross-sectional study, it has been determined that 40% of the patients suffer from malnutrition and 8% have serious protein loss. This is an important risk factor in mortality and morbidity in peritoneal dialysis patients. The reasons for malnutrition are multifactorial. Serum albumin levels are shown to be correlated with protein-catabolism rate (PCR). Nutrition has important effects on the patients' acid-base balance. A decrease in protein catabolism causes acidosis regression. It has been found that hypoalbuminemia correlates with the LVH, left ventricular dilation, and heart failure [26]. Wang *et al.* found a correlation between severity of albuminemia and severity of LVH. In our study, we did not find a relationship between LVH, albumin levels, and protein catabolic rate [27].

There was no any statistical association between the LVH and other parameters (uric acid, total cholesterol, triglyceride, CRP, sodium, potassium) as well.

Conclusions

While hypertension, anemia, hyperparathyroidism, and hypoalbuminemia were important factors in LVH progression found in the literature, it was not found to be of significant difference in our patients with and without LVH. It is concluded that much larger patient group and a longer period of observation are needed in order to reach a significant relationship, but also a lot of other local factors remains to be investigated.

Conflict of interest statement. None declared.

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