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Original Article

Internal Medicine Section

Comparison of Long-term Complications in Patients on Haemodialysis and Peritoneal Dialysis Longer than 10 Years

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ABSTRACT

Introduction: Depending on developments in dialysis techniques and new treatment strategies for comorbid diseases, life expectancy has increased. As a result, dialysis related long term complications could be seen more frequently. We investigated and compared long term complications of the Haemodialysis (HD) and Peritoneal Dialysis (PD) in patients with history if either mode at least 10years.

Materials and Methods: A 13HD & 16PD patients were included to the study. Basic demographic parameters and prevalence of cardiovascular diseases (CVD), uraemic peripheral neuropathy (PNP), parathyroid adenoma, parathyroidectomy and acquired cystic disease (ACD) were assessed.

Results: HD patients were older than PD patients (p=0.035) and duration of dialysis was longer in HD patients (p=0.001).

CVD was present in 18 patients (9 HD, 9 PD). There was no difference in presence of CVD between HD and PD patients (p=0.455). Valvular diseases (n=15), diastolic dysfunction (n=8), left ventricular hypertrophy (n=5), ischemic heart disease (n=3) and congestive heart failure (n=1) were investigated.

Uraemic peripheral neuropathy was observed in 14 of the patients (8 HD, 6 PD patients). Eight patients had mixed type sensory motor neuropathy and 3 patients had mixed type sensorial neuropathy, 2 patients had demyelinating PNP, 1 patient had axonal PNP and 3 of them had CTS related to peripheral neuropathy.

Parathyroid adenoma was detected in 4 patients (2 HD, 2 PD) and 3 patients (1 HD, 2 PD) had history of parathyroidectomy. Serum phosphate and iPTH levels were higher in HD patients (p=0.003, p=0.04, respectively).

ACD was detected in 14 patients (7 HD, 7 PD). There was no difference between PD and HD patients (p=0.75).

Conclusion: HD patients were older than PD patients and had longer duration of dialysis. The prevalence of long term complications was similar in HD and PD modalities. CVD especially valvular diseases were common complication in both modalities

Keywords: Amyloidosis, Acquired cystic disease, Cardiovascular disease, Renal osteodystrophy

INTRODUCTION

Developments in dialysis techniques involving peritoneal dialysis (PD) and haemodialysis (HD) expended the life span of the patients with end stage renal failure (ESRD) attributable to various causes, though this is not without complication [1]. The most frequent long-term dialysis complications relate to cardiovascular disease, peripheral neuropathy, parathyroid adenoma, parathroidectomy and acquired cystic disease of the kidney [1,2].

Few data are available regarding the prevalence of long-term complications, particularly comparison of the prevalence of complications between long-term survivors of different modes of dialysis. We performed a retrospective analysis of patients in a single center who dialysed for at least 10 years and still on dialysis and assessed prevalence of complication of long term dialysis.

MATERIALS AND METHODS

We included all patients who have been commenced dialysis before 2004 with total dialysis history of more than 10 years. All included patients are still on dialysis and attending to the out-patient clinics regularly. The censoring date was 30 June 2014.

Patients who have been switched dialysis therapies, followed up in different centers and died after 10 years of commencement of dialysis, and with policystic kidney disease were excluded from the study. We retrieved demographic, clinical, dialysis, and biochemical data from the most recent follow-up. The dialysis data included dialysis mode (HD, Ambulatory Peritoneal Dialysis (APD), Continous Ambulatory Peritoneal Dialysis (CAPD)) and vascular access for HD patients (location and site of arteriovenous fistula). From clinical records, we retrieved information about complications related to cardiovascular diseases (CVD), parathyroid (PT) adenoma, parathyroidectomy and acquired cystic disease (ACD). Prospective analysis were performed about long term complicatios including CVD, uraemic peripheral neuropathy (PNP), PT adenoma, PT hyperplasia and ACD.

Symptoms related to CVD such as dyspnea, chest pain and oedema were questioned and history of CVD was recorded; cardiovascular medications were documented. A 12-lead electrocardiogram was reviewed for signs of coronary artery disease and left ventricular (LV) hypertrophy. M-mode echocardiography was performed to reveal systolic and diastolic dysfunction, LV hypertrophy and dilatation, valvular disease. LV systolic dysfunction was defined as the ejection fracture less than 40% by echocardiography. Blood pressure was calculated as average of 3 seated measurements taken after a 5-minute rest. It was measured before dialysis on a short (2-day) break in all HD patients and at the time of clinic visit in PD patients.

Signs and symtoms related to uraemic PNP were assessed and electrophysiological studies for diagnosis of PNP and carpal tunnel syndrome (CTS) were performed by the same doctor and device. Detailed history was elicited pertaining to patients' neurological symptom such as tingling and prickling sensation in the legs, paresthesias, hyperalgesia, weakness, numbness of lateral four fingers for compressive neuropathies, pain and stiffness of the hands. Muscle atrophy, loss of deep tendon reflexes, abnormal or absent reflexes (particularly ankle jerk), and impaired sensation (vibratory, light touch pressure, and pain) were assessed objectively.

Nerve conduction studies were performed using Nihon Kohden equipment in the room temperature. Bilateral median, ulnar, peroneal, and tibial motor nerves and median, ulnar, superficial peroneal, sural sensory nerves were evaluated using standard conduction techniques. Distal latency, amplitude and nerve conduction velocity (NCV) of motor and sensory nerves and f wave's minimal latency of all motor nerves were measured. PNP was diagnosed when slowing of nerve conduction velocity and/or decrease of amplitude of muscle action potential and/or lenghtening of distal latencies were present in two or more nerves and longer f wave response was present in one or more nerves. CTS were diagnosed if slowing of NCV and/or decrease of amplitude of muscle action potential and/or lenghtening of distal latency of either sensory or motor median nerve were present. Nerve conduction study was performed only in one upper extremity if the patients did not accept stimulation of median and ulnar nerve on the limb with fistula.

Presence of PT adenoma and history of parathyroidectomy were obtained from clinical records. Ultrasonographic examination of PT gland was performed if the patient had elevated level of iPTH. PT hyperplasia was recognized by enlarged PT glands (larger than 0.5 cm3) and the presence of round or oval masses, hypoechogenic, homogenous, with or without blood flow, located in the rear section of the thyroid gland. If sonographic characteristics of PT glands included homogeneous hypoechogenicity and an extrathyroidal feeding vessel with peripheral vascularity seen on colour-doppler imaging, PT adenoma was diagnosed and then sestamibi nuclear scan was performed to measure the activity of the adenoma.

ACD was confirmed by ultrasonography. Loin pain and (if residual renal function was present) hematuria were questioned. As ACD can be detected prior to ESRD, older ultrasonographic findings were examined and new enhacement of four or more cysts per kidney was accepted as ACD.

STATISTICAL ANALYSIS

Statistical analysis was done by Scientific Package for Social Science (version 17.0; SPSS Inc., Chicago, IL, USA). All continuous data were expressed as mean±SD and were analysed by unpaired t-test. Categorical data were expressed as number (percentage) and were analysed by χ^2 test. Correlation analysis were tested by pearson's correlation statistics for analysing parametric parameters and Spearman's rho test was used for analysing non parametric parameters. Differences were considered statistically significant if p-value was less than 0.05.

RESULTS

The records of 524 HD and 367 PD patients starting dialysis before 2004 were evaluated retrospectively. Totally 29 patients were included into the study [Table/Fig-1]. Participants predominantly were female (55.17%) with a mean age of 45.04±12.88 years and mean follow-up of 12.5±3.2 years. Glomerulonephritis (27.58%) and diabetic nephropathy (17.24%) were the leading causes of ESRD.

Baseline characteristics of the patients are detailed in [Table/Fig-1]. HD patients were older than PD patients (p =0.035) and had longer duration of dialysis (p= 0.001). Twenty three percent of patients in HD group had left sided fistula in cubital area, 61.5% of them had left sided radial fistula and 15.3% of them had right sided radial fistula. Seven PD patients (43.7%) were treated with APD, 9 of them (56.3%) were treated with CAPD.

CVD was present in 18 (62.1%) patients (9 HD, 9 PD). Hypertension was found in 11 (5 HD/ 6PD) of the 29 long-term patients, with similar prevalence in the PD and HD groups (p=0.537). With regard to cardiovascular complications, valvular diseases have found in 15 patients, diastolic dysfunction in 8 patients, left ventricular hypertrophy (LVH) in 5 patients. History of

		Overall (n= 29)	HD patients (n= 13)	PD patients (n= 16)	p
Age (years)		45.04±12.88	51±14.6 (32-74)	40.2±11.5 (22-59)	0.035
Sex	M	13 (44.8%)	6 (46.1%)	7 (43.7%)	
	F	16 (55.1%)	7 (53.8%)	9 (56.2%)	0.214
Age at initiation of dialysis		34.0±13.1	38.9±13.0 (21-57)	28.6±11.4 (12-49)	0.057
Duration of dialysis		12.5±3.2	13.9±3.6 (10-19)	10.4±0.7 (10-22)	0.001

[Table/Fig-1]: Baseline characteristic of the patients.

ischemic heart disease was noted in 3 patients that did not require angioplasty or bypass surgery after angiographic examination. LV systolic dysfunction was present only in one patient. The most frequent valvular diseases were mitral regurgitation (n=10) and aortic regurgitation (n=7). Valvular calcifications were present in 8 (27.5%) patients, 4 with mitral valve calcifications and 4 with aortic valve calcifications. There was no difference in prevalence of CVD between HD and PD patients (p=0.455).

In the patient cohort, 8 of the (3 HD, 5 PD) patients had complain of weakness and tingling and prickling sensations in the legs. None of them had loss of deep tendon reflexes, abnormal or absent reflexes and impaired sensation on physical examination. Electodiagnostic finding reveal that 48.2% of patients (8 HD, 6 PD) had PNP, 8 with mixed type sensory motor neuropathy, 3 with mixed type sensorial neuropathy, 2 with demyelinating motor and sensory PNP, 1 with axonal sensory PNP. Statistically significant relationship was not found between uraemic PNP and age, sex, mode of dialysis, the duration of dialysis, iPTH level, presence of diabetes mellitus and history of parathyroidectomy.

CTS related to PNP was noted in 3 patients (2 PD, 1 HD). Only one PD patient had numbness of lateral four fingers, pain and stiffness of the hands and tenar atrophy. In 3 HD patients, one with documented CTS, nerve conduction study were performed in only one upper extremity because these patients did not accept stimulation of median and ulnar nerve on the limb with fistula. There was no significant difference in frequency of CTS between the two groups (p=0.60). Our results revealed that PT adenoma was present in 4 patients (2 HD, 2 PD). PT hyperplasia was found in one HD patient. Three patients (1 HD, 2 PD) had history of subtotal parathyroidectomy. Fracture of femur head has occured in 3 HD patients. Lower serum phoshate and iPTH level were observed in PD patients (p= 0.003, p= 0.04, respectively) [Table/Fig-2].

A 60.8% of the patients (7 HD, 7 PD) have had documented ACD of which 9 patients (6 HD, 3 PD) have had loin pain. Two PD patients with residual renal function did not have hematuria and 2 PD patients had cystic disease before initiation of dialysis. One of HD patient had history of cystectomy and none of participants had

	Overall (n= 29)	HD patients (n= 13)	PD patients (n= 16)	p
Urea (mg/dl)	114.5±37.8	127.8±±26.7 (71-163)	100.0±43.8 (53-206)	0.078
Creatinin (mg/dl)	8.7±1.7	8.4±1.7 (6.1-10.9)	9.1±1.8 (6-12,7)	0.290
Ca (mg/dl)	8.9±1.1	9.0±1.1 (6.4-10.4)	8.9±1.3 (7.4-10.8)	0.935
P (mg/dl)	4.9±1.3	5.5±1.1 (4.1-7)	4.2±1.1 (2.8-5.8)	0.003
Ca*P	43.1±13.0	47.4±11.3 (29-65)	38.5±13.6 (20-62)	0.099
iPTH (pg/ml)	925.0±1069.6	1153.4±1323.9 (230-4160)	675.8±676.8 (73-2523)	0.04
Albumin(g/l)	3.8±0.5	3.9±0.2 (3.5-4.4)	3.6±0.6 (2.3-4.6)	0.075
Haemoglobin (g/dl)	10.6±2.2	11.4±1.7 (9.4-15)	9.8±2.3 (6.6-14.9)	0.066
ALP (U/L)	207.0±175.5	212.1±198.3 (17-700)	201.5±156.3 (46-505)	0.878
CRP (mg/L)	18.2±26.4	12.0±13.3 (3-47)	25.1±35.4 (22-59)	0.306

[Table/Fig-2]: Biochemical parameters of patients.

	Overall (n= 29)	HD patients (n= 13)	PD patients (n= 16)	p
Cardiovascular disease	18(62.1%)	9(69.2%)	9(56.2%)	0.455
Uraemic polyneuropathy	14 (48.2%)	6 (46.1%)	8 (50.0%)	0.600
Parathyroid adenoma	4 (13.7%)	2 (15.3%)	2 (12.5%)	0.750
Parathyroidectomy	3 (10.3%)	1 (7.6%)	2 (12.5%)	0.560
Acquired cystic disease of kidney	14 (48.2%)	7 (53.8%)	7 (43.7%)	0.750

[Table/Fig-3]: Prevalance of long term complications.

malignant change. There was no difference between PD and HD patients (p= 0.75). Prevalance of long term complications among the patients are given in [Table/Fig-3].

DISCUSSION

HD patients were older and had longer duration of dialysis in comparison to the PD patients. HD patients had higher serum phosphate and iPTH levels. The prevalence of long term complications was similar in both HD and PD modalities. Cardiovascular-related problems especially valvular heart diseases were the most common complications in both modalities.

Although the life expectancy of patients with ESRD has improved in recent years, it is still far below that of the general population. Over the last two decades, based on 2014 USRDS Annual Report, adjusted death rates fell by 9 percent from 1993 to 2002, and by 26 percent from 2003 to 2012. Moreover, 54% of HD patients and 65 % of PD patients were alive three years after ESRD [3]. In Turkey, according to Society of Turkish Nephrology 2013 Report, survival rate at the end of the 5 years is similar in HD (66,35 %) and PD 70.2% [4]. Since we have excluded the patients who commenced dialysis in our centre and then transferred to other dialysis units in subsequent years, we did not estimate survival rate of our patient groups.

According to 2009 USRDS Annual Report, new ESRD patients who choose PD as their initial treatment modality tend to be younger than those starting HD [5]. Similar to literature, we found that mean age of the PD patients were 10.8 years younger than that of the HD patients

Compared with the general population, patients undergoing maintenance dialysis have a significantly increased incidence of CVD including LVH, accelerated valvular damage, atherosclerosis, coronary heart disease. This is due to both an increased prevalence of traditional risk factors for CVD and nontraditional risk factors related to uremia [6,7]. Approximately 80% of 1846 patients enrolled in HAEMO study had some form of heart disease, prevalance of LVH was 75%, of coronary heart disease was 40%, of congestive heart failue was 40% and of valvular heart disease was nearly 50% [8]. The available evidence from a few studies, although limited due to bias, suggests that similar cardiovascular outcomes between HD and PD [9]. Kai-Chung Tse et al., showed that CVD was present 83.3% of the patients treated with HD or PD for more than 12 years, the most common types being LVH and ischemic heart disease. The prevalence of cardiovascular involvement was found similar in the PD and HD groups in this study [1].

Suskic SH et al., has evaluated 30 dialysis patients with the average length of dialysis 5.8 years. Morphological and functional changes in the valves were present in 90% of the patients, suggesting that valvular disease is extremely present in patients on chronic haemodialysis. They also reported frequency of LVH 66.6% and coronary heart disease 16.6% [10]. We have observed that CVD was present in 62.1% patients and the most frequent subgroup was valvular diseases. Our results differed from most of the other studies emphasizing that the most frequent cardiovasculer problem in ESRD was LVH. One of the possible explanations is the death of the patient as a result of CAD and heart failure in the early years of dialysis. There was no difference in prevalence of CVD between HD and PD patients. Limited number of the patients may be another possible reason for this difference.

Polyneuropathy due to uraemic toxins is a distal, motor and sensory polyneuropathy in which there is segmental demyelination, axonal degeneration, and segmental remyelination. The condition is of insidious onset and has been estimated to be present in 60 to 100% of patients on dialysis [11]. In the EPINEURIM study, carried out in Colombia in 2003, PNP was affected 30% more women than men, predominantly in those over 40, and mononeuropathy was predominant in 65.8% of case [12]. Adriana Ondina et al., investigated 27 out of 78 patients on HD treatment for six to sixty months and observed PNP in 92.6% of patients [13]. Our results showed that uraemic PNP were present in 48.2% of the patients.

CTS is the most common complication of dialysis-related amyloidosis (DRA) and can ocur due to acumulation of Beta-2 Microglobulin in carpal tunnel. Duration of dialysis treatment is significant risk factor for the development of CTS. Investigations found that one-third of chronic haemodialysis patients suffered CTS/DRA after less than 4 years of dialysis and reached nearly 100% after 20 years [14-16]. PD is associated with similar risk as HD, a finding that would be expected since there is limited removal of Beta-2 Microglobulin by PD. Three of our patients had CTS related to peripheral neuropathy. Symptoms related to CTS were present only in one patient. There was no significant difference between groups (p=0, 60).

Secondary hyperparathyroidism (SHPT) is one of the major causes of serious morbidity in long-¬term dialysis patients. Although the majority of patients are successfully managed medically, in a considerable number of patients with refractory symptoms, palliative surgical treatment is necessary. Approximately 10% of patients with ESRD undergo parathyroidectomy for SHPT [17]. The prevalence of parathyroidectomy in almost 14,180 patients who received RRT between 1983 and 1996 was 9.2% after 10 to 15 years, and increased with the duration of RRT to 20.8% after 16 to 20 years [18]. We showed that PT adenoma was present in 13.8% of patients. Parathyroidectomy was performed in 10.34% of patients (1 HD, 2 PD).

Chronic kidney disease (particularly in patients on maintenance HD or PD) is frequently associated with the development of multiple and bilateral renal cysts, which are usually less than 0.5 cm in diameter, but can be as large as 2 to 3 cm. The incidence of ACD increases progressively with duration of dialysis. Fifty to 80 percent of patients are affected after 10 years on dialysis [19,20]. In a study evaluating 130 patients with advanced renal disease or ESRD, the incidence of multiple cysts was noted to be 7 percent in those with chronic renal failure and 22 percent in those on maintenance dialysis [21]. Most patients with ACD are asymptomatic. In one review, only 14 percent of patients developed symptoms, with hematuria being most common, followed by lumbar pain and urinary tract infection. Park JH et al., examined 49 HD and 49 CAPD patients who had received dialysis therapy for at least 12 months and found that the prevalence of ACKD is not different according to the mode of dialysis, and the major determinant of acquired cyst formation is duration of dialysis [22]. The development of renal cell neoplasms ranging from adenoma to metastatic carcinoma is the most serious complication of ACD. A comprehensive review of the pertinent literature shows that there is up to 50-fold increased risk of renal cell carcinoma in ACD compared to the general population [23]. In our study, ACD was detected in 60.8% patients and renal neoplasm has been demonstrated in none of them as a complication. There was no difference between PD and HD patients.

CONCLUSION

HD patients were older than PD patients and had longer duration of dialysis. HD patients at their 10th and subsequent years of follow-up had higher serum phosphate and iPTH levels than PD patients. The prevalence of long term complications such as CVD, uremic PNP, PT adenoma, parathyroidectomy and CAD was similar in HD and PD modalities. CVD especially valvular disease was the most common complication in both modalities.

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