International Journal of Urology and Nephrology ISSN: 2091-1252 Vol. 1 (1), pp. 069-073, January, 2015.
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Full Length Research Paper

Comparison of anemia and bone metabolism in hemodialysis and peritoneal dialysis patients

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Accepted 30 September, 2014

In this study, we compared anemia and bone metabolism in patients undergone hemodialysis and peritoneal dialysis replacement therapy. We aimed to demonstrate superiority of the replacement therapies in terms of anemia and bone metabolism. The levels of serum iron, iron binding capacity, ferritin, hemogram, calcium, phosphorus and parathormone were measured in the patients. In all patients were recorded ıron, erythropoiesis stimulation therapy, phosphorus lowering medications containing calcium and active vitamin D therapy and the mean therapy doses were calculated. No differences were found in the distribution of mean age and gender and mean duration of dialysis between the groups. Mean hemoglobine and mean hematocrit values of the dialysis groups were found to be similar. Hemodialysis patient group was observed to receive erythropoiesis stimulation therapy in higher doses than the peritoneal dialysis patient group. There was not significant difference between both the groups in terms of phosphorus binding therapy and active vitamin D therapy. No significant difference was observed between the dialysis groups in terms of anemia and bone metabolism.

Key words: Anemia, bone metabolism, hemodialysis, peritoneal dialysis, superiority of dialysis treatments.

INTRODUCTİON

Replacement therapies were used in end stage renal diseases (ESRD) can be listed as peritoneal dialysis, hemodialysis and transplantation. Despite replacement therapies, expected success in morbidity and mortality could not be achieved in the patients with ESRD. However, there is no consensus on the superiority of peritoneal dialysis and hemodialysis replacement therapies in terms of the morbidity and mortality.

Incidence of cardiovascular disease which is known to be the most important cause of ESRD is reported to be 20 to 40 fold higher compared to normal population. Many factors developing in dialysis patients such as bone mineral metabolism disorders and anemia contribute to development of cardiovascular disease.

It was demonstrated that hospitalization, morbidity and mortality rates reduced by elevation of hemoglobin (Hb) levels to 11-12 g/dL, when any of hemodialysis and/or peritoneal dialysis replacement therapies were administered in the dialysis patients **[**Coyne.,2010]. In the cases of unresponsiveness to the treatment; causing factors such as inadequate dialysis, iron deficiency, fluid retention and secondary hyperparathyroidism should be eliminated and erythropoiesis stimulation should be maintained with the doses as low as possible. It is believed that, absence of fluctuations at the Hb levels and in therapy doses of erythropoiesis stimulation, affect success of the treatment [de Francisco et al., 2011].

In chronic kidney disease, physiological metabolism of the serum calcium (Ca), phosphorus (P), intact parathormone (iPTH) and vitamin D impairs by the glomerular filtration rate lower than 60ml/dk 1,73m^2 and changes may be occur in the skeletal system.While the risk for fracture increased by 20 folds in the moderate to severe chronic kidney disease compared to normal population, this risk was shown to increase by 40 folds in the dialysis patients [Nickolas,2006]. It is well known that duration of dialysis, age, gender,receiving treatment and co-morbid factors (inactivity, steroid usage) have important effect

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on the bone microarchiture in all the dialysis patients [Pelletier et al., 2012].

General approache, in the dialysis patients are initiated of 1 α hydroxyvitamin D_3 therapy when serum levels of parathormone elevated by three or five folds. As a result of close monitoring during the 1 α hydroxyvitamin D_3, phosphorus therapies containing calcium risk for the vascular calcification can be decreased by prevention of hypercalcemia. Long-term positive effects of the proper treatment on the morbidity and mortality was demonstrated [Poulikakos et al.,2014]. Levels of iPTH lower than 65 pq/mL were found to be associated with a high rate of mortality. Likewise, levels of iPTH higher than 480 pq/mL were reported to increase the risk for mortality by 1,17 folds, while levels of iPTH higher than 600 pq/mL were associated for an increase in risk by 1,24 fold [Coen,2005, Abreu et al., 2013].

It was demonstrated in the previous studies that a serum levels of Ca higher than 11mg/dL increased the risk for mortality, while the serum levels of CaxP lower than 42-52 mg^2/dL^2 decreased the risk for mortality by more than 34% [Coen, 2005, Brunkhorst, 2014].

In this study, we compared the bone metabolism and of anemia treatment in the patients undergone peritoneal dialysis and hemodialysis who were similar in terms of age, gender and comorbid factors. We aimed to demonstrate superiority of the replacement therapies.

MATERIALS AND METHODS

Thirty-six patients were received hemodialysis and 39 patients were received peritoneal dialysis therapies whose aged between 30 and 65 years and they were followed-up and treated in our nephrology clinic and undergone dialysis replacement therapy for at least 6 months were included in this study. The provision of both the patients groups to have similar gender distribution and dialysis adequacy were provided. Patients with malignancy, connective tissue disease and chronic inflammation (diabetic feet etc.) were excluded from this study. Also; patients with treatment compliance and non-voluntary were excluded from the study.

Anemia parameters and calcium, phosphorus and parathormone in order to evaluation of bone-mineral metabolism were studied in the same period. Also; the means of the therapy doses were calculated to receive the patients; including iron, erythropoietin, phosphorus binding containing calcium and active vitamin D.

Following a fasting period of 12 hours, venous blood samples were simultaneously collected from all the patients and the levels of iron, iron binding capacity, ferritin, hemoglobin, calcium, phosphorus and intact parathormone were analyzed. The ratio of Ca,x P was recorded for each patient.

Clinic and kinetics evaluations were carried out for dialysis adequacy. For this purpose, it was considered that the patients had not uremic symptoms, blood pressure to be under control, had not cardiac failure and pericarditis. The mean 24-hour urines volum of hemodialysis and peritoneal dialysis group patients were calculated and their' urine volumes found to be the less than 100-200 cc/day and it was not included to the evaluation since it was considered that residual renal function would not be effective on our the results.

At the kinetics evaluation; Kt/V was measured in the computer program of the HD apparatus (trademark, Braun Germany) for hemodialysis patients. [URR= (postdialysis urea/ predialysis urea)] formula was used to calculate URR value. Kt/V >1,4 and URR>70% were accepted as a adequate dialysis. Peritoneal dialysis patients were received continuous ambulatory peritoneal dialysis (CAPD). Change for a mean of 4 times were used in CAPD patients. CAPD 2 stay safe peritoneal dialysis solutions of 2000/2500 mL were used in CAPD patients. Glucose (1,5% glucose, 2,3% glucose) and calcium content (1,25 mmol/L, 1,75 mmol/L) of the dialysis solutions were varied according to the patient.

At the Kt/V evaluation; peritoneal Kt was taken into consideration and Watson (V= 2.447- 0.009516 (age) + 0.1704 Height (cm) + 0.3362 Weight (kg) (in males), (V= 2.097 + 0.1069 Height (cm) + 0,2466 Weight (kg) (in females)) formula was used in calculation of the total body water. Kt/V >1,7 values were accepted as an adequate peritoneal dialysis.

Hemoglobin and hematocrit values were studied with Beckman Coulter device using Beckman method. Serum levels of calcium were analyzed with Abbott Architect 1600 device using Arsenazo method, while phosphorus levels were analyzed with Abbott Architect 1600 device using Phospho Molybdate UV method and the levels of intact PTH were measured with Siemens Immulite 2000 device using Radioimmunometric method.

This study was approved by the Ethics Committee of Bakirkoy Medical Hospital and conducted in accordance with the principles of the Declaration of Helsinki. All participants were given their written informed consent prior to participation in the study.

STATİSTİCAL ANALYSİS

In this study, statistical analysis was performed using NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package software.

In evaluation of the data; Mann-Whitney-U test was used for the comparison of descriptive statistics (mean, standard deviation, median, inter qurtil range) as well as for the comparison of two groups not showing a normal distribution. Chi-square test was used to compared the qualitative data. P values < 0.05 were considered as statistically significant.

RESULTS

Comparison of demographic features of the patients

Table 1. Comparison of the hemodialysis and peritoneal dialysis patient groups demographic features and in terms of anemia, calcium, phosphorus and vitamin D metabolisms parameters.

		Hemodialysis Group	Peritoneal Dialysis Group	MW	P
Age (years)	**Mean±SD**	51.56±15.16	48.41±14.68		**0.340**
Gender (female/male)		16/32 (50.00%)	21/39 (53.80 %)		**0.747**
Dialysis duration (years)		16/32 (50.00%)	18/39 (46.20%)		**0.729**
		3.81±3.36	3.62±2.48		
Hemoglobin (g/dl)	**Mean±SD**	10.21±1.67	10.83±1.39	505.50	**0.170**
	Median (IQR)	10.35 (9.17-11.2)	10.50 (9.9-12)		
Hematocrit (%)	**Mean±SD**	31.10±5.10	32.75±4.19	517.50	**0.218**
	Median (IQR)	31.25 (27.82-34.6)	32.4 (29.8-36.2)		
	Median (IQR)	394.5 (206.25-717)	207.0 (141-390)		
Calcium (mg/dl)	**Mean±SD**	8.23±0.8	8.67±1.06	468.50	**0.072**
	Median (IQR)	8.35 (7.83-8.6)	8.6 (8.1-9.4)		
Phosphorus (mg/dl)	**Mean±SD**	4.87±1.86	5.02±1.15	528.00	**0.267**
	Median (IQR)	4.55 (3.7-5.4)	4.86 (4.23-5.57)		
intact Parathormone (pg/mL)	**Mean±SD**	587.01±574.65	451.7±326.62	578.00	**0.595**

Table 2. Comparison of the treatments of hemodialysis and peritoneal dialysis patients.

		Hemodialysis Group	Peritoneal Dialysis Group	MW	P
Erythropoietin Therapy (IU/ml)	**Mean±SD**	6547±2873.13	4835.39±3203.34	316	**0.02**
	Median (IQR)	7500 (4000-8000)	4000 (2500-6000)		
Phosphorus Binding Therapy (mg/day)	**Mean±SD**	2996.53±1060.41	2651.67±1485.38	422.5	**0.317**
	Median (IQR)	2975 (2100-3887.5)	3000 (1325-4000)		
Active Vitamin D therapy (µg/day)	**Mean±SD**	0.43±0.42	0.49±0.36	255.5	**0.302**
	Median (IQR)	0.25 (0.13-0.62)	0.25 (0.25-1)		

receiving hemodialysis and peritoneal dialysis treatment were performed , also they were compared to the mean values of hemogram, ıron, ıron binding, ferritin, Ca, P and erythropoietin,phosphorus binding containing calcium and active vitamin D treatments administered for at least 6 months.

No statistically significant difference was found between the patients given hemodialysis replacement and peritoneal dialysis therapy in terms of age distribution (p=0.340) (Table 1). No statistically significant differences were found between both groups in terms of gender distribution (p=0.747) and mean duration of dialysis (p=0.729) (Table 1).

Mean hemoglobin (p=0.170), hematocrit (p=0.218), calcium (p=0.072), phosphorus (p=0.267) and intact parathormon (p=0.595) values of the dialysis groups were found to be similar (Table 1).

Between of the dialysis groups were not found statistic-

Table 3. Comparison of the ratio of treatments in the patients received hemodialysis and peritoneal dialysis therapies.

		Hemodialysis Group		Peritoneal Dialysis Group		
EPO Therapy	**No**	0	0.00%	8	20.50%	
(n %)	**Yes**	31	100.00%	31	79.50%	**p=0.007**
Phosphorus Binding Therapy	**No**	2	6.30%	6	15.40%	
(n %)	**Yes**	30	93.80%	33	84.60%	**p=0.226**
Active Vitamin D Therapy	**No**	10	31.30%	11	28.20%	
(n %)	**Yes**	22	68.80%	28	71.80%	**p=0.780**

ally significant difference of the phosphorus binding containing calcium therapy (p= 0.317) and active vitamin D therapy (p= 0.302) (Table 2). Hemodialysis patient group was observed to receive erythropoiesis stimulation therapy in higher doses than the peritoneal dialysis patient group (p=0.02) (Table 2).

No significant difference was found between the amount of phosphorus binding therapy (p=0.226) and active vitamin D therapy that in the patients receiving hemodialysis and peritoneal dialysis therapies (p=0.780) (Table 3). The amount of receiving erythropoiesis stimulation therapy was found to be higher in hemodialysis patient group (p=0.007) (Table 3).

DISCUSSION

The number of patients undergone hemodialysis replacement therapy are more compared to the peritoneal dialysis patients worldwide. Studies have been reported to the different results about superiority of both the replacement therapies. However, recent general view is that, long-term effects of the dialysis therapies on morbidity and mortality are similar, provided the proper therapy is selected for patients [Suzuki et al., 2012, Jefferey et al., 2011].

In our the study, we compared the patient groups undergone peritoneal dialysis and hemodialysis in terms of anemia and bone diseases. No significant different was found between the patients who were regularly followed-up and treated, and were similar in age, gender and duration of dialysis, in terms of anemia.

Anemia is a complex event developing in the kidney disease . Erythropoiesis stimulation is used the most appropriate approach in the treatment, considering to prevention the comorbidity status. Opinion of the prevention fluctations of the hemoglobin levels have been accepted [Coyne, 2010]. In the studies, comparison of development of anemia and erythropoiesis stimulation in the patients receiving peritoneal dialysis with those receiving hemodialysis, different results have been obtained. Some studies were shown superiority of peritoneal dialysis on hemodialysis, since the residuel renal function protected [Jefferey et al., 2011, Synder et al., 2004]. Whereas in the different studies; it was shown that hemodialysis was as successful as peritoneal dialysis when it was initiated after opening of the arteriovenous fistula in the elective conditions and problems such as catheter infections and malnutritions were prevented and both the therapies had no different in terms of morbidity and mortality. Regularly followed-up and treatment of the patients receiving peritoneal dialysis and hemodialysis therapies were compared and hemoglobin and hematocrit values were found to be lower in the first 5 months of the treatment,in the hemodialysis patients whose hemoglobin and hematocrit values reached to similar values after the 5th month and there erythropoietin doses were administered in high doses but was not detected negative effect on the survival [Suzuki et al.,2012]. In their study, Del Vecchio, Cavalli and Locatelli (2012) was demonstrated that, iron deficiency, occult blood loss, ınflammation, oxidative stress, inadequate dialysis and hyperparathyroidism being under control that dose of erythropoiesis stimulatation would be lower and in the hemodialysis patients are the same as in the peritoneal dialysis patients would be obtained successful results with lower eritropoes stimulation [Del Vecchio, et al.,2012].

In our the study, in the patient of hemodialysis group, their' dialysis adequacy and age, gender, duration of dialysis and co-morbid factors were similar to be the peritoneal dialysis patients. Although we did not find a difference , the levels of anemia between the patient groups and also; we observed that hemodialysis patients used erythropoiesis therapy in higher doses. We believe that; the necessary for more erythropoiesis stimulation was seen in some patients due to the loss of blood in dialysis sets because of the arteriovenous fistula and worsening of anemia because of the need for dialysis in emergency conditions with catheter insertion. Different results of the treatment success in peritoneal dialysis and

hemodialysis therapies could be attributed to the existence of age, gender, duration of dialysis, dialysis adequency and co-morbid factors (occult blood loss, vascular access problems, infections etc.).

Besides of the quality of life, bone-mineral metabolism disorders and risk of fracture are very common problems and can be affected on the survival in the patients with chronic kidney disease. High or low serum levels of iPTH are lead to high levels of CaxP; therefore are contributed to ınflammation and the development of cardiovascular disease by causing vascular calcification [Pelletier etal.,2012,Coen,2005, Abreu et al., 2013]. Risk of the fracture in low turnover bone diseases is higher and it is known to increase incidence of low turnover bone disease and vascular calcification in elderly and diabetic patients, especially. Similarly; it is seen that levels of parathormone would be supressed the more easily in the peritoneal dialysis patients [Adragao et al., 2008]. Hypercalcemia can develop with the use of phosphorus binding containing calcium and active vitamin D therapy in seconder hyperparathyroidism; therefore can be contributed to the development of calcification by increasing the rate of CaxP. In conclusion, they may be negative effected on morbidity and mortality. However, it is possible to be positive effects on the mineral metabolism by regulating the treatment, dialysate content and nutrition in the dialysis patients who are regularly followed-up and treated. Especially in the treatment of low turnover bone disease has been shown that keeping dialysate contents might be positive effects on the bone turn over [Haris et al.,2006, Ambrus et al., 2010].

It has been showed in previous studies that age,

gender, body mass index, serum levels of albumin and parathormone might be affected on the bone-mineral metabolism in the dialysis patients [4 Pelletier et al., 2012, Coen,2005]. A few number of studies were compared the bone microarchitecture in hemodialysis and peritoneal dialysis patients. In one study, it was found that trabecular bone volume and tibia microarchitecture were more lower in hemodialysis patients than in peritoneal dialysis patients. This study was reported that peritoneal dialysis therapy might be positive effective for the prevention of bone disease [Yaginuma, et al.,2009]. In a study comparing the markers of bone activity and mineral metabolism, no significant difference was found between hemodialysis and peritoneal dialysis patients. However; we could not perform bone biopsy due to the technical incompetence. Bone biopsy is suggested as a gold standard in determination of bone disease in the dialysis patients. Although; this is not used widely practicable due to the technical difficulties. Limited number of studies could be performed evaluation through bone biopsy.

Recently, different results have been obtained regarding data on superiority of the dialysis replacement therapies to each other by increasing the number of studies including larger number of patients with longer duration of follow-up and treatment. Generally view is accepted that; excluding co-morbid factors of patients, the rates of morbidity and mortality in peritoneal dialysis and hemodialysis replacement therapies are indifferent provided regular follow-up and treatment.

In our study, we found that, both of dialysis groups effected similar on anemia and bone metabolism. This results were caused by the similar characteristic of both the groups (age, gender, body mass index, existence of comorbidite diseases like diabetes mellitus etc.) and the groups receiving a regular and proper therapy in the same center. However; more need for erythropoiesis stimulation in hemodialysis patient group, this condition might be associated with the characteristics of the patient group.

CONCLUSION

General view is accepted that; dialysis replacement therapies to be similar, in long term and proper replacement therapy in the proper patients also; this condition can be increased success of the treatment. We obtained similar results in our the study. We believe that; especially checking of anemia and bone- mineral metabolism can contribute to decrease of the chronic ınflammation thereby life expectancy of dialysis patients may increase.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

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