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Comparison of Serum Parathyroid Hormone (PTH) Levels in Hemodialysis and Peritoneal Dialysis Patients

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A B S T R A C T

Increase in serum PTH levels is one of the earliest disorders in mineral metabolism in patients with CKD. Since in a number of studies, high PTH levels have been significantly associated with better life expectancy in hemodialysis and peritoneal dialysis patients (114 and 117 and 133); therefore, due to the high prevalence of mineral metabolism and renal osteodystrophy in dialysis patients and the importance of parathyroid hormone in calcium and phosphate homeostasis, in this study PTH levels in hemodialysis and peritoneal dialysis patients were compared. In this cross-sectional study conducted in Ahvaz Imam Khomeini Hospital, 68 patients undergoing peritoneal dialysis and hemodialysis in the time period between March2014andFebruary2015 were selected by using convenience samplingmethod. Patients were studied in terms of age, gender, body mass index (BMI), calcium, phosphorus, alkaline phosphatase, Parathyroid hormone (PTH), number of dialysis and dialysis duration. Data were analyzed using SPSS software. In hemodialysis group, serum calcium level, phosphates level, alkaline phosphatase level and PTH level were 8.10 ± 8.40, 5.21± 4.90,574.61±390.00 and 233.00±330.89, respectively. Also, in peritoneal dialysis group, serum calcium level, phosphates level, alkaline phosphatase level and PTH level were8.59±8.50, 4.92±4.90, 374.00±251.00 and 363.76±313.50, respectively. There is a significant difference regarding calcium levels between patients on hemodialysis and peritoneal dialysis (P = 0. 001).Based on age, gender and underlying disease of diabetes, there is no significant difference regarding PTH levels between patients on hemodialysis and peritoneal dialysis (P> 0.05). In this study, it was observed that factors measured in hemodialysis and peritoneal dialysis patients, particularly PTH change with in Iranian society with low correlation and this finding could possibly be due to different genetic ora history of different underlying diseases. In this study, only calcium levels are significantly different in hemodialysis and peritoneal dialysis patients and it is suggested to put more emphasis on this variable in future studies. Moreover, it is suggested to increase information on changes in PTH levels followed by chronic kidney disease, through designing further studies and conducting longer follow-ups and evaluation of morbidities and mortalities in patients.

Introduction

Chronic kidney disease is a health-threatening problem with high mortality rate (1).The incidence of chronic kidney failure is 242 cases per 10,000 people in the world and about 8% is being annually added to this amount and today the mortality rate of this disease in America is 18% (2).Renal osteodystrophy and mineral and bone disorder (MBD) is a common clinical finding in patients with chronic kidney disease (CKD) on dialysis (stage 5) and the majority of patients at stage 3-5 CKD (3). This occurs when the GFR (glomerular filtration rate) goes below 60 ml/min/1.73 m2 (4). CKD-MBD is defined as a systemic disorder of mineral and bone metabolism, caused by impaired metabolism of calcium, phosphate, PTH and vitamin D which leads to the destruction of bone tissue, impairment of bone mineralization and growth, vascular calcification and soft tissue (3). Secondary hyperparathyroidism is a common, important and curable complication of kidney disease in later stages (5) and it is known as the most common form of osteodystrophy (6). Hyperphosphatemia and hypocalcemia and reducing the number of calcium and vitamin D receptors are among the major causes of resistance to PTH (7). PTH is a polypeptide, composed of 84 amino acids with a short half-life (2 to 4 minutes) (8) and most possibly exerts its effect by acting on the receptor activator of nuclear factor kappa B (RANK) (9) and under different physiological conditions, such as low blood calcium, it stimulates renal conversion of 25 (OH) D3 to 1.25 (OH) 2 D3 (10). Kidney patients cannot produce 1.25 (OH) 2 D3; therefore the circulating PTH levels in these patients are high. Increase in serum PTH levels is one of the earliest disorders in mineral metabolism in patients with CKD. PTH plays role in urinary excretion of phosphate and the flow of calcium and phosphate from bones (11); therefore, lack of vitamin D increases bone destruction which leads to rickets in children and osteomalacia in adults and hyperparathyroidism as well (12).At the same time, reduced kidney filtration leads to phosphate retention which again increases the secretion of PTH (13).Since in a number of studies, high PTH levels have been significantly associated with better life expectancy in hemodialysis and peritoneal dialysis patients (14-16); therefore, due to the high prevalence of mineral metabolism and renal osteodystrophy in dialysis patients and the importance of parathyroid hormone in calcium and phosphate homeostasis, in this study PTH levels in hemodialysis and peritoneal dialysis patients were compared.

Materials and Methods

After obtaining permission from the university ethics committee, in a cross-sectional study conducted in Ahvaz Imam Khomeini Hospital, 68 patients undergoing peritoneal dialysis and hemodialysis in the time period between March 2014 and February2015 were selected by using convenience sampling method. Patients were studied in terms of age, gender, body mass index (BMI), calcium, phosphorus, alkaline phosphatase, Parathyroid hormone (PTH), number of dialysis and dialysis duration. Also fasting venous blood samples were taken before starting the dialysis and without using anticoagulant. After centrifugation, serums were separated and were stored in the freezer, in 1 ml volumes and at -20 ° C until conducting the analysis. Also, analyses included measurement of serum PTH, alkaline phosphatase, calcium and phosphorus levels.

It should be noted that dialysis patients who were undergoing dialysis at least for three months and were willing to cooperate were enrolled in the study and patients who didn't provide necessary cooperation and cases of

inadequate samples and kidney transplantation were excluded. In addition, groups were unified in terms of dialysis duration. Using data from the reference article (17) the mean of the first group and the second group were 2.4 and 2.2 and standard deviation of the first group and the second group were 0.2 and 0.3, respectively. In this study, sample size in each group was determined as 27 subjects which was calculated by using NCSS software, power of 80 percent and Type I error (α=0.05). Finally, descriptive statistical methods, such as frequency tables, graphs and measures of central tendency and dispersion were used to analyze the data. Chi-square test was used and in the case of normality of data independent t-test was conducted for two groups; also, in cases of non-normal data, its non-parametric equivalent -Mann-Whitney- was used. Significance levels of these tests were considered <0.05.Data analysis was performed using SPSS software version 22.

Results and Discussion

In this study, 34 patients were included in the hemodialysis group and 34 other patients were included in peritoneal dialysis group. Mean Age in patients was 54.55±15.01 that for hemodialysis group was 56.55±13.56 and for peritoneal dialysis group was 52.55±16.29 and no statistical difference was shown in this groups (P=0.27). Also Gender differences was shown on chart 1.In hemodialysis group, serum calcium level, phosphates level, alkaline phosphatase level and PTH level were 8.10 ± 8.40, 5.21± 4.90, 574.61±390.00 and 233.00±330.89, respectively. Also, in peritoneal dialysis group, serum calcium level, phosphates level, alkaline phosphatase level and PTH level were 8.59±8.50, 4.92±4.90, 374.00±251.00 and 363.76±313.50, respectively. Serum PTH levels in hemodialysis and peritoneal dialysis patients are not different (P = 0.513).There is a significant difference regarding calcium levels between hemodialysis and peritoneal dialysis patients (P = 0. 001).There is no significant difference regarding phosphorus levels between hemodialysis and peritoneal dialysis patients (P = 0. 118). There is no significant difference regarding alkaline phosphatase levels between hemodialysis and peritoneal dialysis patients (P = 0. 208). Also, there is no significant difference regarding PTH levels between different age groups of peritoneal dialysis patients (P = 0. 185). Also, there is no significant difference regarding PTH levels between different age groups of hemodialysis patients (P = 0. 862). Also, there is no significant difference regarding PTH levels between different groups of peritoneal dialysis patients in terms of gender (P = 0. 339). Also, there is no significant difference regarding PTH levels between different groups of hemodialysis patients in terms of gender (P = 0. 659). There is no significant difference regarding PTH levels between different groups of peritoneal dialysis patients in terms suffering from underlying disease of diabetes (P = 0. 054). Also, there is no significant difference regarding PTH levels between different groups of hemodialysis patients in terms suffering from underlying disease of diabetes (P = 0. 219). There is no significant difference regarding PTH levels between different groups of peritoneal dialysis patients in terms dialysis frequency (P = 0. 650). Also, there is no significant difference regarding PTH levels between different groups of hemodialysis patients in terms dialysis frequency (P = 0. 117). There is no significant difference regarding the mean of calcium, phosphorus, and alkaline phosphatase between different groups of hemodialysis patients with different categories of PTH and there is no significant difference regarding the mean of calcium, phosphorus, and alkaline phosphatase

between different groups of peritoneal dialysis patients with different categories of PTH. Also, there is no significant difference regarding the mean of PTH and alkaline phosphatase between different groups of hemodialysis patients with different categories of phosphorus; however, the mean of calcium was lower in patients with higher levels of phosphorus. There is no significant difference regarding the mean of calcium, PTH and alkaline phosphatase between different groups of peritoneal dialysis patients with different categories of phosphorus. Also, there is no significant difference regarding the mean of PTH and alkaline phosphatase between different groups of hemodialysis patients with different categories of calcium; however, the mean of phosphorus was higher in patients with lower levels of calcium. There is no significant difference regarding the mean of phosphorus and alkaline phosphatase between different groups of peritoneal dialysis patients with different categories of calcium; however, PTH was significantly higher in patients with higher levels of calcium. Also, there is no significant difference regarding the mean of calcium, phosphorus, alkaline phosphatase and PTH between different groups of hemodialysis patients in terms of suffering from underlying disease of diabetes. There is no significant difference regarding the mean of PTH, phosphorus and alkaline phosphatase between different groups of hemodialysis patients in terms of suffering from diabetes; however, the mean of calcium was significantly lower in patients with diabetes. Also, in this study, patients in each group were divided into three levels of normal, high and low PTH. In hemodialysis group, 6 patients and in peritoneal dialysis group, 9 patients had normal PTH; so, there is no significant difference between two groups in this regard (P = 0/38).Also, in the hemodialysis group,15 patients and in peritoneal dialysis group, 18 patients had high PTH; so, there is no significant difference between two groups in this regard (P = 0/47). Finally, in the hemodialysis group,13 patients and in peritoneal dialysis group, 7 patients had low PTH; so, there is no significant difference between two groups in this regard (P = 0/11).In this study, patients in each group were divided into three levels of normal, high and low phosphorus. In hemodialysis group,16 patients and in peritoneal dialysis group, 19 patients had normal phosphorus; so, there is no significant difference between two groups in this regard (P = 0/47).Also, in the hemodialysis group,13 patients and in peritoneal dialysis group, 10 patients had high phosphorus; so, there is no significant difference between two groups in this regard (P = 0/44).Finally, in the hemodialysis group, 5 patients and in peritoneal dialysis group, 5 patients had low phosphorus; so, there is no significant difference between two groups in this regard (P = 1/00).In this study, patients in each group were divided into three levels of normal, high and low calcium. In hemodialysis group,16 patients and in peritoneal dialysis group, 27 patients had normal calcium; so, there is a significant difference between two groups in this regard (P = 0/00).Also, in the hemodialysis group,3 patients and in peritoneal dialysis group, 1 patients had high calcium; so, there is no significant difference between two groups in this regard (P = 0/31).Finally, in the hemodialysis group,15 patients and in peritoneal dialysis group, 6 patients had low calcium; so, there is a significant difference between two groups in this regard (P = 0/01).

According to the results, the only statistically significant results in this study are associated with calcium levels in hemodialysis and peritoneal dialysis patients. Also, in hemodialysis group, 16

patients and in peritoneal dialysis group, 27 patients had normal calcium; so, there is a significant difference between two groups in this regard (P = 0/00) and in the hemodialysis group, 15 patients and in peritoneal dialysis group, 6 patients had low calcium; so, there is a significant difference between two groups in this regard (P = 0/01). Also, the mean of calcium was lower in patients with higher levels of phosphorus. The mean of phosphorus was higher in patients with lower levels of calcium. PTH was significantly higher in patients with higher levels of calcium and finally the mean of calcium was significantly lower in patients with diabetes.

Before any speculation about the results of any study, it is necessary to compare the results with reports obtained from other studies; so we can achieve a better understanding of studied patients and their conditions comparing to other patients in other studies. Hence, in this section we will review other similar studies and will compare their results with the present study.

In one of these studies conducted in the U.S, Morrell Michael Avram *et al*. (1996) in a prospective study investigated the relationship between different levels of PTH and morbidity and mortality of patients who are undergoing hemodialysis and peritoneal dialysis. In this study, 175 hemodialysis patients and 113 patients with peritoneal dialysis were studied for over 9 months and their demographic characteristics including age, race, gender diabetic status and biochemical parameters such as albumin, creatinine, calcium, phosphorus and PTH were examined. This study showed that older age and lower creatinine levels are significantly associated with mortality rate in both groups. Regarding PTH levels, it was found that patients with PTH≤65pg/ml had higher (doubled) mortality rate compared with patients with PTH≥200pg/ml. Patients with higher levels of PTH have higher 5-year life expectancies –in hemodialysis patients- and higher 4-year life expectancies–in peritoneal dialysis patients- compared with those with lower levels of PTH. The study also showed that PTH has a direct correlation with albumin and serum creatinine in hemodialysis patients; however, in peritoneal dialysis patients, this correlation has been seen only with creatinine (14).However, in this study that is conducted with a smaller sample size and a shorter time period, no significant correlation was found between PTH levels and other variables and also no significant correlation was found between different levels of PTH in hemodialysis and peritoneal dialysis groups. Therefore, the results of this study are inconsistent with the study of Morrell Michael Avram *et al*. Also, Jinnan Li *et al*. (2013) conducted a study on PTH concentrations in hemodialysis patients in the US. In this study, 106760 hemodialysis patients were studied with biomarkers of PTH, Ca, P, over a period of 8 years (2001- 2009).The average age of the patients was 61±(16), 59% of them were female, 33% were black people and 59% had diabetes. This study showed that low levels of PTH (<100 pg / mL, OR: 2.45, 95% CI: 2.27-2.64) and very high levels of PTH (≥800 pg / mL: OR : 2.13, 95% CI: 1.95-2.33) are correlated with hypercalcemia and a PTH between 100-200 is correlated with hyperphosphatemia and alkaline phosphatase (18). An interesting issue is that the average age of both studies is very close; however, the majority of patients in our study are males, while in this study females constitute the majority of patients. Also, the majority of patients in this study had diabetes; while in our study, only 3.38% of patients had a history of diabetes. Regarding other findings, unlike their study there was no statistically significant results in this study.

Table.1 Mean of Ca, P, Alk.P and PTH in two Groups

Group	Variables	Mean	SD	Min	Max
Hemodialysis	**Ca**	8.1029	8.4000	3.10	9.90
	P	5.2176	4.9000	2.50	10.00
	Alk.P	574.6176	390.0000	177.00	2895.00
	PTH	330.8912	233.0000	9.30	1014.00
Peritoneal	**Ca**	8.5941	8.5000	7.80	10.30
	P	4.9265	4.9000	2.60	8.00
	Alk.p	374.0000	251.0000	20.00	2016.00
	PTH	363.7647	313.5000	21.00	1456.00

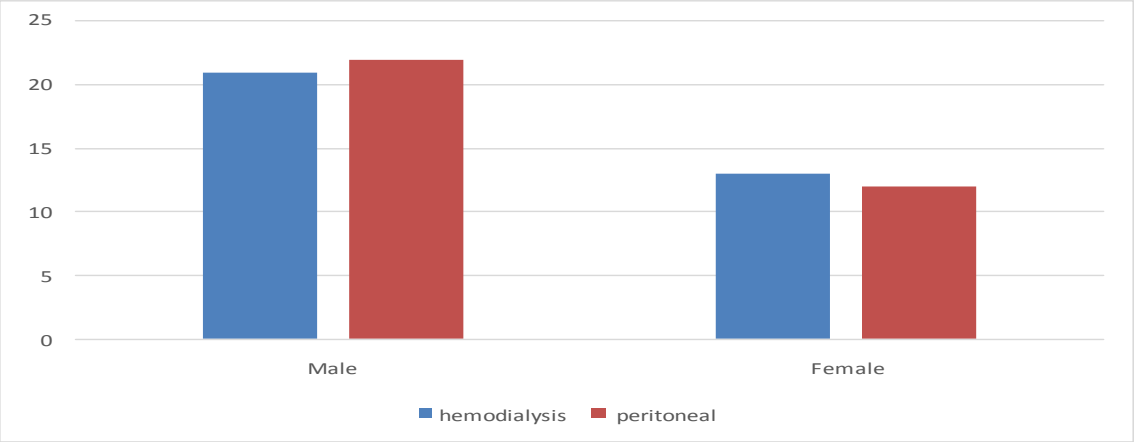
Table.2 Comparison of two Groups with level differences in PTH, P and Ca

Variable	Level	Group	Number	Percent	Mean	SD	P-Value
PTH	**Normal**	**hemodialysis**	6	17.6	218.1667	31.40966	0/38
		peritoneal	9	26.5	194.5556	27.82585	
	High	**hemodialysis**	15	44.1	604.0000	254.154	0/47
		peritoneal	18	52.9	552.2222	302.91613	
	Low	**hemodialysis**	13	38.2	67.7923	31.39948	0/11
		peritoneal	7	20.6	96.7143	41.45164	
P	**Normal**	**hemodialysis**	16	47.1	4.5125	.54391	0/47
		peritoneal	19	55.9	4.6000	.54772	
	High	**hemodialysis**	13	38.2	6.9462	1.33829	0/44
		peritoneal	10	29.4	6.4500	.68840	
	Low	**hemodialysis**	5	14.7	2.9800	.32711	1/00
		peritoneal	5	14.7	3.1200	.31145	
Ca	**Normal**	**hemodialysis**	16	47.1	8.7062	.25682	**0/00**
		peritoneal	27	79.4	8.6593	.29255	
	High	**hemodialysis**	3	8.8	9.7667	.15275	0/31
		peritoneal	1	2.9	10.3000	.	
	Low	**hemodialysis**	15	44.1	7.1267	1.31826	**o/o1**
		peritoneal	6	17.6	8.0167	.17224	

Table.3 Comparison of Ca, P, Alk.P and PTH in Diabetic and Non-Diabetic Patients

Group	Variables	Diabetic Status	Number	Mean	SD	P-Value
Hemodialysis	**Ca**	Diabetic	15	8.4000	1.64056	P>0.05
		Non-Diabetic	19	7.8684	.87372	
	P	Diabetic	15	5.1400	1.93973	P>0.05
		Non-Diabetic	19	5.2789	1.58730	
	Alk.p	Diabetic	15	412.1333	157.70264	P>0.05
		Non-Diabetic	19	702.8947	697.30719	
	PTH	Diabetic	15	258.3533	274.81732	P>0.05
		Non-Diabetic	19	388.1579	317.75659	
Peritoneal	**Ca**	Diabetic	11	8.6273	.33494	**P<0.05**
		Non-Diabetic	23	8.5783	.53339	
	P	Diabetic	11	4.5364	.86403	P>0.05
		Non-Diabetic	23	5.1130	1.37620	
	Alk.p	Diabetic	11	424.3636	536.90377	P>0.05
		Non-Diabetic	23	349.9130	296.74153	
	PTH	Diabetic	11	221.4545	141.96011	P>0.05
		Non-Diabetic	23	431.8261	333.14870	

Chart.1 Gender Difference in Patients



Also, Morrell M. Avram *et al*. (2001) conducted a study in the U.Sto investigate the importance of low levels of PTH as a predictor of mortality in hemodialysis and peritoneal dialysis patients. In this study, 345 hemodialysis and 277 dialysis patients were followed up and studied for 14 years. Results showed that life expectancy is significantly higher in PTH levels over200. For hemodialysis and peritoneal dialysis patients, age and duration of hemodialysis are inversely correlated with PTH levels. This is while, the black race, creatinine and phosphorous have direct correlations with PTH levels. Also, PTH levels lower than expected levels are accompanied with increased mortality (15) and these findings are inconsistent with the results of our study, too. In Iran, Abbas Ali Zeraati *et al*. (2013), in a study investigated the relationship between serum zinc levels and serum PTH levels in hemodialysis patients. This cross-sectional study was conducted in Imam Reza (AS) Hospital, Mashhad in 2011. In one group, hemodialysis patients (30 patients) who were on hemodialysis on a regular basis and were undergoing dialysis at least for three months and had a minimum age of 15 years and had a stable condition in the last two months were enrolled. Levels of zinc, calcium, phosphorus, PTH, albumin and alkaline phosphatase were measured. In hemodialysis patients, nosignificant correlation was observed between serum zinc levels and PTH levels. Also, no significant correlation was observed between serum zinc levels andserum calcium, phosphorus, albumin and alkaline phosphatase levels. However, in hemodialysis patients, a significant correlation was observed between serum albumin levels and PTH levels (19). In this study-that its study population is much closer to the present study- more consistent results are also observed; because less statistically significant relationships were observed between studied variables. In fact, in this study and in our study, it was observed that factors measured in hemodialysis and peritoneal dialysis patients, particularly PTH change within Iranian society with low correlation and this finding could possibly be due to different genetic or a history of different underlying diseases.

Conclusion

In addition, as mentioned earlier, in this study only calcium levels are significantly different in hemodialysis and peritoneal dialysis patients and it is suggested to put more emphasis on this variable in future studies. Moreover, it is suggested to increase information on changes in PTH levels followed by chronic kidney disease, through designing further studies and conducting longer follow-ups and evaluation of morbidities and mortalities in patients.

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