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Evaluation Bone Disease in Hemodialysis Patients

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Abstract: Renal osteodystrophy is one of the most common potentially debilitating complications affecting patients with chronic renal failure. The most reliable markers of bone turnover are intact PTH,and bone alkaline phosphatase. The evaluation of bone mineral densitometry is a useful tool for the detection of hyperparathyroid bone disease. The aim of this study, was the evaluation of effects of hemodialysis on metabolic bone disease in patients with chronic renal failure. A prospective and analytical study was performed to evaluate the bone disease in hemodialysis patients from 2004 to 2005 in hemodialysis ward of Emam Khomeini hospital of Tabriz medical university. Thirty hemodialysis (14 male) patients and 30 non- hemodialysis patients (13 male) with chronic renal failure (Glomerular Filtration Rate <20 mL min^{-1}) as control groups, were enruled the study. Bone mineral densitometry of vertebral spine and neck of femur were performed in all patients. X-ray was performed at knee and wrist in the all patients. Data analyzed by SPSS 11.5 software and T-test and Chi-Square test and the level of meaningfulness was considered as $p<0.05$. The mean of alkaline phosphatase in hemodialysis patients was 301.53±250.10 mg dL^{-1} and in non-hemodialysis patients was 248.53±106.52 mg dL^{-1} ($p = 0.290$). The mean of intact parathyroid hormone in hemodialysis patients was 69.17±45.41 pg mL^{-1} and in non-hemodialysis patients was 66.64±46.94 pg mL^{-1} ($p = 0.833$). The mean of Z score of Spine in hemodialysis patients was -1.25±1.15 and in non-hemodialysis patients was 0.45±1.35. ($p = 0.000$). The mean of Z score of femur in hemodialysis patients was -0.45±1.54 and in non-hemodialysis patients was 1.2±1.01 ($p = 0.000$). This study showed a marked decrease in bone mineral density in a high number of dialysis patients. Z score was significantly lower in hemodialysis patients comparing non-hemodialysis patients. Bone mineral densitometry is useful method in evaluation of bone disease in hemodialysis patients.

Key words: Hemodialysis patients, bone disease, bone mineral densitometry

INTRODUCTION

Kidney function impairment leads to disturbance in metabolism of many substances. The after-effects are found in all tissues and organs of the body. One of the most affected tissues is bone. It has been known for over 100 years that bone disease accompanies renal failure and renal bone disease is one of the most common potentially debilitating complication affecting patients with chronic renal failure (Yonova and Dukova, 2004). There are several pathophysiologic mechanisms, which lead to different types of renal osteodystrophy. The common characteristic for all of them is worsening of the quality of bone followed by loss of bone tissue with a decrease of its biomechanical stability. Definitive diagnosis of renal osteodystrophy is made by a bone biopsy sample examination and bone histology remains the gold standard for the diagnosis of renal osteodystrophy and the distinction between high and low bone turnover disease. However, bone biopsy is an invasive procedure accompanied by technical difficulties in the processing and studying of the specimens and because of its invasiveness this method is not suitable for routine clinical practice and is often re-placed by non-invasive procedures like assessment of biomechanical stability according to bone mineral density and bone turnover according to markers of osteoblast and osteoclast activity. Renal osteodystrophy reaches its maximum in-patients dependent on kidney function replacement and in all forms leads to predominant damage of cortical bone. Bone mineral density was shown to be the most accurate predictor of the risk of bone fracture (Antonsn *et al*., 1999). The physiological bone turnover is necessary for a steady, good biomechanical stability of bone high as

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well as a low one leads to a decrease of the bone mineral density (Baskn *et al*., 2004). The most reliable markers of bone turnover are intact Parathyroid Hormone (iPTH), bone Alkaline Phosphates (ALP) and in-patients without liver disease also total alkaline phosphates. There are various patterns of the types of bone turnover in different centers. The relationship between markers of bone turnover and bone mineral density is discrepant (Baskn *et al*., 2004). For that reason, specific and sensitive serum biochemical markers are required for monitoring bone turnover in uremia. The ideal biochemical marker of bone turnover should be unique to bone and reflect total skeletal activity and be well correlated with histomorphometric and radiocalcium kinetics results:

- Serum alkaline phosphates has been used as a biochemical marker of bone disease for many years. But total alkaline phosphates originates from different organs (liver, bone, intestine, placenta etc.) and sometimes it lacks specificity. In the last decade it has been shown that measurement of iPTH is a useful predictor of bone histology and a noninvasive tool in distinguishing between high turnover, normal and low turnover bone disease in large patient groups.
- However, in an individual patient serum iPTH alone is frequently unable to distinguish adynamic bone from hyperparathyroid bone disease.
- Combined with other biochemical markers it may be useful in solving this problem (Baskn *et al*., 2004).

Skeletal complications in maintenance hemodialysis were first reported in the early era of hemodialysis (Hasegawa *et al*., 2004) which slightly varies among dialysis centers and has some relation-ship to dialysis duration (Antonsn *et al*., 1999). It was reported that in hemodialysis patients, Bone Mineral Densitometry (BMD) in the vertebrae or illume is preserved, but BMD at the distal radius site is reduced (Hasegawa *et al*., 2004). Until now trabecular and cortical BMD have been assessed separately at different sites, e.g., vertebrae for assessment of trabecular bone and forearm, metacarpus and total body for that of cortical bone (Hasegawa *et al*., 2004). In addition, complete information regarding bone structure and architecture in hemodialysis patients has not been available. It is necessary to measure trabecular and cortical bone separately at the same site and to examie both bone structure and architecture for a more accurate analysis of metabolic bone disease in hemodialysis patients (Hasegawa *et al*., 2004).

Purpose: The aim of this study was the evaluation of effects of hemodialysis on metabolic bone disease such as bone cysts, osteoprosis and detect laboratory, radiological and clinical marker and predictive value of them on bone disease. Also relation between biochemical markers and BMD and dialysis duration in hemodialysis patients were studied.

MATERIALS AND METHODS

In a prospective and analytical study that were performed for evaluation of effects of hemodialysis on metabolic bone diseases in chronic renal failure patients (comparing hemodialysis patients with non-hemodialysis patients), Hemodialysis patients selected randomly from patients of hemodialysis ward of Emam hospital that were under hemodialysis over than one year duration 2004 to 2005.

The present study was based on 30 patient's undergoing hemodialysis. Fourteen of patients were male and sixteen of them were female. Mean of age in male patients was 36.92±15.25 years and in female patients was 34.68±11.99 years. Dialysis duration in male patients was 18.07±6.05 months and in female patients was 18.93±5.28 months. As a control group (age and gender match with hemodialysis group), Thirteen of the patients were male and seventeen of them were female. Mean of age in male patients was 33.38±10.85 years and in female patients was 37.23±12.77 years.

Significant difference was not found between means of age in two groups of patients and two groups of patients match in age ($p = 0.960$) and significant difference was not found in gender distribution in two groups ($p = 0.795$). Subjects who were under medical treatment for conditions known to affect bone metabolism such as hyperthyroidism, liver disease, collagen disease, or ovarian tumors and patients who had had a hysterectomy were excluded from the study. All subjects who had a history of symptomatic fractures of the hip, radius or vertebra were also excluded. All patients and controls got informed consent prior to the study. The serum level of intact PTH, total alkaline phosphates, Calcium (Ca^{+2}), phosphor, urea, Creatinine (Cr), Hemoglobin (Hb), Sodium (Na^{+}) and Potassium (K^{+}) were measured in all patients. Bone mineral densitometry of the spine vertebral and neck of femur were performed in all patients and x-ray of knee and wrist performed in all patients. Other demographic information such as age, gender and dialysis duration collected from patients documented. Descriptive finding reported as mean±S.D (SD) and frequency.For analysis data, used SPSS 11.5 for windows and T-test,Chi-square test and perason correlation. The level of meaningfulness was considered as $p<0.05$.

Table 1: Laboratory finding in two groups of patients

	HD		NHD		
Variable	Mean	S.D	Mean	S.D.	P V
Body Mass Index (kg m^{-2})	20.54	4.10	21.37	3.07	0.380
Calcium (md dL^{-1})	8.66	0.74	8.99	.63	0.070
Phosphor (mg dL^{-1})	5.93	1.40	4.87	1.26	0.003*
ALP (IU L^{-1})	301.53	250.10	248.53	106.52	0.290
iPTH (pg mL^{-1})	69.17	45.41	66.64	46.94	0.833
Urea (md dL^{-1})	125.7	38.4	58.4	7.4	0.000*
Creatinine (md dL^{-1})	8.8	2.3	2.6	.6	0.000*
Na^+ (meq L^{-1})	140	2	138	3	0.833
K^+ (meq L^{-1})	4.8	0.4	4.9	.8	0.741

*-Significant

Table 2: Results of X-ray of wrist and knee in all patients

		Wrist X-ray*		Knee X-ray**	
Groups	Gender	Normal	Abnormal	Normal	Abnormal
Hemodialysis patients	Male	5	9	9	5
	Female	9	7	11	5
Non hemodialysis	Male	9	4	12	1
patients	Female	17	0	16	1

*: p = 0.001, **: p = 0.011

RESULTS

Laboratory finding in 2 groups of patients show than in Table 1. Results of X-ray of wrist and knee inding in two groups of patients show than in Table 2 and BDM finding in all patients showes in Fig. 1 and 2.

The mean of Z score of Spine in hemodialysis patients was -1.25±1.15 and in non-hemodialysis patients was 0.45±1.35. (p = 0.000). The mean of Z score of femur in hemodialysis patients was -0.45±1.54 and in non-hemodialysis patients was 1.2±1.01 (p = 0.000).

Liner`s correlation between parameters: Z score of Spine tubercle had a significant negative liner correlation with serum phosphor of all patients (p = 0.021).

Z score of femur had a significant negative linear correlation with serum phosphor of all patients (p = 0.006).

Z score of Spine tubercle had a significant positive linear correlation with serum calcium of all patients (p = 0.045).

Z score of femur had a significant positive linear correlation with serum calcium of all patients (p = 0.019).

Z score of Spine tubercle had a significant positive linear correlation with Z score of femur of all patients (p = 0.045).

Intact PTH had a significant positive linear correlation with age of all patients (p = 0.000). Intact PTH had not a significantly positive liner correlation with other laboratory parameter in all patients (p = 0.000).

ALP had not a significant positive linear correlation with laboratory parameter in all patients (p>0.05).

Serum calcium had a significant negative linear correlation with serum urea of all patients (p = 0.011).

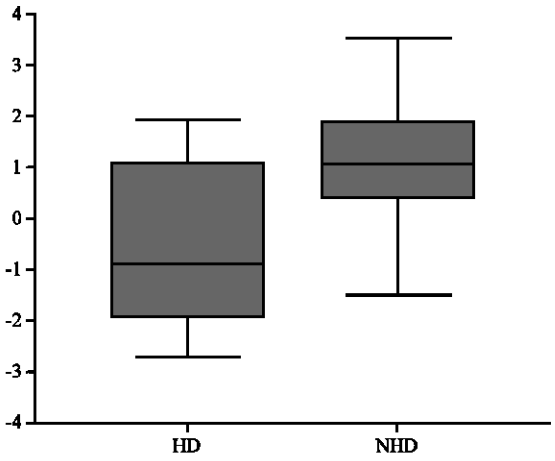

Fig. 1: Comparison Z scores of Spine between two groups of patients. HD: Hemodialysis patients, NHD: Non- Hemodialysis patients

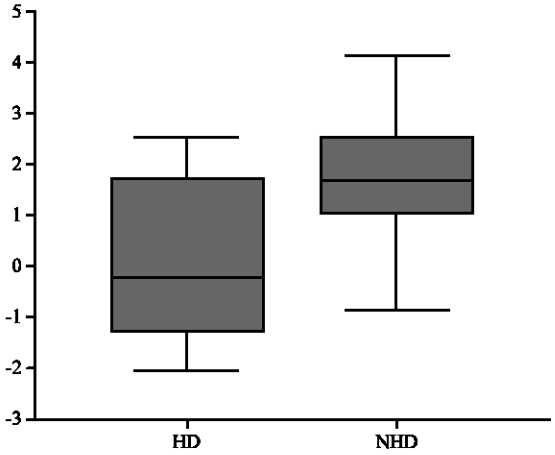

Fig. 2: Comparison Z scores of Femur between two groups of patients. HD: Hemodialysis patients, NHD: Non- Hemodialysis patient

Serum phosphor had a significant positive linear correlation with serum urea of all patients (p = 0.017).

Serum Cr had a significant positive linear correlation with serum phosphor of all patients (p = 0.016).

Serum Cr had a significant negative linear correlation with serum urea of all patients (p = 0.000).

Dialysis duration in hemodialysis patients had No significant linear correlation with laboratory parameter in all patients (p>0.05).

Hb had a significant positive linear correlation with serum phosphor in all patients (p>0.05).

DISCUSSION

BMD of hemodialysis patients was not significantly different from that of the control group. In contrast, BMD

was significantly decreased in hemodialysis patients in comparison with control group (Hasegawa *et al*., 2004).

Hasegawa *et al.* (2004) reported that 72% of patients with end-stage renal failure have some form of histologically apparent bone disease before the commencement of hemodialysis. Moreover, it has been found that a long d-HD will cause skeletal complications (Hasegawa *et al*., 2004).

In the present study, HD duration of our subjects ranged from 13-36 months.

It was found that both hemodialysis and chronic renal failure, or chronic renal failure itself influenced the bone condition of the patients (Hasegawa *et al*., 2004).

In practice, however, it is difficult to distinguish between the skeletal complications of hemodialysis and those of renal failure itself. It is therefore, necessary to assess the state of bone both accurately and harmlessly when treating patients by hemodialysis or for chronic renal failure (Hasegawa *et al*., 2004).

In this study, bone alkaline phosphates indicated no significant correlation with iPTH.

The evaluation of bone turnover should include a combination of different markers so that the balance between bone formation and bone resorption can be evaluated. Alkaline phosphates and osteocalcin seem to be good markers for bone formation but measurement of other markers such as pyridinoline are needed to determine bone resorption (Baskn *et al*., 2004).

In the present study, we used measurement of ALP and iPTH to evaluate of bone disease in hemodialysis patients.

Hyperparathyroid (high turnover) bone disease in-patients with chronic renal failure is found most frequently followed by mixed osteodystrophy, low-turn over bone disease and osteomalasia (Tokumoto *et al*., 2004).

In our study, mean of iPTH in hemodialysis patients was higher than that non hemodialysis patients and normal range and not significant.

Greater level of Parathyroid Hormone (PTH) than normal level is required to maintain appropriate bone turnover in dialysis patients. The skeletal resistance to PTH is the most important genesis of this phenomenon and the mechanism has been elucidated by the recent molecular biological techniques. Insufficient level of PTH induces not only adynamic bone disease but also cardiovascular diseases by ectopic calcification in soft tissues (Shiizaki *et al*., 2004).

In children with ESRF the degree of osteopenia is correlated with laboratory markers of renal osteodystrophy and patients with biochemical findings of secondary hyperparathyroidism are more osteopenic than the others (Bakr, 2004).

In the present study, no significant linear correlation between Z-score of spine tubercle and femur with age ($p>0.05$).

Renal osteodystrophy is a metabolic bone disease and a common complication of end-stage chronic renal failure and maintenance dialysis treatment.

Quantitative bone scintigraphy is a sensitive and useful method for evaluating bone metabolism in hemodialysis patients (Kurata *et al*., 2004).

In this study, we used BMD for evaluation bone disease in CRF patients.

In chronic renal failure, hyperphosphatemia, hypocalcemia, hyperparathyroidism, reduced activation of vitamin D, decreased level of calcium-sensing receptor, osteitis fibrosa and osteomalacia are features related to calcium abnormalities. Hyperparathyroidism is a risk factor for survival of hemodialysis patients as well as hypoparathyroidism, which is another feature in hemodialysis patients (Morii *et al*., 2004).

In the present study, Z-score of spine tubercle and femur had significantly liner correlation with Ca^{+2} of serum ($p<0.05$).

Bone remodeling is a continuous process of removal of microscopic amounts of bone tissue due to synchronized actions of osteoclasts and osteoblasts with the purpose of renewal and repair of bone tissue (Kusec and Smalcelj, 2004).

Hemodialysis patients had significantly lower values for cortical bone area, cortical thickness, moment of inertia and polar moment of inertia than the age-matched controls (Hasegawa *et al*., 2004).

In this study, mean of Z-score in spine tubercle and femur in hemodialysis patients were significantly lower than mean of Z-score in control groups.

Renal osteodystrophy may present with low, normal, or high bone turnover (Malluche *et al*., 2003).

In an unselected population of ESRF patients already, 62% of them have an abnormal bone histology (Spasovski *et al*., 2003).

Increase in radial BMD may not be a useful marker of the improvement in bone lesions in ABD patients (Nakashima *et al*., 2003).

In the present study, abnormality of X-ray of radius in hemodialysis patients was significantly higher than non hemodialysis patients and also we get good information for evaluation bone disease in hemodialysis patients and BMD finding was significantly differ in two groups.

Determination of plasma Parathyroid Hormone (PTH) is routinely performed to diagnose and monitor renal bone disease. Whole PTH and intact PTH assays give similar information (Reichel *et al*., 2003).

CONCLUSION

Renal bone disease is one of the most common potentially debilitating complication affecting patients with chronic renal failure. This study showed that a marked decrease of bone mineral density affects a high number of dialysis patients. Mean of phosphor in hemodialysis patients was significantly higher than non-hemodialysis patients ($p = 0.003$).

Significant difference was not found between mean of iPTH in two groups of patients ($p = 0.833$). Mean of Z score of Spine tubercle in non-hemodialysis patients was significantly higher than hemodialysis patients ($p = 0.000$). Mean of Z score of Spine tubercle in non-hemodialysis patients was significantly higher than hemodialysis patients ($p = 0.000$).

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