TIBIAL ULTRASOUND EVALUATION OF BONE DENSITY IN DIALYZED PATIENTS

DIYALIZE HASTALARDA KEMIK YOĞUNLUĞUNUN TIBIAL ULTRASONOGRAFIK DEĞERLENDIRILMESI

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ÖZET

Son dönem böbrek yetmezi iMi hastalar(SDBY), hastalığa bağlı ve genel faktörlerin etkisi ile düşük kemik yoğunluğuna (KY) sahip olma riski taşırlar. Bu çalışmada diyaliz hastalarında kortikal KY, tibial ultrasonografik yöntemle değerlendirildi ve ostec neni risk faktörleri araştırıldı. Çalışmaya 40 SDBY'li vz 37 sağlıklı kontrol alındı. İki grup genel risk faktörleri açısından homojendi. Tibial ses hızı (SH) ve t skoru Soundscan 2000 cihazı ile değerlendirildi. Bu değerler SDSY'li hastalarda anlamlı olarak düşük bulundu(p=0.001). Hemodializ ve devamlı ayaktan periton diyalizi hastaları arasında SH ve t skoru açısından fark bulunamadı. Serum iPTH ve diyaliz süresi ile bu parametreler arasında negatif korelasyon saptanırken; yaş, vücut kitle indeksi ve heparin kullanımı ile korelasyon saptanmadı. Diyaliz hastalarında kortikal KY ve kemik kalitesi düşüktür, olası kırık riski fazladır.

Anahtar kelimeler: Kemik yoğunluğu, ultrason, diyaliz

SUMMARY

End stage renal disease (ESRD) patients are at risk of having low bone density (BD) due to disease related and general risk factors. This study was to designed to assess the cortical BD and risk factors, by tibial ultrasound evaluation, in dialysis patients. We included 40 ESRD patients and 37 healthy subjects with matched properties for osteopenia. Tibial ultrasound velocity (TUV) and t score were investigated by Soundscan 2000 device. ESRD patients had lower TUV and t score than control subjects(p=0.001). BD did not change between hemodialysis and continuous ambulatory peritoneal dialysis patients. Serum iPTH levels and dialysis duration negatively correlated with SOS and t scores. No such correlation was found out for age, BMI and heparin exposure. Cortical BD lessens and quality deteriorates increasing probability of fractures in cortical bone in dialysed patients.

Key Words: Bone density, ultrasound, dialysis

INTRODUCTION

End stage renal disease (ESRD) patients are at risk of having low bone density (BD) in both cortical and trabecular bones, due to metabolic, endocrine disorders and drug exposure in addition to general risk factors of osteopenia (1). Reduced BD have been found out in various sites of the skeleton in most of the studies (2,3), whereas some investigations failed to demonstrate such a reduction, in ESRD (4). Disease related risk factors like hyperparathyroidism, chronic acidosis, previous immunosupressive therapy, secondary amenorrhea and malnutrition as well as general risk factors like age, sex, body mass index (BMI), menopausal status, parity, smoking, alcohol intake, mobility, diary intake and drug exposure having either bone formation or resorption effect, all have small or big contributing roles in origination of BD (5,6). Although BD is known to be a good determinant of bone strength and future fractures, turnover and microarchitectural quality of bone were shown to be additional, important determining factors in fracture origination (3,7).

QTU is a precise assessment method of BD, without exposing the patient to radiation risk (8). In this method, spreading velocity of ultrasound waves on the

longitudinal surface of a cortical bone is measured. Tibial ultrasound velocity(TUV) has been shown to have significant correlations with BD and material properties of tibial cortical bone(9) as well as BD of other probable fracture sites like spine and femur(8,10). This study was designed to assess the cortical BD, bone microarchitecture quality and the effect of risk factors on BD, by QTU evaluation in dialysis patients.

PATIENTS AND METHODS

Regular hemodialysis(HD) or continuous ambulatory peritoneal dialysis(CAPD) patients, in Nephrology Dept. of Trakya University Hospital were included in the study. Patients with metabolic and systemic disorders and using drugs known to effect bone metabolism other than low dose Vitamin D and elemental calcium, were excluded. 17 female and 21 male, totally 38 dialysis patients agreed to participate in the study. Of these patients 28 were on regular HD and 10 on CAPD. Thirty-seven healthy control subjects matched for general risk factors were also included. Data on general risk factors, such as age, gender, BMI, smoking, alcohol intake, coffee drinking, diary nutrition, mobilisation, menopausal and parity status as well as on disease related factors like duration of dialysis, secondary amenorrhea, parathyroidectomy and underlying renal pathology were collected either from medical records or by physical examination, where necessary. TUV and t score values were measured by Soundscan 2000 (Myriad Ultrasound System). Middle point of tibia was chosen as the QTU application area because this region consists low amount of soft tissue. The average TUV in an individual patient was supplied by taking 10 highest TUV values measured into account. Serum calcium (Ca), phosphorus (P), intact PTH (iPTH) and total protein(TP) were measured in all patients and subjects in blood samples. TUV and t score values in both groups were defined and compared. Also this comparison was made between HD and CAPD patients and between the groups constituted according to the underlying renal pathology. The correlations of age, BMI, dialysis duration and serum iPTH with TUV and t score values were investigated in patient group. Additionally, the patients were classified according to iPTH levels as having low turnover (<100 pg/ml), normal (between 100 and 300 pg/ml) and high turnover (>300 pg/ml) bone disease. Comparison was also made among these subgroups. Statistic analysis was performed in "SPSS for Windows" program by using Mann Whitney U, Chi Square, Posthoc Student-Newmann-Keul-Duncan and Spearman Rank correlation tests.

RESULTS.

No statistically significant difference was found out in terms of age, gender and BMI between the patient and the control group(p>0,05). Mean age and and BMI(kg/m^2) values were 44.0 ± 13.8 and 21.9 ± 3.06 respectively in patient group while were 41.3 ± 11.9 and 23.6 ±3.9 in control group (p>0,05). The groups were homogenious in terms of mobility and all nutritonal habbits as well as menopausal and parital status. Of the women patients, %41.2 were in postmenopausal period while %33,3 of control subjects were postmenopausal(p>0,05). We met only one patient and one subject having had prior parathyroidectomy, and only four(23.5%) patients with secondary amenorrhea, so we could not use these parameters in statistical analysis.

Mean TUV and t score values as well as laboratory findings of the patients and control subjects are demonstrated in Table I. We found out TUV and t score values to be significantly lower in patient group. Serum iPTH, P and ALP levels showed significant increase in this group.

Tqble I: TUV, t score values and laboratory findings in both g.oups.

	Dialysis Patients	Control group	Significance
TUV (m/sn)	3731.2±228.7	3977.0Ü20.4	p<0.001
t score	-2.21i2.06	0.013±l.1	p<0.001
PTH (pg/ml)	249.4±308.4	11.4±16.5	p<0.001
Ca (mg/dl)	10.2Ü.4	10.7±0.2	p > 0.05
P (ng/dl)	**5.7±1.8**	3.7±0.7	p<0.001
TP (g/dl)	6,74±0,62	7,49±0,42	p<0.001

In patient group, 28 patients were being managed by regular HD therapy, while 10 were performing CAPD themselves. The mean TUV and t score values we measured in HD group (3722.4±236.2; -2.29±2.1, respectively) were not significantly different from the values determined in CAPD group (3755.8±216.3; -2.0±1.97),(p>0.05). On the other hand, QTU results in male patients of the patient group when compared with those of female patients were not different. The mean TUV and t score in male patients were 3679,7±223,6 and -2.69±2.03 consecutively, whereas in female patients were 3772.9±229.5 and -1.8±2.06 (p>0.05). BMI and age were not in any correlation with TUV and t score. However dialysis duration(R:- 0.33, p= 0.045)

and serum iPTH (R:- 0.33, p=0.048), inversely correlated with TUV. In ESRD patients with high-turnover bone disease, TUV and t score values in tibia were significantly lower when compared with normal and low turnover groups **(Table II).** Patients with heparin exposure did not have low BD values(p>0,05).

Table II: TUV and t score values of dialysis patients in various bone turnover types.

	TUV	t score
Low turnover (PTH<100pg/ml) (n=18)	3788.8Ü77.6	- 1.7±1.6
Normal turnover (100>PTH>300pg/ml) (n=8)	3811.2±160.9	- 1.4±1.4
High turnover (PTH>300pg/ml) (n=12)	3579.9±292.0*	-3.8±2.4*
SIGNIFICANCE	*p<0.05	*p<0.05

The main underlying renal pathologies in ESRD patients were glomerulonephritis, pyelonephritis and reflux nephropathy in the study. BD and bone quality in reflux nephropathy patients were found out to be lo *ver* than the patients with other renal pathologies **(Table III).**

Tablo III: BD and quality indicators in patients with various underlying renal pathologies.

UNDERLYING RENAL PATHOLOGY	TUV	T score
Idiopathic (n=4)	Insufficient case amount for statistics.	
Glomerulonephritis (n=18)	3772.8±195.4	- 1.8±1.7
Pyelonephritis (n=8)	3810.7Ü51.6	**- 1.5*1.3**
Reflux nephropathy (n=8)	3528.1±282.8*	- 4.6±2.5*
SIGNIFICANCE*	*p<0.05	*p<0.05

DISCUSSION

Despite the fact that, BD measurement does not seem to be a good tool to monitor the renal bone disease process, it has been consistently accepted that, investigating BD is an important part of predicting the future fractures(1,11). In this study we used QTU, a precise and reliable method, able to assess BD as well as bone quality without radiation risk and able to evaluate cortical bone involved dominantly in ESRD (9,11,12). Most reports have claimed BD to be lower in ESRD patients (2,3,13). On the other hand some of the authors have not reported osteopenia (4). Osteopenia is a consequence of many complicated factor interrelations. The control group homogenisation in BD studies should be given extreme importance. Perhaps, inconsistency in the results originates from different study designs. We found out mean TUV and t score values in ESRD patients to be lower than those of control subjects. Bone loss is believed to begin with disease onset prior to commencement of dialysis (14). We could not have opportunity to investigate disease duration on BD because of limited data on the disease onset. Gabay et al reported no bone mineral density (BMD) difference between HD and CAPD patients in lumbar spine, femoral shaft and femoral neck using DEXA (3). However, Mottet et al found out HD patients to have lower BD than CAPD patients in tibial diaphysis that is mainly cortical bone (15) They thought this kind of a difference might be due to higher residual renal function in their CAPD patients. Our finding did not support this claim. QTU has an advantage of evaluating bone material properties, that is not the case in DEXA.

Age did not seem to effect BD in our patient population. Asaka et al reported age factor to correlate with total BMD in female HD patients, but not in male patients(16). However, Aguado et al demonstrate no correlation of age with BD at any skeleton sites with DEXA in premenopausal female patients(17). In a study investigating BD by QTU, TUV seemed to decline with age, beginning from the fourth decade(10). As our patients had a low mean age of 44 and most of the relatively little amount of women in patient group were premenopausal, we think age did not have a great influence on BD, in such conditions. Perhaps disease related factors had more dominant effect than age did on BD, changing normal decline by age. The same thing might have happened for BMI parameter in our patient group. Rix et al claimed BMI to be a strong predictor of BMD in predialysis patients(l). However our study findings in dialysed patients were not so, similar to Aguado et al's findings suggesting no influence of weight on TUV(17).

There exists another controversy about effect of duration dialysis on BD, in studies using DEXA. Many investigations determined a negative correlation between BMD and dialysis duration(3,13), while some not(18). Adversely, some authors reported bone gain within the first year of dialysis which they think might

be due to improvement in uremic state or supplementation of 1,25 dihydroxy-vitamin D(19). In a study using QTU like we did, a negative correlation was found out and this finding was confirmed in our study(13). Deterioration of bone quality additional to bone loss continuing during dialysis period may be responsible for this correlation and this process can successfully determined by QTU, in cortical bone which this deterioration is more prominent.

The effect of hyperparathyroidism(HPT) have been demonstrated to begin in early stages of ESRD(1). As GFR declines and during dialysis period, many patients exhibit impaired bone mineralisation due to HPT(1). Although some authors reported no correlation between BMD and PTH(20), many studies opposed to this data by finding low BD in high turnover bone disease caused by HPT(5,16). HPT causes increased bone resorption which is more dominant than increased bone formation, leading BD decreases(5). Also prior parathyroidectomy has been shown to improve BD in some studies confirming this effect of HPT(21).

Stein et al have reported percentage of secondary amenorrhea to be 20% in women with ESRD and found out BD to be lower in these women(14). We only could found out 4(23.5%) premenopausal women with secondary amenorrhea history, thus could not analyse BD differences in this group. BD reduction may be due to absence of sex hormones with protective effect on bone.

Patients exposed to heparin are in risk of having generalised osteoporosis likely to be due to its direct effect on osteoclast development and activity(7). It has been suggested that deleterious effect of heparin on bone begins if daily doses exceed 10000 IU(14). Daily heparin doses our haemodialysis patients exposed were too much lower under this dosage. Although ESRD patients in our study used D vitamin and elemental calcium, BD was found out to be lower and PTH levels higher than normal subjects. We think we should increase the daily vitamin D dosage and try bone resorption inhibitors for bone gain.

It has been suggested that tubulointerstisial diseases leading to more prominent changes in calcium metabolism and to persistent chronic acidosis may alter metabolic balance of bone much more than glomerular diseases(1). Seven patients with reflux nephropathy had significantly lower BD when compared with patients with glomerulonephritis and pyelonephritis. We accuse chronic renal tubular acidosis affecting reabsorption calcium and phosphorus from the bones(22).

In conclusion, cortical BD lessens and quality deteriorates in cortical bone increasing the risk of future fracture probability in dialysed ESRD patients.

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