The Evaluation of Renal Osteodystrophy in Patients on Hemodialysis by Biochemical and Radiological Methods

Summary

Aim: We planned this study in order to evaluate the radiological and biochemical parameters that may be useful in the early diagnosis of renal osteodystrophy in the patients with chronic renal failure, prospectively.

Material and Methods: In this study, 50 cases on hemodialysis due to chronic renal failure were included and 50 cases without renal and bone pathology were included as control group. Serum levels of calcium, phosphate, alkalen phosphatase, βm, osteocalcin (BGP) and intact parathormon (PTH) were measured. Right hand graphies of both case and control groups were taken by magnifying techniques. Bone mineral densities (BMD) of lumbar vertebra and femur neck were calculated by DEXA method.

Results: The average disease duration and the average of duration of hemodialysis of cases were 8.38±5.61 years and 6.9±4.01 years, respectively. There were significant differences between case and control groups in all biochemical parameters, except calcium levels (p<0.05). There were a negative correlation between iPTH and BMD (r=-0.4, p<0.05), and pozitif correlations between iPTH and BGP (r=0.6, p<0.05). A low level negative but statistically significant correlation between dialysis duration and femur neck bone mineral density was determined (r=0.2, p<0.05). There were positive correlations between dialysis duration and PTH levels (r=0.3, p<0.05), and between dialysis duration and BGP (r=0.4, p<0.05). In the hand graphies, osteopenia, subperiostial resorption, radial artery calcification and endoosteal resorption were seen. Osteopenia was determined in 80% of our cases, however, subperiostial resorption was found in 58% of patients. The cases that had iPTH levels over than 200 pg/ml and cases that have osteopenia have sensitivity of 93% and specificity of 92% for RO diagnosis. Sensitivity and specificity for high iPTH-BGP levels were 90.3% and 87%, respectively. Sensitivity and specificity in the evaluation of high iPTH-subperiostal resorption were 83.9% and 84.2%, respectively.

Conclusion: Measure of iPTH, BMD, BGP and evaluation of hand graphies may be used in early diagnosis and follow-up of RO. (Turkish Journal of Osteoporosis 2013;19: 7-11)

Key words: Bone mineral density, hemodialysis, renal osteodystrophy

Özet

Amaç: Bu çalışmada kronik böbrek yetmezliği olan olgularda renal osteodistrofinin erken tamsında faydali olabilecek radyolojik ve biyokimyasal parametreleri prospektif olarak araştırmayı planladık.

Gereç ve Yöntem: Kronik böbrek yetmezliği nedeni ile hemodializasyon giren 50 olgu ve dahil etildi. Böbrek problemi ve kemik hastalığı olan olgunun 50 olgu kontrol grubu olarak çalışmaya dahil edildi. Serum kalsiyum, fosfor, alkalen fosfataz, β-mikroglobulin (βm), osteokalsin (BGP), intact parathormon (iPTH) seviyeleri ölçülür. Hem iki grupta sağ el grafileri magnifiye teknikle çekildi. Lomber vertebra ve femur boyun kemik mineral yoğunluğu (KMY) DEXA yöntemi ile ölçüldü.

Bulgular: Olgularımızın ortalama hastalık süresi 8,38±5,61 yıl, dialize girme süresi 6,9±4,01 yılı. Kalsiyum dışındaki bütün biyokimyasal parametrelerde olgu ve kontrol grubundaki değişiklikler derecede fark mevcuttu (p<0,05). iPTH ve KMY aralarında negatif korelasyon mevcuttu (r=-0,4, p<0,05). iPTH ve BGP, iPTH ve βm aralarında pozitif korelasyon mevcuttu (r=0,6, p<0,05), (r=0,5, p<0,05). Dializ süresi ve femur boyun KMY aralarında istatistiksel olarak anlamlı, düşük düzeyde negatif korelasyon mevcuttu (r=0,2, p<0,05). Dializ süresi ve iPTH, dializ süresi ve βm aralarında pozitif korelasyon mevcuttu (r=0,3, p<0,04, p<0,05). El grafilerinde osteopeni ve subperiostial resorbsiyon, radyal arter kalsifikasyonu ve endoosteal resorbsiyon görüldü. Olgularımızın %80’dede osteopeni, %58’de subperiostial resorbsiyon saptandı. iPTH seviyesi 200 pg/ml üzerinde...
Introduction

The number of patients with chronic renal failure (CRF) is increasing with the development of new diagnostic methods. Although the average life span of the patients with CRF has increased with treatment modalities such as hemodialysis and peritoneal dialysis, many complications began to be seen more frequently. Renal osteodystrophy (RO) is one of these complications and it causes mineral and bone metabolism impairment, and morbidity and mortality in most of patients (1-3). Osteitis fibrosa cystica, osteomalacia, skeletal abnormalities related to $\beta_2$-microglobulin ($\beta_2$-m), osteosclerosis and osteoporosis are histopathologically observed in RO (4). Hypocalcemia, phosphate retention, changes in vitamin D metabolism, decrease of PTH degradation, changes in calcium regulation are led to secondary hyperparathyroidism pathophysiological. Increase of PTH levels results in rise of osteoclastic activity and bone resorption. Such an osteoclastic activity occurs in Haversian channels of cortical bone and subperiostal and endosteal surfaces. Cortical bone resorption occurs with PTH stimulated increased osteoclast activity. Possible causes of osteoporosis in CRF include changes in vitamin D levels, immobilisation and chronic protein deficiency. Hyperphosphatemia can be observed in the phases which the catabolism increases due to the protein metabolism and catabolism. RO which becomes clinically evident with cases like bone aches, myopathy, muscle cramps, calciphylaxis and skeleton deformities affects the life quality of the cases with CRF and causes serious mortality and morbidity (5).

Material and Method

Fifty patients on chronic hemodialysis were included in this study which was planned prospectively in order to examine RO with noninvasive methods in the patients on hemodialysis. Fifty voluntary subjects without any primary renal problem and bone disease were also included in this study as a control group. The physical examinations of members of both patient and control groups were performed. The serum calcium, phosphorus, alkalen phosphatase, $\beta_2$-microglobulin ($\beta_2$-m) and intact parathormon (iPTH) levels of both groups were measured. Osteocalcin (BGP) levels were determined by Enzyme-linked immunosorbert assay (ELISA) method. Right hand graphies of both case and control groups were taken by magnifying techniques. Thereafter, bone mineral densities were measured from lumbar vertebra and femur neck by Dual energy X-ray absorptiometry (DEXA) method.

T-test, chi-square test and Pearson correlation analysis were used for statistical analysis of study parameters of patient and control groups. Statistically $p<0.05$ value was considered as significant.

Results

The average age of our cases; 30 of whom were male, whereas 20 of whom were female; was 46.4±11.5 (19-69) years. The average disease duration of our cases was 8.38±5.61 (1-23) years and the duration of hemodialysis was 6.9±4.01 (1-16) years. Thirty-one members of the control group were male and 19 of them were female, and their average age was 45.8±11.5 (25-66) years. There was no significant difference between case and control groups in age and sex distribution ($p>0.05$). The distribution of cases according to etiologies were shown at Graphic 1.

The average and standard deviation values of alkalen phosphatase (ALP), calcium, phosphorus, $\beta_2$-microglobulin, osteocalcin (BGP) and parathormon of cases and controls were given at Table 1. There was significant difference between case and control groups in all biochemical parameters, except calcium levels ($p>0.05$).

The bone mineral densities of femoral neck and lumbar vertebra were measured in both groups; and Z-value and T-value were calculated. Both of lumbar vertebra (BMDL) values and femoral neck (BMDF) values have shown significant difference between two groups ($p<0.05$) (Table 2).

The correlation of iPTH with BMD, BGP, ALP and $\beta_2$-m were examined, there was negatif correlation between iPTH and BMD ($r=-0.4$, $p<0.05$), whereas, there were positive correlations between iPTH and BGP ($r=0.6$, $p<0.05$), and between PTH and $\beta_2$-m ($r=0.5$, $p<0.05$).

When the correlations of dialysis duration with BMDF, BMDL, iPTH, BGP, ALP and $\beta_2$-m were evaluated, there was low level
but statistically significant negative correlation between dialysis duration and BMDF (r=-0.2, p<0.05), whereas, there were positive correlation between dialysis duration and PTH (r=0.3, p<0.05) and between dialysis duration and \( \beta_2 \) (r=0.05, p<0.05) (Table 3). The right hand (dominant hand) graphies of all patients in both case and control groups were evaluated radiologically (Figure 1). The hand graphies were prepared by a special magnifying technique. Osteopenia and subperiostal resorption were found to be most frequent findings. Less frequently, radial artery calcification and endosteal resorption were determined. Osteopenia was found in 80% of cases, and subperiostal resorption were determined in 58% of cases (Table 4). Subperiostal resorption were frequently determined at radial, ulnar and radioiulnar sites of phalanges (Graphic 2). For diagnosis of RO occurring as a result of secondary hyperparathyroidism, we investigated the sensitivity and specificity values of parameters evaluated in our cases. When we take into account osteopenia cases which have iPTH values higher than 200 pg/ml, we determined sensitivity as 93% and specificity as 92%. By such a similar evaluation, the sensitivity was 90.3% for high iPTH-BGP levels, whereas specificity was 87%. In the presence of high iPTH values and the subperiostal resorption, the sensitivity and specificity were found 83.9 and 84.2%, respectively.

### Table 2. The comparision of DEXA BMD results of cases and controls

<table>
<thead>
<tr>
<th></th>
<th>Case (n=50)</th>
<th>Control (n=50)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Femur Total Z score</td>
<td>-1.4±0.8</td>
<td>0.01±0.8</td>
<td>p&lt;0.05</td>
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<tr>
<td>Lumbar Total Z score</td>
<td>-1.2±0.9</td>
<td>0.01±0.08</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Femur Total T score</td>
<td>-1.6±0.9</td>
<td>0.2±0.8</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Lumbar Total T score</td>
<td>-1.4±0.9</td>
<td>0.4±0.1</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>BMD Lumbar</td>
<td>0.8±0.1</td>
<td>1.0±0.1</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>BMD Femur</td>
<td>0.7±0.1</td>
<td>0.8±0.1</td>
<td>p&lt;0.05</td>
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</table>

### Table 3. The comparison of dialysis duration with some parameters in case group

<table>
<thead>
<tr>
<th></th>
<th>Dialysis Duration</th>
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<tbody>
<tr>
<td>iPTH</td>
<td>r=0.3 p&lt;0.05</td>
</tr>
<tr>
<td>( \beta_2 )</td>
<td>r=0.4 p&lt;0.05</td>
</tr>
<tr>
<td>BMD (F)</td>
<td>r=0.2 p&lt;0.05</td>
</tr>
<tr>
<td>BMD (L)</td>
<td>r=0.1 p&gt;0.05</td>
</tr>
<tr>
<td>BGP</td>
<td>r=0.1 p&gt;0.05</td>
</tr>
<tr>
<td>ALP</td>
<td>r=0.4 p&gt;0.05</td>
</tr>
</tbody>
</table>

### Table 4. The distribution of radiological findings

<table>
<thead>
<tr>
<th>Radiological Finding</th>
<th>%</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteopenia</td>
<td>80%</td>
<td>40</td>
</tr>
<tr>
<td>Subperiostal resorption</td>
<td>58%</td>
<td>29</td>
</tr>
<tr>
<td>Radial artery calcification</td>
<td>20%</td>
<td>10</td>
</tr>
<tr>
<td>Interdigital artery calcification</td>
<td>16%</td>
<td>8</td>
</tr>
<tr>
<td>Soft Tissue calcification</td>
<td>8%</td>
<td>4</td>
</tr>
<tr>
<td>Endosteal resorption</td>
<td>4%</td>
<td>2</td>
</tr>
</tbody>
</table>

### Figure 1
Right hand graphy of one of our case with evident osteopenia. Subperiostal resorption at radial side of middle phalanges of third finger and radioiulnar side of middle phalanges of second finger are present. Interdigital artery calcification at radial side of third phalanges and radial artery calcification at wrist are seen.

### Graphic 1
The distribution of cases according to etiologies.

### Graphic 2
The distribution of subperiostal resorption according to fingers.
Discussion

RO; which is seen in patients with chronic renal failure; is a pathology that causes morbidity and disturbs the life quality. It was firstly defined by Liu and Chu in 1943. Osteitis fibrosa cystica, osteomalacia, adynamic bone disease (ABH) and osteoporosis are the clinical components (8,9,16,17). In recent studies, it is mentioned that, bone loss on femur neck is higher than lumbar vertebra, because decrease in load at femur neck is more prevalent than lumbar vertebrae due to decreased physical activity (10,11). It is known that risk of hip fracture is increased in hemodialysis patient when compared with normal population (12-14). Although no fracture was determined, the DEXA values of cases were found to be significantly lower than the control group (p<0.05). Therefore, when the hemodialysis durations were compared with femur neck and lumbar vertebra, there was an inverse and weak relationship with femur neck BMD (r=-0.2). Because twelve postmenopausal subjects were present among women cases, effect of postmenopausal period on BMD values could not be ignored. This condition cause some limitations in this study. However, BMDF and BMDL T values of other 8 subjects which have regular menstrual period were respectively -1.7 and -1.5. On the other side, when all of the women subjects (n=20) were evaluated it was seen that BMDF values were smaller than BMDL values. This results support the effect of RO on BMD.

In the evaluation of secondary hyperparathyroidism, it was mentioned that the measure of iPTH values were found to be more sensitive, and it was shown that there was an inverse relationship between BMD and iPTH (10,15). Similarly, there was a inverse correlation between iPTH and BMD values in our cases (r=-0.4).

Serum level of BGP is accepted as indicator of bone formation. If the bone formation and degradation process is together in evaluated patients, it is accepted that BGP reflects the formation and degradation rates. It is also known that, decrease in clearence of BGP in patients with CRF may cause increase in serum BGP levels (19,20). In our study, the BGP values of cases were found higher than control group, and the difference was found to be statistically significant (p<0.05).

It is pointed out that iPTH level is important in evaluation of RO (21). It has been shown that there is correlation between BGP level and iPTH level. Similarly, a significant correlation between iPTH and BGP was shown in case group (r=0.6). In our study, significant difference was determined between case and control groups in iPTH level (p<0.05).

It is known that there is no correlation between serum ALP level and clinical types of RO (22). It is mentioned that ALP level is decreased with calcitriol therapy and this shows parallelism with decrease in PTH level. The ALP level was compared between case and control groups, and the difference was found to be statistically significant (p<0.05). However, no correlation was determined between ALP and iPTH in our case group.

In hemodialysis cases, \( \beta_2 \) m; which accumulates within osteoarticular structures; is responsible for dialysis amiloidosis, and it frequently causes carpal tunnel syndrome and supraspinatus tendinitis. The relationships of \( \beta_2 \) m levels with hemodialysis duration and iPTH levels were shown (23,24). In our study, significant difference was determined between cases and controls in \( \beta_2 \) m level (p<0.05). Moderate positive correlations were found between \( \beta_2 \) m and hemodialysis duration, and between \( \beta_2 \) m and iPTH in our case group (r=0.4,r=0.5).

It was mentioned that, the bone changes that are caused by secondary hPTH are most frequently seen in hand bones (25,26). When the graphs of dominant hands were evaluated in our case group, osteopenia was found in 80%, subperiosteal resorption was found in 58%, radial artery calcification was found in 20% and interdigital artery calcification was found in 16% and endosteal resorption was found in 4% of the patients.

In our study, subperiosteal resorption was most frequently seen in third and second phalanges; respectively. It was prominent especially in radial side (Graphic 2). Although bone biopsy is accepted as gold standart in classification of RO, the disadvantage of this method is being an invasive method (27,28). A recent study; in which iPTH level was evaluated with radiologically evident erosions; the sensitivity, specificity and positive estimate value of iPTH levels over than 200 pg/ml for the diagnosis of osteitis fibrosa cystica were found 83%, 88%, and 88%; respectively (29).

According to these findings, we determined the sensitivity and specificity related with the diagnosis of RO in our cases with iPTH levels over than 200 pg/ml (31 cases) and in our cases with osteopenia (40 cases) as 93% and 92%; respectively. By such a similar evaluation, the sensitivity was 90.3% for high iPTH-BGP levels, whereas sparsity was 87%. When the high iPTH and the presence of subperiosteal resorption was evaluated, the sensitivity and specificity were found 83.9 and 84.2%, respectively.

Conclusion

We are opinion that when osteopenia and subperiosteal resorption detected radiologically and high iPTH values with high BGP values in CRF cases were evaluated, RO diagnosis related with secondary hPTH may be foreseen. For that purpose, measure of iPTH, BMD, BGP and evaluation of hand graphs may be used in early diagnosis and follow-up of RO.

References

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