Hypoparathyroidism In Dialysis Patients of Bagalkot

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ABSTRACT

Introduction: Chronic kidney disease (CKD) is associated with a variety of bone disorders and abnormality of “Calcium” and “Phosphate” metabolism. Chronic kidney disease associated mineral bone disorder (CKD-MBD) is an area of ongoing discussion because of its role in morbidity and mortality in dialysis patients. Both Indian and international data, regarding parathyroid levels in chronic kidney disease patients highlight predominant hyperparathyroidism in dialysis patients and very few as hypo parathyroidism. We undertook this study to determine the prevalence of hypo and hyper-parathyroid state in our dialysis patients and for better understanding and management of CKD-MBD.

Materials & Methods: 40 adult patients (> 18 years age) who met the inclusion criteria and were on hemodialysis in SNMC and HSK HOSPITAL AND RESEARCH CENTER and end stage renal disease (ESRD) (glomerular filtration rate <15 ml/kg/m²) patients attending nephrology clinics were enrolled in the study. Patients’ parathyroid status was defined as per target recommendation of Kidney foundation disease outcomes quality initiatives [KDOQI] – hypo parathyroid when, intact parathyroid (iPTH) < 150 pg/ml as group (A), hyper parathyroid, iPTH > 300pg/ml as group (B) and patients with values between 150pg/ml-300pg/ml to group(C) as per standard protocol.

Results and conclusion: A total of 40 patients all (100%) were on hemodialysis. Mean age of these patients was 51.3 ± 5.3 years. 30 (75%) were males and 18 (45%) were diabetics. Mean duration on dialysis was 15.77±8.8 months. Twenty out of 32 patients (50%) had hypoparathyroidism, 12 (30%) hyperparathyroidism and remaining 8 (20%) were in normal ranges. Hypoparathyroidism is more common (50%) in our dialysis patients as compared to hyperparathyroidism (30%).

KEYWORDS: MBD, CRF, ESRD, Hemodialysis, HPTH, iPTH

INTRODUCTION

Chronic kidney disease (CKD) is associated with variety of bone disorders and abnormality of calcium and phosphate metabolism. Chronic kidney disease associated mineral bone disorder (CKD-MBD) [osteitis fibrosa cystica, osteodystrophy, adynamic bone disease and osteomalacia] is an area of ongoing discussion because of its role in morbidity and mortality in dialysis patients. Impaired production of 1,25
(OH)2D, hyperphosphotemia, MBD and uraemic state contributes to impaired calcium absorption. By dietary restrictions and drug supplements, each patient must be monitored closely to restore normal calcium balance, to prevent MBD by maintaining biologically active iPTH between 150-300pg/ml. Treatment involves administering supraphysiologic amounts of vitamin D or calcitriol for correction and to reduce manifestations of secondary HPTH.[1]

However, besides hyperparathyroid (HPTH), hypoparathyroid state low iPTH is also associated with increased risk of pelvic and vertebral fractures in CKD patient.[2,3] and studies have shown increased risk of death among dialysis patients with low serum iPTH.[4,5] The risk of vascular calcification is also increased in CKD and is a surrogate marker of cardiac disease.[6]

Hence, this study was undertaken to look at the prevalence of hypoparathyroidism and hyperparathyroidism in our dialysis patients.

**MATERIALS AND METHODS:**

**Inclusion criteria:** 50 ESRD adult patients (> 18 years age) who were on hemodialysis patients in our SNMC and HSK HOSPITAL AND RESEARCH CENTER and ESRD patients attending nephrology (speciality clinics) were included in the study after oral consent. Exclusion criteria: Patients with HIV positive serology, active systemic infection, surgery or interventions in last 4 weeks were excluded as they alter iPTH levels. New patients less than 1 month on dialysis were also excluded because iPTH levels may be that for normal patients and the recommended levels in long time dialysis differs from them. Also excluded were chronic renal failure (CRF) patients on conservative treatment who were not on dialysis. And finally 40 patients fulfilling the above mentioned criteria’s were included and Institutional Ethical Committee clearance obtained.

Patients were classified group (A) hypoparathyroid depending on iPTH levels < 150pg/ml, group (B) hyperparathyroid whose iPTH > 300 pg/ml and group (C) with normal range as per standard guidelines for ESRD patients recommendation by KDOQI [7].

However, besides hyperparathyroid (HPTH), hypoparathyroid state low iPTH is also associated with increased risk of pelvic and vertebral fractures in CKD patient.[2,3] and studies have shown increased risk of death among dialysis patients with low serum iPTH.[4,5] The risk of vascular calcification is also increased in CKD and is a surrogate marker of cardiac disease.[6]

Hence, this study was undertaken to look at the prevalence of hypoparathyroidism and hyperparathyroidism in our dialysis patients.

**RESULTS**

After exclusion, 40 patients were finally included in the analysis. All patients (100%) were on hemodialysis dialysis.

Table 1 shows the demographic characteristics of patients included in the study. Mean age of these patients was 51.3 ± 5.3 years. 30 (75%) were males and 18 (45%) were diabetics. Mean duration on dialysis was 15.77 ± 8.8 months. Table 2 shows the baseline and biochemical characteristics of 3 groups, there was statistically significant values in all parameters except in serum calcium and phosphates.

Table 3 shows that 20 out of 40 patients (50%) had hypoparathyroidism, 12 (30%) hyperparathyroidism and remaining 8 (20%) were in normal ranges.
Table 1: Demographic characters of dialysis patients

<table>
<thead>
<tr>
<th></th>
<th>Total patients (40)</th>
<th>Group A (20)</th>
<th>Group B (12)</th>
<th>Group C (8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>51.3 ± 5.3</td>
<td>38.8 ± 11.4</td>
<td>54.8 ± 1.3</td>
<td>45.1 ± 4.7</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>75%</td>
<td>23%</td>
<td>44%</td>
<td>8%</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>45%</td>
<td>18%</td>
<td>22%</td>
<td>5%</td>
</tr>
<tr>
<td>Dialysis duration months</td>
<td>15.77±8.8</td>
<td>14.8 ± 1.4</td>
<td>16.8 ± 0.3</td>
<td>14.98±2.04</td>
</tr>
</tbody>
</table>

Table 2: Biochemical characters of dialysis patients

<table>
<thead>
<tr>
<th></th>
<th>Total (40)</th>
<th>Group A(20)</th>
<th>Group B(12)</th>
<th>Group C(8)</th>
<th>f</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin gm%</td>
<td>9.8 ± 1.3</td>
<td>9.8 ± 0.7</td>
<td>8.8 ± 0.5</td>
<td>9.2±0.2</td>
<td>11.7</td>
<td>0.00</td>
</tr>
<tr>
<td>Blood urea mg/dl</td>
<td>109.3 ± 8.3</td>
<td>110.8 ± 2.4</td>
<td>105.8 ± 6.4</td>
<td>112±5.6</td>
<td>5.8</td>
<td>0.00</td>
</tr>
<tr>
<td>Sr.creatinine mg/dl</td>
<td>6.9 ± 0.6</td>
<td>5.8 ± 0.2</td>
<td>6.8 ± 1.4</td>
<td>6.3±0.5</td>
<td>5.84</td>
<td>0.00</td>
</tr>
<tr>
<td>Sr sodium meq/l</td>
<td>134.5± 2.3</td>
<td>130.8 ± 2.5</td>
<td>141.8 ± 0.9</td>
<td>136±1.43</td>
<td>11.92</td>
<td>0.00</td>
</tr>
<tr>
<td>Sr potassium meq/l</td>
<td>5.8 ± 1.3</td>
<td>5.2 ± 0.17</td>
<td>5.8 ± 0.4</td>
<td>5.1±1.23</td>
<td>4.84</td>
<td>0.01</td>
</tr>
<tr>
<td>Random blood sugar mg /dl</td>
<td>153.28 ± 21.3</td>
<td>144.8±1 0.4</td>
<td>170.8 ± 2.4</td>
<td>144.3±6.32</td>
<td>44.3</td>
<td>0.00</td>
</tr>
<tr>
<td>Sr.Albumin g/dl</td>
<td>3.8 ± 0.3</td>
<td>3.38 ± 0.14</td>
<td>2.0 ± 1.4</td>
<td>2.6±2.8</td>
<td>3.54</td>
<td>0.03</td>
</tr>
<tr>
<td>Sr.Calcium mg/dl</td>
<td>9.8 ± 0.7</td>
<td>8.8 ± 0.14</td>
<td>9.7 ± 3.2</td>
<td>9.2±0.46</td>
<td>0.98</td>
<td>0.38</td>
</tr>
<tr>
<td>Sr.Phosphate mg/dl</td>
<td>4.8 ± 0.4</td>
<td>5.0 ± 0.7</td>
<td>4.7 ± 0.7</td>
<td>4.3±1.3</td>
<td>2.01</td>
<td>0.14</td>
</tr>
<tr>
<td>Sr.Cholesterol mg/dl</td>
<td>139.8 ± 2.8</td>
<td>144.8±2.4</td>
<td>1394.8 ± 5.4</td>
<td>155.3±3.3</td>
<td>477184</td>
<td>0.00</td>
</tr>
<tr>
<td>iPTh pg/ml</td>
<td>156.8 ± 90.4</td>
<td>33.48 ± 0.4</td>
<td>254.8 ±5 0.4</td>
<td>161.4±2.03</td>
<td>263</td>
<td>0.00</td>
</tr>
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</table>
DISCUSSION

Mineral bone disorder secondary to chronic kidney disease is ongoing concern and important cause of morbidity and mortality in dialysis patients. Adynamic bone disease has become increasingly frequent since it has become possible to suppress PTH with calcium and potent vitamin D analogs. In certain dialysis centers, it has become the most common bone disorder. The degree to which it increases morbidity and mortality is unknown, but the limited available data increasingly raise concerns about these issues. The main concerns are related to the inability of bone to contribute to mineral homeostasis in the absence of kidney function and the risk of hip fracture. Accumulating data suggest that the adynamic histology is not benign. A 4-fold increase in hip fracture risk has been found in the dialysis population compared to the general population. Age, duration of dialysis, female sex, and diabetes appear to confer an increased risk for fracture an unanswered question is how adynamic bone lesions and osteoporosis are related.

Many of the risk factors noted for adynamic bone disease also predispose to osteoporosis in the general population. In addition, low bone turnover is seen in the majority of osteoporotic subjects who do not have kidney disease. Finally, the aging of the dialysis population results in a population that would be expected to be at high risk for osteoporosis. Adynamic bone is treated by increasing bone turnover through an increase in PTH. This can best be accomplished by lowering doses of calcium-based phosphate binders and vitamin D or entirely eliminating such therapy. The lowering of dialysate calcium (1.0 to 2.0 mEq/L) has also been suggested as a possible approach in a study, of this therapy (in peritoneal dialysis patients) did lead to a substantial increase in the number of patients with marked PTH elevation; however, this approach must be considered[7,8]

Hypoparathyroidism is also reported differently from different countries. Dialysis outcomes and practice patterns study (DOPPS) reports the prevalence of hypoparathyroidism in 36.2% of overall dialysis patients with US, UK, and Japan having 20.5%, 46.6%, and 49.7% respectively. We found high prevalence of hypoparathyroidism in our dialysis population (50%). The prevalence of hyper parathyroidism in our dialysis population is 30%. Normal iPTH in 20 %.(Table 3)

In view of paucity of Indian data regarding this, we had one from urban Indian study from Pune by Tarun jeloka[10] et al in which hypoparathyroidism 45.58%, hyperparathyroidism in 27.94% and remaining normal iPTH were 26.48% and no statistically significant difference among modes of dialysis whether peritoneal or hemodialysis. (table3) Hyperparathyroidism is more common and reported in 47 – 78% of

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Table 3: Comparision of our results with other similar studies.

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<tbody>
<tr>
<td></td>
<td></td>
<td>UK</td>
<td>USA</td>
</tr>
<tr>
<td>Hypoparathyroidism</td>
<td>50%</td>
<td>45.58%</td>
<td>46.60%</td>
</tr>
<tr>
<td>Hyperparathyroidism</td>
<td>30%</td>
<td>27.94%</td>
<td>33.10%</td>
</tr>
<tr>
<td>NORMAL</td>
<td>20%</td>
<td>26.48%</td>
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</table>
Dialysis patients in the west [11, 12, 13]. Dialysis outcomes and practice patterns study (DOPPS) has data from 11 different countries and has reported the overall prevalence of hyperparathyroidism, based on KDOQI guidelines, to be 34.3%, with US, UK and Japan having 47.6%, 33.1%, and 19.9% respectively.

There could be many causes of higher prevalence of hypoparathyroidism in our dialysis population. Asian dialysis patients could be at higher risk of hypoparathyroidism due to their ethnicity, as it is a common observation from countries like Japan and Taiwan [14, 15]. However this has not been verified in many studies.

This is the pilot study in our center which is considered to be one of the backward areas of Karnataka, to look at the prevalence of hypoparathyroid status in representing Indian dialysis patients of north Karnataka. Not all patients in our set up get these investigations done because of various reasons, one of the most backward areas with financial burdens and many more reasons. We too looked into the point prevalence of hyper- and hypoparathyroidism, which in fact is a changing variable with treatment. However, it still gives an outlook of the problem and justifies monitoring and improvement in their management.

It is a single center study and small sample size. Comparison with age and sex related matching not done because recommended iPTH levels for normal patients 15-65 pg/ml. In the present study we noted, that all most half (50%) had low iPTH and we observed that though the mean dialysis duration was 15.77±8.8 months these patients were recently diagnosed and on HD for lesser duration, many were non diabetics and younger compared to 30% of hyper parathyroid patients who were on long time HD, more diabetics and older than hypo parathyroid patients. In patients of normal iPTH (20%) we had a combination of both these groups. (table 1 and table 2)

In contrast to similar study by Tarun jeloka[10] whose hypo parathyroid patients were also older as compared to the hyper parathyroid group but were similar in diabetic status our center it was reverse. These changes could be because of regional, dietary differences and etiological cause of ESRD, dialysis duration at that point. The most likely explanation could be varied dietary habits, excess of vit D3, compared to long term patients who were irregular in taking drugs because of pill burden, depression socioeconomic problems. However we could not generalize this statement as the sample size was small to divide into groups and this was not our aim. A large study is needed to confirm this.

Another factor leading to higher incidence of hypoparathyroidism in dialysis patients is inadvertent use of active vitamin D3. This happens at two levels: first, blind prescription of active vitamin D3 without monitoring iPTH levels in early stages of CKD patients, which is uncommonly seen in clinical practice in India. Secondly, use of combination pills (calcium carbonate and active vitamin D3) as phosphate binders, carry with it excess dose of active vitamin D3 thereby over suppressing the PTH [14].

Guh[15] et al, a Japanese study shows high incidence of Hypo was observed in the HD patients with diabetes mellitus (DM) and old age (> or = 70 years old) compared with that of a nationwide epidemiological report for dialysis patients by Japanese Society for Dialysis Therapy. Hypo parathyroid patients who were treated by CAPD had a background of being younger, having a shorter duration on dialysis, and were less frequently diagnosed with diabetes than in those hypoparathyroid patients on dialysis. Bone pain and metastatic calcification were observed in. These results suggest that a very high incidence and specific backgrounds (diabetes and aging) of Hypo parathyroid exist in Japanese dialysis patients irrespective of mode of dialysis. Our results variation could be because of regional differences and different drug combination and pill intake.
CONCLUSION:
Since this is only point prevalence study, the results may be variable. Our observation and results show that hypoparathyroidism is more common than hyperparathyroidism in dialysis patients. Excessive use of active vitamin D3 preparations and calcium based phosphate binders leads to suppression of PTH in the body resulting in hypoparathyroid state and adynamic bone disease which can be prevented by regular iPTH monitoring in order to maintain the bone mineral integrity.

Hence screening of all dialysis patients at least once in 6 months and patients of severe bone pain, once in 3 months for iPTH levels should be done, to prevent fractures, soft tissue calcifications, adynamic bone diseases and to improve the quality of life.

REFERENCES:


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