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Original Article

Bone Mineral Density In Chronic Kidney Disease Patients

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ABSTRACT

Background: Metabolic bone disease is common in the case of renal failure. The aim of this study is to compare mineral changes, hormonal changes and bone mineral density in pre-dialysis and post-dialysis renal failure patients. Hypothesis: Secondary hyperparathyroidism may be the cause for skeletal changes in renal failure. Materials and Methods: 20 patients of both sexes, with chronic kidney disease formed the subjects of the present study. Studies are done in pre and post dialysis states. In this study bone mineral density is measured by dual energy X-ray absorptiometry and bone minerals are estimated by using standard lab techniques. Results and Conclusion: The results of this study indicate no gross variation in both genders in all parameters. The serum calcium levels (P-0.073) are statistically decreased. In contrast, serum phosphorus levels (P-0.98) are raised but statistically not significant. Parathyroid hormone levels (P-0.50) are increased but statistically not significant. Vitamin D_3 levels (P-0.02) are significantly increased in post dialysis compared to pre-dialysis subjects. Bone mineral density in lumbar spine (L1 to L4) T-Score (P-0.007), Z–Score (P-0.009), neck of the femur T-Score (P<0.001), Z–Score (P-0.008) statistically decreased. The forearm T-Score (P-0.97), Z–Score (P-0.12) indicates small variation and statistically not significant. The mineral changes are mainly due to increased secretion of parathyroid hormone. Dialysis has no effect on in bone mineral density. There is skeletal resistance to parathyroid hormone, due to reduction in number of hormone receptors and decreased level of calcitriol and loss of negative feedback on parathyroid hormone secretion by calcitriol.

1. Introduction

Early diagnosis of skeletal changes in chronic kidney disease may decrease the risk of fractures. The advanced procedure is measuring bone density using DEXA(dual energy X-Ray absorptiometry).It is used to determine the amount of matter per cubic centimeter of bones[3]. The development of secondary hyperparathyroidism in renal failure is associated with disturbances of the endocrine parathyroid hormone, vitaminD-axis 7 . In advance renal failure hyperparathyroidism progresses even in the presence of normocalcemia or hypercalcemia. Skeletal resistance to the calcium mobilizing action of PTH, another factor responsible for maintenance of hyperparathyroidism in renal failure4. These changes depend on several factors including 1, 25-(OH) 2 Vit-D3 status, type of nephropathy and individual dietary habits. In order to understand the causes of bone changes in chronic kidney disease, the serum mineral content and hormone concentrations (PTH, 1, 25-(OH) 2 Vit-D3) are estimated. This may help in the prevention of bone fractures in chronic kidney disease patients.

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2. Materials and Methods

The institutional ethical committee's approval was obtained **Patients:** The study was done in nephrology Department of Sri Venkateshwara Institute of Medical Sciences after obtaining permission from medical ethics committee of the institute. Studies were carried out in stages 3, 4 and 5 of 20 CKD patients aged between 28-75 years, 10 males and 10 females attending Nephrology o.p for the past 6 months. The studies were done before dialysis and after dialysis of the patients. The dialysis patients were treated by conventional haemodialysis for 4-5 hours, two times a week. None of the patients had a past history of alcohol or smoking. Acute renal failure cases, paediatric patients, patients with primary endocrine abnormalities, diabetes mellitus, pulmonary tuberculosis and hypertension were excluded from this study.

Biochemistry:

Sample collection:

For estimation of serum calcium, phosphorus, parathyroid hormone and vit-D_3 the fasting blood sample was collected into a clean tube allowed the blood to clot for at least 30 min at room temperature. Separated the serum by centrifugation and stored in a refrigerator and serum calcium and phosphorus were assessed by using standard laboratory methods. 1, 25-(OH) 2, vit-D_3 was measured by RIA (diasorin, catalog no: 68100E) and serum parathyroid hormone was measured by using N-tact Parathyroid hormone SP IRMA (Diasorin, catalog no.26100).

Bone mineral density:

Bone mineral density (BMD) of the lumbar spine, total hip and femoral neck were measured by using Dual energy X-ray absorptiometry (Discovery A, Hologic inc.version-12.6.1 USA). All Bone Mineral Density measurements were performed by the same experienced operator. Bone Mineral Density results were obtained in absolute values (g/cm2), in T-score and in Z- score. T-score is the number of standard deviations from the mean of a healthy adult population and is used to determine osteoporosis or osteopenia. Z-score is the number of standard deviations from the mean of a healthy age and gender-matched normal population, which allows the comparison of Bone Mineral Density between patients of different age and gender. Osteoporosis was defined as a Bone Mineral Density T- score at any site less than -2.5 and osteopenia as a Bone Mineral Density T-Score between -1 and –2.5. The reference values were obtained from an Italian normal population.

Statistical Analysis:

Results were statistically analyzed by applying student't' test and calculated 'p' values

3. Results

The results of this study indicate no gross variation in both genders of all parameters. The mean values of bone minerals and hormones for chronic kidney disease patients before and after dialysis are presented in the tables below. Serum calcium (table-1&graph-1) and vitamin D_3(table-2&graph-2) levels were significantly decreased in chronic kidney disease patients. Phosphorus (table-1&graph-1) and parathyroid hormone (table-2&graph-2) levels were significantly increased in chronic kidney disease patients. In this study osteopenia was found in 50% in lumbar spine, 33.3% in femur neck and forearm. 33.3% of the patients had osteoporosis in lumbar spine, forearm and neck of the femur. (table-3&graph-3).

Table:-1: Comparison of SCa^{2+}, SPO_4, levels in Group I and Group II

	Group-I		Group-II			
	Mean	SD	Mean	SD	't'	P
SCa^{2+}(mg/dl)	9.41	0.33	9.75	0.46	1.89	0.078;NS
SPO_4 (mg/dl)	4.57	1.35	4.58	0.91	0.01	0.98;NS

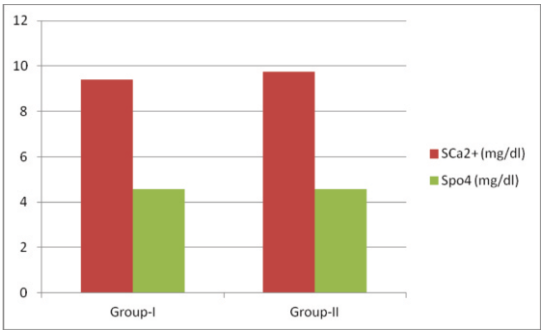
Table:-2: Comparison of serum levels of PTH and Vitamin D3 in Group –I and Group-II

	Group-I		Group-II			
Mean		SD	Mean	SD	't'	P
PTH(pg/ml)	172.53	161.77	132.30	95.46	0.67	0.50;NS
VIT-D_3 (ng/ml)	20.99	13.53	9.32	5.44	2.53	0.02;S

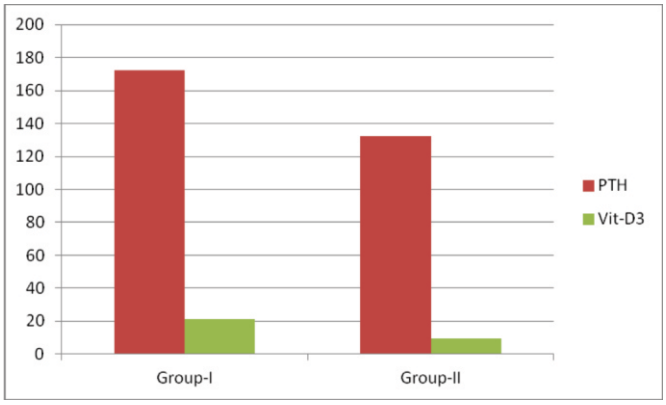
Table:-3: Comparison of BMD T and Z scores of LS, Hip and Forearm in Group I and II

	Group-I		Group-II			
	Mean	SD	Mean	SD	't'	P
LS T-Score	-2.40	1.50	0.46	2.63	2.98	0.007;S
LS Z-Score	-1.87	1.65	1.01	2.69	2.88	0.009;S
Hip T-Score	-2.34	0.43	-0.79	1.05	4.31	<0.001;S
Hip Z-Score	-1.47	0.60	-0.31	1.04	2.97	0.008;S
Fore arm T-Score	-2.66	1.64	-1.39	1.34	1.89	0.97;NS
Fore arm Z-Score	-2.01	2.05	-0.85	1.01	1.60	0.12;NS

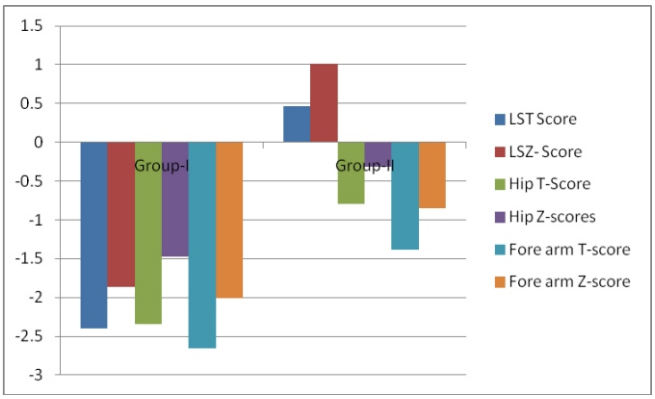
Graph:-1: Comparison of SCa_2+, SPO_4, levels in Group I and Group II



Graph:-2: Comparision of serum levels of PTH and Vit D_3 in Group –I and Group-II



Group:-3: Comparison of BMD T and Z scores of LS, Hip and Forearm in Group I and II



4. Discussion

Metabolic bone disease is common in the course of renal failure. It is observed in a number of studies that renal osteodystrophy is common in End Stage Renal Disease (ESRD) patients under dialysis treatment. It is the most common cause for mortality in End Stage Renal Disease. Secondary hyperparathyroidism is the main cause for renal osteodystrophy [8]. There is no gross variation in men and women of this study.

It is observed that Serum calcium is decreased in chronic kidney disease patients and the values are not much altered in pre and post dialysis conditions. In contrast Serum Phosphorus levels are raised in chronic kidney disease patients and not much change is observed in post and pre conditions. The serum calcium and phosphate levels are controlled by renal mechanisms. So damage of kidneys disturbs the calcium and phosphate levels in serum. In these patients abnormalities in Glomerular filtration rate are also found (filtration rate <60 ml/min.

In Last stages of chronic kidney disease serum calcium levels decrease and serum phosphate levels increase. These changes are mainly due to secondary hyperparathyroidism. These results are also supported by the studies of Hou SH et al [8]. The Serum Calcium levels are decreased in this study because Hypocalcaemia is common but not invariably present in patients with advanced renal failure, and modest reductions in the concentration of serum calcium may be noted in patients with mild renal insufficiency. The hypocalcaemia may be more pronounced in uremic patients with marked and widespread osteomalasia. In contrast, the serum levels of calcium may be normal or elevated in the patients with marked secondary hyperparathyroidism and generalized osteitis fibrosa. The levels of total, diffusible, and ionized calcium are reduced while those of complexed calcium are elevated. The percentages of diffusible and ionized fractions are not different from normal. A direct relationship between the serum levels of ionized calcium and the degree of reduction in Glomerular filtration rate. The patients with marked decreases in the serum concentrations of ionized calcium are those who have the lowest levels of Glomerular filtration rate. Acidosis may increase the serum levels of ionized calcium, but the relative contribution of uremic acidosis to the values of ionized calcium in patients with renal failure within 3 to 5 minutes after initiation of regular hemodialysis, Predialysis concentration of serum calcium generally reaches levels between 9.0 and 10.0 mg/dl a rise in serum calcium occurs in patients with hypocalcemia[12].

The serum phosphorus levels are increased in this study because the concentrations of serum phosphorus during the fasting state are usually normal or lower than normal in the early stages of renal failure. Hyperphosphatemia becomes apparent when Glomerular filtration rate falls below 20ml/min10.The serum phosphorus levels decrease during dialysis secondary to its removal by dialytic procedure. Serum phosphorus concentration increases during the interdialytic period, the rapidity of the rise depending on the dietary intake of phosphorus, the adherence to therapy with phosphate – binding antacids, and the severity of secondary hyperparathyroidism.

In the present study parathyroid hormone levels are increased significantly and Vit-D_3 levels are decreased in renal failure patients. These results are also supported by the study of Sanjay K Agarwal, et al., [1]. The mineral changes are mainly due to increased secretion of parathyroid hormone. Parathyroid hormone secretion occurs in response of hypocalcaemia, hyperphosphatemia and 1, 25 Dihydroxy Cholicalciferol deficiency. However Calcium is more important in parathyroid hormone release and calcitriol is important in inhibiting parathyroid hormone release. According to Dunstan, et al.,

hyperparathyroidism develops even with normal calcium levels or hypercalcemia. This is independent of serum calcium levels. While normal parathyroid glands have almost no proliferative activity, uremia leads to hyperplasia of the parathyroids and to an increase in the number of parathyroid hormone secreting cells in untreated uraemic, patients3. A study by Menders et al [10] showed that there is a transition from simple hyperplasia to multinodular transformation and finally pseudoadenoma formation in cases with severe hyperparathyroidism. Another factor is skeletal resistance to the action of parathyroid hormone to mobilize calcium from bone. This depends on several factors including reduction in the number of hormone receptors and diminished levels of calcitriol. In renal failure the synthesis of calcitriol decreases due to destruction of renal parenchyma. This interrupts negative feedback mechanism on parathyroid hormone secretion.

Vitamin-D_3 deficiency also develops in renal failure. Haemodialysis reduces the serum calcium and Vitamin D3, due to loss in the dialysate. So loss of serum calcium is prevented by higher amount of Calcium in dialyzing fluid. Loss of Vitamin D3 metabolites lead to osteomalacia. This may be prevented by Vitamin D_3 administration. Synthesis of interleukins is stimulated in dialysis. Interleukin-1 has bone resorbing activity.

The results of Bone Mineral Density testing are reported in comparison of ranges in SDs of the T-Score and the Z-Score. In the present study the Bone mineral density T and Z Scores are lower in post dialysis and Pre-dialysis Chronic kidney disease patients. Same results were seen in similar work by Ha SK et al(1996). Hormone that are important in bone remodeling, including parathyroid hormone, Vitamin D_3, estrogen, glucocorticoids, interleukins, prostaglandins and the members of the TGF- super family of cytokines. One quality is impaired in Chronic Kidney Disease because there is an increased prevalence of hip fracture in dialysis patients compared with the general population in all age groups. Dialysis patients in their 40s have a relative risk of hip fracture 80-fold that of age-and sex-matched controls. Furthermore, a hip fracture in a dialysis patient was associated with a doubling of the mortality rate observed in hip fractures in non-dialysis patients. In a multivariate analysis, the risk factors for hip fracture include age, gender, and duration of dialysis and presence of peripheral vascular disease. Other analyses found race, gender, duration of dialysis and low or very high Parathyroid hormone levels as risk factors. These data, and advances in other imaging modalities to a National Institutes of Health consensus conference to redefine osteoporosis as "a skeletal disorder characterized by compromised bone strength that results in an increased risk of fracture. Bone strength reflects the integration of two main features. Bone density and bone quality. These "quality" factors include abnormal base turnover on remodeling and other indices of bone architecture such as geometry, connectivity, mineralization and collagen cross linking[2]. These factors appear additive to bone mineral density as determinants of bone strength.

5. Conclusion

The prolonged treatment with maintenance hemodialysis is associated with worsening of radiographic evidence of bone disease in most patients, irrespective of the calcium concentration in dialysate. Adequate controls of the serum levels of phosphorous within the normal range may possibly ameliorate or reverse this trend. The Bone mineral density T and Z scores are lower in patients in both before and after dialysis conditions. This study was concluded as the dialysis has no effect on skeletal changes. It is observed that secondary hyperparathyroidism may be the cause for skeletal changes in renal failure

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7. References

[1] Agarwal S.K.: "Assessment of Renal Bone mineral Disorder in naïve CKD patients": A single centre prospective study: Indian Journal of Nephrology. 2007: 17.

[2] Cole RE. "Improving clinical decisions for women at risk of osteoporosis dueal femur bone mineral density testing". JAM osteopath Asoc 2008:108(6): 289-95 PMD: 18587077.

[3] Delmez, J. A. Tindira. C., Grcons. P:, Dusso, A: Windus, D. Wand slatopolsky. T. "Parathyroid hormone suppression by intravenous 1-25 dihydroxyvitamin D3. A role for increased sensitivity to calcium". Journal of clinical Investigation: 1989:8. 3, 1349-55.

[4] Dunstan.C.R.,et al.(1985a). The pathogenesis of renal osteoporosis:Role of vitamin D,aluminum,parathyroid hormone,calcium and phosphorus.Quarterly Journal of Medicine.217.127-44.

[5] 4. Ersoy FF, passadakis SP, Tam P, memos ED, katopodis PK, Ozenerc Akcicek F, Camsari T, Ates K, Ataman R, Vlachojannis, JG, DombroSAN, utas C, AKpolat T, Bozfakioglu S, WUG, Karayaylal:I, Arinsoy T, stathkis PC, yavuz M, Tsakiris JD, Dimitriodes CA, yilmaz ME, Gultekin M, karayalcin B, yardimserver M, oreopoulos DG: "Bone mineral density and its correlation with clinical and laboratory factors in chronic peritoneal dialysis patients". J Bone miner metab. 2006:24(1):79-86. PMID: 16369903 (pubmed: indexed for MEDLINE).

[6] Godkar B. Praful, Godkar P. Darshan: "Text book of medical laboratory Technology":1994: 2:16, 406.

[7] Ha Sk, park CH, Seo JK, park SH, Karg SW, choi KH, Lee Hy, Han Ds : "Studies on bone markers and bone mineral density in patients with chronic renal failure": Yonsel med J. 1996 oct : 37(5) : 350-6.

[8] Hou SH, Zhao, J. Ellman CF, Hu J, Criffin Z, Spiegel DM, Bourdeau JE: "Calcium and phosphorus fluxes during haemodialysis with low calcium dialysate". Am J kidney Dis: 1991: Aug, 18(2): 217-24.

[8] Mario Coco, MD, and Heather Rush, MD: "Increased Incidence of Hip fractures in dialysis patients with low serum parathyroid hormone". American Journal of kidney diseases. 2000: 36:6:1115-21.

[10] Murray R. L. "Non protein Nitrogen compounds, In clinical chemistry; Theory, Analysis and co-relation" Kaplan L. A. and pesce A. J., Eds. C . V. Mosby, Toronto, 1984, 1230-1268.

[11] Sharon M. Moe, Stuart M. Sprague. "Mineral bone disorder in chronic kidney disease". The kidney: Brenner: 2006:2:52: 1784-1792.