Serum Calcium, Phosphorous, and Parathyroid Hormone in Sudanese Patients under Regular Haemodialysis

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Abstract

Background Secondary hyperparathyroidism (SHPT) is an important complication of end-stage renal disease. Bone disease, a well-recognized complication of SHPT, represents only a small concern in light of the evidence that correlates SHPT with cardiovascular disease and an increased risk of morbidity and mortality in patients with CKD. Identifying patients at risk and evaluating for SHPT is imperative because early intervention may slow or arrest the progression of both bone and cardiac disease. Dietary concerns, pharmacotherapy, and patient adherence are all important considerations in creating a successful treatment plan.

Aims To evaluate serum calcium, phosphorus and parathyroid hormone concentrations in hemodialyzed renal failure patients.

Materials and Methods The study involved a control group of apparently healthy (N = 50) matched for age with a test group of hemodialyzed renal failure patients (N = 50). The age range of both groups was 25-65 years.

Calcium, phosphorus and parathyroid hormone concentrations were measured according to the standards. Appropriate statistical tests were used to assess significant difference in the means of the studied concentrations between cases and the control group.

Results The patients showed lower Calcium concentrations (M±SD = 9.5±.83 mg/dl) compared with controls (M±SD = 9.7±.57 mg/dl), this difference did not reach statistical significance (*P* = 0.07). In contrast phosphorus concentrations were significantly higher in the patients (M±SD = 4.7±1.8 mg/dl) compared with control group (M±SD = 3.6±.47 mg/dl *P* =0.00). Also parathyroid hormone concentrations were significantly higher in the patients (M±SD = 752±677 pg/ml) compared with control group (M±SD = 55±15 pg/ml *P* =0.00).

Conclusion This study shows that high serum parathyroid hormone level is significantly more common in chronic renal failure. It may be useful to do early screening and treatment of secondary hyperparathyroidism to prevent the bone disease, cardiovascular disease and their complications.

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Introduction

Disturbances in mineral metabolism that are secondary to chronic kidney disease (CKD), such as hypocalcaemia, hyperphosphatemia and impaired synthesis of 1,25-dihydroxyvitamin D3 (calcitriol), result in excess parathyroid hormone (PTH) secretion that is a characteristic of secondary hyperparathyroidism (sHPT) [1;2]. In contrast to low levels of parathyroid gland proliferation and growth in normal adults, hyperparathyroidism secondary to CKD is characterized by abnormally increased parathyroid cell proliferation [3]. Increased parathyroid cell proliferation has also been observed in patients with primary hyperparathyroidism with demonstrable parathyroid hyperplasia [4]. Although molecular mechanisms controlling parathyroid cell proliferation and gland size are not yet clear, the endogenous cyclin-dependent kinase (CDK) inhibitor p21, which inhibits progression from the G1 to the S phase of the cell cycle [5;6], may play a role in decreasing parathyroid cell proliferation [7] and attenuating parathyroid hyperplasia [8].

PTH is an 84 amino-acid peptide released from the chief cells of the parathyroid gland. PTH increases plasma Ca, primarily by stimulating Ca resorption from bone and Ca reabsorption in the kidney. PTH stimulates the renal Ca reabsorption, predominantly in the distal tubule via TRPV5, the distal tubule epithelial Ca transporter [9]. PTH increases the expression of TRPV5 and also increases TRPV5 Ca transport [10;11].

In patients with end stage renal disease measurement of PTH is helpful in assessing parathyroid function, estimating bone turn over and improving management [12].

This study was conducted to evaluate serum calcium, phosphorus and parathyroid hormone levels in Sudanese patients under regular hemodialysis**.**

Materials and Methods

The study involved two groups: a control group of apparently healthy (N = 50) matched for age with a test group of chronic renal failure patients under regular haemodialysis and take calcium supplement (N = 50). The age range of both groups was 25-65 years. All volunteers were recruited from Khartoum Teaching hospital – Khartoum - Sudan Venous blood samples were collected from each volunteer in appropriate containers. Serum Calcium and Phosphorus were measured by stander chemical method using chemistry analyzer (cobas c311 analyzer – Germany). Parathyroid hormone levels were determined by electrochemiluminescence using hormone analyzer (cobas e411 analyzer - Germany). Statistical evaluation was performed using the Microsoft Office Excel (Microsoft Office Excel for windows; 2007) and SPSS (SPSS for windows version 19). Normal distribution of the studied variables was examined using Kolmogorov-Smirnova and Shapiro-Wilk tests. Unpaired T-test and Mann-Whitney U test were used to assess significant difference in the means of the studied variables in chronic renal failure patients and healthy individuals. Correlations between serum biochemical profile and the duration of disease were assessed using bivariate correlations. $P < 0.05$ was considered statistically significant.

Results

This study was carried out on 50 hemodialyzed renal failure patients (cases) and 50 apparently healthy individual (control) to determine the effect of chronic renal failure on calcium, phosphorus and parathyroid hormone level. The age of the patients (M±SD =47.5±13.3 years) was comparable with control group (M±SD =43.1±13.4 years, $P = 0.102$).

After conducting the appropriate tests the following results were obtained:
Calcium concentrations were lower in the patients (M±SD = 9.5± 0.83 mg/dl) compared with controls (M±SD = 9.7±0.57 mg/dl), this difference did not reach statistical significance ($P = 0.07$). In contrast phosphorus concentrations were significantly higher in the patients (M±SD = 4.7±1.8 mg/dl) compared with control group (M±SD = 3.6±0.47 mg/dl $P =0.00$). Also parathyroid hormone concentrations were significantly higher in the patients (M±SD = 752±677 pg/ml) compared with control group (M±SD = 55±15 pg/ml $P =0.00$), Table (1).

Table 1: the mean of analyzed parameters in studied group

Parameter	Study Group (n=100)		95% confidence interval for mean in patients group		P.value
	Patients (n =50) Mean±SD	Control (n =50) Mean±SD	Lower	Upper	
Parathyroid hormone (pg/ml)	752±677	55±15	91	2838	0.000
Calcium (mg/dl)	9.5±0.83	9.7±0.57	8.3	11.4	0.070
Phosphorus (mg/dl)	4.7±1.8	3.6±0.47	1.1	11.9	0.000

There is statistical significant correlation between phosphorus and duration of disease *(P* =0.02), and statistical significant correlation also observed between parathyroid hormone and duration of disease *(P* =0.01). But there is no statistical significant correlation between calcium and duration of disease *(P* =0.3).

Discussion

The results obtained that there is no statistically significant difference in levels of calcium, in the hemodialyzed renal failure patients (cases) compared with apparently healthy individuals (control), with the cases showing lower levels of calcium, also the results showed significant increase the levels of phosphorus and parathyroid hormone, this indicates that chronic renal failure have effect on the levels of calcium, phosphorus and parathyroid hormone.

There is a certain risk that secondary hyperparathyroidism with long-term low Ca therapy will develop, even if normocalcemia is maintained. Hyperphosphatemia is one of the main factors in the pathogenesis of secondary hyperparathyroidism.

These results agree with study conducted by Gallieni M, et al. who showed significant increase in phosphorus and parathyroid hormone level [13].

Any alteration in kidney function will lead to altered in calcium, phosphorus and parathyroid hormone level. Chronic Kidney Disease disrupts calcium homeostasis, low calcitriol Reduced intestinal calcium absorption, low serum calcium and high serum phosphorus at low GFR [14].

As the glomerular filtration rate (GFR) declines to < 60 ml/min/ 1.73 m^2, phosphorus excretion becomes altered in the nephron. Although half of the nephrons are not working to excrete phosphorus, the remaining nephrons compensate by hyper-excreting the daily phosphorus load to maintain normal serum phosphorus concentrations. Compensation can generally continue until the GFR declines to < 25–40 ml/min/1.73 m^2. With progressive CKD, when the remaining nephrons can no longer sufficiently excrete the phosphorus load, hyperphosphatemia is detected [15].

Previously it was reported elevation of PTH levels are common among patients with moderate CKD [16].

Silver J et al., reported small decreases in serum Ca^{2+} and more prolonged increases in serum phosphate stimulate the parathyroid gland to secrete parathyroid hormone (PTH) [17].

Excess PTH synthesis and secretion leads deficient inhibition of PTH transcription, so hyperplasia and parathyroid gland enlargement contribute to elevated serum PTH [14].

Calcium, a divalent cation, and phosphorus, a monovalent anion, have a high binding affinity for each another. In serum, as the concentration of one or both ions increases, there is an increased risk for an ionic bond to form, creating an insoluble complex. This process may lead to extraskeletal calcification and potentially calciphylaxis or cardiac disease [18]. Additionally, the precipitation may decrease serum calcium concentrations, further stimulating PTH secretion. In fact, PTH production and secretion may be stimulated by hypocalcaemia, hyperphosphatemia, and vitamin D deficiency [19;20]. Because PTH is chiefly responsible for preventing hypocalcaemia, it stimulates osteoclasts to lyse bone, releasing calcium into the serum. Under normal conditions, there is homeostasis involving osteoclast activity and osteoblast synthetic activity. SHPT produces an imbalance of these activities leading to enhanced bone breakdown that eventuates in renal osteodystrophy [21; 22].

Conclusion

SHPT is a complex and challenging condition. Metabolic parameters such as calcium, phosphate, PTH, and vitamin D must be maintained within target ranges to prevent bone disease and extraskeletal calcification, and decrease cardiac disease risk.

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