

Calcium and Phosphorus Metabolism in Stable Renal Transplant Recipients

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Objectives: This study sought to elucidate the status of calcium, phosphorus, and parathyroid hormone in patients following kidney transplant.

Materials and Methods: In this cross-sectional study, 20 renal transplant recipients were evaluated. For each patient, age, sex, time since transplant, and body weight were recorded. Inclusion criteria were age > 14 years and good allograft function defined as a serum creatinine level < 132.6 $\mu\text{mol/L}$ for at least 6 months after transplant. Exclusion criteria were immunosuppressive therapy other than the standard triple regimen (cyclosporine, prednisolone, and mycophenolate mofetil or azathioprine) and use of any drug known to alter calcium hemostasis. Levels of 24-hour urine calcium, phosphorus, creatinine, and uric acid, as well as concentrations of hemoglobin, serum creatinine, calcium, and phosphorus were measured. To obtain a mean value of serum intact parathyroid hormone in transplant recipients at our center, serum intact parathyroid hormone levels were additionally quantitated in another group of 30 renal transplant recipients.

Results: The mean hemoglobin level was 135.6 ± 17.7 g/L, the mean serum creatinine level was 105.0 ± 15.3 $\mu\text{mol/L}$, and the mean serum calcium and phosphorus levels were 2.25 ± 0.17 mmol/L (normal range, 2.02-2.60 mmol/L) and 1.28 ± 0.24 mmol/L (normal range, 0.81-1.61 mmol/L), respectively. The mean serum intact parathyroid hormone level was 33.17 ± 14.67 ng/L (normal range, 10-60 ng/L). Mean 24-hour urine calcium and phosphorus values were 2.32 ± 1.68 mmol/day (normal, 2.49-6.24 mmol/day)

and 19.77 ± 8.31 mmol/day (normal, 12.91-41.98 mmol/day), respectively. A positive correlation was found between serum calcium and alkaline phosphatase levels ($r = +0.71$, $P = .006$). Hemoglobin level was negatively correlated with serum phosphorus level ($r = -0.65$, $P = .003$) and sex ($r = -0.57$, $P = .003$) and positively correlated with urine creatinine levels ($r = +0.69$, $P = .001$).

Conclusions: Renal transplant recipients with stable allograft function may have normal serum calcium, phosphorus, and intact parathyroid hormone levels. However, presence of hypocalciuria and elevated serum alkaline phosphatase levels might imply impaired calcium metabolism in these patients.

Key words: Parathyroid, Kidney transplantation, Biodegradation, Biotransformation

Defects in calcium and phosphorus metabolism, which usually parallel bone diseases, may complicate the period after renal transplant (1,2,3). Compared with the general population, patients with end-stage renal disease have a 4.4 times greater risk of hip fracture, and the prevalence of vertebral fractures is as high as 21% among persons in this population (3). In renal transplant recipients, serum intact parathyroid hormone concentrations decrease progressively during the first 6 months after transplant, and then decrease at a lower rate for many years after that. However, persistent hyperparathyroidism has been detected in 25% to 43% of renal transplant recipients with normal serum creatinine levels 1 year after transplant, which has been attributed to a slow involution of the hyperplastic parathyroid glands (4,5,6). Recipients of a successful renal transplant experience rapid bone loss during the first year after transplant and may continue to experience persistent bone loss for many years thereafter (2,3). Although this bone loss may be attenuated by bisphosphonates, oversuppression of intact parathyroid hormone levels may lead to dynamic bone disease (7). Cyclosporine

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and glucocorticoids, which are usually used as immunosuppressive drugs, also are known to induce bone loss (1). Disorders of the parathyroid gland and bone could be associated with impaired calcium metabolism either directly or indirectly. Overall, the issue of calcium metabolism following kidney transplant remains controversial. The aim of the present study was to evaluate the status of calcium, phosphorus, and intact parathyroid hormone in such patients.

Materials and Methods

In this cross-sectional study, 20 renal transplant recipients were evaluated. Written informed consent was obtained from all patients. The study protocol, which had been approved by the ethics committee of Tabriz University of Medical Sciences prior to the onset of the study, conformed to the ethical guidelines of the 1975 Helsinki Declaration. Age, sex, duration of pretransplant dialysis, time since transplant, and body weight were recorded for each patient. Inclusion criteria were age > 14 years, recipient of a first or second living-donor kidney transplant, and good allograft function (defined as a serum creatinine level < 132.6 $\mu\text{mol/L}$ for at least 6 months after transplant). Exclusion criteria were immunosuppressive therapy other than the standard triple regimen (cyclosporine, prednisolone, and mycophenolate mofetil or azathioprine), pretransplant administration of a corticosteroid, history of total parathyroidectomy, and use of any drug known to alter calcium hemostasis (bisphosphonates, fluoride, or calcitonin). Hemoglobin and serum calcium, phosphorus, and creatinine levels were measured. Levels of 24-hour urine calcium, phosphorus, creatinine, protein, and uric acid also were measured. Additionally, to obtain a mean value of serum iPTH in transplant recipients in our center, serum intact parathyroid hormone levels were quantitated in another group of 30 renal transplant recipients. Statistical analyses were performed using SPSS for windows (Statistical Package for the

Social Sciences, version 11.0, SPSS Inc, Chicago, IL, USA). All data are expressed as means $\pm$ SD. The Pearson product moment correlation analysis and Kendall tau rank correlation were used for correlations between variables. Values for *P* less than .05 indicated statistical significance.

Results

The mean age of renal transplant recipients was 42.0 ± 13.5 years, and the male:female ratio was 2:3. All patients received cyclosporine (5-8 mg/kg), mycophenolate mofetil (2 g/day), and a corticosteroid (1 g/day methyl prednisolone for 3 successive days followed by a tapering dose of oral prednisolone starting with 1 mg/kg/d). The patients' mean body weight was 66.9 ± 13.5 kg (range, 36-90 kg), and the mean duration of pretransplant dialysis was 26.6 ± 4.4 months (range, 20-38 months). The mean time since renal transplant was 34.8 ± 30.16 months (range, 9-110 months). The mean hemoglobin level was 135.6 ± 17.7 g/L. The mean serum creatinine level was 105.0 ± 15.3 $\mu\text{mol/L}$. The mean 24-hour urine creatinine and uric acid concentrations were 9172.8 ± 3982.5 μmol (normal, 7072-17680 μmol) and 2761.2 ± 982.1 μmol (normal, 1487-4461 μmol), respectively.

Serum calcium, phosphorus, and intact parathyroid hormone concentrations as well as urine calcium and phosphorus levels all were within normal limits (Table 1). The mean alkaline phosphatase level was elevated at 6.16 ± 8.22 $\mu\text{kat/L}$ (normal range 1.22-5.10 $\mu\text{kat/L}$). A positive correlation was found between serum calcium and alkaline phosphatase levels ($r = +0.71$, $P = .006$). Hemoglobin level was negatively correlated with serum phosphorus level ($r = -0.65$, $P = .003$) and sex ($r = -0.57$, $P = .003$) and positively correlated with urine creatinine levels ($r = +0.69$, $P = .001$). Urine creatinine also was negatively correlated with sex ($r = -0.43$, $P = .037$). There were no significant correlations between age, sex, duration of dialysis, time since transplant, serum calcium and phosphorus levels, and 24-hour urine calcium and phosphorus concentrations ($P > .05$).

Table 1. Variables related to Ca metabolism in the present study.

	Mean value $\pm$ SD	Range	Normal range
Serum Ca (mmol/L)	2.25 ± 0.17 (8.97 ± 0.66)	2.00-2.64	2.02-2.60
Serum P (mmol/L)	1.28 ± 0.24 (3.98 ± 0.74)	0.90-1.74	0.81-1.61
Alkaline phosphatase ($\mu\text{kat/L}$)	6.16 ± 8.22 (369.8 ± 492.8)	1.22-31.37	1.22-5.10
Urine Ca (mmol/day)	2.32 ± 1.68 (92.8 ± 67.2)	0.45-5.34	2.49-6.24
Urine P (mmol/day)	19.77 ± 8.31 (612.5 ± 257.3)	13.56-31.64	12.91-41.98
iPTH (ng/L)	33.17 ± 14.67	15-68	10-60

Abbreviations: Ca, calcium; iPTH, intact parathyroid hormone; P, phosphorus

Discussion

The results of this study show that serum calcium, phosphorus, and intact parathyroid hormone levels are, more often than not, normal in renal transplant recipients. Previous studies have shown a relatively high percentage of hyperparathyroidism and hypercalcemia in renal transplant recipients (8,9). Evenepoel and colleagues revealed that in hyperparathyroid recipients, intact parathyroid hormone levels declined rapidly during the first 3 months after transplant, which was related to posttransplant changes in serum calcium and phosphorus levels (8). These authors detected a high prevalence of hypercalcemia and hypophosphatemia in the early posttransplant period and attributed this finding to decreased tubular reabsorption of phosphate. However (and similar to our results), Berczi and colleagues found normal serum calcium and phosphorus levels in patients after kidney transplant (10).

Relative hypocalciuria and elevated serum alkaline phosphatase levels were found in patients in this study. The former implies a state of increased renal tubular calcium reabsorption after transplant. Elevated serum alkaline phosphatase levels also may indicate heightened bone turnover. While successful kidney transplant reverses many problems associated with uremia that are not corrected by dialysis therapy, renal osteodystrophy (a long-term complication of end-stage renal disease) usually persists. Bisphosphonates and vitamin-D metabolites are used to prevent and diminish early bone loss after renal transplant. It has been shown that 90% to 100% of renal transplant recipients have histologic evidence of osteodystrophy and osteopenia (2,3). Moreover, enhanced loss of bone mass in the early and late posttransplant period has been observed (2,11). Babarykin and colleagues also noted hypocalciuria in the late period after renal transplant (more than 5 years) and suggest that this might be due to parathyroid gland hyperfunction and the negative effects of the steroid therapy (1).

The pretransplant status of the parathyroid gland was not examined in this study. However, the finding

in renal transplant recipients in Iran of a normal calcium, phosphorus, and parathyroid hormone status might be related to the availability of living-donor kidneys and early transplant. In this study, the mean duration of pretransplant dialysis was approximately 2 years.

In conclusion, renal transplant recipients with stable allograft function might have normal serum calcium, phosphorus, and intact parathyroid hormone levels. However, the presence of hypocalciuria and elevated serum alkaline phosphatase might imply impaired calcium metabolism in these patients. We hope this information proves useful for clinicians dealing with kidney transplant issues.

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