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Parathyroid Gland Function in Kidney Transplanted Patient: A single Center Experience

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Abstract
Introduction: Information on the time course of serum parathormone levels after renal transplantation is scanty. Both the abrupt cessation of calcium-containing phosphorus binders and vitamin D (analogs) at the time of surgery and the recovery of renal function may be hypothesized to affect parathyroid gland. This study firstly examined frequency distribution of various biochemical parameters such as alkaline phosphatase (ALP), phosphorus (P), intact parathormone (iPTH) and calcium (Ca) in renal transplanted patients and secondly examined the relationship between these parameters and various demographic data of renal transplanted recipients. *Material and Methods*: we studied 72 renal transplanted patients (47 men and 25 women with mean ages of 44 ± 12 years and mean body mass index of 24.2 ± 3.9. Serum Ca, P, ALP and serum iPTH were measured. Results: In this study, mean serum Ca and iPTH were 9.5 ± 0.7mg/dL and18.4 ± 8.2 Pg/mL (median=16.5). Mean serum ALP was 169 ± 133 IU/L (median=131). In this study, there was a negative relationship between serum iPTH and creatinine clearance (r=-0.44 P< 0.001). There was no correlation between the duration of renal transplantation and serum iPTH (P> 0.05). There were inverse correlations of serum ALP with age (r=-0.35 P= 0.02) and duration of kidney transplantation (r=-0.29 P= 0.01). *Conclusions*: In contrast to previous findings, in this group of patients, there was not secondary hyperparathyroism or significantly increased bone activity. The results showed suppressed parathormone secretion. The reason may be due to excessive intake of calcium and Vitamin D analogues, which suppress the parathyroid gland, and may prone these patients to adynamic bone disease.

Keywords: Parathormone; Kidney; Transplantation; Renal function test.

Introduction

Renal Transplantation (RTx) is a treatment of choice for patients with end-stage kidney disease [1, 2]. Kidney transplantation corrects most of the metabolic disorders [1-3]. Post-transplant bone disease is a heterogeneous disease due to the effects of age, gender, persistent hyperparathyroidism, corticosteroids and therapy with calcineurin inhibitors [2-5]. During the last decade, several investigators have been studying parathyroid hormone status and bone metabolism in renal transplant recipients [6-10]. Indeed, increasing life expectancy after kidney transplantation seeks the

prevention of long-term complications, such as bone disease. Bone disease is one of the long-term complications that can significantly influence quality of life [8-13]. Hypercalcemia is reported in up to 66% of the transplant recipients and typically occurs within the first 3 months after transplantation (10-17]. Successful renal transplantation excludes a number of etiological factors that lead to the development of hyperparathyroidism during renal insufficiency [15-17] and parathyroid function tends to normalize over time in many patients. Therefore, it is necessary to evaluate parathyroid gland function as a regular follow up of these patients. Our aim was to evaluate the post-transplant natural history of parathyroid function and calcium metabolism in a group of Iranian patients with a functional renal graft .Therefore, this study investigated the parathyroid gland function and associations between various indexes of bone turn-over with serum intact parathormone level in stable kidney transplant patients.

Material and Method

Patients

This cross-sectional study was conducted on a group of stable kidney transplanted patients who referred to the clinic of nephrology for continuing their treatment. All patients signed the consent form for participation in this study. Exclusion criteria were any of the following: presence of acute rejection, any active or chronic infection, taking antibiotics during the past two months, and taking drugs such as non steroidal anti-inflammatory drugs. After admission, all patients were examined and patient's histories concerning the timespan since they had undergone kidney transplantation and their treatments were obtained. Patients were also examined for blood pressure (BP) and body mass index. The etiology of renal failure of the patients was various, including diabetic nephropathy, hypertension, various glomerulonephritis [18-21], cystic disease and infection. Body mass index (BMI) was calculated using the standard formula (weight in kilograms/squared height in square meters). The basic immunosuppressive regimen of the recipients consisted of a combination of Cyclosporine at a mean dosage of 190 ± 60 mg/d (median=200 mg/d), Prednisolon 7.5 mg/d for all of the patients and Mycophenolate mofetile in 46% of the patients at a dosage of 1500 ± 500 mg/d (median=1500 mg/d)/or Azathioprine at a dosage of 50 to 100 mg/d in the rest of the patients. Also patients were under treatment with Calcium carbonate and Rocaltrol at various doses.

Laboratory methods

Serum intact parathormone (iPTH) levels were measured as follows: blood samples were drawn after an overnight fast, and were centrifuged within 15 minutes of drawing and measured by Radioimmunoassay method (normal range of values: 10-65 pg/mL). Blood samples were collected for biochemical analysis including serum creatinine (Creat), blood urea nitrogen (BUN), serum magnesium (Mg), phosphorus (P), calcium (Ca), alkaline phosphatase (ALP) and serum albumin (Alb) levels, using standard kits. Creatinine clearance (CrCl) was evaluated from serum creatinine, age and body weight [22].

Statistical Analysis

Descriptive results were expressed as the mean ± SD and median values. A statistical correlation was assessed using a partial correlation test. Comparisons between groups were done using student's t test. For normalization of the iPTH data, their second square values were used. All statistical analyses were performed with the SPSS statistical package (version 11.5 for Windows; SPSS, Chicago, USA). Statistical significance was determined at a P-value < 0.05.

Results

A total of 72 patients were enrolled in this study, including 47 men and 25 women. Among them, 11 patients had diabetes mellitus. The mean patients' age was 44 ± 12 years. The mean length

of time since patients had received a transplanted kidney was 67.5 ± 42 months (median: 62 months).

Table 1. Data of the patients

N=72	Minimum	Maximum	Mean ± SD	Median
Age (year)	13	61	44 ± 12	44
DKT (month)*	4	162	67.5 ± 42	62
BMI (kg/m2)	15	33	24 ± 4	17
Ca (mg/dL)	6.7	10.7	9.5 ± 0.7	9.6
P (mg/dL)	2.5	5	3.7 ± 0.6	3.7
iPTH* *(Pg/mL)	4	40	18.4 ± 8.2	16.5
Alb (g/dL)	2.5	6.2	4.2 ± 0.5	4.2
Mg(mg/dL)	1.5	2.5	1.9 ± 0.2	1.9
ALP(IU/L)	35	963	169 ± 133	131

*duration of kidney transplantation, **Intact PTH (iPTH)
SD = standard deviation

Table 1 shows descriptive data of the patients. Mean serum Ca and iPTH were 9.5 ± 0.7mg/dL and 18.4 ± 8.2 Pg/mL (median=16.5). Mean serum ALP was 169 ± 133 IU/L (median=131). We found a negative relationship between serum iPTH and creatinine clearance (r=-0.44 P< 0.001; Figure 1).

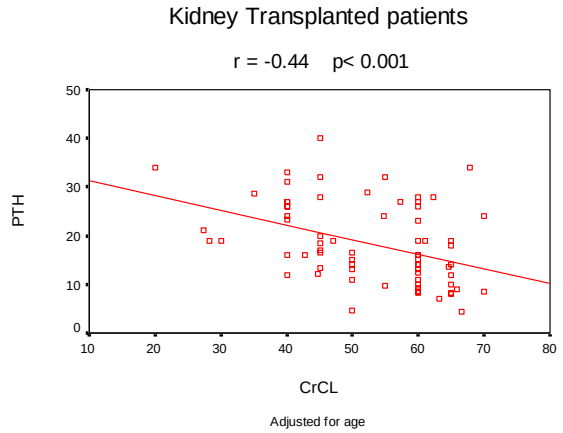

Figure 1. Negative relationship between serum iPTH (Pg/mL) and creatinine clearance (cc/min)

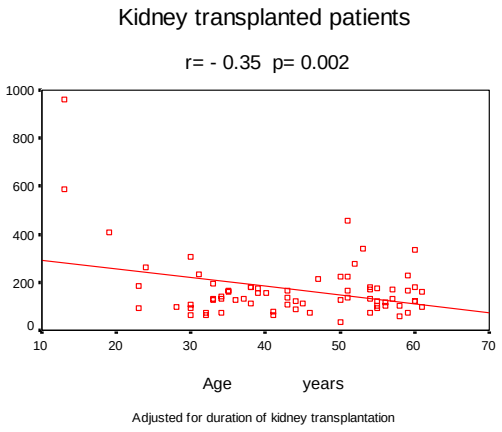

Figure 2. Inverse correlation of serum ALP (IU/L) with age (years)

There was no correlation between the duration of renal transplantation and serum iPTH (P> 0.05). There were inverse correlations of serum ALP with age (r=-0.35 P= 0.02; Figure 2) and duration of kidney transplantation (r=-0.29 P= 0.01; Figure 3).

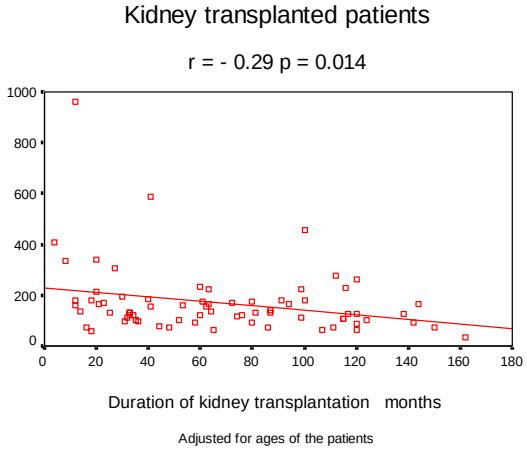

Figure 3. Inverse correlation of serum ALP (IU/L) with duration after RTx (months)

Discussion

Knowledge of the natural history might help in determining the time at which specific treatment should be initiated in order to minimize any detrimental effect of parathormone on bones. The presence of risk factors in kidney transplant recipients may warrant a closer follow-up. In the current study we found a negative relationship between serum iPTH and creatinine clearance. There was no correlation between the duration of renal transplantation and serum iPTH. There were inverse correlations of serum ALP with age and duration of kidney transplantation. This study used the association between parathyroid hormone and alkaline phosphatase with serum creatinine to define bone turn over in kidney transplanted patients. The natural history of parathyroid function after successful RTx and the factors predisposing to consistent hyperparathyroidism (HPT) are not well established. A better knowledge of these data may be helpful in the development of algorithms for optimal surveillance and treatment of HPT after successful RTx. Evenepoel et al. studied 1332 kidney allograft recipients, transplanted between 1989 - 2000, and found that 4.1% of their patients had persistent hyperparathyroidism and needed parathyroidectomy after a first successful kidney transplantation. They concluded that persistent hyperparathyroidism requiring parathyroidectomy after successful kidney transplantation is a common clinical problem [23]. It seems that secondary hyperparathyroidism and its associated bone and vascular complications are highly prevalent in patients undergoing renal replacement therapy (24-36). However, in the present study, our results were different. Our patients' mean iPTH was 18.4 (± 8.2) pg/mL (median: 16.5), which means that there was no hyperparathyroidism. In contrast, the level of parathormone was suppressed. Also, the mean ALP was 169 ± 133 IU/L (median=131), and best showed that in these patients there was not a significantly increased bone activity due to secondary hyperparathyroidism. One reason may be due to excessive intake of calcium and Vitamin D analogues. Indeed, secondary hyperparathyroidism is a frequent complication in patients with chronic renal failure [2, 3, 23-36]. Successful kidney transplantation corrects the abnormalities responsible for secondary hyperparathyroidism in the first months [37, 38]. However, elevated intact PTH (iPTH) levels have been observed in >25% of patients one year after transplantation in the presence of good renal function [37-40].

Conclusion

This study was designed to examine the frequency distribution of various biochemical parameters such as ALP, P, iPTH and Ca in a group of RTx patients and secondly examined the relationship between these parameters with various demographic data of renal transplanted recipients. We concluded that, the reason may be due to excessive intake of calcium and Vitamin D analogues, which suppress the parathyroid gland, and may prone these patients to adynamic bone disease.

Ethical Issues

This study was approved by the ethical committee of Shahrekord University of Medical Sciences.

Conflict of Interest

The authors declare that they have no conflict of interest.

Authors' Contributions

HN defined the aim of research and the study design and carried out the experiments. AB participated in the design of the study and performed the statistical analysis. All authors read and approved the final manuscript.

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