

Parathyroidectomy After Kidney Transplantation: A Single-Center Experience

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ABSTRACT

Objective: Even after successful kidney transplantation, 10% to 50% of kidney transplant recipients have persistent hyperparathyroidism. Parathyroidectomy (PTX) has been reported to be associated with deterioration of renal function and reduced graft survival. The aim of this single-center, retrospective study was to analyze the long-term effect of PTX on calcium, phosphorus, and parathyroid hormone (PTH) levels, as well as the estimated glomerular filtration rate (eGFR), in renal transplantation patients who underwent PTX.

Methods: The study population consisted of 154 patients followed between January 2014 and December 2017, 9 of whom underwent PTX. The median PTH, calcium, phosphorus, and eGFR values were recorded before and after PTX.

Results: The median preparathyroidectomy PTH, calcium, phosphorus, and eGFR values were 311.57 pg/mL, 11.02 mg/dL, 2.35 mg/dL, and 90.88 mL/minute, respectively. When compared with the baseline figures, there was a decrease in PTH (311.5 vs. 147.5 pg/mL; $p=0.015$), calcium (11.02 vs. 9.01 mg/dL; $p=0.017$), and eGFR (90.88 vs. 75.44 mL/minute; $p=0.008$), and an increase in the phosphorus level (2.35 vs. 3.4 mg/dL; $p=0.06$) 1 month after surgery. The eGFR returned to the baseline rate 1 year after surgery (90.88 vs. 79.39 mL/minute; $p=0.11$).

Conclusion: PTX in renal transplant recipients appears to be a safe procedure. Although renal function deteriorates in the acute period following PTX, long-term stabilization occurs.

INTRODUCTION

It is supposed that hyperparathyroidism (HPT) improves in the first year after renal transplantation.^[1] Nevertheless, 10%–50% of the cases still show persistent HPT even after a successful renal transplantation,^[2] and its occurrence is thought to be related to the period elapsed under dialysis prior to transplantation.^[3] Although HPT has been recognized after a long time from renal transplantation, management of the disease is still controversial.^[4] Vitamin D is the suggested treatment method for cases with persistent HPT; however, hypercalcemia limits its usage.^[5] Following transplantation, parathyroidectomy (PTX) is the preferred choice of treatment because nodular hyperplasia of the

parathyroid glands shows monoclonality and aggressive proliferation that is resistant to medical therapy.^[6]

If hypercalcemia is refractory to medical treatment for more than a year following transplantation, PTX is the best choice of treatment.^[7]

On the other hand, there are controversial opinions for consequences of PTX. After PTX, a decrease in kidney function may be observed after transplantation.^[8] However, Tseng et al.^[9] did not confirm this deterioration following surgery.

The aim of the present study was to analyze the effects of PTX on parathyroid hormone (PTH), phosphorus, and calcium concentrations as well as its impact on kidney function.

MATERIAL AND METHODS

We retrospectively evaluated renal transplant recipients who had undergone PTX due to HPT after transplantation between January 2014 and January 2017. Demographic data, such as age, gender, type of dialysis, time on dialysis, time of PTX after transplantation, immunosuppressive treatment applied, and usage of vitamin D or cinacalcet, were obtained from medical records. We checked the blood concentrations of PTH, calcium, phosphorus, and estimated glomerular filtration rate (eGFR) before PTX and at postoperative first month, first year, and the last record of follow-up. The Chronic Kidney Disease Epidemiology Collaboration formula is used to determine eGFR. PTH is measured as intact PTH (reference range: 10–65 pg/mL).

The SPSS 17.0 package program was used for statistical analysis. Continuous variables were expressed as median.

Wilcoxon rank test was used for comparison of calcium, phosphorus, PTH, and eGFR before and after PTX. A p-value <0.05 was considered statistically significant.

RESULTS

The mean age of two female and seven male patients was 51.78 (44–64) years.

Between January 2014 and December 2017, 9 out of 154 renal transplant patients underwent PTX due to persistent HPT. The rate of PTX in our transplant clinic was found to be 5.8% during the study. Renal replacement therapy before transplantation was hemodialysis for all patients.

The median period of dialysis prior to renal transplantation was 9.56 (5–13) years.

The median time for parathyroid surgery after renal transplantation was 34 (5–64) months (Table 1).

The method of surgery was subtotal PTX.

The median pre-operative values were 311.57 (102.8–685.3) pg/mL for intact PTH, 11.02 (9.8–12.6) mg/dL for calcium, 2.35 mg/dL for phosphorus, and 90.88 (50–141) mL/min for eGFR. One month after surgery, PTH (311.57 vs. 147.5 pg/mL, p=0.015), calcium (11.02 vs. 9.01 mg/dL, p=0.017), and eGFR levels (90.88 vs. 75.44 mL/min, p=0.008) decreased, and phosphorus (2.35 vs. 3.4 mg/dL, p=0.06) increased compared with pre-PTX levels. There were a decrease in PTH (311.57 vs. 134.54 pg/mL, p=0.008), calcium (11.02 vs. 9.56 mg/dL, p=0.038), and eGFR levels (90.88 vs. 81.55 mL/min, p=0.11) and an increase in phosphorus (2.35 vs. 3.06 mg/dL, p=0.038) 1 year after surgery.

There were a decrease in PTH (311.57 vs. 112.2 pg/mL, p=0.008), calcium (11.02 vs. 9.51 mg/dL, p=0.021), and eGFR (90.88 vs. 79.39 mL/min, p=0.06) levels and an increase in phosphorus (2.35 vs. 2.82 mg/dL, p=0.08) at the end of follow-up. eGFR was found to decrease significantly 1 month following PTX. It was observed that this decrease was reversed after 1 year of follow-up (Table 2).

A decrease in eGFR (p=0.066) and an increase in serum phosphorus (p=0.08) were not found to be statistically sig-

Table 1. Demographic and clinical characteristics of kidney transplantation patients who underwent PTX

n=9	
Age, years (median)	51.78 (44–64)
Dialysis vintage, years (median)	9.56 (5–13)
Immunosuppressive regimen (n, %)	
Containing TAC	5 (55.6)
Containing CsA	1 (11.1)
Containing everolimus	3 (33.3)
Time from transplantation to surgery, month	33.67 (5–64)
Use of cinacalcet, n (%)	2 (22.2)
PTH level at the time of transplantation, pg/mL (median)	887.33 (475–1378)
Calcium level before surgery (mg/dL)	11.02 (9.8–12.6)
Phosphorus level before surgery (mg/dL)	2.35 (1.7–3)
PTH level before surgery (pg/mL)	311.57 (102.8–685.3)

TAC: Tacrolimus; CsA: Cyclosporin A; PTH: Parathyroid hormone.

Table 2. Calcium, phosphorus, PTH, and eGFR levels before and after PTX

	Pre-PTX	1 month level/p value	1 year level/p value	End of follow-up level/p value
Calcium (mg/dL)	11.02	9.01/0.017	9.56/0.038	9.51/0.021
Phosphorus (mg/dL)	2.35	3.4/0.066	3.06/0.038	2.82/0.08
PTH (pg/mL)	311.75	147.5/0.015	134.54/0.008	112.2/0.008
eGFR (mL/min)	90.88	90.88/0.008	81.55/0.11	79.39/0.066

PTH: Parathyroid hormone; eGFR: Estimated glomerular filtration rate; PTX: Parathyroidectomy.

nificant at the end of the follow-up period. Calcium and PTH levels were found to be significantly decreased at the end of follow-up ($p=0.021$ and $p=0.008$, respectively).

During follow-up time, three patients relapsed and were administered cinacalcet.

DISCUSSION

In case of HPT following renal transplantation, successful PTX prevents various consequences of prolonged hypercalcemia and improves symptoms of established complications, as well.^[10,11]

In the current analysis, PTH and calcium levels decreased significantly, and phosphorus levels were normalized in the long term following PTX. Stabilizing normal serum calcium levels positively affects allograft survival.^[12] Therewithal, cessation of loss of phosphorus in urine due to PTH results in increase in bone mineral density.^[13] Although PTX is thought to play a role in graft protection,^[14] Garcia et al.^[6] suggested that PTX itself has a deteriorating effect on allograft function, resulting in allograft dysfunction in the long term.

The reason of renal allograft function deterioration following PTH is unclear. However, acute decrease in serum PTH following PTX may cause a decrease in kidney perfusion. PTH plays a role on kidney blood flow and glomerular filtration rate. It has an important role in both preglomerular vasodilatation and efferent vasoconstriction.^[15]

Finding out how acute deterioration of renal function occurs shortly after PTX may enable better selection of the right cases.^[16]

Consistently, we observed a significant decrease in eGFR at the first month following PTX in transplant recipients; however, eGFR approaches to presurgery levels 1 year after PTX. Deterioration of renal function at the last follow-up visit was statistically insignificant compared with baseline. This suggests that deterioration persists only for a short term. Schwarz et al.^[17] showed that higher PTH levels prior to PTX and total PTX with autotransplantation are significant predictors of kidney allograft deterioration in 76 cases. Schlosser et al.^[18] also reported that factors including decreased renal function during PTX and total PTX rather than subtotal PTX increase the incidence of allograft function deterioration. In our study, PTX type was subtotal PTX. Longer dialysis treatment is thought to increase the possibility of tertiary HPT.^[19] In our analysis, the duration of dialysis prior to transplantation was 9.56 years.

PTX has a negative hemodynamic effect on renal perfusion. This may be more important in the first year because calcineurin inhibitor-induced renal vasoconstriction is prominent,^[20] and acute rejection may occur.

HPT following renal transplantation improves gradually in the first year of transplantation,^[1] and early post-transplant PTX increases the risk of renal allograft dysfunction. For this reason, PTX may be delayed for 1 year after transplantation. During this period, cinacalcet is administered. Late post-transplant PTX is not expected to have a detrimental effect on kidney function.^[21] Cruzado et al.^[22] reported that PTX is better than cinacalcet in normalizing blood calcium concentrations and PTH levels.

Three patients were found to have recurrent HPT in the long-term follow-up and were treated with cinacalcet.

Since our study was performed with a small number of retrospective patients, future prospective studies should be conducted to further elucidate the relationship between PTX and eGFR.

CONCLUSION

In HPT after renal transplantation, PTX decreases GFR level at 1 month but does not cause deterioration of GFR level in the long term. For this reason, PTX is a safe procedure for HPT after renal transplantation.

Ethics Committee Approval

This was a retrospective study, therefore no ethics committee approval was taken.

Informed Consent

Retrospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: E.P.; Design: E.P.; Data collection &/or processing: E.P., M.M.; Analysis and/or interpretation: E.P., S.F.Y.; Literature search: O.A., A.B.H.; Writing: E.P.; Critical review: Z.B.B.

Conflict of Interest

None declared.

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Böbrek Nakli Sonrası Paratiroidektomi: Tek Merkez Deneyimi

Amaç: Başarılı böbrek transplantasyonundan sonra bile, alıcıların %10–50'sinde kalıcı hiperparatiroidi görülebilir. Paratiroidektominin (PTX) böbrek fonksiyonlarında ve graft sağkalımında bozulma ile ilişkili olduğu bildirilmiştir. Çalışmamızda, merkezimizde takip edilen ve PTX uygulanan böbrek nakli hastalarında PTX'in kalsiyum, fosfor, parathormon (PTH), tahmini glomerüler filtrasyon hızına (eGFR) uzun dönem etkilerini geriye dönük olarak değerlendirmeyi amaçladık.

Gereç ve Yöntem: Ocak 2014–Aralık 2017 tarihleri arasında takip edilen 154 olgudan dokuzuna PTX uygulanmıştı. PTX öncesi ve sonrası medyan PTH, kalsiyum, fosfor ve eGFR değerleri kaydedildi.

Bulgular: Paratiroidektomi öncesi medyan PTH, kalsiyum, fosfor ve eGFR değerleri sırasıyla 311.57 pg/mL, 11.02 mg/dL, 2.35 mg/dL ve 90.88 mL/dk idi. Bazal değerler ile bir aylık kontrol değerleri karşılaştırıldığında PTH (311.5 pg/mL vs. 147.5 pg/mL, p=0.015), kalsiyum (11.02 mg/dL vs. 9.01 mg/dL, p=0.017) ve eGFR (90.88 mL/dk vs. 75.44 mL/dk, p=0.008) değerlerinde azalma, fosfor seviyelerinde artma (2.35 vs 3.4 mg/dL, p=0.06) görüldü. Bir yıllık kontrolde eGFR bazal seviyelerine döndü (90.88 mL/dk vs. 79.39 mL/dk, p=0.11).

Sonuç: Böbrek nakli sonrası PTX uygulanması güvenilir bir metoddur. Her ne kadar PTX sonrası böbrek fonksiyonlarında erken dönemde bozulma görülse de, uzun dönemde stabilizasyon sağlanır.

Anahtar Sözcükler: Böbrek nakli; kalsiyum; paratiroidektomi.