EFFECTIVENESS AND SAFETY OF ORAL PARICALCITOL ON LONG-TERM TREATMENT OF SECONDARY HYPERPARATHYROIDISM IN KIDNEY TRANSPLANT PATIENTS.

C. Massimetti, G. Imperato, L. De Galasso, S. Feriozzi
Centro di Riferimento di Nefrologia e Dialisi, Ospedale Belcolle, Viterbo, Italy

INTRODUCTION

Posttransplant secondary hyperparathyroidism (sHPT),which occurs in 40–60% of kidney transplant (RTx) recipients 1 year posttransplant, and in 20–40% of patients in long-term follow-up. That can be responsible of: greater bone mass loss; increased fractures risk; hypercalcemia and risk of nephrocalcinosis with loss of renal function, and vascular calcification; need for parathyroidectomy. Paricalcitol is a vitamin D analog and selective activator of the VDR has been shown to be effective in the control of sHPT IPS associated with CKD stages 3-5, with little effect on the levels of serum calcium and phosphorus. However there are few studies on the long-term use and safety of PCT in RTx.

Therefore we wanted to evaluate the efficacy and safety of the use of PCT in a group of patients with RTx affected by sHPT.

SUBJECTS AND METHODS

On this purpose we perspectively selected 24 RTXs with high PTH levels, as defined by the guidelines KDOQI (AJKD 2003). The main selection criteria were: RTx vintage > 6 months; increased PTH levels for at least 6 months; serum calcium levels < 10.2 mg/dl; serum phosphate levels < 4.5 mg/dl; eGFR (CKD-EPI) steadily > 15 ml/min/1.73 m2 . Laboratory tests were performed every 6-8 weeks and included: sCr, eGFR, sCa, sPO4, PTH, alkaline phosphatase, urinary calcium, urinary phosphate, proteinuria, cyclosporine (CsA) and tacrolimus (Tac) levels. Proteinuria was performed on samples in the morning and expressed as mg/g Cr. Paricalcitol was started at a dose of 1 µg/d, but if the serum calcium level was > 10.5 mg/dl or if there was a substantial increase in the urinary calcium, expressed as uCa/uCr (mg/mg), paricalcitol was reduced to 1 µg every other day, if the serum calcium was higher than 11 mg/dl was temporarily stopped. The dose of paricalcitol was reduced even when the serum phosphorus was > 5 mg / dl.

RESULTS

Table 1 shows the main baseline characteristics of the patients studied. Table 2 shows the trend of the main clinical and laboratory parameters evaluated during the study. During the study a mild increase in sCa and sPO4 was observed, and were recorded only two episodes of hypercalcemia and hypercalciuria which required temporary reduction of PCT dose or its interruption, urinary calcium increased significantly at six months without significant increased in sCa levels, there were not episodes of hyperphosphatemia. Parathormone levels decreased significantly at F-U (P <0.05) with a decrease of -56% (Figure 1 and 2). During the study we did not observed any change in kidney function. At baseline, only 5 of the 24 patients had proteinuria > 500 mg/g Cr and during this study did not change. Serum levels of cyclosporine and tacrolimus were stable during the observation. Bloodpressure and antihypertensive therapy showed no changes during the study.

Table 1. Main clinical characteristics

Age, y/o	58 ± 12	Urinary Ca/Cr, mg/mg	0.10 ± 0.08
Gender (M/F)	18/6	Urinary phosphorous, mg/24 h	760 ± 355
Dialysis vintage, months	25 ± 24		288 ± 302
Graft vintage, months	85 ± 86	Proteinuria, mg/L	371 ± 353
Serum creatinine, mg/dl	1.9 ± 0.8	Proteinuria, mg/g Cr	133 ± 13
eGFR, mL/min/1.73 m^2	45 ± 26	Systolic BP, mmHg	77 ± 7
Serum calcium, mg/dl	9.4 ± 0.5	Diastolic BP, mmHg	96 ± 7
Serum phosphorus, mg/dl	2.9 ± 0.5	Mean Blood Pressure, mmHg	5.1 ± 2.1 (19)
Ca x PO_4 product, mg^2/dL^2	28 ± 5		10
PTH, pg/ml	232 ± 166	Steroids, mg/d (n° pts)	9
total ALP, mU/ml	103 ± 40	Cyclosporin, n° pts	8
25OHD_3, ng/ml	18.4 ± 14.4	Tacrolimus, n° pts	8
Albumin, gr/dL	3.8 ± 0.3	RAAS blocking agents, n° pts	9
Hemoglobin, g/dl	13.3 ± 1.4		9
Urinary calcium, mg/24 h	113 ± 60	CCBs, n° pts	0.97 ± 0.10
		B-blockers, n° pts	
		Diuretics, n° pts	
		Paricalcitol, µg/d	

Table 2. Main clinical changes during paricalcitol treatment

Months	-6	0	6	12	18	24
sCr, mg/dl	1.9±0.7	1.9±0.8	1.9±0.9	1.9±0.9	1.9±1.0	1.9±0.9
eGFR, ml/m'/1.73 m^2	44±23	45±26	44±21	45±25	43±22	45±25
sCa, mg/dl	9.4±0.4	9.4±0.5	9.7±0.5	9.7±0.5	9.6±0.4	9.5±0.3
sPO4, mg/dl	2.7±0.6	2.9±0.5	3.2±0.7	3.1±0.7	3.0±0.6	3.0±0.6
Ca x PO4, mg^2/dl^2	26±5	28±5	31±7	30±7	29±6	29±6
PTH, pg/ml	203±147	232±165	138±82	141±103	121±88	83±35*
PTH reduction, %			-37	-36	-40	-56
ALP, mU/ml	92±36	103±40	83±27	82±23	76±23	80±24
Urinary Ca, mg/24h	107±76	113±40	138±80*	123±82	152±105*	129±73
uCa/uCr, mg/mg	0.09±0.10	0.10±0.08	0.15±0.14*	0.10±0.09	0.11±0.09	0.11±0.10
Urinary PO4, mg/24h	751±287	760±355	677±267	723±364	674±267	642±277
Proteinuria, mg/gr Cr	387±481	371±353	368±451	534±1095	301±571	321±423
Mean BP, mmHg	97±6	96±7	94±7	93±7	96±6	95±7
ACEi/AT1-b	8	8	8	8	9	9
CsA, ng/ml (n° pts)	93±46 (9)	95±49	118±75 (10)	83±37	85±45	71±48
Tac, ng/ml (n° pts)	6.2±2.9 (8)	(10)	5.8±1.8 (9)	(10)	(10)	(10)
Paricalcitol, µg/d		6.4±2.3	1.0±0.0	5.9±1.9	4.7±1.1	5.4±0.9
		(9)		(9)	(9)	(9)
				0.9±0.2	0.8±0.2	0.6±0.2

* $P < 0.05$ vs baseline

Figure 1. Percent decrease of serum PTH levels during F-U

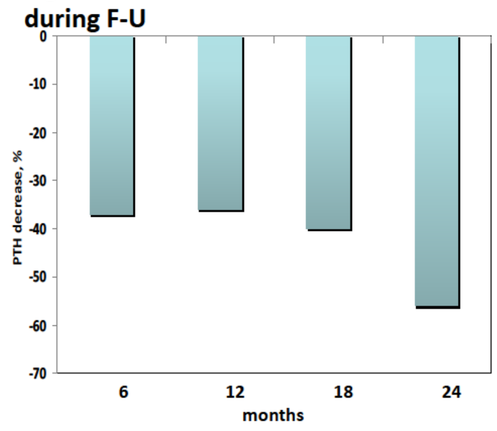
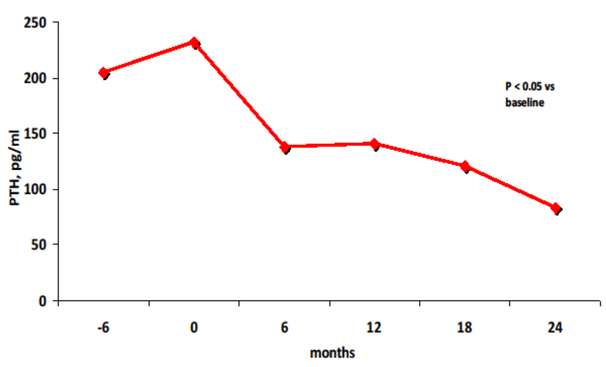


Figura 2. Changes in PTH levels during the study



FINAL THOUGHTS

- Paricalcitol has proven effective in controlling sHPT in RTx.
- Paricalcitol showed few side effects such as hypercalcemia, hypercalciuria and hyperphosphatemia.
- Paricalcitol did not have negative effects on renal function or on blood levels of CsA or Tac.
- We do not have sufficient data to show any impact of paricalcitol therapy on proteinuria.

DOI: 10.3252/pso.eu.52era.2015