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Abstract: BACKGROUND: Cinacalcet rapidly normalizes serum calcium and reduces intact parathyroid hormone (PTH) levels in renal transplant patients with hypercalcaemia and persistent hyperparathyroidism. The aim of this study is to evaluate the 6 months efficacy of cinacalcet and the effect of cinacalcet withdrawal on serum calcium and PTH in such patients. Furthermore, the impact of cinacalcet on bone turnover and quality of life was assessed. METHODS: Twelve renal allograft recipients with hypercalcaemia due to persistent hyperparathyroidism were treated with cinacalcet for 26 weeks. Cinacalcet was then withdrawn to check for recurrence of hypercalcaemia. RESULTS: Cinacalcet maintained normocalcaemia in all patients from week 4 to 26, and PTH significantly decreased and remained suppressed. Serum phosphate increased, whereas the serum calcium-phosphate product remained unchanged. The excretion of calcium and phosphate in the 24 h urine had tendency to decrease. After cinacalcet was withdrawn, hypercalcaemia recurred rapidly and PTH increased to baseline values. Renal function remained stable, proteinuria was unchanged and no allograft rejection was observed. During treatment with cinacalcet, total and bone-specific alkaline phosphatase increased, whereas the urinary deoxypyridinoline-creatinine ratio did not change significantly, suggesting enhanced bone formation. Quality of life assessed at weeks 10 and 26 remained unchanged compared with baseline. CONCLUSIONS: In conclusion, continued treatment with cinacalcet is required to maintain long-term normocalcaemia and to suppress the enhanced PTH production in renal transplant recipients with persistent hyperparathyroidism.

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Effective control of persistent hyperparathyroidism with cinacalcet in renal allograft recipients

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Abstract

Background. Cinacalcet rapidly normalizes serum calcium and reduces intact parathyroid hormone (PTH) levels in renal transplant patients with hypercalcaemia and persistent hyperparathyroidism. The aim of this study is to evaluate the 6 months efficacy of cinacalcet and the effect of cinacalcet withdrawal on serum calcium and PTH in such patients. Furthermore, the impact of cinacalcet on bone turnover and quality of life was assessed.

Methods. Twelve renal allograft recipients with hypercalcaemia due to persistent hyperparathyroidism were treated with cinacalcet for 26 weeks. Cinacalcet was then withdrawn to check for recurrence of hypercalcaemia.

Results. Cinacalcet maintained normocalcaemia in all patients from week 4 to 26, and PTH significantly decreased and remained suppressed. Serum phosphate increased, whereas the serum calcium–phosphate product remained unchanged. The excretion of calcium and phosphate in the 24 h urine had tendency to decrease. After cinacalcet was withdrawn, hypercalcaemia recurred rapidly and PTH increased to baseline values. Renal function remained stable, proteinuria was unchanged and no allograft rejection was observed. During treatment with cinacalcet, total and bone-specific alkaline phosphatase increased, whereas the urinary deoxypyridinoline–creatinine ratio did not change significantly, suggesting enhanced bone formation. Quality of life assessed at weeks 10 and 26 remained unchanged compared with baseline.

Conclusions. In conclusion, continued treatment with cinacalcet is required to maintain long-term normocalcaemia and to suppress the enhanced PTH production in renal transplant recipients with persistent hyperparathyroidism.

Keywords: calcium; cinacalcet; hypercalcaemia; hyperparathyroidism; kidney transplantation; PTH

Introduction

Persistent hyperparathyroidism with subsequent hypercalcaemia after renal transplantation occurs frequently. These metabolic imbalances are evident soon after renal transplantation and resolve in only 50% of patients 1 year after transplantation [1,2]. Persistent hyperparathyroidism is a risk factor for bone loss after renal transplantation [3,4]. Furthermore, the high PTH levels in renal transplant patients are associated with vascular calcifications and correlate with inferior graft function in patients with interstitial calcifications in renal allograft [5]. Hyperparathyroidism and/or hypercalcaemia are also associated with depression and non-specific psychological distress and can have a negative impact on general quality of life [6]. Besides parathyroidectomy, there are only limited therapeutic options. Most patients remain untreated because they do not meet the currently accepted guidelines for parathyroid surgery, or do not wish to undergo parathyroidectomy.

In a previous study, we have shown that cinacalcet effectively normalized serum calcium and reduced intact PTH in the short term in renal transplant patients with persistent hypercalcaemia [7]. The present article describes the results of a prospective study to investigate the efficacy and safety of a 6-month treatment with cinacalcet. Furthermore, the effect of cinacalcet withdrawal after 26 weeks of treatment and the impact of cinacalcet on bone turnover and quality of life was assessed.

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Patients and methods

Patient population

This prospective single-centre, open-label study was performed in renal transplant recipients with persistent hyperparathyroidism and normal stable allograft function. Study approval was obtained from the local ethics committee, and all patients gave written, informed consent. Twelve renal allograft recipients, six men and six women, aged 49–70 years with a dialysis vintage of 32 months (median, range 0–84 months) were enrolled. The patients were 28 months (median, range 6–384 months) after renal transplantation and the immunosuppressive regimes were as follows: four patients were taking cyclosporine A (CyA) and mycophenolate (MMF), three patients CyA, MMF and prednisone (P), two patients CyA and azathioprine (AZA), one patient was taking tacrolimus and MMF, one patient tacrolimus, MMF and P and one patient AZA and P. One patient was switched form cyclosporine to tacrolimus at the discretion of the treating physician at week 10. For all patients taking steroids, the administered doses of prednisone were $\leq$10 mg/day. Preliminary results of 11 of these patients were published elsewhere [7].

Study design

Inclusion criteria included renal transplantation at least 6 months before the start of cinacalcet treatment, stable graft function with a calculated glomerular filtration rate according to the modification of diet in renal disease study group (MDRD GFR; extended version) $\geq$40 ml/min/1.73 m^2, persistently elevated serum calcium >2.60 mmol/l (normal range 2.10–2.60 mmol/l) measured at least twice within 6 months before cinacalcet treatment started, plasma intact PTH (iPTH) (Roche Diagnostics, Basel, Switzerland) greater than 65 pg/ml (normal range 15–65 pg/ml) and normal 25-hydroxyvitamin D_3 (normal range 10–42 µg/l) and 1,25-dihydroxyvitamin D_3 (normal range 19.9–67.0 ng/l) levels. Total plasma calcium and phosphate levels were recorded 3, 6 and 12 months prior to inclusion. Treatment with diuretics, vitamin D sterols, calcium supplementation and bisphosphonates or fluoride was not permitted during the study period. Because cinacalcet inhibits P450 2D6 substantially, patients requiring drugs that are metabolized by this enzyme and have a narrow therapeutic index (e.g. flecainide, thioridazine and many tricyclic antidepressants) were excluded. Patients received 30 mg cinacalcet once daily in the evening. The cinacalcet dosage was adapted in the first 2 weeks of treatment to keep the serum calcium in the predefined target range of 2.10–2.60 mmol/l, independently of PTH values. All patients continued to take the study medications without interruption until week 26, except one subject who discontinued after 2 weeks. At week 26, cinacalcet was withdrawn, and the trial ended at week 30.

Study parameters

Blood samples were collected every 2 weeks for the first 10 weeks and thereafter every 4 weeks. The following values were measured: total and ionized calcium (normal range 1.10–1.30 mmol/l), phosphate (normal range 0.87–1.45 mmol/l), alkaline phosphatase (normal value <129 U/l) and bone-specific alkaline phosphatase (normal range 3.4–21.1 µg/l), creatinine (normal range male 70–105 µmol/l, female 60–90 µmol/l), urea (normal value <11.9 mmol/l), albumin (normal range 32–46 g/l) and liver enzymes. Three different assays were performed to evaluate PTH concentration: iPTH (Roche), iPTH (Nichols) (normal range 10–65 pg/ml; Nichols Institute, San Juan Capistrano, CA, USA) and bio-intact PTH (biPTH, normal range 6–40 pg/ml; Nichols Institute, San Juan Capistrano, CA, USA). Whole-blood trough levels of cyclosporine or tacrolimus were also measured at each study visit. The MDRD GFR was calculated by using the following values: plasma creatinine, serum urea, serum albumin, gender, race and age [8]. After a rest of 5 min, sitting blood pressure was measured at every study visit by an automatic blood pressure monitor (Boso-Medicus, Jungingen, Germany).

Urine was collected over 24 h at week 0, 10 and 26 for the measurement of creatinine clearance and fractional calcium and phosphate excretion rates. At every visit, the spot urine was analysed for protein/creatinine, albumin/creatinine and deoxypyridinoline/creatinine ratios.

The quality of life was assessed at week 0, 10 and 26 using the self-rating SF-36 questionnaire, which measures quality of life in various physical conditions [9]. For the assessment of anxiety and depression, the Hospital Anxiety and Depression Scale (HADS) [10,11], a 14-item self-rating questionnaire, was used.

Statistical analysis

Means of continuous data were compared by the Student's *t*-test. *P*-values were two sided for the comparison with the baseline value, and those <0.05 were considered statistically significant. All results were expressed as means $\pm$ SE. Linear regression analyses were performed for biPTH and iPTH (Nichols), as well as biPTH and iPTH (Roche) from week 0 to 30. Regression lines were fitted through the intercept of biPTH and iPTH (Nichols), and biPTH and iPTH (Roche), respectively. Mean comparisons of continuous variables of SF-36 and HADS were tested using Friedman's test; categorical data were analysed with Cochrane's test. All tests were two-sided, and the significance level was set at $P < 0.05$. Mood and quality of life data were available for 10 patients. All analyses were performed using SPSS software (version 12.0, SPSS Inc., Chicago, IL).

Results

Cinacalcet treatment normalizes total and ionized calcium

At inclusion, all patients had hypercalcaemia and persistent hyperparathyroidism. The baseline serum calcium was 2.73 ± 0.04 mmol/l, the ionized calcium was 1.40 ± 0.02 mmol/l and the PTH values were elevated—iPTH (Roche) 190.3 ± 26.1 pg/ml, iPTH (Nichols) 266.6 ± 43.1 pg/ml and biPTH 137.0 ± 21.9 pg/ml. The initial 30 mg cinacalcet dose was adjusted within 2 weeks as follows: eight patients remained at 30 mg, one patient reduced to 15 mg and two patients increased to 60 mg (one patient was withdrawn after 2 weeks of treatment).

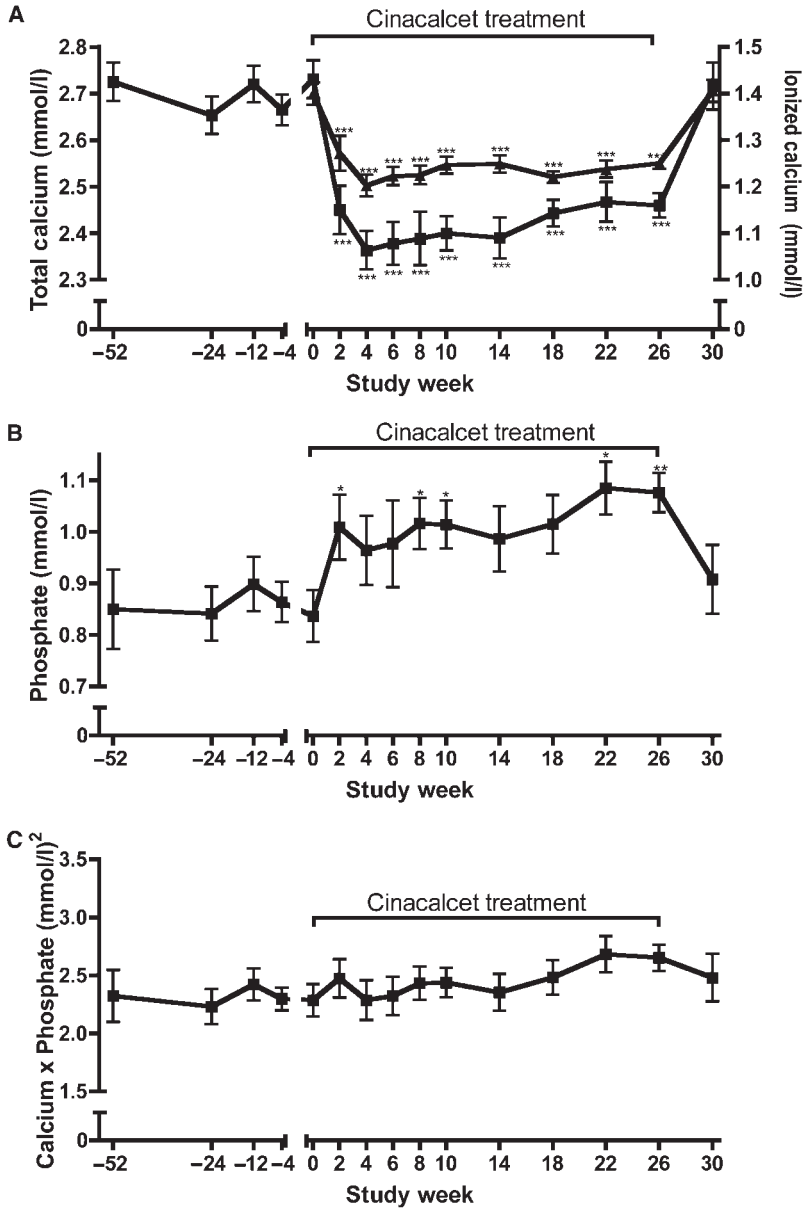

Fig. 1. Effect of cinacalcet on serum levels of total calcium, ionized calcium, phosphate and calcium–phosphate product. (**A**) Cinacalcet normalized total serum calcium rapidly, and ionized calcium was below 1.35 mmol/l in all patients from weeks 2 to 26. Hypercalcaemia recurred after cinacalcet was withdrawn at week 26. Filled squares indicates total serum calcium, and filled triangles indicates ionized calcium. (**B**) Cinacalcet increased mean serum phosphate significantly at week 2, 8, 10, 22 and 26. After cinacalcet withdrawal, serum phosphate returned to baseline values. (**C**) The mean serum total calcium–phosphate product remained unchanged throughout. $^{***}P < 0.001$, $^{**}P < 0.01$, $^{*}P < 0.05$, as compared with week 0 (mean ± SE).

After adjustment of the cinacalcet dose, total and ionized serum calcium levels were maintained within normal limits in all patients until week 26 (Figure 1). No further cinacalcet dose adjustment had to be performed later. Total calcium and ionized calcium were reduced by 11.7 ± 0.5 and 17.7 ± 2.1% with a mean dose of 31 mg/day cinacalcet after the dose-finding period.

Parallel reduction of bio-intact and intact PTH during cinacalcet treatment

Plasma iPTH (Roche), iPTH (Nichols) and biPTH were rapidly reduced during the dose-finding period, with a maximal reduction after 8 weeks (by 32.2 ± 6.0, 36.8 ± 5.7 and 40.5 ± 6.1%, respectively) and remained suppressed until week 26 (Figure 2). Reductions in biPTH paralleled reductions in iPTH throughout the study (Figure 2). Regression analysis of biPTH and iPTH (Roche) showed a highly significant correlation ($R = 0.981$, $P < 0.001$). A similar significant correlation ($R = 0.982$, $P < 0.001$) was observed between biPTH (Nichols) and iPTH (Nichols). The ratio of biPTH (Nichols) to iPTH (Roche) and biPTH (Nichols) to iPTH (Nichols) was maintained at 52 ± 0.3% and 49 ± 2%, respectively, throughout the study.

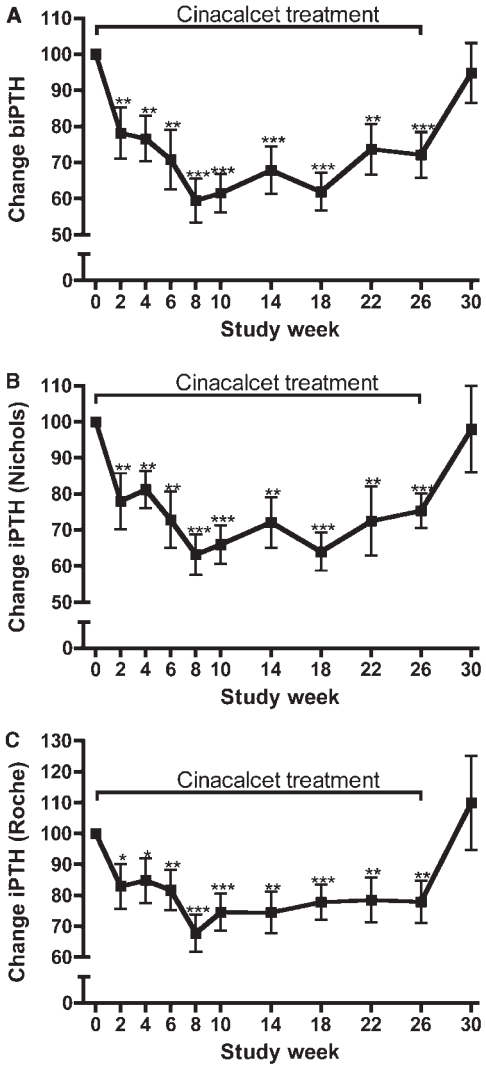

Fig. 2. Mean percentage change of biPTH and iPTH (Roche and Nichols) compared with baseline values (100% value of week 0) over time. (**A**) After cinacalcet dosage adaptation, mean percentage bio-intact PTH (biPTH) was about 35% reduced compared with week 0. (**B**) In parallel, mean percentage intact PTH (iPTH) (Nichols) and (**C**) iPTH (Roche) were significantly reduced. After cinacalcet was withdrawn, PTH values returned to baseline values. $^{***}P < 0.001$, $^{**}P < 0.01$, $^{*}P < 0.05$, as compared with week 0 (mean ± SE).

Impact of cinacalcet on serum phosphate and urinary phosphate excretion

At inclusion, 58.3% of the patients were hypophosphataemic despite oral phosphate supplementation in three of the 12 patients. Cinacalcet significantly increased serum phosphate concentrations at study week 2, 8, 10, 22 and 26, and oral phosphate supplements could be stopped in all patients at week 6 (Figure 1). At week 26, more than 90% of the patients were normophosphatemic, and the lowest individual serum phosphate level was 0.80 mmol/l. Fractional phosphate excretion measured after 10 and 26 weeks of treatment with cinacalcet had a tendency to decrease compared with week 0 (Table 1).

Table 1. The 24 h urine analysis at study week 0, 10 and 26

Parameter	Study week		
	0	10	26
CrCl (ml/min/1.73 m^2)	54.9 ± 2.2	50.0 ± 3.6	56.0 ± 4.8
24 h urine Ca/Cr	0.43 ± 0.11	0.36 ± 0.10	0.26 ± 0.06
FE Ca (%)	1.54 ± 0.30	1.56 ± 0.28	1.22 ± 0.23
24 h urine P/Cr	3.00 ± 0.43	2.50 ± 0.19	2.68 ± 0.21
FE P (%)	39.05 ± 3.44	31.16 ± 2.98	31.81 ± 3.27

CrCl, measured creatinine clearance; Ca, calcium; Cr, creatinine; FE, fractional excretion; P, phosphate.

The serum calcium–phosphate product remained unchanged (Figure 1).

Cinacalcet withdrawal leads to recurrent hypercalcaemia

After cinacalcet treatment was withdrawn, hypercalcaemia recurred, PTH values increased and serum phosphate concentrations decreased to baseline level. This shows that cinacalcet is necessary to maintain normocalcaemia and to continuously suppress enhanced PTH production in renal transplant recipients with persistent hyperparathyroidism.

Renal function and calcineurin inhibitor trough levels remain unchanged

Tables 1 and 2 show that renal allograft function remained stable throughout the 6-month treatment phase. Proteinuria (Table 2), albuminuria and blood pressure (both data not shown) remained unchanged and no allograft rejection was clinically suspected. Table 2 shows also that cyclosporine doses and cyclosporine trough levels remained unchanged throughout the study. The switch from cyclosporine to tacrolimus in one patient at week 10 led to a reduced mean cyclosporine dose from weeks 14 to 30. The cyclosporine trough levels remained unchanged throughout the study. The doses of tacrolimus, mycophenolate mofetil, azathioprine and prednisone remained constant.

Influence of cinacalcet on biochemical markers of bone metabolism

We also examined the effect of cinacalcet on biochemical markers of bone turnover. At inclusion, the alkaline phosphatase and bone-specific alkaline phosphatase were 92.2 ± 10.8 U/l and 20.45 ± 3.8 µg/l, respectively. Alkaline phosphatase increased by 7.1 ± 5.7% (P = ns) and 20.0 ± 6.3% ($P < 0.01$), and bone specific alkaline phosphatase by 9.8 ± 5.7 ($P < 0.01$) and 19.5 ± 4.8% ($P < 0.01$) from week 4 to 10 and 14 to 26, respectively (compared with dose-finding period). Figure 3 shows that the deoxypyridinoline/creatinine ratio in the spot urine

Table 2. Renal parameters, cyclosporine dose and whole-blood trough levels at study week 0, 10, 26 and 30

Parameter	Study week			
	0	10	26	30
Serum creatinine (μmol/l)	116.1 ± 8.7	128.2 ± 10.7	127.6 ± 11.1	124.0 ± 9.0
MDRD GFR (ml/min/1.73 m^2)	56.0 ± 4.8	49.9 ± 4.5	50.4 ± 3.5	51.2 ± 4.2
Protein/Cr (mg/mmol)	14.1 ± 2.5	7.9 ± 2.8	11.4 ± 3.3	9.9 ± 3.2
Cyclosporine dose (mg/day)	188.9 ± 13.9	193.8 ± 14.8	162.5 ± 26.3	162.5 ± 26.3
Cyclosporine dose (mg/kg/day)	2.98 ± 0.18	2.93 ± 0.17	2.52 ± 0.39	2.51 ± 0.39
Cyclosporine trough level (μg/l)	110.0 ± 12.9	117.6 ± 10.1	111.6 ± 6.5	111.0 ± 11.7

MDRD GFR, calculated glomerular filtration rate according to the modification of diet in renal disease study group (extended version); Cr, creatinine.

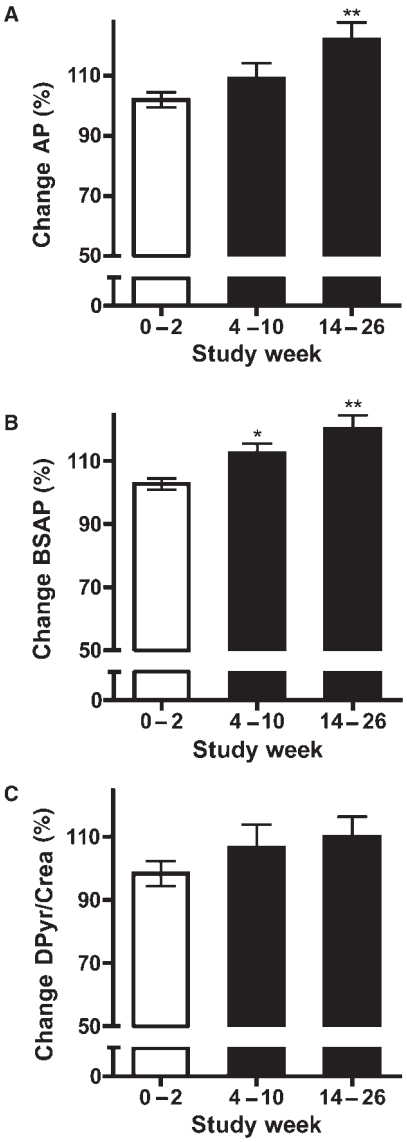

Fig. 3. Mean percentage change of AP, BSAP and Dpyr/Crea ratio during week 4 to 10 and 14 to 26 compared with dose-finding period. (**A**) Cinacalcet increased alkaline phosphatase (AP) and (**B**) bone-specific alkaline phosphatase (BSAP), expressed as mean percentage of initial AP and BSAP (100% value of week 0). (**C**) The mean percentage change of deoxypyridinoline/creatinine (Dpyr/Crea) ratio remained unchanged. $^{**}P < 0.01$, $^{*}P < 0.05$, as compared with dose-finding period (mean ± SE).

tended to increase (P = ns). Table 1 shows that the fractional excretion of calcium and 24 h urine calcium to creatinine ratio had a tendency to decrease compared with baseline values. The 25-hydroxyvitamin D_3 and 1,25-dihydroxyvitamin D_3 levels measured at week 0 (22.1 ± 4.0 μg/l, 43.6 ± 4.0 ng/l), 10 (16.9 ± 1.9 μg/l, 32.9 ± 6.0 ng/l) and 26 (21.8 ± 3.2 μg/l, 34.5 ± 3.2 ng/l) remained in the normal range.

Effect on mood and quality of life

Using quality-of-life questionnaires (HADS and SF-36), we examined the impact of cinacalcet treatment on the patients' well-being. On the depression scale in the HADS, the score was 5.6 ± 1.8, 4.9 ± 1.6 and 5.7 ± 1.5 and on the anxiety scale 6.0 ± 1.5, 5.1 ± 1.4 and 5.6 ± 1.6 at week 0, 10 and 26, respectively (cut-off for all scales: 8). All changes were not significant using the Cochrane test. In the SF-36, there were no changes between week 0, 10 and 26 for physical and mental health. The mean values for both components of the SF-36 and all eight subscales were within the norm at all three assessment points.

Adverse events

Overall cinacalcet was well tolerated, no specific side effects were reported and no serious adverse events occurred during the 26-week treatment phase. All patients but one continued to take the study medications without interruption. As mentioned earlier, one patient discontinued the study after 2 weeks because she feared a possible deterioration of a pre-existing retinitis pigmentosa. Ophthalmological examination showed no changes in vision compared with pre-study tests.

Discussion

Cinacalcet treatment was highly effective in rapidly normalizing serum calcium and significantly reducing PTH in renal transplant patients with chronic hypercalcaemia and persistent hyperparathyroidism. The effect was sustained over 6 months, but reversed

rapidly when cinacalcet was stopped. Cinacalcet treatment also corrected hypophosphataemia and normalized serum phosphate in more than 90% of the patients, without increasing the serum calcium–phosphate product. These results confirm and extend the findings of previous short-term studies with cinacalcet in renal allograft patients with persistent hyperparathyroidism [7,12].

Treatment with cinacalcet for 6 months did not prevent recurrence of hypercalcaemia and PTH increase to baseline values after cinacalcet was withdrawn. It is known that the development of hypercalcaemia correlates with severity of the hyperplasia and nodular transformation of the parathyroid gland [13]. Although cinacalcet attenuates parathyroid hyperplasia in a rat model of secondary hyperparathyroidism [14], and although successful renal transplantation reverses hyperparathyroidism via involution of the parathyroid glands in renal transplant patients [15], the hyperfunctional potential of the parathyroid gland often persists, and is only controlled as long as cinacalcet is given. Therefore, cinacalcet needs to be given continuously to control normocalcaemia in these patients. We cannot exclude that longer treatment duration (>6 months) may lead to permanent inhibition of parathyroid function in renal transplant patients.

The PTH levels were measured by three different methods, and all values decreased significantly by approximately 25–35% after the dose-finding period. It should be noted that these values represent hormone concentrations 12 hours after the evening dose of cinacalcet and may underestimate PTH reduction over 24 h. Pharmacodynamic data in patients with primary hyperparathyroidism demonstrated that plasma PTH levels were reduced by 60% from baseline 2 to 4 h after dosing [16]. Regression analysis revealed statistically significant correlation between the bio-intact assay and two different intact PTH assays. Because the correlation between plasma biPTH and iPTH was excellent, we propose that full-length PTH can be reasonably estimated by multiplying iPTH (Roche) by 0.52 and iPTH (Nichols) by 0.49 in renal transplant patients with persistent hyperparathyroidism. Several studies have shown statistically significant correlations between bio-intact and intact immunometric PTH assays for patients with primary hyperparathyroidism [17] and for patients with end-stage renal disease [18]. Similar strong correlations between PTH assays were also reported in patients with ESRD during cinacalcet treatment [19].

During the 26 weeks of treatment with cinacalcet, renal allograft function remained stable. Infusion of PTH is known to increase GFR and renal blood flow, most likely through a hemodynamic effect [20]. Cinacalcet might, therefore, decrease GFR via its PTH-lowering effect. But a conclusion on GFR changes cannot be drawn from this study because of the limited number of patients. Albuminuria and proteinuria remained at a very low level in the spot urine during the study. There was no allograft rejection, and the blood pressure remained unchanged. An important aim of our study was to exclude effects of cinacalcet on CsA trough levels since *in vivo* interaction data of cinacalcet with immunosuppressive drugs are missing. The cyclosporine whole-blood trough levels showed no relevant fluctuations, and the dosage could be held constant. The cytochrome P450 3A4 (CYP3A4) is the enzyme that is primarily responsible for the elimination of cyclosporine and tacrolimus. The CYP3A4 IC_{50} for cinacalcet is 100 mM (Amgen, internal data). That is 1000 times higher than the highest unbound cinacalcet concentrations that can be achieved clinically. Because cinacalcet mainly inhibits CYP 2D6 and has a low inhibitory potential for CYP3A4, no interactions with the metabolic transformation of cyclosporine or tacrolimus were expected. Indeed, we could not demonstrate an effect of cinacalcet treatment on CsA trough levels. Formal pharmacokinetic–pharmacodynamic studies are needed to exclude subtle effects of cinacalcet on CsA pharmacokinetics.

Persistent hyperparathyroidism, together with steroid use, causes a decrease in bone density in renal allograft patients [4]. Studies have shown decreased levels of bone-specific alkaline phosphatase after renal transplantation [21,22], reflecting decreased osteoblast activity [23]. We found that cinacalcet treatment increased alkaline phosphatase and bone-specific alkaline phosphatase in renal allograft recipients. In patients with primary hyperparathyroidism, cinacalcet treatment also increased bone-specific alkaline phosphatase, and the urine deoxypyridinoline/creatinine ratio remained unchanged compared with placebo [16]. A possible explanation is that the cycling PTH levels that are induced by cinacalcet treatment may stimulate bone formation. Cinacalcet treatment induces such cycling PTH levels in patients with primary [16] and secondary hyperparathyroidism [24]. By analogy, daily PTH (1-34) injections have a stimulatory effect on bone turnover [25]. Preliminary evidence also suggests that cinacalcet increases bone mineral density [26] and reduces the risk of fractures [27] in patients with secondary hyperparathyroidism. Altogether, our data suggest that cinacalcet stimulates bone formation and may have a favourable effect on bone metabolism. Further studies are needed to confirm that cinacalcet has a beneficial effect on the skeletal system in patients with persistent hyperparathyroidism.

Depression and non-specific psychological symptoms are frequent in patients with hyperparathyroidism and account for impaired quality of life in patients after kidney transplantation. In our patients, five out of 10 scored above the cut-off for depression and/or anxiety before treatment. Although changes of depression and anxiety scores are not significant, it is remarkable that two of the five patients with anxiety and/or depressive symptoms at week 0 were no longer anxious or depressive after 26 weeks of treatment. Due to the small sample size and the relatively low

depression and anxiety scores, this improvement is not statistically significant.

In conclusion, continued treatment with cinacalcet maintains normocalcaemia and significantly reduces PTH in renal transplant recipients with persistent hyperparathyroidism. Cinacalcet appears to have favourable effects on bone formation. Further studies with larger patient samples and larger treatment duration are needed to examine the effect of cinacalcet on patient outcomes such as bone disease, cardiovascular morbidity and allograft function after renal transplantation.

Conflict of interest statement. None declared.

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