

Case Report

Successful use of low-dose intravenous paricalcitol in the treatment of severe secondary hyperparathyroidism in a haemodialysis patient

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Introduction

Haemodialysis (HD) patients are commonly affected by secondary hyperparathyroidism (SHPT), hyperphosphataemia and calcitriol deficiency [1]. Classically, serum high PTH levels cause bone-associated diseases, such as osteitis fibrosa and renal osteodystrophy. More recently, the link between SHPT and a systemic toxicity has been elucidated, with SHPT playing a major role in determining cardiovascular disease, including vascular calcification [2,3].

Treatment with calcitriol, the active form of vitamin D, reduces serum PTH levels, but may result in elevations in serum calcium (Ca), phosphorus (P) and Ca × P product levels, increasing the risk of cardiovascular calcification in the HD population [4]. Several new vitamin D analogues have been developed and investigated with the rationale to treat SHPT with a reduced risk of hypercalcaemia and hyperphosphataemia in HD patients [5,6]. Paricalcitol (1,25-dihydroxy-19-nor-vitamin D₂, 19-Nor-D₂) is a vitamin D receptor activator that suppresses PTH secretion with minimal increases in serum calcium and phosphate levels [7,8]. Furthermore, it has recently been demonstrated that paricalcitol prevents vascular calcification in experimental models of renal failure, compared to calcitriol [9,10].

The purpose of the present case report is to analyse the possibility of using low-dose intravenous (i.v.) paricalcitol in the treatment of severe SHPT in HD patients with elevated serum Ca and P levels.

Case report

A 34-year-old man on maintenance HD with severe SHPT, hypercalcaemia and hyperphosphataemia refused parathy-

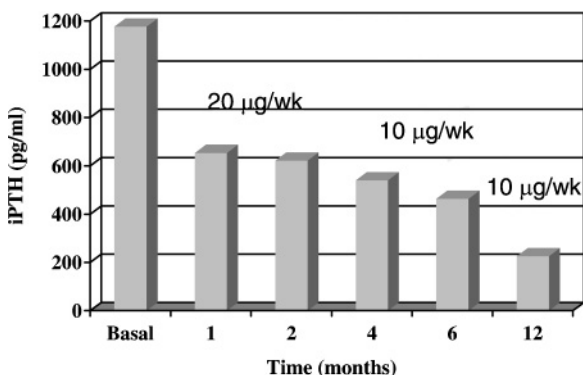
roidectomy. His diet and pharmacological incomppliance was dramatic from the beginning. Oral calcitriol was prescribed to reduce serum iPTH levels, but the patient's adherence was close to zero. Consequently, he had a poor control of serum phosphate (7.8 ± 1.2 mg/dl) and iPTH (650 ± 128 pg/ml) since the beginning of HD 36 months earlier. No data are available on the pre-dialysis period since he was diagnosed with chronic kidney disease (CKD) stage V immediately before starting HD treatment. Also the etiology of renal failure remains unknown. After 3 years of HD, the patient presented the following biochemistry: iPTH = 1177 pg/ml, alkaline phosphatase (ALP) = 428 U/l, Ca = 9.6 mg/dl, P = 10.6 mg/dl and Ca × P = 102 mg²/dl². He was not regularly taking any prescribed calcium-free phosphate binder (either sevelamer hydrochloride or aluminium hydroxide). Moreover, it was not possible to continue any therapy with either oral or i.v. calcitriol due to several episodes of hypercalcaemia. At that time, we proposed the parathyroidectomy, but he unfortunately refused it. Regrettably, we did not have the possibility to use cinacalcet hydrochloride to suppress parathyroid function. Finally, we had the opportunity to use i.v. paricalcitol in our HD unit and the patient gave us his informed consent, only because of i.v. administration way. We decided to start with a low-dose paricalcitol treatment at the dose of PTH/180, because of his tendency to develop hypercalcaemia with i.v. calcitriol.

The biochemistry is reported in Table 1. An initial starting i.v. dosage of 20 µg weekly divided into three doses was used (PTH/180). This dose was adjusted according to iPTH, Ca, P and Ca × P product levels. During the study, Ca dialysate concentration (1.5 mmol/l) did not change. Serum iPTH levels decreased rapidly during the first 4 weeks of therapy (from 1177 to 654 pg/ml), and reached a reduction of 61% after 6 months of treatment (463 pg/ml). As defined in the K/DOQI guidelines, the target for PTH concentration is 150–300 pg/ml in stage V of CKD [11]. Interestingly, after 12-month low-dose i.v. paricalcitol serum iPTH was 225 pg/ml. Figure 1 shows the serum iPTH levels and decreasing doses of i.v. paricalcitol. Throughout the course of the study, serum Ca levels were maintained within the normal range, while the serum P, Ca × P product and ALP consensually decreased. No adverse events possibly related to paricalcitol were observed.

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Table 1. Patient's biochemistry

	Basal	1 month	2 months	4 months	6 months	12 months
iPTH (pg/ml)	1117	654	622	540	463	225
ALP (U/l)	428	265	186	188	168	152
Ca (mg/dl)	9.6	10.0	9.8	9.3	8.9	9.3
P (mg/dl)	10.6	9.3	6.6	6.6	6.5	6.9
Ca × P (mg ² /dl ²)	102	93	65	61	58	69

**Fig. 1.** Changes in serum iPTH levels after 12 months of low-dose intravenous (PTH/180) paricalcitol, during the course of the clinical observation.

Discussion

SHPT is a common complication of HD patients. Several new vitamin D receptor activators (VDRAs) have been developed to treat SHPT with a reduced risk of hypercalcaemia and hyperphosphataemia in CKD patients. In addition, VDRAs have variable affinity for the components of the vitamin D system, including the vitamin D-binding protein and the nuclear VDRA [5].

Paricalcitol has the side chain of vitamin D₂ and differs from 1,25(OH)₂D for the lack of carbon 22. It was the first VDRA approved for use in CKD patients and is administered intravenously, commonly three times a week after HD. It may be dosed according to a 4:1 ratio to calcitriol, even though a ratio 3:1 was proposed for a safer approach [12]. Alternatively, its initial dosage may be calculated from circulating PTH concentrations (PTH concentration/80) or body weight (0.04 µg/kg of dry body weight) [13]. In their study, Martin *et al.* [13] demonstrated that the median number of days for patients in the 0.04 µg/kg treated group to achieve the first of four consecutive 30% or greater reductions from baseline iPTH levels was 45 days, and for patients in the PTH/80 treated group only 31 days.

In this severe SHPT case report, we use the minimum paricalcitol dose required to control serum iPTH secretion with no side effects. The above results establish that 19-norD₂ rapidly suppresses PTH with no episodes of hyperphosphataemia or hypercalcaemia. In addition, in a recent study, Mitsopoulos *et al.* [14] demonstrated that paricalcitol at a lower initial dose of iPTH/120 has an efficacy similar to that of iPTH/80 in reaching target iPTH levels, with lower risk of excessive parathyroid function suppres-

sion, less paricalcitol dose adjustments and fewer episodes of hypercalcaemia. During the course of that study [14], only two patients from the iPTH/120 group versus eight patients from the iPTH/80 group experienced at least one episode of hypercalcaemia. Furthermore, there were less episodes of increased serum Ca × P product levels in the iPTH/120 compared to the iPTH/80 group.

In conclusion, the modern strategies to prevent SHPT in CKD patients give great relevance to vitamin D replacement therapy. A sound approach to treatment requires taking into account many factors, including stage of CKD, serum levels of iPTH, bone status, vitamin D deposits, serum calcium and phosphate levels. This case report demonstrates that low-dose i.v. paricalcitol (PTH/180) safely, rapidly and effectively suppresses iPTH levels in a HD patient, without any effect on serum Ca and P levels. We suggest that paricalcitol, as one of the VDRAs with low risk of both hypercalcaemia and hyperphosphataemia, could be tried in untreated patients with severe SHPT.

Conflict of interest statement. None declared.

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