Dear Sir,

In patients with chronic renal failure (CRF), the restriction of dietary phosphorus results in serum phosphate reduction and improvement of secondary hyperparathyroidism. These data are usually ascribed to a concomitant increase in the production of calcitriol [1, 2]. However, it has been reported in patients with advanced renal failure [3] and in severe experimental renal failure [4, 5] that phosphorus restriction reversed hyperparathyroidism without significant change in plasma calcitriol levels.

The aim of the present investigation was to examine the effects of phosphorus restriction on calcium phosphate metabolism and more especially on plasma calcitriol levels. Our study comprised 23 patients with advanced CRF (GFR: \(11.63 \pm 3.9 \text{ ml/min per } 1.73 \text{ m}^2\)) receiving a diet providing daily, per kilogram body weight, 0.4 g protein of vegetable origin, 3-5 mg of inorganic phosphorus and 35 kcal. The diet was supplemented with ketoanalogues (CSW 20/4, Clintec, France) and with calcium carbonate to keep unchanged their habitual calcium intake: 758 ± 124 mg/day at the start of the study. No other phosphate binder was prescribed. The patients additionally received a multivitamin preparation providing 1,000 IU of vitamin D\(_2\) per day. Serum calcium, serum phosphorus, serum bicarbonate, PTH activity (intact hormone), calcitriol, alkaline phosphatase and osteocalcin were measured at the start of the study and 3 months later. The evolution of renal function was assessed by \(51\text{Cr}-\text{EDTA} \) clearances.

Results were expressed as mean ± standard deviation (SD). Student’s t test was used for paired data. Multiple regression analysis was applied to analyze the relationship between the concentrations of PTH and calcitriol and the different variables.

At the start of the study, PTH concentration was directly correlated with GFR (\(r = 0.46; p = 0.04\)), with inorganic phosphorus (\(r = 0.59; p = 0.01\)) and with osteocalcin (\(r = 0.5; p = 0.02\)). On the other hand, PTH did not correlate with either calcitriol or calcium concentrations, no correlation was found between calcitriol and the other biochemical variables.
After 3 months of phosphorus and protein restriction, GFR did not change significantly from initial values: $11.63 \pm 3.98$ and $11.00 \pm 4.05$ ml/min, respectively. During this period, serum bicarbonate increased significantly while alkaline phosphatase, serum inorganic phosphorus and PTH decreased significantly. At the same time, calcitriol levels decreased slightly from 16.91 ± 7.39 to 13.51 ± 6.3 pg/ml (NS), while serum calcium was not significantly modified. Table 1 summarizes the evolution of the different biochemical parameters.

Beneficial effects of dietary protein and phosphorus restriction on acidosis and calcium phosphate metabolism have been described in previous studies [6-8].

Although it has been known for 20 years that in patients with CRF dietary phosphorus restriction prevents and ameliorates secondary hyperparathyroidism [9, 10], the mechanisms that may mediate these effects are still controversial. It is generally postulated that phosphorus restriction results in a decrease in serum phosphorus with secondary increase in 25-hydroxyvitamin D $\alpha$-hydroxylase activity and calcitriol production and lastly a decrease in the PTH level favored by the improvement in the calcemic response to PTH [5]. However, it has been reported in severe clinical and experimental uremia that phosphorus restriction could reverse secondary hyperparathyroidism without any change in plasma calcium or plasma calcitriol levels [3-5]. Actually Lucas et al. [3] observed in 7 patients with severe CRF (creatinine clearance : $6.1 \pm 0.9$ ml/min) that after 3 months on a low-phosphorus diet, plasma concentration of PTH and plasma phosphorus level significantly decreased whereas serum calcitriol levels which were initially below normal, decreased significantly. In 5 uremic dogs (with $\frac{1}{2}$ nephrectomy), Lopez-Hilker et al. [4] pointed out that phosphate intake restriction was able to decrease PTH levels despite nor-mocalcemia and low plasma calcitriol levels. Recently, Rodriguez et al. [5] have shown that, in rats with normal function or with moderate CRF, reduced phosphorus intake increased serum calcitriol levels whereas in animals with a more severe degree of renal failure the same diet did not affect the serum calcitriol level which was not modified by a PTH infusion either. It is likely that in advanced renal failure, calcitriol synthesis which is continually stimulated by the elevated PTH levels and produced at a maximum rate by a reduced renal mass cannot be stimulated by phosphorus restriction anymore.

We confirm that in severe CRF, the beneficial effect of phosphorus restriction on secondary hyperparathyroidism is independent of changes in calcitriol and plasma calcium. The mechanism of this effect is not yet known, Lopez-Hilker et al. [4] have proposed that the improvement of secondary hyperparathyroidism may be related to a direct effect of the low-phosphorus diet which may affect the phosphohpid composition of the parathyroid cell membranes modifying local calcium fluxes and/or regulation of calcitriol receptors of the parathyroid cells.

References


