Is Administration of Vitamin D Metabolite Needed for the Treatment of Secondary Hyperparathyroidism at the Predialytic Stage?

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Dear Sir,

Concerning the treatment of secondary hyperparathyroidism (HPT) in patients with chronic renal failure at the predialytic stage (nondialyzed patients), opinions are divided over the time of beginning the remedy [1]. Although the possibility exists that administration of vitamin D metabolite may induce impairment of renal function due to an elevation of the serum calcium concentration, a rise of the calcium $\times$ phosphate product, an increase in the plasma renin activity or the drug per se [2], vitamin D metabolite has been prescribed for the treatment of secondary HPT in nondialyzed patients [3]. On the other hand, it has been reported that dietary phosphorus restriction prevented secondary HPT by increasing the serum 1,25-dihydroxyvitamin D₃ [1,25(OH)₂D₃] concentration in animals [4] and humans [5], since a low phosphorus diet stimulates 25-hydroxyvitamin D₃ 1 α -hydroxylase activity [6]. We suggest therefore that there is no need to administer vitamin D metabolite in nondialyzed patients, because their kidneys can produce adequate doses of 1,25(OH)₂D₃ by reducing their serum phosphate concentration sufficiently resulting from the prescription of phosphate binder.

We administered calcium carbonate (3 g/day) for a period of 4 weeks to 7 nondialyzed patients with a 24-hour creatinine clearance (Ccr) of between 10 and 30 ml/min who were not treated with phosphate binder and vitamin D metabolite. Their renal function had been relatively stable for more than 6 months, and there was no diabetes mellitus. Their mean age was 62 ± 4 years, and the mean Ccr was 14.5 ± 1.3 ml/min. The patients came to the investigating room at 9.00 h a.m. after a light breakfast for blood sampling. The level of serum phosphate was significantly decreased from 5.1 ± 0.4 to 3.8 ± 0.3 mg/dl ($p < 0.05$), and the level of serum 1,25(OH)₂D₃ was appreciably increased from 18.5 ± 4.2 to 39.7 ± 7.7 pg/ml ($p < 0.01$). The levels of serum total calcium and ionized calcium were significantly elevated from 8.6 ± 0.4 to 9.1 ± 0.3 mg/dl ($p < 0.05$) and from 4.5 ± 0.2 to 4.6 ± 0.2 mg/dl ($p < 0.02$), respectively. The levels of midportion parathyroid hormone and calcium $\times$ phosphate product were significantly reduced from 2.7 ± 1.1 to 1.6 ± 1.4 ng/ml ($p < 0.05$) and from 43.9 ± 4.9 to 35.0 ± 3.6 ($p < 0.05$),

respectively. There were no appreciable changes in serum creatinine concentration, calcitonin concentration, pH and bicarbonate concentration.

In the present study, decreasing serum phosphate concentration was thought to induce an increase in serum 1,25(OH)₂D₃ concentration because other stimulations of 1 α -hydroxylase activity, such as those related to the levels of parathyroid hormone [7] and calcitonin [8], were not activated. Since the serum 1,25(OH)₂D₃ was elevated to the normal range, there was no reason to administer vitamin D metabolite. Although Farrington et al. [9] have reported that administration of 0.25 μ g/day 1 α -hydroxy-vitamin D₃ to nondialyzed patients did not increase the calcium absorption and did not impair the renal function, we found that prescription of 0.25 μ g/day 1 α -hydroxyvitamin D₃ with calcium carbonate led to deterioration of renal function in 2 out of 7 nondialyzed patients [10]. Accordingly, we firstly recommend administration of phosphate binder to stimulate 1 α -hydroxylase activity for the treatment of secondary HPT in nondialyzed patients with a Ccr below 30 ml/min where the serum 1,25(OH)₂D₃ concentration is generally below the normal range. In addition, phosphate binder is considered better than vitamin D metabolite since phosphate restriction im-

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proves secondary HPT independently of the levels of serum 1,25(OH)₂D₃ or ionized calcium [11], chelation of intestinal phosphate absorption delays the progression of chronic renal failure [12] and vitamin D metabolite itself may induce exacerbation of the renal function [2]. In the case of employing calcium carbonate as a phosphate binder in nondialyzed patients, it is desirable that the calcium carbonate be used in a low dose and gradually increased with care, paying attention to any exacerbation of renal function due to a rise in serum calcium concentration. Needless to say, dietary phosphorus restriction should be carried out.

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