Oral 1,25-Dihydroxyvitamin D₃ Minipulse Therapy

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400
300
175
200
D-
100

Fig. 1. Change in serum intact PTH concentration.

minimum accumulation, for the treatment of mild to moderate secondary HPT.

Five patients whose parathyroid hormone (PTH) concentration before hemodialysis was between 200 and 400 pg/ml were selected. All patients were hemodialyzed for 5 h three times weekly, employing a dialysate calcium concentration of 3.5 mEq/l. The age of the patients was $62 \pm (\text{SE}) 7$ years, the duration of hemodialysis was 8.5 ± 2.3 years, the doses of $1\alpha(\text{OH})\text{D}_3$ administered were 0.6 ± 0.1 $\mu\text{g}/\text{day}$, and the doses of calcium carbonate were 3.5 ± 0.5 g/day. After the levels of serum total calcium, inorganic phosphate (Pi), alkaline phosphatase (ALP) and intact PTH had been measured, the prescription was changed. 2 μg 1,25-(OH) 2D_3 was ad-

Dear Sir,

Intravenous administration of 1,25-dihydroxyvitamin D₃ [1,25-(OH) 2D_3 ; intravenous pulse therapy] has been reported to improve severe secondary hyperparathyroidism (HPT) which is refractory to conventional therapy through a transient increase in the serum 1,25-(OH) 2D_3 concentration [1-3]. Although daily oral administration of 1,25-(OH) 2D_3 leads to hypercalcemia because of accompanying intestinal calcium absorption when the doses increase, it has been demonstrated that oral administration of 1,25-(OH) 2D_3 at high doses twice a week combined with an aluminum-containing phosphate binder (oral pulse therapy) can improve severe secondary HPT with little effect of the serum calcium concentration. [4]. However, hypercalcemia was sometimes experienced with such oral pulse therapy. In our view, even small doses of aluminum should not be prescribed to patients with chronic renal failure, since aluminum is absorbed from the intestine in chronic renal failure more than in normals [5]. Prescription of aluminum hydroxide together with vitamin D metabolites further increases the intestinal absorption of aluminum [6], the majority of the serum aluminum

combines with serum protein which cannot be removed by general hemodialysis [7]. A decrease in the rate of bone turnover following intravenous 1,25-(OH)₂D₃ pulse therapy [2] and accumulation of aluminum in dialysis patients [8] can lead to aluminum bone disease. In addition, we consider that treatment of secondary HPT by intravenous or oral pulse therapy has a better effect when it is performed at an earlier stage. Since 1,25-(OH)₂D₃ for intravenous injection is not commercially available in Japan, we attempted oral minipulse therapy, in order to avoid alu-

0 4 8 12 16 20 24 Time, weeks

ministered once a week after the first hemodialysis session of the week, and the same doses per day of 1α(OH)D₃ were prescribed from the next day after the second hemodialysis session to the day of the first hemodialysis session of the next week. The same doses per day of calcium carbonate were prescribed from the evening after the second hemodialysis session to lunch after the first hemodialysis session of the next week in order to avoid either the occurrence of hypercalcemia during the first 2 days during which the serum 1,25-(OH)₂D₃ concentration increased or the appearance of hyperphosphatemia during the last 5 days. The same parameters were measured every 4 weeks. As shown in figures 1-3, the levels of intact PTH and ALP were

500 -i

400

* p < 0.05 vs. week 0 ** p < 0.01 vs. week 0 p < 0.001 vs. week 0

12

10

p < 0.05 vs. week 0 | 12

MO

300 H

s

200

E

-5/8-H

100

1.4

0J

i 1 1 1 1 1 -i

0 4 8 12 16 20 24 Time, weeks

i 1 1 1 1 1 i

0 4 8 12 16 20 24

Time, weeks

Fig. 2. Change in serum ALP concentration.

Fig. 3. Changes in serum total calcium concentration and Pi.

significantly decreased at 4 weeks despite no change in the levels of total calcium and Pi, indicating that the increase in the level of serum 1,25-(OH)₂D₃ due to the oral minipulse

therapy directly induced the decreases in intact PTH and ALP levels. The level of total calcium was significantly increased 16 weeks after intact PTH and ALP levels decreased to the normal range, suggesting that normalization of bone turnover induced the increase of the total calcium level. However, there was no appearance of hypercalcemia. The level of Pi underwent no significant changes during the study. The peak level of serum 1,25-(OH) $2D_3$ was from 118 to 148 pg/ml.

Our results indicate that oral minipulse therapy is effective for the treatment of mild to moderate secondary HPT without the occurrence of hypercalcemia and hyperphosphatemia. In addition, calcium carbonate as a sole phosphate binder could maintain the level of Pi within a satisfactory range during the oral minipulse therapy, resulting in no risk of aluminum accumulation. Since the serum 1,25-(OH) $2D_3$ concentration was increased to approximately 120-150 pg/ml following oral administration of 2 μ g 1,25-(OH) $2D_3$, such an increase in the level of serum 1,25-(OH) $2D_3$ for a while exerts a suppressive effect on parathyroid function. We, therefore, recommend that oral minipulse therapy is employed for the treatment of progressive secondary HPT at an earlier stage. We further need to examine the effect of the oral minipulse therapy in terms of the bone morphology.

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