Pharmacological Parathyroidectomy by Oral 1,25(OH)₂D₃ Pulse Therapy

Y.	Yusuke	Tsukamoto
M.	Masanori	Nomura
F.	Fumiaki	Marumo

Department of Medicine, Kitasato University School of Medicine, Sagamihara, Japan

Dr. Yusuke Tsukamoto, Department of Medicine, Kitasato University School of Medicine, 1-15-1 Kitasato, Sagamihara, Kanagawa 228 (Japan)

Dear Sir,

Renal osteodystrophy is one of the major complications of chronic renal failure. Many uremic patients, especially those who have been receiving hemodialysis for a long time, suffer from bone pain and bone fractures caused by this disorder. Avoidance of this disorder can be achieved by prevention or treatment of secondary hyper-parathyroidism (HPT). Prevention of secondary HPT can be accomplished by oral administration of 1,25-dihydroxycholecalciferol [1,25(OH)₂D₃] combined with phosphate binders. However, the treatment of secondary HPT cannot always succeed by a maintenance dose of 1,25(OH)₂D₃ when the serum parathyroid hormone (PTH) level is very high. In order to treat secondary HPT without a surgical procedure, Slatopolsky et al. [1] reported that intravenous administration of high-dose 1,25(OH)₂D₃ was effective in suppressing PTH secretion. Although their attempt was very successful, this therapy is not available for patients at the present time, because the 1,25(OH)₂D₃ preparation for intravenous administration is no longer on the market.

We report here that periodic oral administration of high doses of 1,25(OH)₂D₃ was also very effective in reducing the high serum PTH level. 1,25(OH)₂D₃ was administered orally to 9 patients undergoing hemodialysis at the end of each dialysis session twice a week for a period of 20 weeks. The serum PTH (carboxy-terminal) level was higher than 7.0 ng/ml, and the average value was 17.2 ± 7.7 ng/ml (normal range in our facility 0.20–1.00 ng/ml) at the beginning of the therapy. Initially, the dose was 2.0 µg and was increased to 6 µg. The dose was determined so that the serum calcium level did not exceed 11 mg/dl. Aluminum hydroxide was administered to maintain the serum phosphorus level below 5.0 mg/dl. The results are shown in table I. One of the clinical courses of therapy is also depicted in figure 1. The serum PTH-level(c-terminal and midregion) decreased dramatically in every patient under therapy, and the average decrement was 41% of the initial level after 5 months of treatment. The serum alkaline phosphatase level (normal range 73–248 IU) also decreased significantly, suggesting improvement of an excessive bone calcium turnover. In most cases, serum PTH and alkaline phosphatase levels

*p < 0.01 compared with the data before therapy, analyzed by Wilcoxon's test for paired data.
Pharmacological Parathyroidectomy by Oral 1,25(OH)₂D₃ Pulse Therapy

1,000
500
50-

venous administration in suppressing the PTH secretion in uremic patients with secondary HPT, we found that this is not true. If high oral doses of 1,25(OH)₂D₃ are administered periodically and not daily (we call this pulse therapy), this method can be very effective in the treatment of secondary HPT in uremic patients (pharmacological parathyroidectomy).

20
0 4 8

Duration of therapy, weeks

Fig. 1. Typical clinical course of pharmacological parathyroidectomy. 1,25(OH)₂D₃ administration (twice a week) is shown in the horizontal column at the top of the figure. ALP = Alkaline phosphatase activity.

Reference

1 Slatopolsky, E.; Weerts, C; Thielan, J.; Horst, R.; Harter, H.; Martin, K.J.: Marked suppression of secondary hyperparathyroidism by intravenous administration of 1,25-dihydroxycholecalciferol in uremic patients. J. clin. Invest. 74:2136–2143 (1984).

started to fall significantly within 5 weeks of therapy, and a dose of 4–6 µg of 1,25(OH)₂D₃ was considered to be adequate to maintain these effects.

Although Slatopolsky et al. [1] reported that oral administration of 1,25(OH)₂D₃ was not as effective as intra-