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Secondary Hyperparathyroidism in Patients on Maintenance Hemodialysis: Study of Optimal Hemopurification and Parathyroidectomy

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We have found that hemofiltration and direct hemoperfusion combined with hemodialysis removed significant amounts of parathyroid hormone. Hemofiltration and direct hemoperfusion combined with hemodialysis seemed to have better effects on secondary hyperparathyroidism. Surgical parathyroidectomy is indicated when medical parathyroidectomy has failed to prevent progressive bone disease. We had ten patients with refractory secondary hyperparathyroidism. In these patients, subtotal parathyroidectomy was attempted. The results obtained were: 1) Subtotal parathyroidectomy was successful in all patients. 2) Preoperative serum parathyroid hormone values were useful for diagnosis of secondary hyperparathyroidism. 3) The average serum N and C-terminal parathyroid hormone values measured preoperatively were 4,491.00 ± 892.13 pg/ml and 4,580.00 ± 474.48 pg/ml, respectively. 4) The average N and C-terminal parathyroid hormone values measured postoperatively were 298.60 ± 128.68 pg/ml and 2,631.00 ± 719.51 pg/ml, respectively.

(Key Words: Secondary hyperparathyroidism, Maintenance hemodialysis, Hemofiltration, Direct hemoperfusion, Parathyroidectomy)

INTRODUCTION

In maintenance dialysis patients, musculoskeletal disorders can influence the quality of life and contribute to the morbidity (1, 2). When radiological and clinical findings of secondary hyperparathyroidism (2°HPT) are present, it is logical to use all the therapeutic measures available, i.e. the control of hyperphosphatemia, oral supplement of calcium and active vitamin D ($1\alpha(OH)D_3$, 1α, $25(OH)_2D_3$), and optimal hemodialysis (HD) conditions. In this paper, we present results concerning the advantages of hemofiltration (HF) and direct hemoperfusion (DHP) to 2°HPT, and the changes in values of parathyroid hormone (PTH), total calcium (Ca), ionized calcium (Ca^{++}), phosphate (P), total alkaline phosphatase (ALP) and bone alkaline phosphatase (ALP_3) in serum measured preoperatively and postoperatively in 10 patients with refractory 2°HPT in whom subtotal parathyroidectomy (PTX) was attempted.

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MATERIALS AND METHODS

Three cases with 2°HPT were treated with HF. The Toray filtryzer B_1 (Toray, Japan) with a PMMA membrane was used. Substitution fluid was infused into a venous line to compensate for water and solute removal (post-dilution method) and contained: Na^+: 140 mEq/L, K^+: 2 mEq/L, Ca^{++}: 3.5 mEq/L, Mg^{++}: 1.5 mEq/L, Cl^- : 107 mEq/L and acetate: 40 mEq/L, Osmolarity was 291.5 mOsm/Kg. One case with 2°HPT was treated by DHP combined with HD. The DHP-1 (hydron hemoperfusion cartridge) (Kuraray, Japan) was used. In ten patients with 2°HPT (Table 1), subtotal parathyroidectomy was attempted. We measured the concentration of PTH (radioimmunoassay), Ca (autoanalyzer), Ca^{++} (Orion calcium analyzer-model SS-20), P (autoanalyzer) and ALP (densitometer at 590 mμ followed by gel electrophoresis) in serum before and after subtotal PTX.

Table 1 Clinical Features

Case	Age	Sex	Diagnosis	Duration of Hemodialysis	Chief Complaints	Date of Operation
1	26	Male	Glomerulonephritis	66 months	Pathological fractures, hyperosteosis of jaw	1978.11.17
2	32	Female	Glomerulonephritis	64 months	Left anterior neck-mass, knee joint pain and swelling	1979. 8.31
3	40	Male	Glomerulonephritis	122 months	Itching, bone pains, metastatic calcification	1980. 4.25
4	37	Male	Glomerulonephritis	75 months	Joint pains, loss of height, hyperosteosis of jaw	1981. 7. 1
5	34	Male	Clomerulonephritis	58 months	Lumbago, joint pains metastatic calcification	1982. 1.26
6	36	Male	Glomerulonephritis	72 months	Pathological fractures, metastatic calcification	1982. 1.26
7	34	Female	Glomerulonephritis	50 months	Joint pains	1982. 2.26
8	59	Male	Glomerulonephritis	45 months	Itching, joint pains	1982. 3. 2
9	55	Female	Glomerulonephritis	49 months	Itching, joint pains	1982. 5.21
10	50	Male	Glomerulonephritis	108 months	Itching, joint pains	1982.11.19

RESULTS

1) Fig. 1 shows the change in serum N and C-PTH levels during HD and HF. Serum N and C-PTH levels decreased during both HD and HF. The decrease in serum C-PTH levels was not significantly steeper during HD and HF. There were no significant differences between HD and HF. The decrease in serum N-PTH levels was significantly steeper during HF than during HD.

2) The serum C-PTH level was 4,020 ± 200 pg/ml in patients treated by HD and the level was 4,090 ± 450 pg/ml one month after induction HF.

There were no significant differences between HD and HF. The serum N-PTH level was 3,000±250 pg/ml in patients treated by HD and 1,500±2 000 pg/ml one month after induction HF. These levels were lower than the corresponding values for patients on HD (Fig. 2).

3) A decrease in serum P levels one month after the initiation of HF, and an increase in serum Ca levels one month after the initiation of HF were observed (Fig. 3).

4) Fig. 4 shows the change in serum N and C-PTH levels during DHP combined with HD. The decrease in serum N and C-PTH levels, especially N-PTH levels, was significantly steeper during DHP combined with HD.

5) The average serum N and C-PTH values measured before subtotal PTX were 4491.00±892.13 pg/ml and 4580.00±474.48 pg/ml, respectively. Normalization of serum N-PTH values was observed one month after subtotal PTX. A decrease in serum C-PTH values was also observed one month after subtotal PTX, but serum C-PTH values one month after subtotal PTX did not become normal (Table 2).

6) Normalization of serum Ca^{++} levels was observed one month after subtotal PTX. Serum Ca^{++} level one month after subtotal PTX was 2.41±0.21 mEq/L. Total serum Ca level one month after subtotal PTX was slightly lower than the normal value, i.e. 4.09±0.50 mEq/L (Table 2). All patients were placed on calcium and $1\alpha(OH)D_3$.

7) Normalization of serum P levels one month after subtotal PTX was observed (Table 2). None of the patients required intestinal binding of phosphate postoperatively.

8) An increase in serum ALP activities one week after subtotal PTX was observed followed by a decrease in serum ALP and ALP_3 activities. The decrease in serum ALP and ALP_3 activities after subtotal PTX was slow, elevated serum ALP and ALP_3 activities did not return to normal and the high levels continued one month after the operation (Table 2).

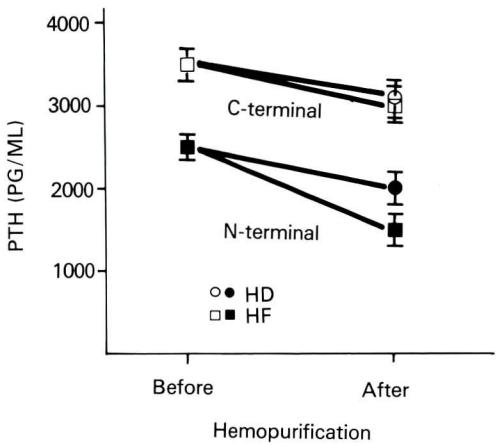

Fig. 1 Changes in plasma PTH levels during hemopurification.

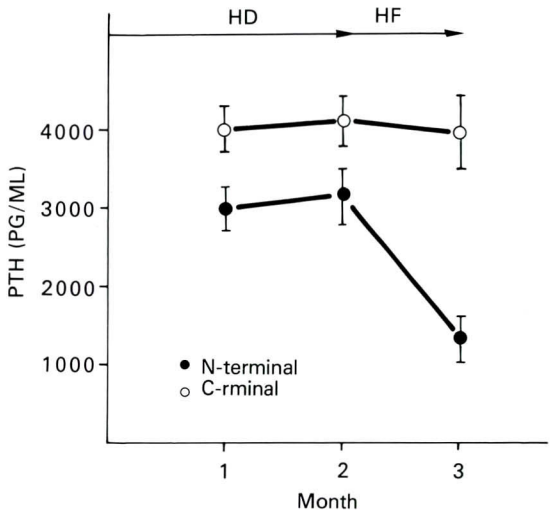

Fig. 2 Changes in plasma PTH levels.

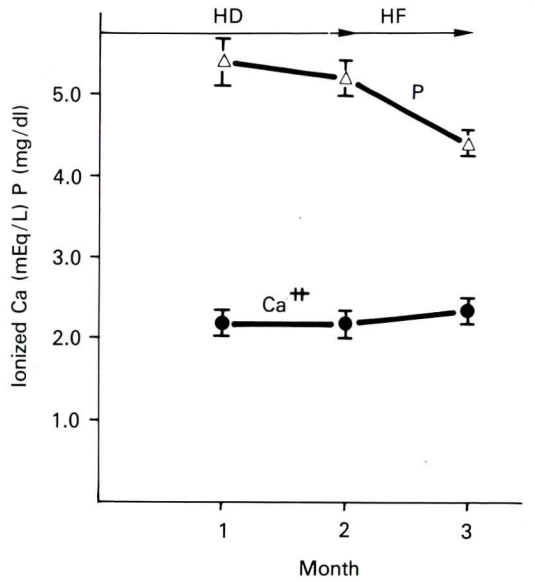

Fig. 3 Changes in plasma P and ionized Ca levels.

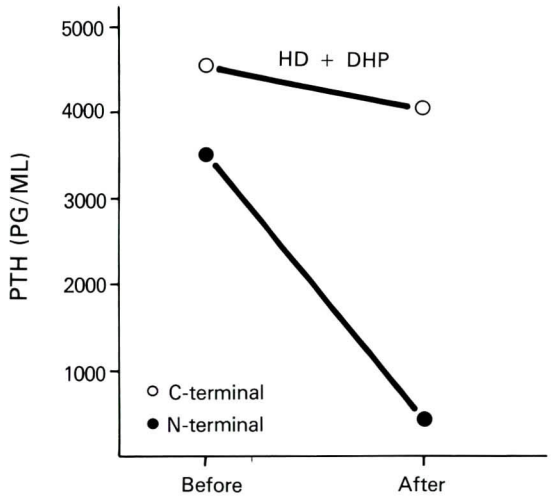

Fig. 4 Changes in plasma PTH levels during hemopurification.

Table 2 Plasma biochemical variables before and after parathyroidectomy

	Before	After
N-PTH (pg/ml)	4491.00±892.13	298.60±128.68
C-PHT (pg/ml)	4580.00±474.48	2631.00±719.51
Total Ca (mEq/L)	4.89± 0.48	4.09± 0.50
Ionized Ca (mEq/L)	2.29± 0.20	2.41± 0.21
P (mg/dl)	5.85± 1.30	3.18± 0.48
Total ALP (U/L)	1067.23±503.60	960.73±345.63
ALP_3 (U/L)	920.48±420.50	840.83±240.55

DISCUSSION

Management of renal osteodystrophy during maintenance hemopurification is very important for patients with end-stage renal failure. Optimal hemodialysis conditions to prevent osteodystrophy (3) were as follows: 1) the water should be treated either by deionization or by reverse osmosis. The dialysate Ca^{++} should be 6.5 when vitamin D is given or 7.0 mg/dl when no vitamin D therapy is given. 2) Between dialysis, the diet should be restricted only concerning dairy products, but protein intake should be around 1 g/kg. 3) Calcium supplements should be given to bring Ca intake up to 1.5 g of elemental calcium per day when vitamin D is given; a dialysate Ca of 6.5-7 mg/dl is used. 4) Sufficient phosphate binders should be administered to maintain predialysis phosphate at 4.5±0.5 mg/dl. This control of hyperphosphatemia is especially critical when the duration of dialysis is short (4 hours) and when vitamin D is administered. 5) Vitamin D therapy is advised

as in the case before dialysis. In accordance with the the results of previous studies by the authors (5) and other reporters (4, 6), we found in the present study that HF and DHP combined with HD can remove significant amounts of PTH, pain due to abnormal calcium deposition was relieved, and administration of phosphate binders such as Al-Gel could be eliminated because of well controlled serum P levels. Unfortunately, when the above therapeutic measures failed to prevent 2°HPT, surgical parathyroidectomy was indicated. Subtotal parathyroidectomy has generally been considered preferable to total removal of the glands. It is important to prevent post PTX hypocalcemia and tetany. To prevent tetany, calcium and 1α derivatives of vitamin D_3 supplements should be given. We had no postoperative complications. Normalization of serum N-PTH values was rapid after PTX, but the decrease in serum C-PTH levels after PTX was slow. Elevated serum ALP and ALP_3 activities did not return to normal rapidly after PTX. We observed normalization of serum ALP and ALP_3 activities one year after subtotal PTX in all patients with 2°HPT. Complete recovery of renal osteodystrophy was only achieved by successful renal transplant.

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