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*The long-term effects of parathyroidectomy (PTx) on blood pressure, anemia, erythropoietin requirement and other clinical features of hemodialysed (HD) patients*

Treatment of severe secondary hyperparathyroidism (HPTH) remains a serious therapeutic problem in hemodialysed (HD) patients. Some HD patients with severe HPTH may not respond to calcitriol and a new vitamin D analogues. However, despite significant progress in the field of HPTH treatment, including the introduction of calcium-free non-absorbable oral phosphate binders and new vitamin D analogues in some patients with severe HPTH surgical intervention is still required. Current indications for PTx in HD patients were published by Schöming and Cazzolino (3, 10).

The aim of the study was to assess the long-term effects of PTx of clinical course of severe secondary HPTH in patients undergoing maintenance HD. A diastolic and systolic blood pressure, Hb level and erythropoietin dosage, as well as other clinical symptoms were evaluated.

MATERIAL AND METHODS

The presented study was performed in 22 HD patients with severe secondary HPTH. The mean age of the patients was 47 years (26–71), an average hemodialysis duration was 97 months (37–203). All the patients were dialyzed three times a week using bicarbonate fluid. The mean length of the follow-up was 39 months (28–56).

Persistent hyperphosphatemia required co-administration of calcium carbonate or sevelamer hydrochloride, agents preventing phosphorus reabsorption from the gastrointestinal tract.

Clinical symptoms of severe HPTH, i.e. persistent pruritus, bone pain, muscle weakness and cardiovascular complications were observed.

In all the patients an initial treatment with active derivative of vitamin D<sub>3</sub> (1- $\alpha$  hydroxy-cholecalciferol) was performed; it was given orally 3 times a week at increasing doses ranging from 0.5 to 4.0  $\mu$ g. An increasing hyperphosphatemia and increase in Ca x P product were found in all patients during the long-term clinical follow-up. Nevertheless, persistent hypercalcemia found despite reduction of calcium concentration in dialysis fluid resulted in termination of 1- $\alpha$  hydroxy-cholecalciferol treatment and consequent surgical interventions in 7 patients. All patients underwent scintigraphy with <sup>99m</sup>Tc MIBI and ultrasonography of the neck. PTx was performed in all patients (8 subtotal, 12 total with autotransplantation of parathyroid tissue into the forearm musculature and 2 total without autotransplantation). The biochemical parameters will be reported in a separate publication.

## RESULTS

Immediately after PTx and during the long-term follow-up all patients showed a marked decrease in systolic and diastolic blood pressure ( $p < 0.01$ ). Relevant increase in Hb levels ( $p < 0.01$ ) has also been noticed, although the weekly erythropoietin doses were significantly lower ( $p < 0.01$ ) (Table 1).

Postoperative improvement of clinical symptoms – persistent pruritus, bone pain, muscle weakness and cardiovascular disturbances was achieved within 1 month in all patients. Seven patients showed gradual increase in PTH levels after PTx (5 subtotal, 2 total with autotransplantation of parathyroid tissue). It has been accompanied by hyperphosphatemia and the elevated Ca x P product level and the recurrence of HTPH and clinical symptoms.

Table 1. Blood pressure, hemoglobin levels and doses of erythropoietin before and after PTx

		Min	Max	Average	Standard deviation	Median	P
Systolic blood pressure	before PTx	100.00	190.00	153.08	22.13	160	<0.01
	after PTx	90.00	160.00	125.00	23.09	130	
Diastolic blood pressure	before PTx	60.00	105.00	83.85	12.10	80	<0.01
	after PTx	60.00	90.00	71.92	9.90	70	
Hb level	before PTx	8.50	13.50	9.73	1.30	9.5	<0.01
	after PTx	9.30	13.60	11.25	1.21	11.4	
Erythropoietin doses (weekly)	before PTx	2,000.00	8,000.00	5,250.00	1,815.34	5,500	<0.01
	after PTx	1,000.00	6,000.00	2,750.00	1,658.31	3,000	

## DISCUSSION

The presented results demonstrated postoperative improvement of clinical symptoms – persistent pruritus, bone pain, muscle weakness within one month in all the patients. In addition, immediately after PTx and during the long treatment follow-up, marked decrease in systolic and diastolic pressure was observed in all patients. Thus hypotension drugs were given in considerably reduced doses or withdrawn. Some other authors report blood pressure decrease after PTx (2, 5, 7). Nevertheless, conflicting reports have been published (1). Hyperparathyroidism has been coupled to normochromic and normocytic anemia with significant improvement observed after parathyroid gland surgery (12). Presented data demonstrated significant increase in the Hb level in the long-term clinical follow-up of patients who had undergone PTx, despite previous reduction of erythropoietin dosage. The subsequent study by Mandolfo and Schiffel strongly supported our data (6, 9). Several previously published papers reported recurrence of severe HPTH in 5–80% of patients after subtotal and total PTx with immediate autotransplantation. In our own experience seven patients showed gradual increase in PTH level after PTx (5 subtotal, 2 total with autotransplantation of parathyroid tissue). It has been accompanied by hyperphosphatemia and the elevated Ca x P product level and the recurrence of HPTH and clinical symptoms (11).

It should be noted that parathyroid cells reveal a strong tendency to proliferation. Therefore, a rupture of parathyroid capsule with seeding of parathyroid cells or incomplete excision of abnormal parathyroid gland may put the patients at risk of local recurrence and lead to increase in the basal PTH level seen in postoperative biochemical parameters. Furthermore, the proliferative growth of tissue detected in parathyroid autografts can be extremely hard to explore.

In our study graft dependent recurrence resulting from parathyroid cells proliferation was found in one patient. To overcome this problem some authors proposed total PTx without autografting (8, 4). In these patients low-dose calcitriol administration allowed to normalize serum calcium.

### CONCLUSIONS

The presented results demonstrated that PTx should be performed in patients with severe secondary HPTH, hyperphosphatemia, elevated level of Ca x P product and large size of parathyroid glands. After PTx surgery a decrease in clinical symptoms, decrease in blood pressure and improvement of anemia was observed.

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### SUMMARY

Treatment of severe secondary hyperparathyroidism (HPTH) remains a serious therapeutic problem. Some HD patients with severe HPTH may not respond to calcitriol and a new vitamin D analogues. The aim of this study was to assess long-term effects of PTx on the clinical course of severe secondary HPTH in patients undergoing maintenance HD. A diastolic and systolic blood pressure, Hb level and erythropoietin dosage, as well as other clinical symptoms were evaluated. Our study was performed in 22 HD patients with severe secondary HPTH. The mean age of the patients was 47 years

(26–71), an average hemodialysis duration was 97 months (37–203). The mean length of follow-up was 39 months (28–56). All patients had scintigraphy with  $^{99}\text{Tc}$  MIBI and ultrasonography of the neck. PTx was performed in all patients (8 subtotal, 12 total with autotransplantation of parathyroid tissue into the forearm musculature, 2 total without autotransplantation). For statistical calculations Wilcoxon's test was used.  $P < 0.05$  was considered statistically significant. Immediately after PTx and during the long-term follow-up all patients had a marked decrease in systolic and diastolic blood pressure ( $p < 0.01$ ). Relevant increase in Hb levels ( $p < 0.01$ ) has also been noticed, although the weekly erythropoietin doses were significantly lower ( $p < 0.01$ ). Postoperative improvement of clinical symptoms – persistent pruritus, bone pain, muscle weakness and cardiovascular disturbances was achieved within one month in all patients. Seven patients showed a gradual increase in PTH levels after PTx (5 subtotal, 2 total with autotransplantation of parathyroid tissue). It has been accompanied by hyperphosphatemia and elevated Ca x P product level and recurrence of HPTH.

#### Wpływ paratyreoidektomii na odległe wyniki nadciśnienia tętniczego, niedokrwiistości oraz stosowane dawki erytropoetyny u pacjentów przewlekle hemodializowanych

Leczenie ciężkiej wtórnej nadczynności przytarczyc (HPTH) pozostaje nadal poważnym problemem terapeutycznym, ponieważ wielu pacjentów nie odpowiada na leczenie calcitriolem oraz nowymi analogami witaminy D. Celem naszej pracy była ocena wpływu paratyreoidektomii (PTx) na odległe wyniki nadciśnienia tętniczego, niedokrwiistości oraz stosowanych dawek erytropoetyny u pacjentów przewlekle hemodializowanych. Ponadto ocenialiśmy inne objawy kliniczne HPTH. Badania przeprowadzono u 22 pacjentów z HPTH. Średni wiek pacjentów wynosił 47 lat (26–71), średni okres leczenia HD – 97 miesięcy (37–203), a średni okres obserwacji – 39 miesięcy (28–56). Wszyscy pacjenci mieli wykonaną scyntyografię przytarczyc z użyciem  $^{99}\text{Tc}$  MIBI oraz ultrasonografię tarczycy przed planowanym zabiegiem. PTx wykonano u wszystkich pacjentów (u 8 subtotalną, u 12 totalną z przeszczepem części tkanki gruczołu przytarczycowego na przedramię, a u dwu totalną bez przeszczepu). W opracowaniu statystycznym posłużono się testem Wilcoxon. Bezpośrednio po zabiegu PTx oraz w obserwacji odległej obserwowano istotny statystyczny ( $p < 0,01$ ) spadek ciśnienia skurczowego i rozkurczowego krwi. Jednocześnie istotnie wzrosło stężenie HB ( $p < 0,01$ ). Obserwowano też istotne ( $p < 0,01$ ) zmniejszenie stosowanych dawek erytropoetyny. Po około miesiącu od wykonania PTx ustąpiły objawy kliniczne HPTH, takie jak: uporczywy świąd skóry, bóle kostne, osłabienie mięśniowe oraz powikłania sercowo-naczyniowe. U siedmiu pacjentów (pięciu po subtotalnej PTx i u dwu po totalnej z autoprzeszczepem tkanki przytarczyc) obserwowano nawroty HPTH. U pacjentów tych obserwowano ponownie znaczny wzrost stężenia PTH, hiperfosfatemię oraz wzrost iloczynu Ca x P.