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ORIGINAL ARTICLE

The Efficiency of Parathyroidectomy and the Comparison of the Complications of Surgical Procedures in Dialysis Patients

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ABSTRACT

Secondary hyperparathyroidism is the hyperplasia and hyperfunctioning of the parathyroid gland in chronic renal failure. The aim of our study was to evaluate the efficiency and complications of surgical methods for secondary hyperparathyroidism in patients requiring dialysis. Forty-one patients operated for secondary hyperparathyroidism before renal transplantation were retrospectively analysed. The efficiency and complications of types of surgery in relation with age, gender, duration of dialysis, symptoms, laboratory test results before and after surgery were evaluated. Mean duration of dialysis was 6.2 ± 3.98 years. Patient's calcium, phosphorus and parathormone levels before surgery were 9.83 ± 1.25 mg/dl, 5.73 ± 2.15 mg/dl, 1847, 0.02 ± 666.602 pg/ml and, after surgery, were 7.85 ± 1.36 mg/dl, 4.5 ± 1.55 mg/dl, 288.05 ± 404.09 pg/ml. The differences betweeen preoperative and postoperative values were statistically significant ($p < 0.05$) recognizing the efficiency of surgery. The age of patients, the duration of dialysis and the type of surgery were not significantly effective on this difference ($p > 0.05$). Fifteen patients had subtotal parathyroidectomy, 25 patients had total parathyroidectomy with autotransplantation and one patient had total parathyroidectomy. The incidence of complications did not differ with age, gender, duration of dialysis and type of surgery ($p > 0.05$). The type of surgery did not possess difference in the improvement in levels of calcium, phosphorus and parathormone and also in the incidence of complications in secondary hyperparathyroidism. Surgeon's experience and individual patient characteristics seem to be more important in determining the type of surgery.

Keywords: Secondary hyperparathyroidism, Subtotal parathyroidectomy, Hypocalcemia, Chronic renal failure.

INTRODUCTION

Secondary hyperparathyroidism (SHPT) is a common complication in chronic renal failure (CRF) and characterized by abnormal mineral metabolism, skeletal anomalies and increase in serum parathormone levels.[1] SHPT appears as a response to damaged renal functions in chronic renal failure. Hyperphosphatemia, hyperuricemia and metabolic acidosis caused by renal failure leads to the inhibition of 1-alpha-hydroxylase enzyme.[2] In collaboration with the progression in renal failure, decreasing $1,25(OH)_2D$ production, hyperphosphatemia and hypocalcemia result in hyperparathyroidism. The risk of development of SHPT is not equal in all patients with chronic renal failure.[3] This disease may cause serious cardiovascular events, acceleration in atherosclerosis and metabolic bone disease. In some cases, SHPT can be controlled with diet and medical treatment. However, parathyroidectomy should be considered in cases with progressive clinical picture despite medical treatment, severe parathyroid gland hyperplasia, calciflaxis, osteitis fibrosa and significant hypercalcemia.[4] Risk factors for SHPT are young age, white race, presence of diabetes and long-term dialysis treatment.[3] Methods, such as subtotal parathyroidectomy (3.5 glands), total parathyroidectomy with or without autotransplantation, are used for the surgical treatment,[5] but the optimal surgical procedure remains controversial.[4]

In this study, our aim was to evaluate the efficiency of the surgery and the effects of the surgical methods on the complications in patients who underwent surgery for SHPT and on dialysis treatment because of chronic renal failure.

PATIENTS AND METHODS

We analyzed 41 patients who were on dialysis treatment because of chronic renal failure and who underwent surgery because of resistant SHPT to medical treatment between October 2005 and July 2010. During this period, subjects who underwent surgery after renal transplantation and whose information files were missing, were excluded from the study group. Patient's records were retrospectively analysed in age, gender, duration of renal failure, symptoms, serum laboratory test results before and after surgery, the efficiency of the surgery and complications. All patient's preoperative serum calcium (Ca), phosphorus (P), alkaline phosphatase (ALP) and parathormone

(PTH) levels were determined. In our hospital, normal range of serum values of the parameters were as follows: Ca: 8.1 to 10.7 mg/dl, P: 2.3 to 4.7 mg/dl, ALP: 95 to 280U/l, PTH: 15 to 65 pg/ml. The indications for surgery were persistant hypercalcemia (> 11 mg/dl) in spite of medical treatment, PTH value > 500 pg/ml, hyperphosphatemia > 6 mg/dl and symptomatic patients with bone pain and pruritus. All tests were repeated after surgery. Intravenous, later oral calcium replacements were given to patients who developed symptomatic hypocalcemia. Hypocalcemia remaining longer than 6 months was accepted as a persistent complication. Likewise, cases with PTH levels higher than 65 pg/ml 6 months after surgery were accepted as persistant hypocalcemia. Subtotal parathyroidectomy or total parathyroidectomy with autotransplantation was frequently performed. Surgical method was selected according to the surgeon's preference. By using Kocher's incision, the thyroid bed was explored for the four parathyroid glands. In subtotal parathyroidectomy, the half of the most normal appearing gland and the other three glands were excised. In total parathyroidectomy and auto-transplantation, the four glands were excised and the half of the most normal appearing gland was implanted inside the sternocleidomastoid muscle after being divided into 15 to 20 pieces of 1 mm thickness. The implanted gland was signed by a metal clip. Frozen section examination was performed on the material intraoperatively. In 32 patients (78%), four glands; in eight patients (19.5%), three glands; in one patient (2.4%), five glands were excised. All patients had received their last dialysis day before the surgery.

Data of the study were encoded, transferred to the computer and analyzed by using SPSS 15.0 version. Continuous variables were expressed as median (min-max) and discrete datas were expressed in numbers (%). Mann-Whitney U-test was used for the comparisons between groups, and Wilcoxon marked rows test was used for intragroup comparison. Chi-square test was used for the comparison of data derived from census. Statistical significance level for all tests was considered to be $p < 0.05$.

RESULTS

The ratio of female/male was 14/27. The mean age was 43.2 ± 14.03. The mean duration of CRF was 6.2 ± 3.98 years. Twenty-six patients (63, 41%) had symptoms of skeletal and gastrointestinal system disorder and fatigue. Patients had hypercalcemia (17.1%), hyperphosphatemia (68.3%), hyper-parathyroidism (100%) and elevated ALP levels (78.0%), before surgery. We performed subtotal parathyroidectomy in 36.6% of patients, total parathyroidectomy with autotransplantation in 61% and total parathyroidectomy in 2.4% (Table 1). The mean calcium, phosphorus and parathyroid hormone values before surgery were 9.83 ± 1.25 mg/dl, 5.73 ± 2.15 mg/dl, 1847.02 ± 666.602 pg/ml respectively. These values after surgery were 7.85 ± 1.36 mg/dl, 4.5 ± 1.55 mg/dl, 288.05 ± 404.09 pg/ml. In 23 of the 41 patients (56.1%), PTH levels were > 65 pg/ml on the first postoperative day. In following control measurements, six of these 23 patients (14.6%) had persistant hyperparathyroidism. Two of them had subtotal, four of them had total parathyroidectomy and autotransplantation. The reason for the persistance could not be determined. The preoperative and postoperative Ca, P and PTH values were compared in order to evaluate the effectiveness of the method selected for surgery, and the values were statistically significantly lower in postoperative period ($p < 0.05$) (Table 2). Decreased laboratory test results after surgery did not differ in terms of patient's age, duration of dialysis and the type of surgical method ($p > 0.05$) (Table 3). Nine patients (21.95 %) developed deep hypocalcemia requiring IV calcium replacement. The patients with appearent postoperative clinical tetany had intravenous calcium gluconate infusion therapy in 5 to 10 minutes. The patients who did not have clinical tetany but with calcium level < 8 mg/dl received oral calcium and vitamin D. The incidence of complications did not differ with age, gender, duration of dialysis treatment and the type of surgical method ($p > 0.05$) (Table 4). There was no mortality and no recurrent laryngeal nerve damage.

Table 1: Clinical and laboratory characteristics of cases

		Number of patients (n = 41)	*Value(%)*
Mean age (year)		43.2 ± 14.03	–
Mean duration of dialysis (year)		6.2 ± 3.98	–
Gender	Female	14	34.1
	Male	27	65.9
Symptom	Bones/joints	13	31.7
	Gastrointestinal	5	12.2
	Fatigue	8	19.5
	None	15	36.6
Laboratory tests before surgery	Hypercalcemia	7	17.1
	Hyperphosphatemia	28	68.3
	ALP increase	32	78.0
	PTH increase	41	100
Surgical method	Subtotal (3.5 glands) parathyroidectomy	15	36.6
	Total parathyroidectomy + autotransplantation	25	61
	Total parathyroidectomy	1	2.4

DISCUSSION

SHPT is defined as the excessive secretion of PTH from the parathyroid glands stimulated by external factors. SHPT is frequently resulted from CRF and that is so-called renal hyperparathyroidism. SHPT develops in a large number of dialysis patients (90%) and the primary treatment for these cases is medical.[6] About 5 to 10% of the cases require surgical treatment after a period of 10 to 15 years, despite significant improvements in technology of the dialysis and medical treatment modalities. Despite these recent improvements, the incidence of parathyroidectomy has not been reduced.[3] In our study, we observed that the mean duration of dialysis was longer than 6 years. Parathyroidectomy seems to be necessary in order to control parathormone synthesis and secretion in long-term hemodialysis patients with uncontrolled SHPT with medical treatment.[3,7] It is well-known that uncontrolled SHPT can result in many metabolic and systemic complications. Therefore, parathyroidectomy is effective in reducing long-term results and can also be effective in preventing mortality in patients with end-stage renal failure.[8-10] PTH supression treatment significantly reduces metabolic bone diseases, bone loss, metabolic complications and reduces morbidity and mortality related with these factors.[11] The comparison of the preoperative and the postoperative Ca, P and PTH levels of our patients, proved the effectiveness of surgical treatment. Furthermore, PTH levels were statistically significantly decreased after the surgery ($p < 0.05$) (Table 2).

Today, the optimal surgical method for SHPT remains controversial, but subtotal parathyroidectomy with bilateral cervical exploration and total parathyroidectomy with or without autotransplantation are currently the most performed surgical methods.[4,6,7,12] In our study, 36.6 % of the patients had subtotal parathyroidectomy, 61% had total parathyroidectomy with autotransplantation and 2.4% had only total parathyroidectomy. Subtotal or total parathyroidectomy with autotransplantation is the most preferred methods according to medical literature.[3,7,13-15] In our study, the comparison of the preoperative and the postoperative laboratory test results indicated no statistically significant difference between surgical methods ($p > 0.05$) (Table 3). Rachad A et al[13] and Richards ML et al[14] expressed that both methods are similar in terms of effectiveness and persistence. Total parathyroidectomy without autotransplantation is a recently used method for SHPT.[6] Furthermore, Lorenz et al[12] reported that solo total parathyroidectomy is just as safe and effective as other methods used in SHPT, and even more successful in terms of recurrence. Similarly, Ockert S et al[16] and Puccini et al[4] reported that total parathyroidectomy without autotransplantation is a safer method with low recurrence rate, compared with parathyroidectomy with autotransplantation. Likewise, Drakopoulos et al[17] underlined the effectiveness and the safety of the parathyroidectomy without autotransplantation in resistant SHPT. However, in our study,

Table 2: The results of statistical evaluation of laboratory values before and after surgery

Test name	*Before surgery*	*After surgery*	*p-values*
Ca (mg/dl)	9.83 ± 1.25	7.85 ± 1.36	< 0.05
P (mg/dl)	5.73 ± 2.15	4.5 ± 1.55	< 0.05
PTH (pg/ml)	1847.02 ± 666.602	288.05 ± 404.09	< 0.05

Table 3: The postoperative laboratory values related with age, duration of dialysis and type of surgery

			Normal	*Abnormal*	*p-values*
Ca	Mean age (year)		41.11 ± 14.27	44.83 ± 13.92	0.324 (NS)
	Mean duration of dialysis (year)		6.56 ± 4.04	5.91 ± 4.01	0.594 (NS)
	Surgery	Subtotal	5-33.3%	10-66.7%	
		Total + autotx	13-52.0%	12-48.0%	0.332 (NS)
PTH	Mean age (year)		41.5 ± 13.08	44.52 ± 14.87	0.454 (NS)
	Mean duration of dialysis (year)		6.39 ± 4.53	6.04 ± 3.59	0.958 (NS)
	Surgery	Subtotal	8-53.3%	7-46.7%	
		Total + autotx	10-40.0%	15-60.0%	0.517 (NS)
P	Mean age (year)		41.24 ± 13.05	44.58 ± 14.79	0.435 (NS)
	Mean duration of dialysis (year)		7.53 ± 5.14	5.25 ± 2.64	0.217 (NS)
	Surgery	Subtotal	5-33.3%	10-66.7%	
		Total + autotx	12-48.0%	13-52.0%	0.512 (NS)

NS: Not significant; Autotx: Autotransplantation

Table 4: Analysis of risk factors for the development of complications

		Complications present	*Complications absent*	*p-values*
Age		40.89 ± 12.75	43.84 ± 14.49	0.514
Surgery	Subtotal	2-13.3%	13-86.7%	0.44
	Total + autotx	7-28.0%	18-72.0%	
Duration of dialysis (year)		6.89 ± 5.75	6.00 ± 3.43	0.987
Preop PTH (pg/ml)		1939.89 ± 630.86	1820.91 ± 678.67	0.654
Preop ALP (U/l)		811.00 ± 449.70	836.56 ± 1105.16	0.219
Preop Ca (mg/dl)		9.43 ± 1.64	9.94 ± 1.13	0.625
Preop P (mg/dl)		6.95 ± 1.99	5.38 ± 2.10	0.065

Autotx: Autotransplantation

only 2.4% of the patients underwent total parathyroidectomy without autotransplantation and the number of cases was inadequate for statistical evaluation; therefore, comparison for this surgical method was impossible.

The most common surgical complications after parathyroidectomy are permanent or temporary hypocalcemia and hoarseness caused by recurrent laryngeal nerve damage. The incidence of postoperative hypocalcemia in patients undergoing parathyroidectomy for primary hyperparathyroidism is expressed between 10 and 46%. This rate is reported to be 20 to 85% in patients undergoing parathyroidectomy for SHPT.[18] Supporting the literature, our rate of transient hypocalcemia after surgery is 21.95%. Risk factors for postoperative hypocalcemia are not yet fully elucidated.[19] Identification of risk factors before surgery seems to be important in the management of postoperative complications. According to the study of Torer N et al,[18] the incidence of early hypocalcemia after surgery in hemodialysis patients is related with age and preoperative Ca, ALP levels, but no relation was found with gender, duration of dialysis, surgical method and preoperative PTH and P levels. Conflicting with the medical literature who reported an increased risk of hypocalcemia in advanced age due to inadequate intake and deficiency of vitamin D.[20] Torer N et al[18] reported a higher risk of hypocalcemia in young patients. In an other study, Mittendorf et al[19] found no correlation between primary and secondary HPT patients in terms of preoperative calcium levels. Torer N et al[18] also showed no association between postoperative hypocalcemia and surgical method. As it was mentioned in above studies, there is no reliable data on risk factors for the development of hypocalcemia after parathyroidectomy. We could not identify any statistically significant relation between postoperative early hypocalcemia and age, length of dialysis, surgical method, preoperative PTH, ALP, Ca and P levels (Table 4).

CONCLUSION

Surgical parathyroidectomy is an effective method in reducing PTH levels in hemodialysis patients who are resistant to medical treatment. It is well-known that continuous high levels of PTH in resistant cases can cause various skeletal and metabolic complications; therefore, surgical treatment at the appropriate time is important. There is no difference between the types of surgical methods in terms of postoperative complications. Therefore, we think that it would be logical to determine the type of surgery according to the surgeon's experience and to the individual patient and the conditions of the hospital.

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