



## Surgical treatment of secondary hyperparathyroidism in chronic hemodialysis

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### ABSTRACT

*Introduction: Secondary hyperparathyroidism is a common complication of chronic renal failure. The surgical management comes after a period of evolution, and it's recommended particularly severe and resistant forms to medical treatment. Purpose: The purpose of this work is to clarify the indication of parathyroidectomy, and assess the follow up of patients. Patient and Methods: This is a cross-sectional study of 14 patients who are chronic hemodialysis, who were parathyroidectomized over a period of four years. We analyzed the clinical, biological and radiological parameters before and after the surgery. Results: The average age of patients at the time of surgery was  $47 \pm 12$  years. The indication for parathyroidectomy was necessary in these 14 patients before resistance to medical treatment, to achieve the targets of the KDIGO guidelines for calcium, phosphorus and the PTH1-84 in 10 patients and the persistence of clinical signs of hyperparathyroidism in 4 patients (bone pain in 3 cases; pathological fractures in one patient). Immediately after surgery, we have identified an immediate postoperative hypocalcemia in six cases (42.8%). After a mean follow up of 12 months, we identified the persistence of secondary hyperparathyroidism in two cases (14.8%). The outcome was favorable in the long term in most cases with a clinical and biological improvement. Conclusion parathyroidectomy is an effective treatment that stops the overproduction of parathyroid hormone with good clinical, biological and radiological results. However, the early treatment of phosphocalcic anomalies with new drugs and the development of renal transplantation would reduce its prevalence.*

**Keywords:** parathyroidectomy, hemodialys, hyperparathyroidism

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### INTRODUCTION

Secondary hyperparathyroidism (SHPT) is a common complication in chronic hemodialysis patients, associated with morbidity and sometimes mortality [1-2]. The treatment of SHPT is primarily preventive, and involves correcting the main pathogenic factors including the phosphorus retention, hypocalcemia and calcitriol deficiency [3]. In the majority of patients with secondary

hyperparathyroidism (SHPT), this can be managed by medical treatment but this does not always give adequate control of the parathyroid disorder. Some patients require intervention treatment of the parathyroid glands including parathyroidectomy [4]. The purpose of this study is to analyze the experience of our unit in the management of secondary hyperparathyroidism, to clarify the indications for surgical treatment and assess the evolution in the short-and long-term.

## MATERIALS AND METHOD

We conducted a monocenter cross-sectional study between October 2009 and March 2013, recruiting all adult patients operated for SHPT, in the University Hospital Mohammed VI (Marrakech, Morocco). Data were collected from medical records.

We clarified demographic parameters (age, gender), dialytic parameters (length of hemodialysis, blood pressure, dry weight, interdialytic weight gain and dose of dialysis), clinical signs of hyperparathyroidism and biological data (serum levels of hemoglobin, ferritin, albumin, calcium, phosphorus, total alkaline phosphatase, and parathyroid hormone). We collected the radiographic parameters and parathyroid ultrasound abnormalities. We performed a parathyroid scintigraphy methoxy-isobutylisonitrile labeled with technetium 99 metastable (<sup>99m</sup>MIBI) in search of focus uptake of the parathyroid glands. A monitoring of serum calcium, phosphorus and parathyroid hormone was performed immediately after surgery, in one month, six months and one year of parathyroidectomy.

The HPTS was defined as a parathyroid hormone that is nine times superior than the upper normal limit. The hyperphosphatemia, hypercalcemia have to be superior than the target rate, recommended by Kidney Disease Improving Global Outcomes (KDIGO) [5].

The parathyroidectomy was indicated in severe hyperparathyroidism (> 500 pg / ml) associated with hyperphosphataemia (> 60 mg / l) and / or hypercalcemia (> 100mg / l) that are refractory to medical treatment, bone pain, pathological fractures, anaemia resistant to erythropoietin, calciphylaxis[6]. Statistical analysis was done on SPSS 11.5 software. Quantitative variables were expressed as average  $\pm$  standard deviation and qualitative variables as percentages.

## RESULTS AND DISCUSSION

There was 14 regular hemodialysis patients who were parathyroidectomized during a period of four years. The average age was  $47 \pm 12$  years (40-59 years). 57.1% of patients were male with a sex ratio of 1.3. Demographic, clinical, biological and radiological parameters of the patients on before the surgery are presented in Table 1.

**Table 1: The demographic, clinical, biological and radiological data of patients operated on before the surgery**

Age (mean $\pm$ SD)	47 $\pm$ 12 ans (40-59)
Male (%)	57,1%
Length of hemodialysis (mean $\pm$ SD)	10 ans $\pm$ 4 (6-15)
Dialytic parameters (mean $\pm$ SD)	
Dose of dialysis (Kt/v)	1,32 $\pm$ 0,16
Dry weight (kg)	62,73 $\pm$ 10,04
Interdialytic weight gain (kg)	2,41 $\pm$ 0,78
Predialysis systolic arterial pressure (cmhg)	13,06 $\pm$ 3,6
Predialysis diastolic arterial pressure (cmhg)	8,83 $\pm$ 2,15
Clinical signs n (%)	
Pruritus	6(42,8%)

Fatigability	10(71,4)
Bone pain	13(92,8%)
Pathological fractures	1(7,1%)
Calciophylaxis	1(7,1%)
Biological parameters (mean±SD)	
Hemoglobin (g/dl)	9,75 ± 2,1
Ferritin (ug/l)	245±35
Albumin (g/l)	39,4± 3,6
Calcium (mg/l)	104±8
Phosphorus (mg/l)	58±5
Total alkaline phosphatase (UI/l)	738±13
Parathyroid hormone (pg/ml)	2121±107
Radiological signs n (%)	
Subperiosteal bone resorption	9(64,2%)
Thinning of the cortical	12(85,7%)
Diffuse demineralization	14(100%)
Bone defects	8(57,1%)
Soft tissu calcifications	6(42,8%)
Ultrasound parameters n (%)	
Diffuse hyperplasia	4 (28,5%)
One or several nodules	6 (42,8%)
Normal	4 (28,5%)
Scintigraphic parameters n (%)	
Parathyroid adenoma	5 (35,7%)
Diffuse hyperplasia	2 (14,2%)
Normal	3 (21,4%)

The indication for parathyroidectomy was necessary before resistance to medical treatment, to achieve the targets of the KDIGO guidelines for calcium, phosphorus and the PTH1-84 in 10 patients and the persistence of clinical signs of hyperparathyroidism in 4 patients (bone pain in 3 cases; pathological fractures in one patient).

The surgery is programmed for all patients was subtotal parathyroidectomy of 7/8. Surgical exploration noted the presence of four cervical parathyroid glands in all patients. Histological study of these glands revealed diffuse hyperplasia without signs of malignancy in 8 cases. Six patients had nodular hyperplasia of the parathyroid glands. In the immediate postoperative period, clinical symptomatology was dominated by cramps in 3 patients, and no seizures or tetany were noticed among the patients. Biologically, the mean values of serum calcium, phosphorus and parathyroid hormone were respectively  $65 \pm 9$  mg / l (54-93 mg / l),  $38 \pm 10$  mg / l (13-45 mg / l), and  $105 \pm 12$  pg / ml (34-456 pg / ml). The correction of biological disturbances consisted intake of calcium gluconate intravenously and active compounds vitamin D orally. No local postoperative complications were noticed. At one month of the intervention, the mean serum calcium was  $76 \pm 10$  mg / l (60-92 mg / l). The mean iPTH was  $102 \pm 59$  pg / ml (1.8 to 231 pg / ml). After a year of development, we noticed that pruritus and neuromuscular manifestations has gone in all cases. 4 patients still suffered from bone pain. The mean serum calcium was  $84 \pm 13$  mg / l (66 to 100 mg / l). The average iPTH was  $445 \pm 102$  pg / ml (22-1788 pg / ml). The treatment consisted in most

cases of calcium carbonate and vitamin D orally, with regular monitoring of serum phosphorus, calcium, parathyroid hormone, and total alkaline phosphatase. The table 2 summarizes the changes in serum calcium, phosphate and parathyroid hormone in the immediate postoperative period, at 1 month, 6 months and 1 year of surgery.

**Table 2: the changes in serum calcium, phosphate and parathyroid hormone in the immediate postoperative period, at 1 month, 6 months and 1 year of surgery.**

	immediate postoperative period n (%)	at 1 months n (%)	at 6 months n (%)	at 1 year n (%)
Serum calcium $\leq 75$ mg/l	2(14,2%)	4(28,5%)	5(35,7%)	3(21,4%)
75 mg/l < Serum calcium $\leq 80$ mg/l	4(28,5%)	6(42,8%)	5(35,7%)	4(28,5%)
Normal serum calcium	8(57,1%)	4(28,5%)	4(28,5%)	7(50%)
Serum phosphorus $\leq 15$ mg/l	1(7,1%)	5(35,7%)	3(21,4%)	2(14,2%)
15 mg/l < Serum phosphorus $\leq 35$ mg/l	3(21,4%)	4(28,5%)	4(28,5%)	3(21,4%)
Normal serum phosphorus	10(71,4%)	5(35,7%)	7(50%)	9(64,2%)
PTH $\leq 150$ pg/ml	6(42,8%)	6(42,8%)	5(35,7%)	4(28,5%)
150 < PTH < 300	7(50%)	6(42,8%)	7(50%)	8(57,1%)
PTH $\geq 300$	1(7,1%)	2(14,2%)	2(14,2%)	2(14,2%)

## Discussion

The HPT is a common complication of chronic renal failure. It is characterized by excessive synthesis and secretion of parathyroid hormone, parathyroid hyperplasia and abnormal calcium and phosphate metabolism with bone and visceral impact [7,8]. Treatment of SHPT should be primarily preventive by dietary restriction of phosphates, phosphate binders, vitamin D native and active derivatives of vitamin D [9, 10]. Surgical treatment of hyperparathyroidism should be discussed when medical treatment cannot control serum calcium, serum phosphorus and iPTH in recommended targets [11].

The parathyroidectomy should be recommended in patients with severe HPT ( $> 500$  pg / ml) associated with hyperphosphataemia ( $> 60$  mg / l) and / or hypercalcemia ( $> 100$ mg / l) that are refractory to medical treatment, bone pain, pathological fractures, anaemia resistant to erythropoietin, calciphylaxis[6]. In our study, patients had the usual indications for surgical treatment, the resistance to medical treatment, to achieve the targets of the KDIGO guidelines for calcium, phosphorus and the PTH1-84 in 10 patients and the persistence of clinical signs of hyperparathyroidism in 4 patients (bone pain in 3 cases; pathological fractures in one patient).

Parathyroidectomy is necessary among 1-2% of dialysis patients each year [12]. More recent studies have shown that the incidence of parathyroidectomy remained stable in recent years [13,14]. The effect of parathyroidectomy increased from 0.3% if the duration of dialysis is less than five years to 3% if the duration is more than ten years [15]. In our study, all the patients have a duration of dialysis that is over 6 years. The average age was 47 years. Our results were similar to the results

found in medical literature. Indeed, the average age of patients treated surgically for HPT series varies between 40 and 50 years [16,17].

Hyperparathyroidism is now frequently detecting on laboratory tests. Preoperative localization of lesions by imaging is required. Among the available techniques, sonography and scintigraphy dominate. The benefits of morphological explorations before parathyroidectomy is questionable since all the glands should be explored by the surgeon. Ultrasound gives an precise anatomical image, but can not view some ectopic adenomas. Parathyroid scintigraphy has improved the efficiency of parathyroidectomy especially in detecting ectopic glands that may be responsible for immediate or delayed failures of the surgery [18,19]. . In our study cervical ultrasound was abnormal in 70.5%. This is consistent with results in the literature, in fact from Tominaga et al, abnormal parathyroid glands in the neck ultrasound is detected between 66 and 75% [10]. Scintigraphy was performed in 10 patients, revealing a diffuse hyperplasia in 2 cases (14,2%), one or several nodules in 5 patients (35,7%). The choice of subtotal parathyroidectomy was done in consultation with surgeons. The results of this technique are the decrease of the secretion of iPTH, hypercalcemia, hyperphosphatemia and bone disease. In our study, the persistent hypersecretion of parathyroid hormone was noted in two cases (14.28%) which is a close rate from those reported in the literature [20]. A parathyroid scintigraphy was performed secondary in the first case and noted an ectopic nodule; then further surgery was indicated with good clinical and laboratory results. The second surgical failure was controlled by medical treatment. However, this surgery has numerous complications including:

- Hypocalcemia: important immediate complication, secondary to sudden hypo secretion of the parathyroid hormone that is induced by the reduction of parathyroid tissue, in a context where the skeleton, was used to HPT in a long time becomes very eager to calcium. In our series, 42.8% of patients had postoperative hypocalcemia corrected by calcium intake and vitamin D derivatives. We noted a profound hypocalcemia in 2 cases, moderate in 4 patients.
- laryngeal nerve paralysis: The parathyroid and thyroid surgery is typically associated with a risk of laryngeal nerve lesions of the order of 1% [21]. In our study, there was no case of laryngeal paralysis;
- Other complications: the compressive cervical hematomas, infections and postoperative abscess is seen in some studies in 5-8% of cases. In ours, we did not notice any of these postoperative complications.

In addition, there is also a risk of permanent postoperative hypoparathyroidism after the reduction parenchyma or parathyroid reoperations [22]. In our study, 4 cases of hypoparathyroidism is reported after a year of surgery. Postoperative mortality due to surgery remains low, ranging from 0-7% according to some important studies [23]. In our series, no specific surgery deaths have been reported.

Currently, the advent of new therapies will probably make the parathyroidectomy an exception indication in the treatment of SHPT [24,25]. In our study, parathyroidectomy seems an effective and economically way to treat severe SHPT. Indeed, the biological results of our study are comparable to most published studies that were done with cinacalcet [25,26] which does not seem a priority in Morocco. Benefits to a long-term treatment remains to show on criteria of morbidity and mortality and comparing conventional therapies to the parathyroidectomy especially in refractory SHPT. Meanwhile, the high cost of cinacalcet is the reason why it's prescription comes in second-line, as recommended in the recent Kidney Disease Improving Global Outcomes (KDIGO) [5].

## CONCLUSION

Surgical parathyroidectomy is an effective treatment to slow the hypersecretion of PTH with good clinical, biological and radiological results. However, the realization of this technique must be careful with bilateral exploration that allows an accurate assessment of the four glands to prevent any persistent or recurrent hyperparathyroidism. Despite these good results, the early treatment of phosphocalcic anomalies in patients with chronic renal failure is necessary. And the use of new drugs such as calcimimetics and the development of renal transplantation, would reduce the prevalence of parathyroidectomy.

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