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Parathyroidectomy in chronic kidney disease: effects on weight gain and on quality of life improvement

Paratireoidectomia na doença renal crônica: efeitos no ganho de peso e na melhora da qualidade de vida

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ABSTRACT

Objective: *to evaluate the benefit of parathyroidectomy in patients on hemodialysis, regarding nutritional and biochemical statuses, body composition and the health-related quality of life.* **Methods:** *this is a longitudinal study involving 28 hemodialysis adult patients with severe secondary hyperparathyroidism evaluated before and one year after surgery. Inclusion criteria: parathyroid hormone levels exceeding ten times the upper normal range and end-stage renal disease in hemodialysis program. We used the body mass index to classify the nutritional status and the biodynamics analyzer to evaluate the body composition. Biochemical analysis included markers of lipid and bone metabolism. We assessed quality of life with the SF36 (Short Form Health Survey) questionnaire. All individuals underwent total parathyroidectomy with a forearm implant.* **Results:** *there were significant gains in body weight (61.7 vs 66.0 kg, p<0.001), body cell mass (22.0 vs 24.5 kg/m², p=0.05) and quality of life (p=0.001) after surgery. With respect to bone metabolism, intact PTH, calcium, phosphorus and alkaline phosphatase all stabilized and there were improvements in biochemical parameters such as albumin and hemoglobin.* **Conclusion:** *parathyroidectomy improves hemodialysis patient survival and is associated with weight and bone cell mass gain and improvement in health-related quality of life.*

Keywords: *Parathyroidectomy. Kidney Failure, Chronic. Survival. Quality of Life. Nutrition Assessment.*

INTRODUCTION

Chronic kidney disease (CKD) has gained importance worldwide, since the morbidity profile of chronic noncommunicable diseases has changed. With the change, challenges have come due to its economic and social implications[1]. CKD is characterized by the presence of renal morphofunctional changes for a minimum period of three months, whose severity varies with the reduction of renal function, and may lead to death if left untreated[2]. Substitutive therapies such as hemodialysis, peritoneal dialysis and renal transplantation become essential when loss of renal function is incompatible with life. Several basic diseases, whose prevalence is increasing each year, can lead to CKD, among them obesity, diabetes mellitus, systemic arterial hypertension and glomerulonephritis[3,4].

Reduced renal function leads to several adaptive changes involving serum levels of calcium, phosphorus, and regulatory hormones, such as parathyroid hormone (PTH) and 1,25-hydroxy-vitamin D[1]. Metabolic changes due to renal failure result not only in bone mineral disease with its effects on the skeleton generating pain, deformities and incapacity due to changes in remodeling and errors in bone mineralization, but they are associated with high mortality mainly due to cardiovascular disease[5-7]. Regarding bone mineral disease, secondary hyperparathyroidism (HPT) is characterized by elevated levels of PTH, usually greater than 800 pg/mL, associated with bone lesions, increased resting energy expenditure (REE) and worsening of quality of life[2,7]. Increased REE leads to weight loss and decreases survival. However, overweight and/or obesity, heavily studied as a risk factor for cardiovascular disease[3] and decreased survival, may be a protective factor in this case[8].

The worsening of quality of life is due to all these factors, and for its evaluation, we use the Short Form Health Survey 36 (SF-36), a questionnaire that evaluates eight physical and mental domains[9]. When quality of life becomes much compromised, the deformities are important and the bone pain intractable, surgery becomes the best option. In

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general, total parathyroidectomy with a forearm implant has been an excellent therapeutic option, reversing these negative factors[10].

The objective of this study was to evaluate the benefit of parathyroidectomy (PTx) on quality of life, body weight, biochemical and metabolic parameters in dialytic chronic renal disease.

METHODS

We carried out a longitudinal study involving 28 adults with CKD who underwent a three-times-weekly hemodialysis program with severe HPT and uncontrolled PTH levels (>1000 pg/mL), and fulfilled the criteria for parathyroidectomy (PTx). All were evaluated before surgery, when they signed an informed consent, and one year after surgery, between the years of 2010-2012, at the Pedro Ernesto University Hospital, UERJ.

Inclusion criteria were serum PTH levels equal to or greater than ten times the upper normality limit, inability to respond to oral medications and one or more of the following: persistent hypercalcemia despite interruption of calcium and calcitriol or after kidney transplantation; Calcium-phosphorus product >70mg/dL; bone pain that did not respond to oral treatment; pathological fractures; bone deformities; ectopic calcification; disabling arthritis or periarthritis; tendon rupture; intractable pruritus; or presence of brown tumor[11].

We excluded subjects with previous hospitalization within three months before the start of this study, with active inflammatory disease or infection, and in use of steroid and/or immunosuppressive agents.

The evaluation before and one year after surgery included anthropometry, body composition analysis by electrical bioimpedance (BIA), biochemical parameters and quality of life by the SF 36. The study was approved by the Ethics in Research Committee of the Pedro Ernesto University Hospital, under the number 2551-030.

Anthropometry

We measured weight and height for evaluation of the body mass index (BMI), using the classification of nutritional status proposed by the World Health Organization (WHO)[3], based on BMI = Kg/m2, namely: underweight <18.5 kg/m$^{2;}$ Eutrophy 18.5 to 24.9 kg/m^2; Overweight 25 to 29.9 kg/m^2; Obesity ≥30 kg/m^2. The evaluation was performed after the hemodialysis session, with the patients wearing light clothes and without shoes.

Analysis of Body Composition by Electric Bioimpedance (BIA)[12]

We used a Biodynamics 310E, version 4.0 analyzer. We placed the electrodes in the standard position, on the side not accessible for hemodialysis. We analyzed: lean mass (LM), fat mass (FM), phase angle (PA) and body cell mass (BCM). Cell mass included evaluation of muscle (60%) and organs (20%), as well as cells and tissues. The loss of BCM is a strong marker of mortality[13]. We performed the examination the day after the hemodialysis session.

Biochemical parameters

We collected blood samples after 12 hours of fasting for the analysis of triglycerides, total cholesterol and HDL-cholesterol by automated methods using commercial kits. The LDL-cholesterol level was calculated by the Friedewald's[14]. The following were considered as altered: triglycerides above 150mg/dL; HDL-cholesterol below 40mg/dL for men and below 50mg/dL for women; LDL-cholesterol greater than 130mg/dL and total cholesterol greater than 200mg/dL.

For the analysis of bone metabolism, we used the colorimetric method to study total alkaline phosphatase, calcium and phosphorus, and the chemo-luminescence to assess intact PTH (iPTH). We considered normal intervals, respectively: 50-250 U/L, 8.6-10.0 mg/dL, 2.5-4.8 mg/dL and 10-65 pg/ml.

For evaluation of nutritional status, we used the colorimetric method to measure hemoglobin and albumin. Levels below 3.5g/dL for albumin and below 12.8g/L for men and 11.3g/L for women for hemoglobin were markers of poor nutritional status.

Assessment of Quality of Life

We evaluated quality of life with a validated Brazilian version of the SF-36, which measures eight health domains related to quality of life (QOL)[15].

We compared the QOL at the time of the study with the QOL one year before the evaluation. The calculation procedures of the scores followed the recommendations of the SF-36 developers. Each component was analyzed individually as the average of a predefined sum of questions, ranging from 0 to 3 or from 0 to 5, depending on the number of possible answers. Each response was linearly transformed to 0 to 100, the higher scores indicating better QOL.

The eight domains of the SF-36 are: functional capacity (ten items), physical aspects (four items), pain (two items), general health status (five items), emotional aspects (three items) and mental health (five items), and two summary measures - PC (physical component) and MC (mental component).

Statistical analysis

We used the Statistical Software for Social Sciences (SPSS) version 20 and the Stata 12 for data analysis. We expressed the frequency distributions of socio-demographic characteristics and anthropometric measurements as percentages (%). We investigated the normality of the variables with the Kolmogorov-Smirnov test. We compared the mean ± standard deviation (SD) of the anthropometric, biochemical, body composition, and quality of life values before and one year after parathyroidectomy using the Student t-test or the Wilcoxon Signed Ranks test. In all cases, we considered p values of less than 0.05 as statistically significant.

RESULTS

The most frequent clinical manifestations were pain, bone high uptake and pruritus. PTx had a positive and significant effect on pruritus reduction (p=0.04), reducing its prevalence from 50% to 22%. The other clinical manifestations also had a significant reduction after surgery. Table 1 shows the baseline characteristics of the 28-people study group.

There was a change in nutritional status after PTx. The prevalence of overweight increased from 31% to 39% (p=0.001) and low weight decreased from 12% to 4% (p=0.343). Surgery did not determine modification in body composition, except for the increase in BCM. Before surgery, the phase angle (PA) varied from 2.9 to 7.1°, BCM= 11.2 to 45.6 kg, LM= 25.9 to 71.7 kg and FM= 1.5 to 42.9 kg. After PTx the variations were as follows: PA= 2.9 to 9.0°, BCM= 12.3 to 50.3 kg, LM= 28.5 to 89.2 kg and FM= 1.5 to 46.0 kg. Table 2 shows the mean ± standard deviation of body composition, SF-36 and biochemical values.

Table 1 - *Baseline Characteristics of the 28 subjects studied: data presented in percentages or mean ± standard deviation.*

Basic Features	Average +-dp or%
Male (%)	39.3
Age (years)	43.7 +-9.9
BMI (Kg/m^2)	23.7 ± 4.8
Time of disease (years)	10.7 +-4.6
Smoking (%)	17.9
Alcoholism (%)	3.6
Non-Caucasian (%)	32.1
Causes of kidney disease (%)	
Systemic hypertension	75.0
Diabetes mellitus	3.7
Glomerulonephritis	7.1
Polycystic Kidney	7.1
Other	7.1
Secondary manifestations of hyperparathyroidism (%)	
Pain	96.4
High bone uptake	78.6
Pruritus	50.0
Bone resorption	32.7
Deformities	32.1
Ectopic calcification	25.0
Calcium/Phosphate ratio > 70	25.0
Arthritis	21.4
Nutritional Status (%)	
Low Weight	3.6
Eutrophic	53.6
Overweight/obese	42.8

BMI= body mass index.

When analyzing only the individuals who gained weight, we observed that this variation was mainly in the fat mass (delta= 37%, p<0.05), a little less intense but present in BCM (16%, p=0, 03), and had no effect on lean mass.

The proportion of subjects with low albumin was 33% before surgery and 26% after surgery. The procedure also significantly reduced the prevalence of anemia. Before, 91% of the patients had reduced hemoglobin and after, only 38% (p=0.02).

Regarding lipid profile, before the surgery, 50% had triglycerides above the reference values, 44% had low HDL-cholesterol levels and more than 20% had elevated total cholesterol. Despite weight gain, the lipid profile did not change significantly after surgery except for the increase in LDL-cholesterol. However, despite this increase, the levels observed both before and after PTx remained within normal values.

Surgery had an important effect in the reduction of bone remodeling and, consequently, in the prevention of future fractures.

Table 2 - *Characteristics of body composition, biochemical parameters and quality of life (SF-36) before and after PTx: mean ± standard deviation.*

General parameters	Pre-PTx	Post-PTx	p
Body Composition (BIA)			
Weight (Kg)	61.7 +-18.5	66.0 ± 20.3	< 0.001
BMI (Kg/m^2)	23.7 ± 4.8	+ 25.1-5.8	< 0.001
LM (Kg)	46.8 +-2.3	47.2 +-2.9	ns
FM (Kg)	16.8 ± 1.9	19.7 +-1.7	ns
BCM (Kg)	22.0 +-7.4	24.5 +-9.1	0.05
PA (degree)	5.4 +-0.5	6.2 +-0.6	ns
Biochemical Parameters			
Intact PTH (pg/ml)	2290.7 +-734.5	215.5 +-90.8	0.000
Calcium (mg/dl)	10.0 +-1.3	8.19 +-1.1	0.000
Phosphorus (mg/dl)	5.6 +-1.5	3.83 +/-1.2	0.000
Alkaline phosphatase (U/l)	1548.1 +-1257.4	362.35 +-128.5	0.000
Albumin (g/dL)	6.7 +-0.9	7.3 +-0.9	0.06
Hematocrit (%)	32.5 +-5.3	36.8 +-1.5	0.05
Hemoglobin (g%)	10.7 +-1.7	12.1 +-2.2	0.02
Total cholesterol (mg/dL)	160.1 +-41.9	166.0 +-40.6	NS
HDL-cholesterol (mg/dL)	44.1 +-13.2	42.3 +-13.7	NS
LDL-cholesterol (mg/dL)	65.3 +-14.1	91.8 +-11.5	0.004
Triglycerides (mg/dL)	166.8 +-83	174.2 +-25.9	NS
SF-36			
Functional capacity	19.3 +-22.1	53.0 +-30.7	0.001
Physical aspects	12.5 +-29.3	52.7 +-43.7	0.001
Pain	29.3 +-23.2	+ 70.2-27.1	0.001
General health	43.8 +-19.3	61.1 +-21.6	0.001
Vitality	45.7 +-41.9	+ 58.9-18.9	0.001
Social aspects	53.8 +-18.7	75.9 +-24.3	0.001
Emotional aspects	15.5 +-33.3	72.6 +-41.6	0.001
Mental health	53.8 +-18.7	+ 60.6-19.7	0.259

BMI= body mass index; LM= lean body mass; FM= fat mass; BCM= body cell mass; PA= the Phase angle.

There was also a positive effect of surgery on QOL. Both the functional capacity and the emotional, vitality and pain aspects, which were important pre-PTx complaints, had a significant reduction, contributing to the improvement of quality of life and satisfaction with the surgical procedure.

DISCUSSION

The most relevant results of surgery in this study were: a) improvement of nutritional status, b) weight gain, and c) improvement in quality of life. The data are in accordance with a recent study showing the importance of parathyroid resection in CKD patients with advanced disease[17].

In large population studies, overweight, low body cell mass and phase angle have shown to increase morbidity and mortality[18,19]. However, in patients with end-stage renal disease, an "obesity paradox" has been consistently reported: High BMI is associated with lower all-cause mortality[19]. The present study showed a gain after PTx, predominantly a change in fat mass. The explanation for this effect would be related to a reduction of PTH[20] associated with a more liberal diet and better quality of life.

Still in relation to body composition, this study showed a BCM increase after PTx that could be explained by some factors already described: 1) Reduction of serum phosphate: phosphate has a toxic cellular effect, reducing the lean and total body masses[21]; 2) Reduction of bone pain: Pain can reduce mobility and contribute to the reduction of BCM, resulting in lower survival; 3) Increased food intake: the improvement in the general state of health favors a higher food intake, with a gain of fat mass, but also with a higher protein intake[22].

Although some patients had their albumin levels increased after surgery, this difference did not have statistical robustness, probably due to the small number of individuals studied. We can infer from this observation that even patients with more adequate levels of postoperative serum albumin require a proper nutritional follow-up, since hypoalbuminemia is associated with higher morbidity and mortality in chronic kidney disease[23].

Surgery had a positive effect on hemoglobin levels. Anemia in CKD is difficult to manage, especially when associated with hyperparathyroidism. The reduction of iPTH and phosphate levels, combined with an improvement in the Ca:P ratio, contribute to the control of anemia and may be associated with a reduction in bone marrow fibrosis and systemic inflammation.

The evaluation of lipids in the pre-dialysis serum may underestimate the true lipemic levels, since before the hemodialysis (HD) sessions the individuals have greater weight (due to a greater amount of free water), impairing results and hindering therapeutic management[24]. In this study, we did not identify pre-PTx elevated lipids and justified the increase in LDL-cholesterol after surgery by other factors, other than nutritional or metabolic, such as oxidative stress, inflammation and possible endothelial dysfunction, as described by Nitta[25]. According to that author, LDL-cholesterol cannot be used as a good marker of cardiovascular risk in CKD.

The poor quality of life was evident before surgery, not directly related to the duration of the disease, as demonstrated[26,27]. However, the procedure had an important beneficial effect, which can be explained by the reduction of the toxic effects of PTH, causing multiple organ damage and exuberant symptomatology[28]. These improvements validate the indication of parathyroidectomy as early as possible in CKD[29,30].

The present study has some limitations that include the low number of participants, due to the financial difficulties of a public hospital, and the lack of information about the body weight gain after PTx. However, it demonstrates the importance of surgery being performed as early as possible, considering all the presented advantages, and that there is concern about the excessive gain of body weight, which can become a predictor of greater cardiovascular risk in end-stage renal disease.

We conclude that parathyroidectomy with forearm implantation (PTx), performed in patients with end-stage renal disease in hemodialysis regimen and with severe hyperparathyroidism, is associated with weight gain, increased body cell mass and improved quality of life.

R E S U M O

Objetivo: avaliar o benefício de paratireoidectomia em pacientes submetidos à hemodiálise, em relação ao estado nutricional e bioquímico, composição corporal e a qualidade de vida. **Métodos:** estudo longitudinal envolvendo 28 adultos em programa de hemodiálise, com hiperparatireoidismo secundário grave, avaliados antes e um ano após a cirurgia. Critérios de inclusão: níveis de paratormônio dez vezes superior ao valor de referencia e doença renal crônica em programa de hemodiálise. O índice de massa corporal foi utilizado para classificação do estado nutricional. A bioimpedância elétrica para avaliação da composição corporal. A análise bioquímica incluiu dosagem de lipídios e marcadores do metabolismo ósseo. A qualidade de vida foi avaliada pelo questionário SF36 (Short Form Health Survey). Todos os pacientes foram submetidos à paratireoidectomia total com implante em antebraço. **Resultados**: houve ganho significativo de peso corporal (61,7 vs 66,0 kg; p<0,001), da massa celular corporal (22,0 vs 24,5 kg/m^2; p=0,05) e da qualidade de vida (p=0,001) após a cirurgia. Com relação ao metabolismo ósseo, PTH intacto, cálcio, fósforo e fosfatase alcalina, se estabilizaram e houve melhora em parâmetros bioquímicos, tais como albumina e hemoglobina. **Conclusão:** a paratireoidectomia melhora a sobrevida em pacientes de hemodiálise e está associada a aumento de peso, ganho de massa óssea e melhoria na qualidade de vida.

Descritores: Paratireoidectomia. Insuficiência Renal Crônica. Sobrevida. Qualidade de Vida. Avaliação Nutricional.

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