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EFFECT OF TOTAL PARATHYROIDECTOMY WITHOUT AUTOIMPLANTATION ON PARATHYROID HORMONE LEVEL IN HEMODIALYSIS PATIENTS WITH SECONDARY HYPERPARATHYROIDISM

By

Ezzat Abdel-Rahman Eletreby, Waleed Ahmed Massoud and Hany Abd EL-Ghany Mohamed

Department of Internal Medicine, Al-Azhar Faculty of Medicine

ABSTRACT

Background: Secondary hyperparathyroidism is a major problem in chronic kidney disease patients, resulting in skeletal complications including enhanced osteoclast activity with accelerated bone turnover and osteitis fibrosa cystica.

Objective: Studying the effect of total parathyroidectomy without autoimplantation on PTH level, and state of parathormone activity in hemodialysis patients.

Patients and Methods: Thirty four hemodialysis patients with secondary hyperparathyroidism were subjected for follow up as regard calcium, phosphorus, parathormone (PTH) level, post total parathyroidectomy without auto implantation between July 2013 and December 2015 after failure of medical treatment.

Results: The studied patients had a mean age of 52.3 ±5.6 years. They were 15 males (44.1 %) and 19 females (55.8%). Mean of hemodialysis duration was 12.4 ±3.8 years.There was a significant decline of the postoperative parathyroid hormone levels when compared with their preoperative assessments. After 6 months 67.6 % had PTH levels of 3-8 folds more than upper normal of assay, while 5.9% had PTH level below 100 pg-ml, and 26.5 % have PTH level more than 8 folds the upper normal of assay,and symptoms of recurrent hyperparathyroidism.

Conclusion: Total parathyroidectomy without autoimplantation was associated with a low rate of hypoparathyroism in hemodialysis patients.

Keywords: Parathyroidectomy, hyperparathyroidism, hemodialysis.

INTRODUCTION

Secondary hyperparathyroidism is a major problem in chronic kidney disease patients resulting in skeletal complications including enhanced osteoclast activity with accelerated bone turnover and osteitis fibrosa cystica ***(Bureo et al., 2015).***

Medical treatment of secondary hyperparathyroidism consists of active vitamin D2, D3 analogues as alfa calcidol and calcitriol. This treatment is limited by hypercalcemia and aggravation of hyperphosphatemia ***(Rodriguez and Rodriguez-Ortiz, 2015).***

Surgical treatment is reserved for patients whose PTH values persist above

800 pg/ ml with hyperphosphatemia and hypercalcemia despite medical treatment. Three surgical approaches for parathyroidectomy have been reported,i.e. subtotal parathyroidectomy, total parathyroidectomy with auto implantation of parathyroid tissue into the forearm musculature and total parathyroidectomy without auto implantation ***(Lorenz et al., 2015).***

Subtotal or total parathyroidectomy with autoimplantation are done but both are associated with a high recurrence rate.The third surgical strategy is total parathyroidectomy without autoimplantation. Most centers perform either subtotal or total parathyroidectomy with autoimplantation to avoid a possible hypoparathyroidism and the need for calcium and vitamin D supplementation. Recurrence of hyperparathyroidism varies from 5 to 80% in different studies for the first two surgical approaches ***(Schneider and Bartsch, 2015).***

The present work aimed to study the effect of total parathyroidectomy without autoimplantation on parathyroid hormone level in hemodialysis patients with secondary hyperparathyroidism.

PATIENTS AND METHODS

The study included 34 patients who were subjected to total parathyroidectomy after consents from the patients.

Inclusion criteria: All hemodialysis patients with secondary hyperparathyroidism above 800 pg / ml after failure of medical treatment for at least 6 months. The duration of dialysis for 18 patients were subjected to the study was 7 years, and 16 patients stayed on dialysis for 9 years. The medical treatment given consisted of alphacalcidole 3 microgm (3 times per week), and calcium based phosphorus binder in form of calcium acetate (700 mg tablet 3 tablets with each meal for 6 months).

Failure of medical treatment was denoted by occurrence of hypercalcemia, increased calcium phosphorus product and failure of PTH levels to decrease after this treatment.

Stastistical analysis: Data obtained from the present study were computed using SPSS versions 17 under the platform of Microsoft Windows 7. Continuous data were expressed in the form of mean ± SD, while categorical data were expressed in the form of count and percent. Tests used were ANOVA, Mann Whitney U test, and using post hoc test with ANOVA test for comparison between groups of data. P value less than 0.05 was considered statistically significant.

RESULTS

After 6 months of follow up, calcium level was much lower than preoperative calcium (Ca) level (9.2 ± 0.1 vs 7.8 ± 0.8 after 3 months and 8.5 ± 0.7 after 6 months respectively (Fig.1) and serum phosphorus (P) level was much lower level than preoperative serum phosphorus level (7.3 ± 1.8 vs 4.5 ± 1.0 after 3 months,and 4.7 ± 1.0 at 6 months respectively Fig. 1).

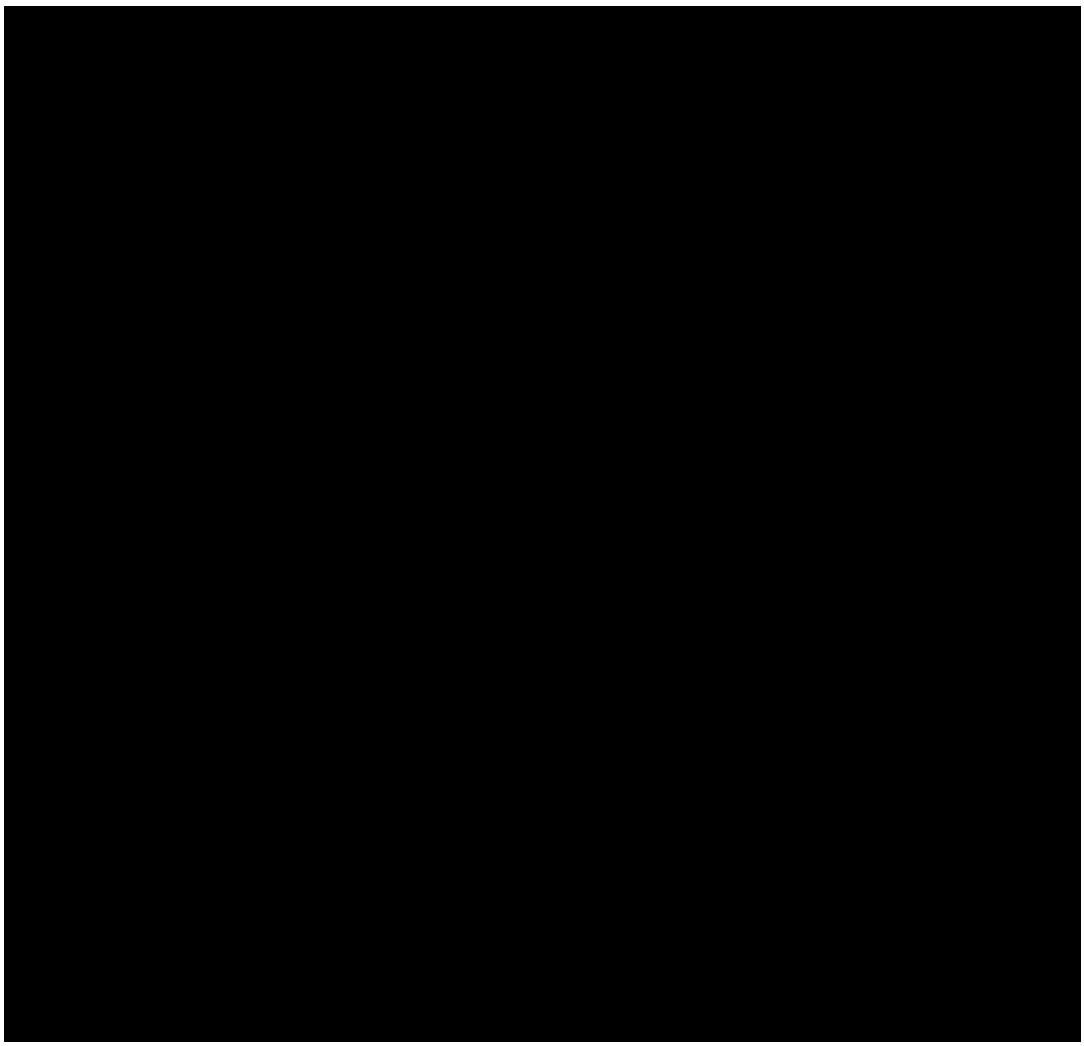

Figure (1): Mean ±SD of Ca and P levels in the studied patients (mg/dl).

Table (1): Mean and SD of Ca, P levels, Ca x P and ALP.

Parameters / **Duration**	**Ca levels (mg/dl)**	**P levels (mg/dl)**	**Ca × P (mg/dl)**	**Repeated Measures ANOVA (P-value)**
Preoperative	9.2±0.1	7.3±1.8	67.5±19.6	**0.0001**
3 months postoperatively	7.8±0.8	4.5±1.0	35.0 ± 7.9	
6 months postoperatively	8.5±0.7	4.7±1.0	40.3±10.2	

After 6 months follow up calcium level was much lower than preoperative level 5.8 ± 0.7 and 9.2 ± 0.1 respectively (Fig. 1 and Table 1).

After 6 months follow up serum phosphorus level was much lower level than preoperative serum phosphorus level (7.3 ± 1.8 vs 4.5 ± 1.0 at 3 months and 4.7 ± 1.0 at 6 months) (Fig. 1and Table 1).

The calcium × phosphorus (Ca × P) product at 6 months follow up revealed a significant decline in comparison of the preoperative assessments (67.5 ± 19.6 vs 35.0 ± 7.9 at 3 months and 40.3 ± 10.2 at 6 months (Table 1).

There was a significant decline of the postoperative Alkaline phosphatase (ALP) levels when compared with their preoperative assessments (554.8 ± 242.3 vs 346.4 ± 123.5 at 3 months and 241.0 ± 72.8 at 6 months respectively - Table 2).

There was a significant decline of the postoperative parathyroid hormone (PTH) levels when compared with their preoperative assessments (1195.5 ± 469.4 vs 130.9 ± 70.9 respectively, Table 3).

Table (2): Mean ± SD of ALP levels in the studied patients (u/L).

Parameters / Duration	ALP	Repeated Measures ANOVA (P-value)
Preoperative	554.8 ± 242.3	**0.0001**
3 months postoperatively	346.4 ± 123.5	
6 months postoperatively	241.0 ± 72.8	

Table (3): Mean ± SD of PTH levels in the studied patients (pg-ml).

Parameters / Duration		PTH	Mann Whitney U Test P-value
Preoperative	**Range**	3.0 – 2850	**0.0001**
	Mean ± SD	1195.5 ± 469.4	
6 months postoperatively	**Range**	3.0 – 500.0	
	Mean ± SD	130.9 ± 70.9	

After 6 months postoperative follow up, 23 patients (67.6 %) had PTH levels up to 3-8 fold the normal value, while 2 patients (5.8 %) had hypoparathyroidism less than 100 pg/ml and 9 patients (26.47 %) had recurrent hyperparathyroidism PTH level more than 8 fold of upper normal value (Table 4). The explanation for occurrence of recurrent hyperparathyroidism is the presence of super-numerary parathyhroid glands which range from 2.5 to 30% ***(Schneider et al.,***

2011), these glands subjected for uremic stimulation and so secondary hyperparathyroidism in spite of doing total parathyroidectomy without autoimplantation.

Table (4): Postoperative PTH outcome.

Patients / parameters	No patients	% of patients	PTH Level Pg/ml
3-8 fold upper normal levels	23	67.6	195-520
Hypoparathyroidism	2	5.9	Less than 100
Recurrent hyperparathyroidism	9	26.5	More than 520

DISCUSSION

The relationship between chronic renal insufficiency and secondary hyperparathyroidism is well established ***(Pitt et al., 2009).***

Parathyroidectomy to treat secondary hyperparathyroidism is indicated in 15%-38% of chronic renal failure patients over 10-20 years, and has been shown to improve survival for dialysis-dependent patients as well as symptomatology and quality of life ***(Schneider et al., 2012).***

Hypoparathyroidism after total parathyroidectomy seems to be rare. in the literature,the presence of supernumerary and ectopic parathyroid glands is quite variable ranging from 2.5 to 30% ***(Schneider et al., 2011).***

The present study aimed to determine the influence of total parathyroidectomy without autotransplantation on the state of parathyroid activity in patients with chronic renal failure under maintenance hemodialysis.

Comparison between preoperative and follow up calcium levels showed a significant decline of the postoperative calcium levels at 6 months when compared with their preoperative assessments. These findings were in agreement with the study of ***Puccini et al. (2010)*** who reported clinical and laboratory long-term follow-up for total parathyroidectomy without autotransplantation for the treatment of secondary hyperparathyroidism associated with chronic kidney disease. The study found significant reduction in Ca, P and ALP levels in the studied patients in the follow up period when compared with controls.

Our study also found a statistically significant differences between preoperative and postoperative PTH levels in the studied patients. There was a complete improvement of the reported symptoms

including bone pain, fatigue and pruritis after performing the operation.

After 6 months postoperative follow up, 67.6 % had the recommended PTH levels 3-8 folds more than upper level of assay, while 5.9 % had PTH level below 100 pg/ml, and 26.5 % had PTH level more than 8 folds of normal assay. These data seemed better than the study of ***Coulston et al. (2010).*** In this study high percentage 28.7% had PTH level below 100pg/ml while in our study, only 5.9% had PTH level less than 100pg/ml.

In our study 26.5% of patients had recurrent hyperparathyroidism. This finding was in agreement with the study of **Thomas and Jacob** (**2016).** In this study, 20% of the patients demonstrated persistent hyperparathyroidism.

CONCLUSION

There was a low rate of hypoparathyroidism and recurrent hyperparathyroidism with total parathyroideetomy without autoimplantation. Total parathyroidectomy without autoimplantation was associated with low rate of hypoparathyroidism and recurrent hyperparathyroidism so it is a better option than the other two surgical modalities.

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تأثير الإستئصال الكلي للغدة جار الدرقية على مستوى هرمون الغدة في مرضى الغسيل الدموي المنتظم الذين يعانون من نشاط ثانوي للغدة الجاردرقية

عزت عبد الرحمن الإتربي – وليد أحمد مسعود – هاني عبد الغني محمد

قسم الأمراض الباطنة- كلية طب الأزهر

خلفية البحث: يحدث إرتفاع في وظائف الغدة الجاردرقية نتيجة للفشل الكلوي المزمن، وينتج عن هذا الإرتفاع مشاكل في عظام المرضى مثل زيادة نشاط الخلايا ناقضة العظام، و إلتهاب العظام الليفي الكيسي .

الهدف من البحث: دراسة تأثير الإستئصال الكلي للغدة جار الدرقية (مع عدم زرع أي فص منها بذراع المريض) على مستوى هرمون جاردرقية ، وبالتالي نشاط الغدة الجاردرقية.

المرضي وطرق البحث: تم متابعة أربعة وثلاثين مريضاً لديهم نشاط ثانوي للغدة الجاردرقية بعد إجراء إستئصال كلي للغدة وذلك للمعايير الآتية:

١. مستوى الفوسفور بالدم.
٢. مستوى الكالسيوم بالدم.
٣. حاصل ضرب الكالسيوم والفوسفور بالدم.
٤. مستوى الغدة الجاردرقية بالدم.

وذلك في الفترة من يوليو ٢٠١٣ وحتى ديسمبر ٢٠١٥م.

وتم اللجوء للحل الجراحي بعد فشل العلاج الدوائي، ومعيار فشل العلاج الدوائي هو إرتفاع مستوى الكالسيوم في الدم عن الحد الطبيعي وزيادة حاصل ضرب الكالسيوم والفوسفور بالدم وعدم نزول مستوى هرمون جار الدرقية بعد هذا العلاج.

النتائج: متوسط عمر المرضى الخاضعين للدراسة هو ٥٢ ± ٥,٦ (سنة) منهم خمسة عشر من الذكور وتسعة عشر من الإناث. ولوحظ بعد متابعة ٦ أشهر ما بعد الجراحة أن ٦٧,٦% من المرضى لديهم مستوى هرمون جار الدرقية يتراوح من ثلاثة إلى ثمانية أضعاف المستوى الطبيعي لذلك الهرمون، بينما ٥,٩% منهم لديهم انخفاض بمستوى الهرمون الجاردرقية أقل من ١٠٠ pg/ml، وان ٢٦،٥% منهم لديهم ارتفاع بمستوى الهرمون أعلى من ثمانية أمثال الطبيعي للهرمون بالدم ،وأيضاً ظهور تكرار أعراض نشاط جارات الدرق .

الإستنتاج : إستئصال الغدة جاردرقية الكلي بدون زرع جزء منها في ذراع المريض مرتبط بمعدلات قليلة من قصور هرمون جاردرقية في مرضي الغسيل الدموي المنتظم.