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Original Article

Evaluation of Parathyroid Hormone Increase After Parathyroidectomy in Primary Hyperparathyroidism

Muhammet Fikri Kündeş, Hasan Fehmi Küçük

Department of General Surgery, University of Health Sciences, Kartal Dr. Lütfi Kırdar Training and Research Hospital, İstanbul, Turkey

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Correspondence: Muhammet Fikri Kündeş, Sağlık Bilimleri Üniversitesi Kartal Dr. Lütfi Kırdar Eğitim ve Araştırma Hastanesi, Genel Cerrahi Kliniği, İstanbul, Turkey
E-mail: fkrkundes@hotmail.com

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ABSTRACT

Objective: In this study, we tried to evaluate retrospectively high levels of parathyroid hormone in patients who received parathyroidectomy due to primary hyperparathyroidism in the light of the literature search.

Methods: In this study, 121 patients who underwent surgery for primary hyperparathyroidism between September 2015 and December 2017 were retrospectively evaluated, according to gender, preoperative calcium and PTH levels, postoperative calcium and PTH levels, diagnosis, histopathological results, type of surgery, follow-up time and recurrence. We excluded patients who were unreachable.

Results: Mean age was 54.83±12.56 (26–82). One hundred three patients were female (85.1%). One hundred nineteen patients were diagnosed (98.4%) as adenoma, whereas two patients were diagnosed as (1.6%) hyperplasia. According to histopathological results, 103 (85.1%) adenoma, four (3.3%) carcinoma, four (3.3%) hyperplasia and 10 (8.2%) adenoma and papillary carcinoma of the thyroid were found. Preoperative mean PTH value was 301.9±470 pg/ml (79-3674 pg/ml). Preoperative mean calcium level was 10.10 mg/dl (10.10 - 13.07 mg/dl). Postoperative mean PTH value was 77.2±11.1 pg/ml (6.0- 907 pg/ml). Postperative mean calcium level was 9.38±0.7 mg/dl (6.3- 11.4 mg/dl). Mean value was 9.38±0.7 mg/dl. Mean follow-up time was 18.75±5.4 (8–28) months. Post-operative PTH elevation persisted in 17 (14.8%) patients. Nine (7.4%) of them had chronic kidney failure, three (2.4%) patients suffered from vitamin D deficiency, and five (4.1%) cases had a recurrence.

Conclusion: Primary hyperparathyroidism is a rare disease. In the absence of postoperative PTH decrease and normocalcemic PTH elevation should be considered as well as recurrence. Renal diseases, bone hunger and Vitamin D deficiency should be evaluated.

INTRODUCTION

Primary hyperparathyroidism is a general endocrine disease with prevalence of 0.3%.[1] Major causes remain as follows: adenoma (80–85%), hyperplasia (15–20%) and carcinoma (1%).[2] In hyperparathyroidism, ionized serum calcium (Ca) level is high and parathyroid hormone (PTH) level is reported to be high 80–90%.[3–5] Laboratory data (high PTH, high Ca, low phosphate) and radiological findings (Ultrasound, Sestamibi scintigraphy) help diagnose primary hyperparathyroidism and localize the pathological gland. In atypical conditions that are difficult to diagnose, 24 hours calcium levels in the urine sample and bone mineral dancytometrie are evaluated.[6] More attention should be required for the management of patients with asymptomatic normocalcemic or moderate hypercalcemic primary hyperparathyroidism.[7]

In our study, we investigated patients who underwent parathyroidectomy for primary hyperparathyroidism in our clinic and whose PTH levels did not improve postoperatively and the possible causes. We retrospectively eva luated high parathyroid hormone levels and evaluated the results concerning vitamin D deficiency, renal function and recurrence in the light of literature.

MATERIALS AND METHODS

In this study, 121 patients who underwent surgery for primary hyperparathyroidism between September 2015 and

December 2017 were retrospectively evaluated, according to gender, preoperative calcium and PTH levels, postoperative calcium and PTH levels, diagnosis, histopathological results, type of surgery, follow-up time and recurrence. PTH, Ca, phosphate, and alkaline phosphatase levels were measured in the diagnosis of patients. 24-hour urine calcium level was investigated in atypical cases. Ultrasound and sestamibi scintigraphy were used as imaging methods. Computed tomography was performed if necessary.

The diagnosis of patients was made in the endocrine and metabolic polyclinic. The patients who were decided to operate by the council were operated. Each patient underwent standard surgical therapy under general anesthasia. PTH and Ca levels were measured on the preop and postop first day and postop 1, 3, 6 months (normal value for calcium was considered as 8.3–10.2 mg/dl, whereas the normal value for PTH was considered as 15–80 pg/ml). PTH was measured using electro-immunoassay.[8] Patients who could not be reached and refused to work were not included in this study. Patients were followed for at least eight months. Mean follow-up time was 18.75±5.4 months. Postoperative elevation in PTH and Ca levels were reevaluated.

RESULTS

In this study, the mean age was 54.83±12.56 (26–82). One hundred three patients were female (85.1%). One hundred nineteen patients were diagnosed (98.4%) as adenoma, whereas two were diagnosed as (1.6%) hyperplasia. According to histopathological results, 103 (85.1%) adenoma, four (3.3%) carcinoma, four (3.3%) hyperplasia and 10 (8.2%) adenoma and papillary carcinoma of the thyroid were found (Table 1). The preoperative minimum PTH level was 79 pg/ml, whereas the maximum level was 3674 pg/ml. Mean value was 301.9±470. Preoperative minimum calcium level was 10.10 mg/dl, whereas the maximum level was 13.07 mg/dl. Mean value was 11.42±0.7. Postoperative minimum PTH level was 6 pg/ml, whereas the maximum level was 907 pg/ml. Mean value was 77.2±111. Postoperative minimum calcium level was 6.3 mg/dl, whereas the maximum level was 11.4 mg/dl. Mean value was 9.38±0.7 mg/dl. Mean follow-up time was 18.75±5.4 (8–28). Postoperative PTH increase continued in 17 (14.8%) patients (Table 2). Nine (7.4%) of them was treated in the nephrology clinic due to renal diseases. Three patients (2.47%) suffered from Vitamin D deficiency. Five (4.1%) cases had a recurrence (Table 3).

Table 1. The outcome of pathology of patients with hiperparatroidizm

Pathology	Patients	
	n	%
Adenoma	103	85.1
Carsinoma	4	3.3
Hyperplasia	4	3.3
Adenoma+thyroid papillary carcinoma	10	8.2
Total	121	100

Table 2. The levels of postoperative parathyroid hormone

Patients n (%)	Levels of postoperative parathyroid hormone
104 (85.9)	Normal
17 (14.1)	High

Table 3. The etiology of high-level parathyroid hormone

Patients number (n=17)	Etiology
9	Renal
3	Lack of Vitamin D
5	Recurrence

DISCUSSION

Parathyroidectomy is the main treatment for primary hyperparathyroidism. After surgery, PTH and Ca levels also improve in most patients. However, some patients may not improve these parameters.[9] When we evaluate our patients with the literature, in our study, the majority of the patients were female (85.1%), this was correlated with the literature.[10,11]

The average age in the literature was between 51–67.[10] In our study, the mean age was 54.83±12.56 years. In general, the adenoma is responsible for primary hyperparathyroidism.[11,12] In our study, we found adenoma in 85.1% of our cases.

Surgical morbidity in various series was reported to be 0–6.3%.[10,11,13] In our series, this rate was found to be 0.83%. We detected seroma in one patient. The mortality rate is very low in the literature (0.9%).[12] Mortality is zero in our series. There are two studies related to thyroid pathologies.[12,14] In these cases, the type of surgical procedure performed at the time of parathyroidectomy is not clear. In our 10 (8.2%) patients, thyroid malignancy was detected during the operation, and additionally, lobectomy was performed. Bergenfelz et al.[15] reported that minimally invasive procedures are promising but do not show the coexisting thyroid pathology.

Inabnet et al.[16] implied systematic surgical exploration rather than minimal procedure since preoperative sestamibi screening and ultrasound could not fully localize. Okudan et al.[17] reported that computed tomography was more accurate than ultrasound in determining preoperative single adenoma in with a patient with primary hyperparathyroidism.

In our study, we were able to locate the gland. Thus, we did not apply extensive surgery. Thyroid US, sestamibi screening and computed tomography were sufficient for our cases.

Nordenström et al.[18] detected 16% recurrence in 5-year follow-up and emphasized the importance of long-term follow-up. Although parathyroidectomy has been reported to be inadequate in patients with high PTH and calcium levels within six months,[19] normocalcemic PTH elevation (NPE) is observed in approximately 12–45% of the patients after successful parathyroidecto.[20,21] Relapsing primary hyperparathyroidism is present in 3–7% of patients with approximately high PTH levels.[22]

In our series, 17 (14.8%) patients showed high levels of PTH. Our recurrence rate (5 patients) was 4.1%. Our recurrence rate shows similarities with the literature.[22] Our rate of normocalcemic PTH elevation was 10.7% (12 patients) with a high PTH level within six months after parathyroidecto. Of the five patients (4.1%) who were evaluated as recurrence, three patients were parathyroid carcinoma, and the other patients were paratroid hyperplasia and adenoma. Three patients with parathyroid carcinoma were found to have elevated PTH and calcium levels on the first postoperative day. They were reoperated. PTH and calcium levels returned to normal. Of the other two cases with parathyroid hyperplasia that we considered recurrence PTH levels started to increase after one day postoperatively, the other with adenoma started to rise PTH levels after three months postoperatively. They reoperated. The values have returned to normal.

Nine cases (7.4%) of the remaining 12 (9.9%) cases were detected renal dysfunction and three cases were detected vitamin D deficiency. In these patients, PTH levels started to increase after three and six months. PTH levels began to decline with the treatment of those with vitamin D deficiency. Patients with renal dysfunction are followed in the Nephrology Clinic.

Our rate of NPE is low compared to the literature. This may be due to the short follow-up period.

The risk factors of NPE are not clear. In studies on this subject, vitamin D deficiency, bone hunger and renal dysfunction have been identified as potential risk factors.[23,24]

Some studies have identified NPE as a risk factor for recurrence.[13,25] Many studies have shown that NPE is not associated with recurrence.[19]

Likewise, Solorzano et al.[25] reported that NPE did not show operative insufficiency but showed recurrence in some patients. In our study, NPE was detected in one of the five patients with recurrence.

The limitations of our study were retrospective and single-center study.

CONCLUSION

Primary hyperparathyroidism is a rare disease. It is successfully treated with parathyroidectomy. However, postoperative hyperparathyroidism is detected in some patients. In this case, NPE should be considered, as well as recurrence. NPE can be due to bone hunger, vitamin D deficiency and renal dysfunction. Long-term prospective studies are needed to better evaluate hyperparathyroidism after parathyroidectomy.

Ethics Committee Approval

Approved by the local ethics committee (no: 2018/514/144/11, date: 26.12.2018).

Informed Consent

Retrospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: M.F.K.; Design: M.F.K.; Supervision: M.F.K., H.F.K.; Fundings: M.F.K.; Materials: M.F.K.; Data: M.F.K.; Analysis: M.F.K., H.F.K.; Literature search: M.F.K., H.F.K.; Writing: M.F.K.; Critical revision: H.F.K.

Conflict of Interest

None declared.

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Primer Hiperparatroidizmde Paratroidektomi Sonrası Paratroid Hormon Yüksekliğinin Değerlendirilmesi

Amaç: Bu çalışmanın amacı kliniğimizde primer hiperparatiroidizm nedeni ile paratiroidektomi uygulanan hastalar da yüksek paratiroid hormon (PTH) seviyelerini geriye dönük olarak literatür eşliğinde irdelemek.

Gereç ve Yöntem: Eylül 2015, Aralık 2017 arasında kliniğimizde primer hiperparatiroidizm nedeni ile ameliyat edilen ve takip edilen 121 hasta yaş cinsiyet, ameliyat öncesi kalsiyum (Ca) ve PTH seviyeleri, ameliyat sonrası Ca ve PTH seviyeleri, tanı, patoloji sonuçları, yapılan ameliyat, takip süresi, nüks açısından geriye dönük olarak değerlendirildi. Kendilerine ulaşılamayan hastalar çalışmaya alınmadı.

Bulgular: Primer hiperparatiroidizm nedeni ile ameliyat edilen hastaların en küçüğü 26 yaşında, en büyüğü 82 yaşında olup yaş ortalaması 54.83±12.56 idi. Bunların 103'ü (%85.1) kadın hasta idi. Klinik tanılarına göre hastaların 119'u (%98.4) adenom, ikisi (%1.6) hiperplazi idi. Patolojik sonuçlarına göre ise 103 hasta (%85.1) adenom, dört hasta (%3.3) karsinom, dört hasta (%3,3) hiperplazi, 10 hasta (%8.2) adenom ve troid papiller karsinoma tanısı aldı. Ameliyat öncesi ortalama PTH seviyeleri 301.9±470 pg/ml (en düşük 79 pg/ml, en yüksek 3674 pg/ml), ortalama Ca seviyesi ise 11.42±0.7 mg/dl (en düşük 10.10 mg/dl, en yüksek 13.07 mg/dl) idi. Ameliyat sonrası ortalama PTH seviyesi 77.2±11.1 pg/ml (en düşük 6.0 pg/ml, en yüksek 907 pg/ml), ortalama Ca seviyesi ise 9.38±0.7 mg/dl (en düşük 6.3 mg/dl, en yüksek 11.4 mg/dl) idi. Takip süresi minimum sekiz ay, maksimum 28 ay olup ortalama 18.75±5.4 ay idi. Ameliyat sonrası PTH yüksekliği 17 (%14.8) hastada devam etti. Dokuz (%7.4) hastada böbrek yetersizliği (bu hastalarda ameliyat sonrası PTH seviyesi normal olup üç-dört ay sonra yükselme tespit edildi), üç (%2.4) hastada vitamin D eksikliği ve beş (%4.1) hastada da nüks tespit edildi.

Sonuç: Pirimer hiperparatiroidizm nadir görülen bir hastalıktır. Ameliyat sonrası PTH seviyesi yüksek olan hastalarda nüks yanında normokalsemik PTH elevasyonu (NPE) ve buna sebep olan renal fonksiyon bozukluğu, kemik açlığı ve vitamin D eksikliği de göz önünde bulundurulmalıdır.

Anahtar Sözcükler: Hiperparatyroid; paratyroid hormon; paratyroidektomi.