ASTR

ORIGINAL ARTICLE
pISSN 2288-6575 • eISSN 2288-6796
https://doi.org/10.4174/astr.2018.94.2.69
Annals of Surgical Treatment and Research

Clinical usefulness of intraoperative parathyroid hormone monitoring for primary hyperparathyroidism

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Purpose: The availability of intraoperative parathyroid hormone (IOPTH) monitoring allows successful focused parathyroidectomy for primary hyperparathyroidism (pHPT). The objective of this study was to report our initial experience in IOPTH monitoring during parathyroid surgery for primary hyperparathyroidsim.
Methods: Between May 2011 and February 2013, 37 patients underwent focused parathyroidectomy due to pHPT. IOPTH monitoring based on Miami criteria was used to confirm complete excision of hyperfunctioning parathyroid gland during surgery. Medical records of patients were reviewed retrospectively.
Results: Preoperative mean maximal calcium level was 11.7 ± 0.9 mg/dL. Preoperative technetium (^{99m}Tc) sestamibi scan and ultrasonography identified 32 of 37 (86.5%) and 29 of 37 (78.4%) of abnormal parathyroid glands, retrospectively. Results of the 2 imaging modalities were discordant for 8 cases (21.6%). The mean pre-excision PTH level was 147.2 ± 201.5 pg/mL. At 5- and 10-minute post tumor resection, PTH levels were 65.3 ± 25.4 pg/mL and 47.5 ± 24.3 pg/mL, respectively. In all cases, IOPTH levels fell by at least 50% after removing all suspected abnormal glands. All patients had a successful return to normocalcemia after surgery (mean follow-up period: 60.2 ± 15.4 months).
Conclusion: Surgeon could confirm complete excision of abnormal hyperfunctioning parathyroid glands by IOPTH monitoring during surgery for pHPT. IOPTH monitoring can maximize performance of successful focused parathyroidectomy for pHPT, especially when preoperative imaging results are discordant.
[Ann Surg Treat Res 2018;94(2):69-73]

Key Words: Focused parathyroidectomy, Parathyroid hormone monitoring, Primary hyperparathyroidism

INTRODUCTION

Primary hyperparathyroidism (pHPT) is a relatively common endocrine disorder characterized by inappropriate secretion of parathyroid hormone (PTH) from one or more parathyroid glands. Although there has been a recent development of a medical therapy, the only curative therapy for pHPT is surgical resection [1,2]. Bilateral neck exploration has been accepted for decades as the gold standard treatment for pHPT and the success of surgery depends on skill and judgment of experienced surgeons.

Recently, there has been a paradigm shift in parathyroid surgery from bilateral neck exploration toward the use of focused parathyroidectomy for pHPT [3-6]. Compared with bilateral neck exploration, focused parathyroidectomy can lead to lower postoperative complications, operation time, and length of hospital stay with equally high cure rates [7,8].

To have successful focused parathyroidectomy, precise pre-

Received May 29, 2017, **Revised** June 19, 2017, **Accepted** July 12, 2017

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operative localization is very important to determine the site of incision. Accurate preoperative imaging techniques such as technetium (^{99m}Tc) sestamibi scan and ultrasonography (US) have reduced unnecessary search and enabled minimally invasive surgery.

Since its first description in 1988 [9], intraoperative parathyroid hormone (IOPTH) monitoring has allowed successful focused parathyroidectomy by confirming if any other hyperfunctioning glands are still present after resection of suspicious lesion seen in preoperative imaging [9,10].

The standard procedure for IOPTH monitoring involves IOPTH measurements shortly before operation (preincision value), after complete mobilization of the adenoma (pre-excision value), 5 minutes and 10 minutes after excision based on Miami criteria [11]. If IOPTH levels are decreased sufficiently, the operation is concluded. If IOPTH levels are not decreased as expected, further exploration of the neck is performed until another gland or more abnormal glands are identified and removed with appropriate decrease of PTH. The objective of this study was to report our initial experience with IOPTH monitoring during parathyroid surgery for pHPT.

METHODS

Between May 2011 and February 2013, 40 patients underwent parathyroidectomy due to pHPT. Based on histopathological evaluation, there were 37 cases of single adenoma, 1 case of double adenoma and 2 cases of multiple hyperplasia. The 37 pHPT patients with one unequivocally enlarged parathyroid gland underwent focused parathyroidectomy. Their medical records were reviewed. Of these 37 patients included in the study, 10 patients were males and 27 were females. Their mean age was 56.9 ± 10.9 years. The mean follow-up period after operation was 60.2 ± 15.4 months (Table 1).

Preoperative technetium (^{99m}Tc) sestamibi scan and US were performed to locate hyperfunctioning parathyroid gland. IOPTH monitoring was used to confirm complete excision of hyperfunctioning parathyroid gland. IOPTH sampling was performed before operation (preincision value), after complete removal of the adenoma (pre-excision value), and 5- to 10-minute post tumor resection using radial arterial line through immunochemiluminometric assay (ICMA, E170, Roche Diagnostics, Indianapolis, IN, USA). A fall in PTH levels from baseline by at least 50% in 10 minutes after removing the hyperfunctioning parathyroid gland was used to define success according to Miami criteria [11]. Collected IOPTH monitoring data were analyzed to determine the accuracy of preoperative imaging techniques, technetium (^{99m}Tc) sestamibi scan and US. Clinical cure was defined when serum calcium level was less than 10.2 mg/dL at least 6 months postoperatively.

Table 1. Patient demographics

Characteristic	Value
Sex, male:female	10:27
Age (yr), mean ± SD (range)	56.9 ± 10.9 (33–80)
Follow-up period (mo), mean ± SD	60.2 ± 15.4

RESULTS

The mean maximal serum calcium level was 11.7 ± 0.9 mg/dL (range, 10.3–14.8 mg/dL). Mean preincision PTH level was 247.1 ± 293.7 pg/mL (range, 74.1–1931.1 pg/mL). All patients underwent both technetium (^{99m}Tc) sestamibi scan and US preoperatively. Technetium (^{99m}Tc) sestamibi scan and US identified 32 of 37 (86.5%) and 29 of 37 (78.4%) of abnormal glands, respectively. Results of the 2 preoperative imaging techniques were concordant for 29 of 37 cases (78.4%). When both technique results were concordant, the sensitivity was increased to 96.6% compared to 86.5% for technetium (^{99m}Tc) sestamibi scan alone and 78.4% for US alone. However, results of those 2 imaging modality were discordant for 8 cases (21.6%). For such cases, the sensitivity was decreased to 77.8%.

IOPTH monitoring was performed for 32 cases. We could not perform IOPTH monitoring for all cases due to uncertain schedule of operation day but we performed IOPTH moniroring especially when preoperative imaging results were discordant. Mean PTH levels are demonstrated in Fig. 1. Mean preincision PTH level was 247.1 ± 293.7 pg/mL (range, 74.1–1,931.1 pg/mL). Mean pre-excision PTH level was 147.2 pg/mL. At 5- and 10-min post tumor resection, PTH levels were 65.3 pg/mL and 47.5 pg/mL, respectively. In all cases (100%), IOPTH level fell from baseline by at least 50% after removal of all suspected abnormal glands. When preoperative imaging results were discordant, surgeon decided to continue or discontinue exploration of

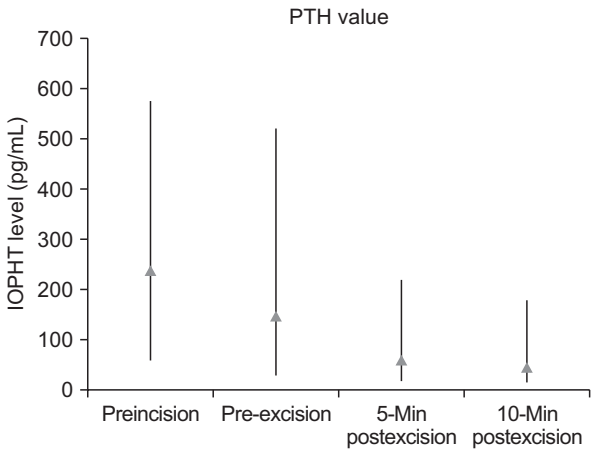

Fig. 1. The overall mean intraoperative parathyroid hormone (IOPTH) levels. PTH, parathyroid hormone.

parathyroid gland depending on IOPTH level.

No intraoperative or postoperative complications were encountered. There was no recurrence during a mean follow-up period of 60.2 ± 15.4 months. In 1 patient, although technetium (^{99m}Tc) sestamibi scan and US results were concordant, IOPTH level did not decrease first after removing suspected abnormal gland. After exploring neck thoroughly, the surgeon found missed parathyroid adenoma. After removing the missed parathyroid adenoma, IOPTH was decreased adequately. All patients achieved normocalcemia (postoperative 6-month mean serum calcium level: 9.7 ± 1.9 mg/dL) during follow-up.

DISCUSSION

The main cause of pHPT is a single parathyroid adenoma which accounts for approximately 85% of cases, followed by multiple hyperplasia, multiple adenomas, and rarely parathyroid carcinomas. For years, surgical treatment for this disease entity has been bilateral neck exploration by visually looking for parathyroid glands and removing all abnormal parathyroid glands confirmed by intraoperative frozen biopsy. The success rate of this method has been reported to be about 95%. However, the main cause of failure of this method is parathyroid tumor which cannot be found during surgery.

Recent development of preoperative localizing imaging techniques such as technetium (^{99m}Tc) sestamibi scan and US has enabled successful focused parathyroidectomy. Compared to bilateral neck exploration, focused parathyroidectomy offers reduced risk of complications such as hypocalcemia and recurrent laryngeal nerve injury, less operating time, shorter length of hospital stay, and lower cost per patient [11-14]. In addition, it is a minimally invasive procedure without sacrificing cure rates [15].

For successful focused parathyroidectomy, preoperative localization is paramount to determine the site of incision [16]. The goal of preoperative imaging for hyperparathyroidism is to identify the location of abnormal parathyroid tissue as precisely as possible. Accurate preoperative imaging techniques such as technetium (^{99m}Tc) sestamibi scan and US can reduce unnecessary search and enable minimal invasive surgery. Technetium (^{99m}Tc) sestamibi scan is the imaging of choice with sensitivity ranging from 54% to 88% [17-21]. The sensitivity of the scan is dependent on size of the lesion and calcium levels [22]. Our study showed that technetium (^{99m}Tc) sestamibi scan had a sensitivity of 86.5%. US is inexpensive, convenient, and noninvasive. Its sensitivity ranges from 59% to 89% for single parathyroid adenomas [17,18]. US is capable of providing precise anatomical details of surgical findings [23]. However, its accuracy is operator-dependent and ectopic adenomas might be missed [24]. In the present study, US had a sensitivity of 78.4%.

When results of the 2 imaging modalities are concordant, the rate of successful localization for single adenoma has increased by at least 10%–20% [16]. The sensitivity of technetium (^{99m}Tc) sestamibi scan and US was increased to 96.6% (28 of 29) for patients with single adenomas in our study. However, when results of technetium (^{99m}Tc) sestamibi scan and US are discordant, surgeon cannot target the hyperfunctioning parathyroid gland precisely. For such cases in our study, the sensitivity was decreased to 77.8%.

By checking PTH level intraoperatively during parathyroid surgery, surgeon can achieve complete excision of all hyperfunctioning parathyroid glands. PTH is produced only in parathyroid glands and intact PTH has a half-life < 5 minutes. Therefore, blood concentrations of intact PTH will decrease rapidly within a short period of time after removing all hypersecreting parathyroid tissues. In the present study, results of the 2 imaging modalities were discordant in 8 of 37 (21.6%). For these discordant cases, surgeon decided whether he should continue exploring parathyroid glands depending on IOPTH level. Combining preoperative imaging with IOPTH monitoring can lead to successful focused parathyroidectomy [2,25-27].

There are ongoing debates about the interpretation of measurement results, i.e., the baseline to use, the appropriate percentage of IOPTH level reduction, and normalization of PTH level. Miami criteria used in this study require more than a 50% decrease in PTH level from the highest of either preincision level or post-mobilization level at 10 minutes after excision of the adenoma. Barczynski et al. [28] have found that Miami criteria have an overall accuracy of 97.3%, which is higher than Vienna criteria (accuracy of 92.3%) and Rome criteria (accuracy of 83.8%) [11,28]. In the present study, PTH levels were decreased by more than 50% but they failed to reach normal level in 4 patients (normocalcemic hyperparathyroidism). PTH levels in these 4 patients became normal within 6 months except for 1 patient (77.3 pg/mL).

In 1 patient, although both technetium (^{99m}Tc) sestamibi scan and US results were concordant, IOPTH level did not decrease first after removing the suspected abnormal gland. Surgeon had to explore ipsilateral side or contralateral side of neck thoroughly until he found the missed parathyroid adenoma or hyperplasia successfully. After that, IOPTH level was decrease adequately.

Patients were regarded as clinically cured if they became normocalcemic postoperatively and remained so for 6 months. This is the traditional definition of operative success. During 6 months and recent follow-up of these patients who underwent surgery, there was no recurrence in any patient.

In summary, IOPTH monitoring can be used to confirm complete excision of all abnormal hyperfunctioning parathyroid glands. Despite the availability of technetium (^{99m}Tc) sestamibi scan and high-resolution ultrasound, combining preoperative imaging and IOPTH monitoring can lead to successful focused

parathyroidectomy for pHPT, especially when preoperative imaging results are discordant.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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