Quick Parathormone Assay in the Surgical Management of Hyperparathyroidism

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Abstract

Background: Among the various new technologies in the field of parathyroid surgery is intraoperative quick parathormone measurements.

Objectives: To evaluate the contribution of QPTH measurements during parathyroidectomy to the achievement of higher success rates.

Methods: QPTH assay using Immulite Turbo Intact PTH was measured in 32 patients undergoing parathyroidectomy: 30 for primary and 2 for secondary hyperparathyroidism. QPTH levels were measured at time 0 minutes (before incision) and at 10, 20, and 30 minutes after excision of the hyperfunctioning gland. Only a drop of 60% or more from the 0' level was considered to be a positive result.

Results: The mean QPTH level at time 0' for PHPT patients was 38.12 $\pm$ 25.15 pmol/L (range 9.1–118 pmol/L). At 10 minutes post-excision of the hyperfunctioning gland (or glands), QPTH dropped by a mean of 73.80% to 9.89 $\pm$ 18.78 pmol/L.

Conclusions: Intraoperative QPTH level measurement is helpful in parathyroid surgery. A drop of 60% or more from 0' level indicates a successful procedure, and further exploration should be avoided.

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Primary hyperparathyroidism is relatively common, with an incidence of about 1:1,000 [1] and a wide spectrum of presentation including asymptomatic hypercalcemia, skeletal pain, osteoporosis, pathologic fractures, nephrocalcinosis, gastrointestinal disturbances and neuropsychiatric symptoms. Prior to the mid 1970s, more than 50% of patients with PHPT had evidence of skeletal or renal disease. Today, the incidental finding of hypercalcemia in an asymptomatic patient is the most common method of diagnosis [1]. Single parathyroid adenoma (80–85%), multiple parathyroid adenoma (2–3%) and parathyroid hyperplasia (12–15%) are the most common causes, with parathyroid carcinomas accounting for the remaining cases (approximately 1%).

While most people have four parathyroid glands situated in well-known anatomic locations, 2–6% of the population have more than four parathyroid glands and in 15% of the population the parathyroid glands are located atypically [1]. It is in this particular group that preoperative localization using intraoperative gamma detection and hormone assay is of utmost importance. We report our experience with intraoperative quick parathormone measurement.

QPTH = quick parathormone
PTH = parathormone
PHPT = primary hyperparathyroidism

Materials and Methods

During an 18 month period 32 patients underwent parathyroidectomy in our center – 30 due to primary and 2 to secondary hyperparathyroidism. The diagnosis of hyperparathyroidism was based on high plasma calcium and PTH levels and low plasma phosphor levels.

All patients underwent preoperative localization including MIBI scan and ultrasound scan of the neck. Biochemical evaluation included plasma calcium, phosphor and PTH levels and quantitative 24 hour urine calcium and phosphor excretion.

During the operation, blood samples were drawn into EDTA tubes, centrifuged for 5 minutes and immediately evaluated. Quick PTH assays were performed using Immulite Turbo Intact PTH (DPC, Los Angeles, USA). Intraoperative QPTH levels were measured at time 0' (before the incision) and at 10, 20 and 30 minutes following excision of the suspected hyperfunctioning parathyroid gland.

In cases of secondary hyperparathyroidism, blood samples were taken after removal of each suspected specimen until normal intraoperative QPTH levels were achieved. Only a drop of 60% or more in intraoperative QPTH levels from time 0' was considered to be a positive result. Blood samples were sent via a pneumatic tubing system and reached the laboratory within 3–4 minutes. All excised specimens were sent for frozen section evaluation. The decision to end the surgical procedure was based on the accumulation of laboratory data and pathologic reports.

A gamma detector was used in all patients. They were injected 1 hour prior to surgery at the Institute of Nuclear Medicine, and the possible location of the hyperfunctioning gland was marked on the skin of the neck in those patients in whom it could be located.

Results

During an 18 month period, 32 patients underwent surgery for hyperparathyroidism, 30 for PHPT and 2 for SHPT. The 23 women and 9 men ranged in age from 23 to 85 years. In the patients with PHPT, the adenoma was located in the right lower neck in 11 patients, the left lower neck in 5, the right upper neck in 6, the left

SHPT = secondary hyperparathyroidism

upper neck in 3, and in an ectopic position in 4 patients. In one patient, two adenomas were found, one in the right lower neck and one in the left upper neck. Preoperative localization with MIBI scan and ultrasound was performed in all patients. In the 30 patients with PHPT, the hyperfunctioning gland was accurately localized by MIBI scan in 22 and by ultrasound of the neck in 17. Both MIBI and ultrasound accurately localized the hyperfunctioning gland in 14 of 30 patients with PHPT. In the SHPT group, preoperative localization failed to localize the hyperfunctioning gland in one patient, but in the second patient with SHPT, ultrasound accurately suggested hyperplasia. Intraoperative localization of the adenoma was in concordance with MIBI preoperative localization scan in 20 of 22 patients with PHPT (positive predicted value 91%) and with ultrasound preoperative localization scan in 14 of the 17 patients (positive predicted value 82%).

The pathologic results concurred with the preoperative diagnosis of adenoma in 29 patients and hyperplasia in 2 patients. In one patient, intraoperative QPTH levels dropped by >60% from 0' levels, although the pathologic report suggested a normal parathyroid.

Bilateral neck exploration was performed in 6 of 30 patients with PHPT and in all patients with SHPT. The reasons for performing a bilateral exploration were as follows: non-localization on preoperative MIBI scan and ultrasound in one patient, hyperplasia and multiple adenomas in three patients, failure of the intraoperative QPTH level to decrease after unilateral neck exploration in three other patients, and report of a normal parathyroid gland found on frozen section, despite a drop of intraoperative QPTH level, in one patient.

The mean QPTH level at time 0' for PHPT patients was 38.12 ± 25.15 pmol/L, ranging from 9.1 to 118 pmol/L (normal 0.99–5.94). At 10 minutes post-excision of the hyperfunctioning gland, intraoperative QPTH levels dropped by a mean of 73.80%, from 38.12 to 9.89 ± 18.78 pmol/L. Since the technique was still under evaluation in the first 20 patients, intraoperative QPTH levels continued to be measured at 20 minutes and in some cases even at 30 minutes [Figure 1]. In the SHPT group the mean QPTH level at time 0' was 195 pmol/L (range 127–263 pmol/L), and as the surgical procedure proceeded QPTH levels were measured following the excision of

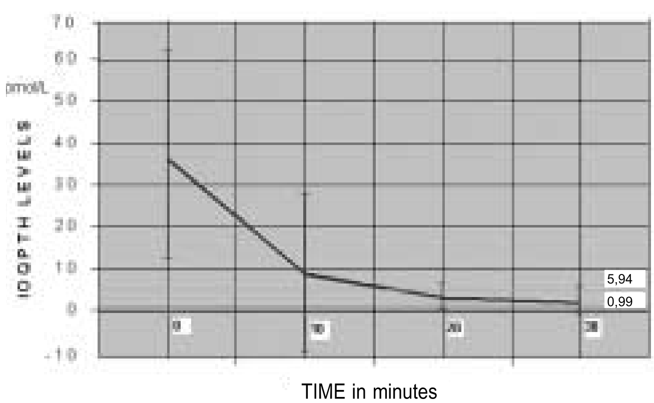

Figure 1. Mean intraoperative QPTH levels in 30 patients with primary hyperparathyroidism

each hyperplastic gland until a decrease of QPTH by 60% or more from 0' levels. In all patients, there was a direct correlation between a decrease in intraoperative QPTH of more than 60% and achievement of postoperative normocalcemia.

Hemithyroidectomy was concomitantly performed in three patients: in two patients because the parathyroid adenoma was located in the right thyroid lobe, and in the third patient because of an unsuspected carcinoma of the right lobe.

In 12 patients, intraoperative QPTH monitoring helped in the surgical process of decision-making, as exploration continued until a drop of 60% or more in intraoperative QPTH levels was achieved. No re-operation was necessary in the two groups of patients.

Since the purpose of this paper is to report the efficacy of intraoperative QPTH analysis in predicting the outcome of surgery for PHPT and SHPT, the use of the gamma detector, the length of the operation, the extent of hospital stay, complications, etc., will not be discussed.

Discussion

The classical approach to parathyroid surgery has changed markedly in the last decade, from bilateral neck exploration without preoperative localization to preoperative localization followed by unilateral exploration with or without the use of radio-guided detection, intraoperative QPTH monitoring [2] and, lately, even to a minimally invasive endoscopic parathyroidectomy [3,4]. Taking into consideration all these developments, which no doubt contribute to the achievement of better results, the personal experience and judgment of the surgeon probably play the most important role. It should be kept in mind that in the past the overall success rate of experienced surgeons was approximately 95% [5]. Hence, all modern developments have two aims: the first is to increase the success rate to as close to 100% as possible, and the second, to do so with better cosmetic results (smaller incisions), fewer complications and, of course, reduced costs.

The modification of the Nichols Institute Diagnostics Immunochemiluminometric Assay for intact PTH, for rapid intraoperative QPTH assay during surgery for PHPT, was developed and documented by Irvin and co-workers [6–9]. This technique has been applied by other investigators in the field of PHPT [10] and SHPT [11] treatment, and has also been adopted by us.

Most failures in parathyroidectomy are due to the inability to identify a multiglandular disease or an ectopic location. Use of the intraoperative QPTH assay could provide several solutions to this problem. Published reports indicate that the incidence of multiple gland involvement may be between 5% and 30% of all cases, and as a result many surgeons consider bilateral exploration to be essential in all cases. Theoretically, biochemical confirmation of the complete removal of all hypersecreting parathyroid tissue provided by the intraoperative QPTH assay renders unilateral exploration sufficient in many cases of HPT. As a result, the use of intraoperative QPTH assay could potentially reduce the length of the operation, enable the use of local anesthetics, shorten hospital stay, and lead to a reduction in the number of re-operations [2].

Since the half-life of PTH *in vivo* is 2–5 minutes, resection of a single affected gland should result in a sharp decline in the PTH level 10 minutes after the excision of the hyperfunctioning gland [12]. Since PTH secretion by the remaining normal or suppressed glands is inhibited by the hypercalcemia, a "time gap" will be formed during which the PTH level will be extremely low.

Most published articles suggest that a 50% drop in the level of QPTH 10 minutes after parathyroidectomy is a marker of successful surgery [12–14]. In multiglandular disease, the QPTH level drops by more than 50% of the initial level only after all affected glands have been excised. To be on the safe side, we arbitrarily decided that the cutoff point would be 60% or more. The QPTH test requires about 20 minutes, making its result relevant to intraoperative decision-making.

Basically, our results do not differ from those reported in the literature. We embarked on the protocol of 10, 20 and 30 minutes intraoperative QPTH measurements in the first 20 patients, but now we only perform the assay at 10 and 20 minutes. We suggest that in cases of SHPT, intraoperative QPTH measurement should continue until all the glands have been identified and removed. Blood samples should be taken 10 minutes after excision of each gland until the intraoperative QPTH drops to normal levels. In order to achieve a 100% success rate, we established an algorithm of treatment that was followed in all patients. In all the procedures, preoperative localization was attempted, and intraoperative QPTH monitoring was used in combination with frozen-section reports. The senior author decided whether or not the surgical procedure should continue, only after collecting all pertinent data.

The introduction of intraoperative QPTH measurement demands close cooperation between the operating surgeon and the laboratory, placing the specialized laboratory staff at the disposal of the surgeon. The question of cost remains a problem, since the price of $100 per patient is not covered by the health insurance funds. However, as this method could potentially eliminate the need for further re-operations, we believe that in the near future this problem will be resolved.

In conclusion, preoperative localization together with intraoperative QPTH monitoring would enable unilateral neck exploration for parathyroidectomy. This new approach would shorten the length of the operation, minimize morbidity (mainly vocal cord paralysis and hypoparathyroidism), enable performance of the operation under local anesthesia, reduce costs, and might improve the success rate of the first operation to almost 100%.

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