Comparison Between Rapid Intraoperative and Central Laboratory Parathormone Dosage in 12 Kidney Transplant Candidates

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ABSTRACT

Background. The rapid intraoperative parathormone (PTH) and at central laboratory PTH dosage gives similar results. The central laboratory provides results in longer times and higher costs. Intraoperative measurement can reduce time and costs during parathyroidectomy.

Methods. Twelve patients undergoing parathyroidectomy for hyperparathyroidism renal transplant candidates were included. Diagnosis was made by laboratory tests (serum calcium, PTH) and imaging techniques (ultrasonography and scintigraphy). All patients presented PTH levels of >400 pg/mL (the limit value to be maintained in list for kidney transplantation) and resistant to medical therapy. For each patient, 2 blood samples were collected before surgery at anesthesia induction for PTH testing intraoperative (rapid assay) and central laboratory, and 10 minutes after the removal of each gland. The times from collection–processing to communication to the surgeon of the results were compared for both the methods. It was considered successful the abatement of PTH of $\geq$70% at rapid intraoperative testing and consequently surgical intervention stopped before communication of central laboratory PTH testing.

Results. The average time of reporting the test results of the central laboratory was 41.5 minutes (SD $\pm$ 9), whereas with the rapid intraoperative PTH (ioPTH) testing the average time was 9.9 minutes (SD $\pm$ 2.02). An average of 33.6 minutes of the duration per intervention (SD $\pm$ 10.27) were virtually saved with the use of ioPTH testing. The 2 values of the Pearson correlation (ρ) of 0.99 obtained (for baseline) and 0.975 (for the 10-minute) lead us to conclude that there is an excellent correlation between the series of data.

Conclusions. Rapid ioPTH testing, owing to its accuracy, permits a dramatic reduction of operating time for patients with secondary hyperparathyroidism that need to be treated before inclusion on the waiting list.

THE ACCURACY of commercial rapid intraoperative parathormone (PTH) testing kits is well-validated and the results are comparable with those obtained from central laboratory methods [1]. The diffusion of intraoperative PTH (ioPTH) devices revolutionized the surgical approach to hyperparathyroidism. Complete surgical neck exploration and the gross anatomy evaluation of parathyroid glands demanded of the surgeon nowadays is enhanced by this powerful and rapid confirmation of an efficient surgery, and helps to avoid prolongation and unnecessary manipulation of patients. Patients on dialysis experience more complications when surgery is prolonged. Central laboratory testing is valid as a tardive guarantee of a correct surgical intervention.

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Table 1. Laboratory Data

Patient	Time of Blood Collection	PTH Central Laboratory (pg/mL)	Central Laboratory Time (min)	ioPTH Values (pg/mL)	ioPTH Testing Time (min)	Operating Time (min)
1	Baseline	780	42	731	8	110
	10 min	28	38	33	9	
2	Baseline	1340	49	1289	10	85
	10 min	83	39	76	11	
3	Baseline	3201	51	3189	7	210
	10 min	96	39	87	10	
4	Baseline	1940	39	1870	9	66
	10 min	159	41	139	11	
5	Baseline	690	42	620	8	79
	10 min	27	39	35	10	
6	Baseline	2020	38	2034	12	96
	10 min	36	40	29	9	
7	Baseline	1125	38	1100	9	110
	10 min	95	41	104	11	
8	Baseline	3134	40	3031	13	77
	10 min	40	42	25	7	
9	Baseline	1340	39	1386	10	101
	10 min	32	39	39	9	
10	Baseline	689	43	598	8	68
	10 min	41	45	34	7	
11	Baseline	530	48	499	14	79
	10 min	21	39	18	11	
12	Baseline	458	43	515	14	115
	10 min	52	42	43	11	

Abbreviation: ioPTH, intraoperative parathormone.

The circulating PTH molecule as intact 84 amino acid peptide has a half-life of 3–5 minutes in patients with normal renal function. After parathyroidectomy, PTH presents a biphasic pattern of decrement with a very rapid initial phase (2–4 minutes) and a subsequent smothering of curve with a lower elimination speed (21–82 minutes) [2].

Nussbaum et al. [3] described the first use of PTH monitoring during parathyroidectomy. Other groups [4,5] independently described the use of ioPTH monitoring to guide the surgeon during parathyroidectomy.

The central laboratory of our Institution uses the PTH intact STAT (short turnaround time) electrochemiluminescence immunoassay of the Cobase 411 analyzer (Roche Diagnostics, Basel, Switzerland). This third-generation assay uses a biotinylated monoclonal antibody, which reacts with amino acids 26–32, and a capture ruthenium-complexed monoclonal antibody, which reacts with amino acids 55–64, and requires 9 minutes to provide results. The STAT-IO-I-PTH System (Future Diagnostics, Nieuweweg, the Netherlands) is a third-generation PTH assay (immunochemiluminometric) that requires 7 minutes to perform the assay. Briefly, it uses a 2 affinity-purified goat polyclonal antibodies against PTH with a sandwich technique for measuring (1–84) PTH (1 antibody specific for the 1–34 amino acid segment and the other for the 35–84 or 39–84 carboxy segment). The kit consists of an instrument on a trolley in the actual or immediate proximity of the operating room.

The criterion for evaluation of results in primary hyperparathyroidism is based on a cutoff of a 50% decrease in PTH in plasma levels; the evaluation of the results in secondary hyperparathyroidism is based on a cutoff of a 70% decrease of PTH levels in plasma after 10 minutes from the resection of the last gland or 85% after 15 minutes [6–8]. In both cases, there is a sensitivity of 85% and a specificity of 100% when it is performed 10 minutes after surgical resection; sensitivity increases to 97% when the sample is taken 15 minutes after resection.

The rapid ioPTH assay represents a kind of "extemporaneous histological biochemical examination": a significant reduction of PTH levels, in fact, is able to predict healing in almost 100% of cases, demonstrating the complete excision. On the contrary, a finding of increased PTH values at the end of the intervention is a sign of persistent disease and suggests continuing the surgical exploration until the identification and removal of all pathologic tissue.

Therefore, this method of investigation not only "certifies" the nature of the parathyroid tissue removed, but also documents the absence of residual hyperfunctioning tissue, thus making the exploration of not easily identified parathyroids not always necessary. The protocol adopted for the ioPTH assay provides 2 measurements: one at baseline (induction of anesthesia) the second at 10 minutes after the removal of suspected glands. A decreased value of PTH postablation of >70% (the so-called cutoff) compared with the value before ablation (baseline value) is able to predict the surgical excision of a hyperfunctioning gland with a sensitivity of 98% and a specificity of 94% [6–8]. Failure to

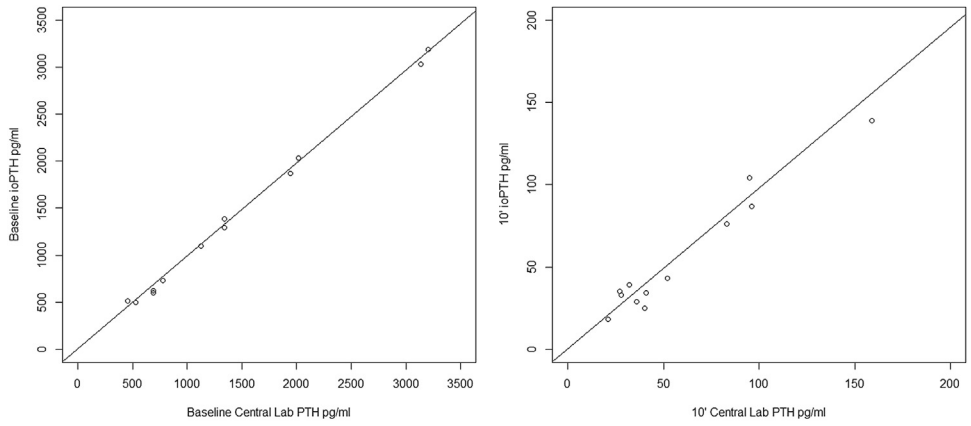

Fig 1. Correlation plot of central laboratory and intraoperative parathormone (ioPTH) assay at baseline and at 10 minutes after complete hyperfunctioning gland excision.

decrease PTH indicates the persistence of hyperfunctioning parathyroid tissue.

In this study, we analyzed the comparison of time needed to perform intraoperative testing and central laboratory testing and the value obtained from the test.

MATERIALS AND METHODS

This study included 12 patients with secondary hyperparathyroidism owing to chronic renal insufficiency who were candidates for renal transplantation, but required parathyroidectomy to staying on the waiting list. The diagnosis was made by laboratory tests (serum calcium, PTH) and localization testing (ultrasonography and scintigraphy). All patients presented PTH levels of >400 pg/mL (the limit for maintaining the list for kidney transplantation; Table 1) and were resistant to medical therapy. For each patient, blood samples (collected by a dedicated peripheral vein cannula on the foot) were taken at baseline (before the surgery but after the induction of anesthesia) and 10 minutes after the removal of suspected gland. Blood samples were analyzed initially with ioPTH assay and the sample sent to central laboratory only in presence of PTH reduction of >70%. The results were compared.

The criterion for evaluation of results was based on a cutoff of ≥70% from baseline of PTH plasma levels at 10 minutes as successful removal of abnormal parathyroid glands.

RESULTS

The average time for central laboratory testing (time from blood collection-processing to reporting to the surgeon) was 41.5 minutes (SD ± 9); the rapid ioPTH testing the average time was 9.9 minutes (SD ± 2.02). For each patient, the reduction in operating time was calculated (the intervention was considered successful in presence of a PTH of >70% from baseline and consequently terminated). An average of 33.6 minutes (SD ± 10.27) were saved when the ioPTH value was sufficient to terminate the intervention before central laboratory results were returned (Table 1).

The correlation between the 2 respective series of data (baseline PTH central laboratory vs baseline ioPTH and 10-minute PTH central laboratory vs 10-minute ioPTH) verified the presence of a similar behavior (at high values of a variable correspond with high values of the other and vice versa). The 2 values of the Pearson Correlation (ρ) of 0.99 obtained (for baseline) and 0.975 (for the 10-minute) lead use to conclude that there is an excellent correlation between the series of same data; therefore, we do find a difference in measurement between the 2 instruments at baseline and 10 minutes after complete excision of the hyperfunctioning parathyroid gland. The analysis of scatter plots supports the thesis (Fig 1).

DISCUSSION

According to our experience and a validated protocol, we consider a decrease of ≥70% from baseline PTH levels at 10 minutes and/or a decrease of ≥85% at 15 minutes as successful removal of abnormal parathyroid glands [6–8].

The use of ioPTH testing has increased dramatically the success of this kind of surgery. Imaging techniques are unable to detect abnormal glands, requiring complete surgical exploration (basing on the gross anatomy morphology). The reduced time required for considering successfully parathyroidectomy permits a reduction of anesthesia time, global operative time up to a decrease of 30 minutes, and costs for treatment.

Candidates for kidney transplantation may have spent years on dialysis, have effects of uremia, and be taking drugs to reduce the value of PTH [9]. In these patients, ioPTH testing has been validated and problems related to a reduced PTH clearance overcome [10]. These fragile patients may take advantage of such a tailored surgery that avoid the complete surgical exploration required in the past and make less difficult the stairway to transplant.

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