Use of Intraoperative Parathyroid Hormone Measurement Does Not Improve Success of Bilateral Neck Exploration for Hyperparathyroidism

Frederic L. Starr, MD; Robert DeCresce, MD; Richard A. Prinz, MD

Hypothesis: Use of intraoperative measurement of intact parathyroid hormone (iPTH) to confirm complete excision of hyperfunctioning parathyroid tissue does not improve overall operative success rates.

Design: Case series of patients undergoing parathyroidectomy with or without intraoperative iPTH measurement.

Setting: University teaching hospital.

Patients and Interventions: Fifty patients undergoing parathyroidectomy before our institution of intraoperative iPTH sampling in March 1999 (group 1) were compared with 50 patients undergoing parathyroidectomy after this technique was adopted (group 2). Overall, 100 patients underwent operation between December 1996 and May 2000. Serum calcium and iPTH levels were measured at 1- and 3-month intervals. Intraoperative frozen sections and operative times were also analyzed.

Results: Mean preoperative calcium levels were 2.85 and 2.82 mmol/L (11.4 and 11.3 mg/dL) in groups 1 and 2, respectively. One-month postoperative calcium values were identical in both groups at 2.35 mmol/L (9.4 mg/dL) (group 1 SD=0.18 [0.74], group 2 SD=0.20 [0.82]). At 1 month, all but 1 patient in group 1 had normalized calcium values (2% failure rate), while 3 patients in group 2 (6%) remained hypercalcemic. All 3 patients in group 2 had intraoperative iPTH levels that returned to normal. There was a significant difference in the number of intraoperative frozen sections between groups, with a mean (SD) of 3.4 (1.7) in group 1 and 2.0 (1.6) in group 2 (P<.01). There was no significant difference in operative times between groups.

Conclusions: Use of intraoperative iPTH sampling did not significantly affect the overall success of parathyroidectomy, as determined by postoperative normocalcemia. There was, however, a significant decrease in the number of frozen sections sent at operation.

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Traditionally, patients with primary hyperparathyroidism have been treated with bilateral neck exploration to identify all 4 glands. The abnormally enlarged glands are then removed, and a biopsy of a normal gland is often performed. In the hands of experienced endocrine surgeons, cure of primary hyperparathyroidism, defined as postoperative normalization of the serum calcium level, has been reported to be as high as 95% to 98% with this approach.1,2 The success rate for reoperative parathyroid surgery is lower, ranging from 65% to 98%, and may be more surgeon dependent.3 Intraoperative measurement of intact parathyroid hormone (iPTH) is being used widely as an adjunct in both initial and reoperative parathyroid surgery.4,5 Its usefulness as an aid in determining adequacy of resection, reducing operative time, and lateralizing the abnormality has been demonstrated in both primary and secondary hyperparathyroidism.4,6 In addition, several groups have reported that intraoperative iPTH levels are predictive of surgical success, as defined by long-term postoperative normocalcemia, with a reported accuracy of 95% to 97%.7,8 Use of the “quick” iPTH assay has also been shown to help improve the success rate in reoperative parathyroidectomy.3 Other surgeons have challenged the need and efficiency of using the intraoperative iPTH assay in primary hyperparathyroidism.3,10

This study sought to determine whether the use of the intraoperative iPTH assay improves the surgical success rate in both initial and reoperative parathyroidectomy. In addition, we examined the impact of the quick iPTH assay on the use of intraoperative frozen sections and overall operative time.

RESULTS

The mean (SD) preoperative calcium level for the 50 patients in group 1 was 2.85
PATIENTS AND METHODS

One hundred twenty-three consecutive patients with primary and secondary hyperparathyroidism underwent parathyroidectomy between December 6, 1996, and May 30, 2000. Sixty-one of these patients were operated on before our institution began using the “quick” intraoperative iPTH assay in March 1999 (group 1), while the remaining 62 patients underwent parathyroidectomy with the aid of this measurement (group 2). Of the patients in group 1, 11 were ultimately excluded from the study because of incomplete follow-up values, including 1-month postoperative serum calcium or iPTH levels, thus leaving 50 patients in the study. For 9 of these excluded patients, 1-week postoperative calcium levels are available, all within the normal range. The remaining 2 patients had single adenomas removed without complication. All 11 patients were doing well according to their primary care physicians. Similarly, 12 patients in group 2 were excluded because of incomplete follow-up data, including missing intraoperative iPTH levels or 1-month calcium and/or iPTH values. Of these 12 excluded group 2 patients, 11 have postoperative calcium levels available, all within the normal range. The remaining patient had an uncomplicated excision of a single adenoma, after which her intraoperative iPTH level decreased from 88 to 18 ng/L. Follow-up discussion with the primary care physicians of these patients did not reveal any evidence of hypercalcemia. The remaining 50 patients were included in the study and constitute group 2.

All operations in both groups, regardless of the use of the intraoperative iPTH assay, consisted of a bilateral neck exploration with attempted identification of all 4 parathyroid glands. All operations were performed at a single institution by the same surgeon (R.A.P.).

The average age of patients in group 1 was 58 years (range, 26-81 years), and 70% were women (Table 1). Thirty-seven patients had a single hyperfunctioning gland removed at operation and 8 patients had double adenomas excised. Two patients had a subtotal parathyroidectomy with 3½ glands removed. The remaining 3 patients, all with secondary hyperparathyroidism, had 4-gland excisions with autotransplantation of parathyroid tissue into the forearm (Table 2). Two patients with recurrent hyperparathyroidism underwent reoperation. Both had previously undergone parathyroidectomy and later developed recurrent hypercalcemia. The first of these patients had a left-sided adenoma removed 20 years previously, after which his calcium level normalized. Five months before our operation, routine screening revealed an elevated calcium level of 2.80 mmol/L (11.2 mg/dL). The other group 1 patient who required a reoperation had a left-sided adenoma removed 19 years earlier. Reevaluation of his calcium level was detected by routine screening 6 months before reoperation. Ten patients had concomitant thyroid surgery. Five lobectomies were performed, 3 for colloid cysts and 2 for Hurthle cell adenomas. The remaining 5 patients underwent total thyroidectomy in addition to parathyroidectomy. These patients all had very large colloid nodules, with a history of radiation exposure.

Of the 50 patients in group 2, 49 had histologically proven benign disease, with 9 of these patients having double adenomas. Two patients had 4-gland hyperplasia and underwent 4-gland excision with autotransplantation of parathyroid tissue into the forearm. One of these patients was diagnosed as having multiple endocrine neoplasia type 1. The other patient had secondary hyperparathyroidism due to chronic renal failure, and is receiving hemodialysis. The final patient in group 2 was diagnosed as having parathyroid carcinoma, which was treated by en bloc thyroid lobectomy with complete excision of the tumor. Eight patients underwent reoperation, each previously having had a single failed neck exploration at other institutions. Seven patients had concomitant thyroid surgery, including 4 lobectomies for colloid nodules. 2 total thyroidectomies (1 for multiple cysts in a patient with a history of radiation exposure and 1 for a multinodular goiter), and 1 total thyroidectomy in a patient with papillary carcinoma. The average age of patients in group 2 was 61 years (range, 18-88 years), and 80% were women.

The modified 2-site antibody immunoluminometric assay (Nichols Institute Diagnostics, San Juan Capistrano, Calif) as described by Irvin and Deriso was used in all operations performed on group 2 patients. Blood specimens were processed in the operating room, with iPTH values available within 12 to 15 minutes. Our sampling method included obtaining a baseline value, drawn from a peripheral vein after the patient was anesthetized. Subsequent samples were drawn from the internal jugular vein under direct vision. The second sample was obtained immediately after exposure of the thyroid gland, but before any manipulation of parathyroid tissue. Additional samples were drawn 5 and 10 minutes after removal of presumed parathyroid tissue. If more than 1 gland was removed, the final sample was obtained 10 minutes after the resection was complete.

Postoperative calcium levels were obtained in both groups at 1-week and 1-month intervals, with 3-month values available for some patients. Serum iPTH values were also measured 1 month following operation, using the traditional 24-hour immunoradiometric assay protocol. Pathology records were reviewed in all patients to determine the number of intraoperative frozen sections utilized. The operating room record was also reviewed to assess the length of operation. All statistics were analyzed with SPSS software (SPSS Inc., Chicago, Ill) using independent samples t test.
did not achieve normal calcium levels at 1 week (normal level, <2.62 mmol/L [<10.5 mg/dL]). Two of these patients became normocalcemic 1 month after operation, one of them after stopping oral calcium supplementation. The third patient who underwent a reoperation had a long-term failure. After the first postoperative week, 8 patients in group 2 remained hypercalcemic (16%), although all but 1 patient was normocalcemic by 1 month after operation. Five of these 8 patients were taking oral calcium supplements postoperatively. After calcium supplementation was discontinued, the calcium level in all 5 patients declined to normal levels. Of these 8 patients, 3 had a reoperation, with normal calcium levels at 1 month after operation.

The mean postoperative calcium level at 1 month was identical in both groups at 2.35 mmol/L (9.4 mg/dL) (group 1 range, 1.75-2.70 mmol/L [7.0-10.8 mg/dL]; group 2 range, 1.62-2.80 mmol/L [6.5-11.2 mg/dL]). One patient in group 1 (2%) failed to achieve normal calcium levels at this time. This 76-year-old man undergoing a reoperation had a partial parathyrectomy 20 years earlier. Before operation, his calcium level was 2.80 mmol/L (11.2 mg/dL) and the iPTH level was 111 ng/L. At operation, a solitary right superior adenoma was removed, after which the intraoperative iPTH level remained normal at 26 ng/L, although her calcium level remained elevated at 2.68 mmol/L (10.7 mg/dL). She did not receive calcium supplementation after his operation, but did have sarcoidosis. The second patient had a preoperative calcium level of 2.70 mmol/L (10.8 mg/dL) that dropped to 2.22 mmol/L (8.9 mg/dL) 1 week after the removal of a single 350-mg adenoma. Intraoperative iPTH levels corrected to normal values at the end of the resection, decreasing from a baseline of 74 to 28 ng/L. By 1 month, however, the calcium level had risen to 2.72 mmol/L (10.9 mg/dL) despite a normal concomitant iPTH level of 40 ng/L. At 3 months, after the cessation of oral calcium supplementation, her calcium level returned to normal levels at 2.60 mmol/L (10.4 mg/dL) although the iPTH level was mildly elevated at 76 ng/L. At 6 months, both calcium and iPTH levels were normal at 2.45 mmol/L (9.8 mg/dL) and 64 ng/L, respectively. The final hypercalcemic patient had preoperative and 1-week postoperative calcium levels of 2.62 mmol/L (10.5 mg/dL) and 2.68 mmol/L (10.7 mg/dL), respectively. The preoperative iPTH level was 145 ng/L; however, the baseline value obtained with the intraoperative quick iPTH assay was 34 ng/L, well within the normal range. A single 350-mg adenoma was removed, after which the intraoperative iPTH level decreased to 5 ng/L. One month after operation, the iPTH level remained normal at 26 ng/L, although her calcium level remained elevated at 2.68 mmol/L (10.7 mg/dL).

Four patients in group 2 failed to achieve normal intraoperative iPTH levels after removal of all presumed hyperfunctioning parathyroid tissue. Three of these 4 patients had substantial decreases from their baseline values (471 to 80 ng/L, 644 to 71 ng/L, and 560 to 187 ng/L) with drops of 83%, 89%, and 67%, respectively. All of these patients were normocalcemic 1 month after operation. However, the 2 patients with intraoperative decreases of 83% and 89% had elevated iPTH levels of 430 and 243 ng/L, respectively, at 1-month follow-up. In the fourth patient, the final intraoperative iPTH level actually increased from the baseline value (138 to 212 ng/L). This patient had undergone a prior parathyrectomy at another institution and subsequently remained hypercalcemic. At reoperation, a single 500-mg adenoma was removed, but the intraoperative iPTH level failed to decrease. The operation was stopped after an extensive exploration revealed no additional abnormalities. After the

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Table 1. Patient Information*

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 50)</th>
<th>Group 2 (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), y</td>
<td>58 (26-81)</td>
<td>61 (18-88)</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>15/35</td>
<td>10/40</td>
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<tr>
<td>Symptomatic, No.</td>
<td>40</td>
<td>42</td>
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<tr>
<td>Reoperations, No.</td>
<td>2</td>
<td>8</td>
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<tr>
<td>Concomitant thyroid surgery, No.</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Operative time, mean (range), min</td>
<td>130 (61-353)</td>
<td>145 (65-313)</td>
</tr>
<tr>
<td>Preoperative serum calcium, mmol/L (mg/dL)</td>
<td>2.85 (2.30-3.82)</td>
<td>2.82 (2.48-3.38)</td>
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<td>Preoperative serum iPTH, ng/L</td>
<td>114 (9.2-15.3)</td>
<td>113 (9.9-15.5)</td>
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<tr>
<td>Preoperative serum IP, mean (range), ng/L</td>
<td>146 (53-789)</td>
<td>229 (74-999)</td>
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</tbody>
</table>

*Group 1 patients are those who underwent parathyrectomy before institution of intraoperative intact parathyroid hormone (iPTH) sampling and group 2, those who underwent parathyrectomy after adoption of this technique.

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Table 2. Parathyroid Gland Histologic Data*

<table>
<thead>
<tr>
<th>Disease type</th>
<th>Group 1</th>
<th>Group 2</th>
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<tbody>
<tr>
<td>Single adenoma</td>
<td>37</td>
<td>38</td>
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<tr>
<td>Double adenoma</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>4-Gland hyperplasia</td>
<td>5</td>
<td>2</td>
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<tr>
<td>Carcinoma</td>
<td>0</td>
<td>1</td>
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<td>Glands removed, No.</td>
<td>73</td>
<td>65</td>
</tr>
<tr>
<td>Gland weight, mean (range), mg</td>
<td>1231 (100-9000)</td>
<td>1190 (100-4250)</td>
</tr>
<tr>
<td>Frozen sections, mean (range), No.</td>
<td>3.4 (1-9)</td>
<td>2.0 (0-6)</td>
</tr>
</tbody>
</table>

*See footnote to Table 1 for explanation of patient groups.
Successful operation for primary hyperparathyroidism is strongly affected by the experience of the operating surgeon, with surgical cures achieved in up to 95% to 98% of patients after traditional bilateral exploration and identification of all 4 parathyroid glands. Operative failure has usually been attributed to either a missed adenoma, generally in an ectopic location, or unrecognized multiglandular disease. Success in reoperative parathyroidectomy is even more surgeon dependent, with reported cure rates ranging from 65% to 98%. The intraoperative quick iPTH assay was developed by Irvin and coworkers in part as an adjunct to eliminate these common causes of operative failure by ensuring that all hyperfunctioning parathyroid tissue has been removed. The use of this technique has increased the surgical cure rate for reoperative parathyroidectomy from 76% to 94%. Irvin and colleagues reported that the quick intraoperative iPTH assay confirmed complete excision of hyperfunctioning tissue in 17 straightforward reoperations. Furthermore, the assay directly influenced operative success in 14 (42%) of the 33 studied patients undergoing reoperation. The assay aided localization of the abnormal gland to a particular side when used for differential venous sampling (9 patients), and in locating an obscure ectopic gland by measuring an increase in hormone level after directed massage (3 patients). They also noted that intraoperative iPTH measurement correctly helped identify abnormal tissue in the face of a false-positive or false-negative sestamibi scan in 4 of their patients. When used in reoperative cases, they found that the quick iPTH assay had a positive predictive value of 97%, a negative predictive value of 100%, and an overall accuracy of 98%.

In patients undergoing initial operation, however, the benefits of intraoperative iPTH measurement are not so clear-cut. Several series have reported limited usefulness of intraoperative iPTH sampling in primary hyperparathyroidism, both with the older immunoradiometric assay protocol as well as the modified immunochemoluminometric assay procedure. Proye and colleagues noted that intraoperative iPTH values were misleading in 40% of patients with multiglandular disease. They found that the intraoperative iPTH levels returned to normal in 4 patients despite the presence of an additional adenoma. The technique was helpful in their patients with secondary hyperparathyroidism, assisting in the identification of a fifth gland, and during forearm graft resection and reoperations. Tan and coworkers reported that 3 of 31 patients with primary hyperparathyroidism who underwent successful parathyroidectomy had intraoperative iPTH levels that either remained unchanged or rose after excision of abnormal tissue. They concluded that reliance on iPTH measurement would have led to unnecessary continued exploration.

In our experience, there was no improvement in operative success using the quick iPTH assay. We had a 2% overall failure rate (1 patient) for correcting postoperative calcium levels without the aid of intraoperative iPTH measurement. Since we adopted the use of this technique in March 1999, our overall failure rate has been 6% (3 patients). Our 1 failed operation in group 1 was in a patient undergoing a reoperation after having had a left-sided adenoma removed 20 years prior. After removing a 150-mg right superior adenoma, postoperative calcium levels remained elevated at 1-week, 1-month, and 3-month intervals, with values of 2.65 (10.6), 2.70 (10.8), and 2.72 mmol/L (10.9 mg/dL), respectively. Serum iPTH levels were elevated at 111 and 101 ng/L at 1-month and 3-month follow-up visits, indicating that this patient represented a true operative failure with additional hyperfunctioning parathyroid tissue likely remaining. The use of the quick iPTH assay in this patient did not normalize the calcium levels and failed to adequately treat the patient. Although the quick iPTH assay did not meet the standard used in our institution for a surgical cure (a decrease of greater than 65% in baseline calcium), the failure may not have been due to an inadequacy of the assay itself. The use of intraoperative iPTH measurement in this patient may have been helpful in identifying additional normal tissue that was missed during the reoperation. This may have allowed for a more complete parathyroidectomy and a successful outcome.
of intraoperative iPTH measurement in this patient might have indicated that additional abnormal tissue had been left behind. All the patients in group 1 undergoing initial parathyroidectomy for primary or secondary hyperparathyroidism were normocalcemic at 1 month after operation and therefore were surgical successes.

Three patients in group 2 (6%) failed to achieve normal calcium levels 1 month after operation. The first patient developed sarcoidosis and had a preoperative calcium level of 2.85 mmol/L (11.4 mg/dL) and an elevated iPTH level of 481 ng/L, indicating that his hypercalcemia was at least in part due to parathyroid disease. At operation, a double adenoma was removed after which his intraoperative iPTH level dropped to within the normal range. One week after operation, the calcium level normalized. However, by 1 month, the calcium level had again risen to 2.80 mmol/L (11.2 mg/dL) while the iPTH level was 1 ng/L. This profile indicates that his persistent hypercalcemia is probably not due to residual parathyroid disease, but most likely secondary to his sarcoidosis. The intraoperative iPTH assay thus was ultimately correct in predicting surgical cure of his hyperparathyroidism despite an elevated 1-month postoperative calcium level, and his parathyroid disease has most likely been eradicated. He continues to take prednisone for sarcoidosis.

The second patient, with an elevated 1-month calcium level at 2.72 mmol/L (10.9 mg/dL), had a single adenoma removed at operation. Her intraoperative iPTH value fell to a normal level 10 minutes after the tumor was excised. One week after operation, her calcium level was 2.22 mmol/L (8.9 mg/dL), at which time she was prescribed oral calcium supplementation 3 times a day. When her 1-month laboratory results showed hypercalcemia, calcium therapy was discontinued. Subsequently, her calcium level has dropped to 2.60 mmol/L (10.4 mg/dL) and 2.45 mmol/L (9.8 mg/dL) at the 3- and 6-month follow-ups, respectively. At her 6-month follow-up, both calcium and iPTH levels had normalized. Aggressive postoperative calcium replacement likely accounted for hypercalcemia at 1 month postoperatively, which has since normalized after calcium therapy was discontinued. Technically, her intraoperative iPTH measurement falsely predicted surgical success (assessed at 1 month after operation) as evidenced by her elevated 1-month calcium level. In reality, the assay was correct in predicting a surgical cure, a fact that was masked temporarily by excessive exogenous calcium intake.

The last patient, with a calcium level of 2.68 mmol/L (10.7 mg/dL) at 1 month, had a single adenoma removed. Although the preoperative iPTH level was elevated at 145 ng/L, her baseline intraoperative measurement was within the normal range at 34 ng/L. Therefore, the quick intraoperative iPTH assay offered no assistance. The level did, however, drop to 5 ng/L after the adenoma was excised. One week postoperatively, her calcium level was 2.68 mmol/L (10.7 mg/dL), and it remained elevated at 1 month at 2.68 mmol/L (10.7 mg/dL). She was never given oral calcium supplementation. This patient represents a possible operative failure, although the 1-month iPTH level is normal at 26 ng/L, indicating that parathyroid disease is likely not responsible for her hypercalcemia. Additional follow-up will be necessary to determine whether continued parathyroid disease or another pathologic process is the cause of her persistently elevated calcium level.

In this series, the rate of surgical success for reoperative patients in group 2 was 100%, with all 8 patients being normocalcemic 1 month after operation. In all but 1 patient, intraoperative iPTH values returned to normal or dropped by greater than 65% of the baseline measurement. As previously mentioned, this one patient outlier actually had an increase in his intraoperative iPTH level (138 to 212 ng/L) despite removal of all apparent abnormal parathyroid tissue. The operation was stopped only after an exhaustive search revealed no additional abnormalities. This patient has been normocalcemic since the operation. The elevation of the final intraoperative iPTH level is unusual and could be due either to improper timing when drawing intraoperative blood samples or a technical error in the steps involved in performing the assay itself. The latter is likely since the time intervals were done in the same manner in all the procedures. In our hands, the quick iPTH assay correctly predicted surgical success in 88% of reoperative patients.

Early studies examining the effect of intraoperative iPTH measurement on the use of frozen sections were disappointing. Madira and coworkers reported the use of the older immunoradiometric PTH assay intraoperatively and concluded that due to the lengthy incubation time (30 minutes), added to the time for the iPTH level to fall more than 70%, use of frozen sections was more time efficient. Today, with the newer quick iPTH assay, values are available intraoperatively within 12 to 15 minutes, making comparison with histopathologic evaluation realistic.

In this study, we have demonstrated a significant decrease in the number of intraoperative frozen sections utilized at operation with the adoption of the quick intraoperative iPTH assay (3.4 for group 1 vs 2.0 for group 2). Furthermore, although the patient numbers are small, the decreased reliance on frozen sections in group 2 patients continues to hold true when only the reoperations are examined (3.0 for group 1 vs 2.12 for group 2). The potential cost savings could be significant, although exact figures have not been calculated. The accuracy of the histopathologic evaluation is dependent on the experience of the pathologist and not without potential error. Despite the decrease in intraoperative histopathologic consultation, there was no significant difference in overall operative time between the groups. Previous reports have described a decrease in length of operation with the use of intraoperative iPTH measurement, but only when used to direct a unilateral dissection. Carty and colleagues, however, report that with the use of both preoperative sestamibi scanning and the quick iPTH assay, they were able to perform a unilateral operation in 62.7% of patients. Even so, there was no significant decrease in operative time compared with operations performed without the aid of these techniques. They attribute this in part because, in all operations, they routinely spent time locating a normal parathyroid gland to undergo biopsy. In our study, all patients underwent bilateral neck exploration to identify all abnormal parathyroid disease.
The use of intraoperative iPTH measurement did not influence our overall rate of operative cure when all patients are considered. We demonstrate a 98% success rate, as evidenced by 1-month postoperative normocalcemia, without the use of this technique, and a 94% success rate when using the quick iPTH assay. The number of frozen sections sent at operation was significantly decreased by the use of intraoperative iPTH measurement, while the overall operative time remained the same.

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REFERENCES


CONCLUSIONS

The use of intraoperative iPTH measurement did not influence our overall rate of operative cure when all patients are considered. We demonstrate a 98% success rate, as evidenced by 1-month postoperative normocalcemia, without the use of this technique, and a 94% success rate when using the quick iPTH assay. The number of frozen sections sent at operation was significantly decreased by the use of intraoperative iPTH measurement, while the overall operative time remained the same.

DISCUSSION

Edwin L. Kaplan, MD, Chicago, Ill: Most surgeons agree that primary hyperparathyroidism is caused by an adenoma in about 85%, by double adenomas in up to 10% of women older than 50 years, and by 4-gland hyperplasia in a smaller number of patients. Currently, most surgeons continue to use a bilateral parathyroid exploration. However, there are a growing number of reports of the use of minimally invasive parathyroidectomy in which a 2-cm incision is made and only 1 gland is seen and removed. There is no question that if minimally invasive parathyroidectomy is performed, intraoperative PTH should be utilized or a number of patients will not be cured. However, this study addresses other questions.

Does intraoperative PTH measurement aid the experienced parathyroid surgeon who performs a bilateral neck exploration?

Dr Prinz and his group suggest that the answer is no. Their results would be more persuasive if all of the data were counted, for 21 patients were eliminated because of incomplete data. Furthermore, it is very hard to beat success. In their group 1 patients, 98% were cured by exploration alone. Thus, it is not very likely that any technique would improve this.

Thus, my first question is, do you think that intraoperative PTH measurement may help the less experienced surgeon to a greater extent?

Second, intraoperative PTH measurement has its own set of pitfalls. Have you found, as we have, that often PTH measurements must be followed longer than 10 minutes? Have you found PTH to fall to normal at 10 minutes after removal of 1 gland only to rise later, signifying that a second abnormal gland was present? We have 2 such patients.

And, last, have you found any difference in the half-life of PTH in your patients with severe secondary hyperparathyroidism?

Jerry M. Shuck, MD, Cleveland, Ohio: 1 note that if you do 2 parathyroid assays during the course of the operation and you wait 10 to 15 minutes for each, that is a half-hour waiting
period during the course of the operation. In this study, you are going to explore the other glands anyway while you are waiting. If the PTH level has fallen after 5 minutes or 10 minutes, do you stop the rest of the exploration or was that irrelevant to the purpose of this study?

I am concerned about a study group that has a 1-month follow-up. It would be very interesting to see if some tiny hyperplastic nodules in normal parathyroids do pop up and become important. Some of those you can see grossly—you can see a slightly enlarged parathyroid, and we have run into that this past week.

Your operation takes over 2 hours in both series. Does the PTH assay contribute to this? The success rate on the first series is as good as the second. Do you really increase your confidence level, since you are just as good in both groups? I understand very well that the directed parathyroidectomy requires the PTH, but I just don’t understand the time management issue (the waiting time) for the gold standard operative procedure if PTH assay is added.

Armando E. Giuliano, MD, Santa Monica, Calif: This was a very nice and timely discussion. Currently, we are wrestling with whether to institute intraoperative PTH assay at our institution. When we looked back at our last 100 cases, it may have helped us in 1 or 2 of our patients who had minimally invasive parathyroidectomy, but I wonder if the cost is justified. You concluded that it did not help you but stated you will continue to do it. Could you share with us the cost of the equipment, the cost of the technologists and the cost of doing the assay? Should you really continue to do it in 4-gland exploration?

Clive S. Grant, MD, Rochester, Minn: The question that seems central to the decision about applying intraoperative PTH measurement to unilateral, minimal access parathyroidectomy is whether the PTH level remained elevated in patients in whom you visualized multiple enlarged glands at the time of your bilateral operation. Did the intraoperative PTH remain elevated until all enlarged glands were removed? Given your apparent skepticism about the value of intraoperative PTH, do you have confidence in utilizing the technique in minimal access parathyroidectomy?

Dr Prinz: Dr Kaplan points out some inadequacies of our follow-up. All of these patients have had queries to their primary care doctors to see if they have had any evidence of hypercalcemia. All have been negative. However, there were missing postoperative calcium or parathyroid hormone values either at 1-week or 1-month time frames, and that is why these patients were deleted.

The first question was, does this technique help the lesser-experienced parathyroid surgeon? I don’t know how to answer that since I am still learning from the technique. It does give you numbers to gauge the efficiency of your procedure, but I think you still need experience in how you interpret those numbers. If the problem for the inexperienced surgeon is finding an abnormal gland, the technique is probably not going to help.

The time of our follow-up was 1 month. We have continued to follow up patients with elevated PTH levels and borderline elevated calcium levels. We are very interested and concerned about what will become of these patients. We have not had patients who have dropped their iPTH levels down to normal and then rebounded to elevated levels. However, it is not uncommon to have a drop in the first 5-minute value after abnormal gland resection and then have a rise later in the 10-minute value. When that occurs we look for another gland if the level of that secondary elevation is out of the normal range.

We treated a small number of patients with secondary hyperparathyroidism. In my experience, the drop in PTH is somewhat delayed in this group, but the methodology is still a useful adjunct when operating on patients with secondary hyperparathyroidism.

Dr Shuck asked about our operative approach. During this study, we did do full exploration of both sides of the neck. The iPTH values were not supposed to influence us, but there is no question that they did have some effect. If we were looking for a missing gland that we presumed was normal, and the PTH values did drop to normal levels, we would terminate our operation and not persist in that endeavor as the study progressed. We have moved to doing focused or directed parathyroid exploration utilizing the intraoperative PTH levels as a means to give us confidence that we are removing all abnormal tissue. There is no question that we have had patients who did not drop appropriately after removing 1 abnormal gland and then converted that procedure to a more formal exploration of the neck.

Dr Giuliano asked about the cost. The setup that we showed originally cost about $1000 per patient. There are now less expensive ways of doing this on the market. We currently utilize an in-house assay that costs about $10 per sample, so approximately $50 to $100 is added to the cost of the procedure. If you are doing a focused operation, the time of the procedure does decrease and more than makes up for the expense of the intraoperative PTH value.