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A Single PTH Measurement on the First Postoperative Day Predicts the Need for Calcium and/or Calcitriol Supplementation following Total Thyroidectomy

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Cayo AK, Yen TW, Misustin SM, Wall K, Wilson SD, Evans DB, Wang TS. Predicting the need for calcium and calcitriol supplementation after total thyroidectomy: results of a prospective, randomized study. Surgery 2012;152:1059-67. Epub October 13, 2012.

SUMMARY

Background

Hypocalcemia from temporary hypoparathyroidism is a common postoperative sequela of total thyroidectomy. Identification of reliable predictors of postoperative calcium and vitamin D requirements would benefit patients by mitigating the risks of postoperative hypocalcemia while reducing unnecessary calcium and/or calcitriol supplementation. The authors of this study hypothesized that a single intact parathyroid hormone (PTH) measurement on the first postoperative day would reliably predict the need for postoperative calcium supplementation. They tested their hypothesis via a single–institution, randomized, prospective trial. They also sought to develop an algorithm for calcium and calcitriol supplementation for patients at risk for postoperative hypoparathyroidism. Although several other studies have evaluated the utility of postthyroidectomy PTH measurements, this is the first hypothesis-driven, randomized, prospective trial on the subject.

Methods

The authors conducted a prospective, randomized trial at a single institution over a 23-month period beginning in February 2010. Patients who were undergoing completion thyroidectomy or total thyroidectomy were included in the trial, and 143 completed the trial. Vitamin D levels were supplemented preoperatively. Routine calcium and vitamin D were not given in the immediate postoperative period. PTH was measured on the morning of the first postoperative day. The patients were stratified by PTH level and then randomly assigned into one of five groups with standard calcium and calcitriol doses. If PTH was >10 pg/ml, no supplementation was given. If PTH was <5 pg/ml, the patient was randomly assigned to calcium supplementation or calcium and calcitriol supplementation. If the PTH was 5 to 10 pg/ml, the patient was randomly assigned to either calcium supplementation or no supplementation. Demographic and clinical data were recorded, including preoperative and postoperative calcium, vitamin D, and PTH levels. Univariate and multivariate logistic-regression analyses were performed to determine the factors associated with symptomatic hypocalcemia or PTH <10 pg/ml.

Results

A total of 112 patients (78%) had a PTH ≥10 pg/ml on postoperative day 1. The remaining 31 patients were stratified and randomly assigned into supplementation groups. Five patients with PTH <5 pg/ml and 15 patients with PTH 5 to 10 pg/ml received calcium alone. Seven patients with PTH <5 pg/ml received calcium and calcitriol. Four patients with PTH of 5 to 10 pg/ml received no supplementation. In 10% of patients with a PTH ≥10 pg/ml and 48% with PTH <10 pg/ml, symptoms of hypocalcemia were reported within the first 72 hours after surgery. The specificity of PTH <10 pg/ml for symptomatic hypocalcemia was 86%. On multivariate analysis, young age and postoperative PTH were independent predictors of postoperative

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hypocalcemia. More extensive surgery did not predict a PTH <10 pg/ml. A total of 55% of patients with a PTH <10 pg/ml on postoperative day 1 were on calcium and calcitriol at 1 week after surgery, whereas no patients with a PTH ≥10 pg/ml on postoperative day 1 were on routine calcium or calcitriol at 1 week after surgery.

Conclusions

Symptomatic hypocalcemia developed in only 10% of patients with PTH ≥10 pg/ml and all were treated successfully with calcium supplements as needed. Symptomatic hypocalcemia developed in 48% of patients with PTH <10 pg/ml . Multivariate analysis yielded no independent predictors of PTH <10 pg/ml on postoperative day 1. The authors conclude that a PTH of ≥10 pg/ml on postoperative day 1 is a strong predictor of postoperative eucalcemia and have limited the use of routine calcium supplementation to patients with a PTH <10 pg/ml on postoperative day 1.

ANALYSIS AND COMMENTARY

This study suffers from some limitations that are clearly discussed in the manuscript. The most significant issue is that after randomization, the number of patients for each PTH <10 pg/ml treatment group was very small, limiting the ability to generate meaningful statistical analyses for these groups. In particular, there did not appear to be any predictors of PTH <10 pg/ml on postoperative day 1, including extent of surgery and number of autotransplanted glands. Nonetheless, the conclusion that PTH ≥10 pg/ml is a strong predictor of postoperative eucalcemia is not affected by this.

This study is the first randomized, prospective trial on the subject and expands on a prior retrospective study by the same authors wherein they determined that PTH on postoperative day 1 was more reliable in predicting independence from vitamin D supplementation than calcium on postoperative day 1 (1). In that study, they concluded that a PTH of >5 pg/ml on postoperative day 1 was indicative of not needing routine postoperative vitamin D supplementation. In a complementary study, Landry et al. retrospectively evaluated 156 patients who underwent thyroidectomy and concluded that calcium supplementation could be limited to the patients with a PTH of <6 pg/ml on postoperative day 1 (2). Sywak et al. measured PTH at 4 and 23 hours after surgery to determine whether either was predictive of hypocalcemia and found that both were predictive and performed equally well (3). Lombardi et al. more extensively evaluated the timing of postoperative PTH measurements by comparing PTH levels drawn at the end of surgery with those drawn at 2, 4, 6, 24, and 48 hours after surgery (4). They found that PTH <10 pg/ml measured 4 or 6 hours after surgery was 100% sensitive and 100% specific for predicting symptomatic hypocalcaemia. Wiseman et al. demonstrated in a cohort of 423 consecutive patients that an algorithmic approach to postoperative calcium replacement, based on PTH measured 1 hour after thyroidectomy, could reduce the risk of severe postoperative hypocalcemia (5). Finally, guidelines have also been developed by the Australian Endocrine Surgeons that cover the topic of postoperative PTH measurement and early discharge (6). In their literature review, they found that a normal PTH had a positive predictive value for eucalcemia of 92.3%. They recommend that all patients undergoing thyroidectomy have PTH drawn 4 hours after surgery and state that patients with a normal PTH can be safely discharged on the first postoperative day either with or without supplements. Patients with undetectable PTH, on the other hand, should be started early on calcium and calcitriol.

After reviewing the literature, it seems clear that measurement of postoperative PTH is useful in predicting the need for calcium and vitamin D analogs following total thyroidectomy. Several studies have

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evaluated the utility of postoperative PTH to prognosticate short- and long-term parathyroid function, and each has come to a similar conclusion. A normal postoperative PTH is a strong predictor of postoperative eucalcemia. This is particularly important now that thyroidectomy is performed as an outpatient procedure in many specialized centers, and the ability to stratify patients into groups of low and high probability of postoperative hypocalcemia could substantially impact the discharge protocol. Questions still remain, however, regarding the cost-effectiveness of routine postoperative measurement of PTH, with one study suggesting that routine calcium and vitamin D supplementation is actually less costly than selective replacement based on PTH levels (7).

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