



Parathormone response to thyroid surgery

Ronan A. Cahill, M.B., B.Ch., A.F.R.C.S.I.^a, Regina Harty, B.Sc.^b, Seamus Cotter, B.Sc.^b,
R. Gordon K. Watson, M.B., B.Ch., F.R.C.S.I.^{a,*}

^aDepartment of Surgery, Waterford Regional Hospital, Waterford, Ireland

^bDepartment of Biochemistry, Waterford Regional Hospital, Waterford, Ireland

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Abstract

Background: Confident determination of adequate residual parathyroid function early after thyroid surgery could facilitate the discharge of patients soon after their operation without the need for subsequent serum calcium monitoring and/or calcium and vitamin D supplementation.

Methods: Thirty-one patients who underwent 33 thyroid operations (22 unilateral lobectomies and 11 bilateral thyroid resections) were prospectively studied. Parathormone (PTH) levels were measured intraoperatively, and serum calcium was monitored before and after surgery to determine PTH and calcium homeostatic response to thyroid surgery.

Results: A significant decrease in circulating PTH occurred during 27 procedures, most markedly after specimen mobilization. Intraoperative PTH and postoperative calcium levels were lowest in those who underwent bilateral operations. Patients who underwent unilateral procedures experienced significant decreases in PTH but not postoperative calcium levels. A PTH level >50% of baseline predicted normocalcemia by postoperative day 3. However, PTH level did not accurately triage other patients' risk for postoperative hypocalcemia.

Conclusions: A decrease in PTH levels intraoperatively is a common event during both unilateral and bilateral thyroid operations. Although normal PTH levels at the end of surgery ensure normocalcemia after surgery, patients with low final PTH measurements may not develop significant hypocalcemia after surgery. © 2006 Excerpta Medica Inc. All rights reserved.

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Permanent hypoparathyroidism after thyroid surgery manifests as persistent hypocalcemia. This may result in increased patient discomfort and delayed discharge from the hospital as well as potentially provoke more serious complications such as tetany and cardiac dysrhythmias. However, transient hypocalcemia of little clinical consequence is a common occurrence after such operations. This confounds the early identification of patients likely to experience significant postoperative impairment of their calcium homeostatic mechanisms. Although parathyroid gland injury during surgery is implicated in the etiology of prolonged postoperative hypocalcemia, the recommended practice of

safeguarding these glands intraoperatively after their direct visualization [1,2] is undermined by the fact that the periglandular tissue dissection necessary to do so may actually compromise their vascular supply and so induce parathyroid dysfunction. Indeed, so difficult is the current inability to identify patients at risk of clinically significant hypocalcemia, some experts advocate a policy of routine postoperative supplementation with calcium and/or vitamin D to facilitate early discharge after surgery.

The development of enzyme-linked immunosorbent assay-linked parathormone (PTH) assay technology has allowed reliable determination of circulating PTH levels to be performed during surgery for adenomatous parathyroid disease. The adoption of this technique in thyroid surgery as a measure of the function of residual parathyroid tissue may be of great potential benefit both to reassure, and perhaps caution, the operating surgeon in the extent of neck dissection performed. Furthermore, it may also allow the early identification and treatment of patients at risk of prolonged hypocalcemia caused by hypoparathyroidism after their sur-

The Statgen Intraoperative PTH Analysis equipment (but no consumables) was supplied free of charge for the study by Cambridge Diagnostic Services (Cambridge, UK). No right of manuscript approval was sought by or granted to the company.

* Corresponding author. Tel.: +1-00353-51-848000; fax: +1-00353-51-848574.

E-mail address: rcahill@rcsi.ie

gery while facilitating early discharge without postoperative calcium monitoring and/or supplementation of those not at risk.

In this prospective clinical study, we examined the utility of intraoperative PTH assay in determining the parathyroid response to thyroid surgery and, in particular, its ability to distinguish those patients likely to develop significant hypocalcemia from those who will not.

Methods

After full approval of the protocol by our local Ethics Committee, all patients who were undergoing thyroid resection for any indication by a single surgeon (R. G. W) between October 2002 and June 2004 were offered participation in the study. All volunteers fully consented and were scheduled and prepared for surgery in the usual fashion. In addition, for the purposes of the study, fasting corrected calcium levels were measured both on the morning of surgery and thereafter, on a daily basis, for 72 hours after surgery. The normal range of calcium in our laboratory is 2.1 to 2.7 mmol/L with the correction for albumin levels being calculated by the following formula: corrected calcium = serum calcium + 0.8 (4 – serum albumin). Hypocalcemia was therefore present when the corrected calcium value decreased to <2.1 mmol/L. Patients also underwent further venesection during their surgery for measurement of serum osmolarity as well as PTH by enzyme-linked immunosorbent assay (Statgen Intraoperative PTH Analysis, Cambridge Diagnostic Services, Cambridge, UK) at four perioperative time points as follows: (1) after induction of anesthetic but before commencement of the operation; (2) immediately after sufficient mobilization the thyroid gland to allow excision of the gland; (3) immediately after resection of the gland; and (4) after surgery but before the patient emerges from the anesthetic. Supplementary calcium was administered after surgery only if the patient developed symptoms and/or signs of hypocalcemia (eg, parasthesia or carpopedal spasm) or if the corrected serum calcium level decreased to <1.8 mmol/L. All data were recorded on Microsoft Excel spreadsheets and analyzed using Analyse-It software (Analyse-it Software Ltd, Leeds, England). Statistical significance was defined as $P < .05$ using Mann-Whitney U test to analysis of differences between groups, and Fisher's Exact test was used to the determine significance of different proportions between groups.

Results

In all, 31 patients underwent 33 thyroid operations during the study period. The median age (interquartile range) of the study group was 43 (range 31 to 55) years. Twenty-eight patients were female, and 3 were male. All patients were

normocalcemic before surgery. Twenty-five individuals underwent surgery for nontoxic nodular goiters, 21 of whom had a unilateral thyroid lobectomy. The remaining 4 underwent total thyroidectomy. Two patients in the former group, however, subsequently underwent completion thyroidectomy after unsuspected neoplasia was discovered in their resected lobectomy specimens. An additional 5 patients had toxic goiters that were not suitable for medical therapy alone (4 required subtotal thyroidectomy for multinodular toxic goiters, and 1 underwent unilateral lobectomy for a solitary toxic nodule). One final patient underwent total thyroidectomy for a preoperatively diagnosed carcinoma. Therefore, in total, 22 unilateral thyroid lobectomies and 11 bilateral thyroid operations were performed. No patient had obvious parathyroid tissue excised as judged by intraoperative inspection and postoperative histologic scrutiny of the excised specimens.

The change in median corrected calcium level on each day after surgery for patients who underwent unilateral and bilateral operations is shown in Fig. 1a, whereas that for patients with hypocalcemia or normocalcemia on postoperative day 3 is shown in Fig. 1b. Seven patients (21%) had persistent hypocalcemia at 72 hours; 6 of these had undergone bilateral procedures. Three of these patients had calcium levels >2.0 mmol/L on postoperative day 3 (including the 1 patient who had undergone a unilateral procedure), whereas 3 had levels that were <1.9 mmol/L at this same time point. Only 1 patient developed symptoms related to hypocalcemia and received supplementary calcium. Those who were hypocalcemic on postoperative day 3 had significantly lower calcium levels on every day after surgery than those in the latter group ($P = .015$ on day 1; $P = .0002$ on day 2, and $P = .0005$ on day 3), with their most significant decrease in calcium occurring by postoperative day 1 ($P = .035$). In contrast, patients who were normocalcemic by postoperative day 3 had shown no significant change in their postoperative calcium levels on any day after surgery. Patients who underwent bilateral neck exploration were significantly more likely to remain hypocalcemic by postoperative day 3 than those who underwent unilateral procedures (45% v 5%, $P = .02$), and they also had significantly lower corrected calcium levels for the first 2 days after surgery ($P = .0016$ on day 1, and $P = .009$ on day 2).

The percentage decrease in median PTH level at each of the 4 intraoperatively measured time points in patients who underwent unilateral and bilateral procedures is shown in Fig. 2 as is that of patients who were either hypocalcemic and normocalcemic on day 3 after surgery. Although there was no decrease in circulating PTH levels during 5 operations (2 of which were bilateral procedures), a marked decrease in PTH level was apparent in 28 procedures. The most significant decrease occurred after mobilization of the specimen, but before its removal, with lesser (not statistically significant) changes occurring thereafter. Patients who underwent bilateral procedures had statistically significantly lower PTH levels at every intraoperative time point after

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