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# An intact parathyroid hormone–based protocol for the prevention and treatment of symptomatic hypocalcemia after thyroidectomy

Yvette Carter, MD, Herbert Chen, MD, and Rebecca S. Sippel, MD\*

Section of Endocrine Surgery, Department of Surgery, University of Wisconsin, Madison, Wisconsin

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### ABSTRACT

**Background:** Symptomatic (SX) hypocalcemia after thyroidectomy is a barrier to same day surgery and the cause of emergency room visits. A standard protocol of calcium and vitamin D supplementation, dependent on intact parathyroid hormone (iPTH) levels, can address this issue. How effective is it? When does it fail?

**Methods:** We performed a retrospective review of the prospective Thyroid database from January 2006 to December 2010. Six hundred twenty patients underwent completion thyroidectomy or total thyroidectomy and followed our postoperative protocol of calcium carbonate administration for iPTH levels  $\geq 10$  pg/mL and calcium carbonate and 0.25  $\mu$ g calcitriol twice a day for iPTH  $< 10$  pg/mL. Calcium and iPTH values, pathology, and medication were compared to evaluate protocol efficacy. A P value  $< 0.05$  was considered statistically significant. **Results:** Using the protocol, sixty-one (10.2%) patients were chemically hypocalcemic but never developed symptoms and 24 (3.9%) patients developed breakthrough SX hypocalcemia. The SX and asymptomatic groups were similar with regard to gender, cancer diagnosis, and preoperative calcium and iPTH. The SX group was significantly younger ( $39.6 \pm 2.8$  versus  $49 \pm 0.6$  y,  $P = 0.01$ ), with lower postoperative iPTH levels. Thirty-three percent ( $n = 8$ ) of SX patients had an iPTH  $\leq 5$  pg/mL versus only 6% ( $n = 37$ ) of ASX patients. Although the majority of patients with a iPTH  $\leq 5$  pg/mL were asymptomatic, 62.5% ( $n = 5$ ) of SX patients with iPTH levels  $\leq 5$  pg/mL required an increase in calcitriol dose to achieve both biochemical correction and symptom relief.

**Conclusions:** Prophylactic calcium and vitamin D supplementation based on postoperative iPTH levels can minimize SX hypocalcemia after thyroidectomy. An iPTH  $\leq 5$  pg/mL may warrant higher initial doses of calcitriol to prevent symptoms.

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## 1. Introduction

Hypocalcemia is the most common complication of thyroid surgery. Occurring most commonly after total thyroidectomy (TT) and completion thyroidectomy (CT), the incidence ranges

from 1.6% to 50% [1,2]. This incidence is dependent on the definition of hypocalcemia, what symptoms are included, permanent versus transient occurrence, and the type of resection. Even rarer is the occurrence of permanent hypoparathyroidism, ranging from 0% to 3%, according to the

\* Corresponding author. Section of Endocrine Surgery, Department of Surgery, University of Wisconsin, K3/704 Clinical Science Center, 600 Highland Avenue, Madison, WI 53792. Tel.: +1 608 263 1387; fax +1 608 263 7652.

E-mail address: [sippel@surgery.wisc.edu](mailto:sippel@surgery.wisc.edu) (R.S. Sippel).

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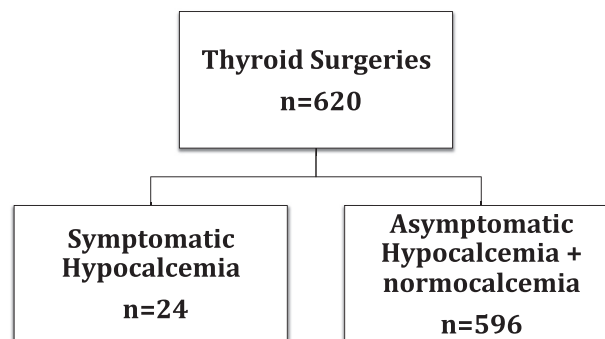
experience of most surgeons [1,3]. Regardless of the underlying cause, the symptoms can be debilitating, hence the need to minimize its occurrence. Studies have demonstrated the efficacy of supplemental calcium and/or vitamin D, in minimizing the occurrence of hypocalcemia and subsequent emergency room visits and hospital readmission [4–6]. Others have debated the efficacy and cost-effectiveness of standardized protocols, which provide supplementation to all patients. There are differences in the protocols used, including the utilization of ionized calcium versus serum calcium, the timing of postoperative laboratory values, and the dosage of vitamin D to administer [6–15]. There are also questions of whether prophylactic vitamin D supplementation further suppresses parathyroid function and hence recovery.

Here, we evaluate the efficacy of our postoperative parathyroid hormone (iPTH)-based protocol and attempt to identify any prognostic clinical factors, which would result in failure of the protocol.

## 2. Methods

We performed a retrospective review of our prospective Thyroid database from January 2006 to December 2010 and identified all patients who underwent a thyroid resection. Included in the study are all patients who underwent a TT or CT, either alone or in conjunction with another procedure. Both benign and malignant pathologies were included. We evaluated differences between patient demographics, including age, gender, preoperative diagnosis, and clinical parameters, including preoperative and postoperative calcium, intact parathyroid hormone (iPTH), operative procedure(s), pathologic diagnosis, hypocalcemia symptoms, and medications and their respective dosages. Patients were stratified into two groups, symptomatic (SX) and asymptomatic (ASX), for comparison (Fig. 1). In an effort to identify those patients with significant SX hypocalcemia while following the protocol, at least one of the following criteria had to be met (1) two or more episodes of perioral or extremity paresthesias, muscles aches, or cramps at any time in the postoperative period; (2) symptoms presenting on or persistent after postoperative d 3; (3) emergency room visitation; or (4) hospital readmission for hypocalcemia management.

Postoperative iPTH protocol: calcium and iPTH levels at 1–4 h postoperatively were evaluated (Elecsys; Roche Pharmaceuticals, Mannheim, Germany). The detection limit of the iPTH assay at our institution is down to <2 pg/mL, with a reference range of 14–72 pg/mL. Patients with an iPTH <10 pg/mL were given 2–6 g of oral calcium carbonate daily, scheduled and as needed for symptom relief, with 25 µg calcitriol twice daily. Patients with an iPTH ≥10 pg/mL were prescribed only 2–6 g daily of oral calcium carbonate scheduled and for symptom relief (Fig. 2). Verbal explanation of the postoperative protocol was discussed during the preoperative clinic visit and at the time of discharge. The initial calcium dosage was based on patient symptoms and the risk of hypocalcemia (i.e., surgery for Graves' disease). The patients were given instructions to start with 2 g of calcium, at the onset of symptoms. If the symptoms persisted or did not show



**Fig. 1 – Breakdown of thyroid resection patients and hypocalcemia from January 2006 to December 2010.**

signs of improvement, they were instructed to take an additional 1 g of calcium every 30 min, until symptom resolution. All SX patients were instructed to increase their scheduled calcium intake to 2 g three times a day, if they were not already taking that much. Patients were provided with written postoperative instructions, followed up by a mid-level practitioner, and had the first postoperative visit within 2 weeks of surgery.

SPSS statistical software (SPSS Inc, Chicago, IL) was used to analyze the data. Student t-test was used to determine the statistical significance between SX and ASX groups.

## 3. Results

From January 2006 to December 2010, 620 patients underwent either a TT or CT (Fig. 1). Five hundred ninety-six patients were classified into the ASX group. In addition to patients who never experienced symptoms of hypocalcemia, this group includes patients with biochemical hypocalcemia without symptoms, those who experienced very mild hypocalcemia symptoms (had two or less episodes of symptoms within 2 d of surgery), and those who did not follow the protocol and had symptom resolution on taking the previously recommended supplemental calcium. Twenty-four patients were considered SX (see definition in Materials and Methods section).

Both groups presented with similar preoperative diagnoses and pathologic results (Fig. 3). The SX group had a higher incidence of both Hashimoto's thyroiditis (16.7% versus 11.5%) and Graves' disease (12.4% versus 8.8%); however, this was not statistically significant, even when combining all causes of autoimmune thyroiditis. Women represented the majority of patients in both groups. The SX group was significantly younger ( $39.6 \pm 2.8$  versus  $49 \pm 0.6$  y,  $P = 0.01$ ) and had smaller thyroid glands ( $21.4 \pm 3.2$  versus  $39.6 \pm 1.8$  g,  $P < 0.001$ ). The size of the dominant nodule was similar in the two groups (Table 1). Parathyroid autotransplantations were performed in four (17%) patients in the SX group and 31 patients in the ASX group (5%) ( $P = 0.07$ ). None of the 24 SX patients had a parathyroid gland identified in their pathologic specimen.

Pre- and postoperative calcium levels were similar in the ASX group ( $9.7 \pm 0.4$  and  $9.9 \pm 0.03$  mg/dL), whereas the SX

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