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Pediatric thyroidectomy in a high volume thyroid surgery center: Risk factors for postoperative hypocalcemia☆

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ABSTRACT

Introduction: Hypocalcemia is a common complication following thyroid surgery. We seek to report on our experience in pediatric thyroidectomy in a high volume thyroid surgery center and accurately assess the incidence of postoperative hypocalcemia.

Materials and methods: A retrospective review of patients aged 18 and younger who underwent thyroid surgery between 1992 and 2013. The primary endpoints were the occurrence of postoperative hypocalcemia as by defined as a nadir calcium <8.0 mg/dL and being discharged on oral calcium supplementation, need for intravenous calcium and the occurrence of permanent hypoparathyroidism.

Results: 171 patients who underwent 186 thyroid operations were analyzed. The average age was 15.4 years with 82.3% female. The most common indications for surgery were nodular disease (74.7%) and hyperthyroidism (12.4%). 24 patients (12.9%) experienced postoperative hypocalcemia with 13 (7.0%) requiring intravenous calcium infusion. One patient (0.9%) experienced permanent hypoparathyroidism. Risk factors for postoperative hypocalcemia included total thyroidectomy (OR 7.39, $p < 0.01$), central and bilateral lateral neck dissection (OR 22.26, $p = 0.01$), Graves' disease (OR 3.99, $p = 0.02$), and malignancy (OR 2.96, $p = 0.03$).

Conclusions: Pediatric patients who undergo total thyroidectomy for underlying malignancy or Graves' disease and those who have more extensive nodal dissections are at increased risk of developing this postoperative hypocalcemia. These patients may benefit from more vigilant preoperative preparation and postoperative calcium and vitamin D supplementation.

Thyroidectomy in the pediatric population is a less frequently performed procedure than in adults and published reports noting patient volume and postoperative complications are highly variable. Hypocalcemia is the most common postoperative complication following thyroid surgery in children and adults and is often the cause of prolonged hospital stay and significant morbidity. It is caused by transient or permanent hypoparathyroidism owing to either disruption of the blood supply to the parathyroid glands or inadvertent removal of one or more glands. Symptoms of hypocalcemia are predominantly based on increases in neuromuscular excitability and range from perioral and peripheral paresthesias to generalized tetany.

The incidence of hypocalcemia varies widely depending on how it is defined in each study. In the adult population, rates ranging from 6% to 30% have often been reported [1–3]. Identified risk factors for postoperative hypocalcemia include total thyroidectomy [2,4], younger patient age [3], Graves' disease [5] and incidental parathyroidectomy [2,5]. Temporary hypocalcemia rates in children after thyroid surgery are reported to be between 7% and 52% [6–9]. However, these studies do not consistently define hypocalcemia.

Published data indicates higher postoperative morbidity following pediatric thyroidectomy when compared to the adult population [10–12]. This may be compounded by the relative rareness of pediatric thyroid surgery when compared to adults. However, as we move toward referring children who require thyroidectomy to high volume thyroid surgery centers, the literature suggests that complication rates are becoming more comparable with adult series [8].

In this study, we report on our experience with pediatric thyroidectomy from a high volume thyroid surgery center. We aim to accurately assess the incidence of hypocalcemia following pediatric thyroidectomy and analyze risk factors for this postoperative complication.

1. Materials and methods

We performed a retrospective analysis of all patients aged 18 or younger who underwent thyroid surgery and had their pathology analyzed at the Massachusetts General Hospital between July 1992 and April 2013. Patients who underwent an indicated parathyroidectomy

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at the time of thyroidectomy were excluded from the study. Patient demographics, indications for surgery, and preoperative work-up were obtained from the medical records. Operative and pathology reports were utilized to determine the extent of surgery and final pathological diagnosis.

We defined temporary hypocalcemia as a postoperative nadir calcium value <8.0 mg/dL and treatment with oral calcium supplementation or intravenous calcium during their hospitalization. Patients who were still taking oral calcium supplementation beyond 6 months postoperatively with a serum calcium value <8.0 mg/dL or parathyroid hormone (PTH) level <15 pg/mL were classified as having permanent hypoparathyroidism. Transient recurrent laryngeal nerve (RLN) injury was defined as postoperative hoarseness combined with a laryngoscopic diagnosis of RLN palsy although routine laryngeal examination was not performed. Patients were classified as having permanent RLN injury if these findings persisted beyond 6 months.

All patient data was recorded in Microsoft Excel for Windows 2010 and analyzed using SPSS (version 20, IBM SPSS). Continuous values were compared using the Mann–Whitney U test with the chi-square test utilized for categorical variables. Variables with a p-value of <0.20 were entered into a multivariate analysis. A p-value of <0.05 was considered statistically significant.

Ethics approval for this study was obtained through the Partners Human Research Committee.

2. Results

A total of 171 patients who underwent 186 thyroid operations were included in the study (Table 1). The mean age at time of operation was 15.4 years (range 2.5–18.9). 82.3% of patients were female. Indications for thyroid surgery were nodular disease (74.7%), hyperthyroidism (12.4%), completion thyroidectomy (8.1%) and multiple endocrine neoplasia (MEN) type 2 prophylaxis (4.8%). A family history of thyroid disease was reported by 75 of 160 patients (46.9%) with a specific history of thyroid malignancy in 19 (11.9%).

Table 1
Comparison of patients who did and did not experience postoperative hypocalcemia.

Variable		No hypocalcemia (n = 162)	Hypocalcemia (n = 24)	p-Value
Gender	Female	132 (81.5%)	21 (87.5%)	0.69
Age	≥14	124 (76.5%)	16 (66.7%)	0.42
Indication	Nodule	146 (90.1%)	17 (70.8%)	<**0.01**
	Hyperthyroidism	16 (9.9%)	7 (29.2%)	
	MEN2A prophylaxis	7 (4.3%)	2 (8.3%)	
	Completion	11 (6.8%)	4 (16.7%)	
Family hx thyroid disease	Yes	63 (38.9%)	12 (50%)	0.58
Family hx thyroid cancer	Yes	16 (9.9%)	3 (12.5%)	0.98
Operation	Hemithyroidectomy	79 (48.8%)	0	<**0.01**
	Total thyroidectomy	65 (40.1%)	20 (83.3%)	
	Nodulectomy	7 (4.3%)	0	
	Completion thyroid	11 (6.8%)	4 (16.7%)	
LN dissection	Yes	29 (17.9%)	10 (41.7%)	**0.01**
LN dissection extent	No	133 (82.1%)	14 (58.3%)	<**0.01**
	Yes, central	18 (11.1%)	5 (20.1%)	
	Yes, unilateral	10 (6.2%)	2 (8.3%)	
	Yes, bilateral	1 (0.6%)	3 (12.5%)	
Parathyroid	No	133 (82.1%)	17 (70.8%)	0.37
	Yes, reimplant	11 (6.8%)	2 (8.3%)	
	Yes, inadvertent	18 (11.1%)	5 (20.8%)	
Pathology	Benign	93 (57.4%)	4 (16.7%)	<**0.01**
	Graves	15 (9.3%)	7 (29.2%)	
	Hashimoto	8 (4.9%)	0	
	Malignant	46 (28.4%)	13 (54.2%)	
Median length of stay	Days (range)	1 (0–3)	2 (0–8)	<**0.01**

Thyroid ultrasound was the most commonly used imaging modality performed prior to initial surgery and was utilized in 138 patients (80.7%). Thyroid cytology via FNA was obtained in 98 patients (57.3%) and scintigraphy in 42 (24.6%). Genetic testing was positive in 10 patients (5.9%), resulting in the preoperative diagnosis of MEN type 2 in 8 patients, Cowden syndrome in 1 patient, and familial adenomatous polyposis in another.

The most common initial operation performed was a total thyroidectomy in 85 patients (45.7%). 15 patients (8.1%) underwent completion thyroidectomy following previous thyroid resection. A hemithyroidectomy was performed in 79 patients (42.5%) and a local excision or nodulectomy in 7 (3.8%). In addition to their thyroid resection, 39 patients (21.0%) also underwent a lymph node dissection. The extent of the neck dissection was limited to the central neck (level VI) alone in 23 patients (12.4%), while 12 patients (6.5%) underwent a central plus unilateral (levels II–IV) neck dissection and 4 patients (2.2%) underwent central plus bilateral neck dissection. Average lymph node yield for central neck dissection alone was 9, while it was 27 and 59 for dissection of the unilateral and bilateral lateral neck respectively. More than 85% of the operations were performed by adult thyroid surgeons.

The final pathology was benign in 127 cases (68.3%) with follicular adenoma (31.4%) and Graves' disease (11.9%) being the most common. The remaining 59 specimens (31.7%) were malignant, with 51 cases (27.4%) of papillary thyroid cancer, 5 (2.7%) of medullary thyroid cancer and 3 (1.6%) of follicular thyroid cancer. Of the patients with proven malignancy, 26 (44.1%) had evidence of lymph node metastases. There was evidence of inadvertent parathyroid gland removal in 36 patients (19.4%). 13 of these were autotransplanted back into the patient while the remaining 23 had parathyroid tissue reported in the final pathological specimen but were not reimplanted. Patients who had parathyroid gland resection were more likely to have had central and/or lateral nodal dissection (33% vs 18%, p = 0.04).

Average postoperative follow-up was 3 years (range 0–17 years) with 59.1% of patients having >6 months follow-up. In patients with malignant disease, mean follow-up was 4.6 years with 74.1% of patients having >6 months follow-up. 37 patients (19.9%) received postoperative radioactive iodine ablation therapy. At the time of last follow-up, 6 patients (10.1%) with malignant pathology had developed recurrent locoregional or metastatic disease.

Preoperative vitamin D levels were available in 19 patients with a mean 25(OH)D level of 31.6 ng/mL (range 12–85). Five patients had vitamin D deficiency (<20 ng/mL) and six patients had vitamin D insufficiency (21–30 ng/mL) as defined by the Endocrine Society [13]. Two patients with vitamin D deficiency experienced postoperative hypocalcemia and none with vitamin D insufficiency. However, this variable was not included in the univariate analysis given inadequate power.

Overall, 24 patients (12.9%) experienced temporary hypocalcemia in the immediate postoperative period with 13 patients (7.0%) requiring intravenous calcium administration. When considering only patients who underwent total or completion thyroidectomy, this rate was 24% and 13% respectively. At 6 months follow-up, only 1 patient (0.9%) had PTH <15 pg/mL and remained on calcium supplementation. This patient did eventually recover parathyroid function and her hypoparathyroidism had resolved by 12 months follow-up. As such, by 12 months months postoperatively, there were no cases of permanent hypoparathyroidism. There were 3 cases (1.6%) of temporary recurrent laryngeal nerve injury, but none was permanent. The overall median length of stay (LOS) was 1 day (range 0–8) following thyroid surgery. Patients who experienced temporary hypocalcemia had a median LOS of 2 days (p < 0.01).

On univariate analysis (Table 2), factors associated with an increased risk of postoperative hypocalcemia included total thyroidectomy (odds ratio (OR) 7.39, p < 0.01), need for lymph node dissection particularly combined central and bilateral neck dissection (OR 22.26, p = 0.01), and a final pathological diagnosis of either Graves' disease (OR 3.99, p = 0.02) or malignancy (OR 2.96, p = 0.03). Younger patients aged <14