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Original research

Prophylactic oral calcium supplementation therapy to prevent early post thyroidectomy hypocalcemia and evaluation of postoperative parathyroid hormone levels to detect hypocalcemia: A prospective randomized study

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HIGHLIGHTS

- Intravenous calcium was given to only 1.9% of patients.
- Oral calcium was given to 33.9% of patients in no supplementation group.
- Symptomatic hypocalcemia was found to be 1.9–33.9%.
- Hypoparathyroidism was observed in 8% of patients.

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ABSTRACT

Background: Postoperative hypocalcemia is the most common complication after total thyroidectomy. Postoperative parathyroid hormone (PTH) measurement is one of the methods to detect or prevent postoperative hypocalcemia. Prophylactic oral calcium supplementation is another method to prevent early postoperative hypocalcemia. The aim of this study is to detect the accurate timing of PTH and evaluate efficacy of routine oral calcium supplementation for postoperative hypocalcemia.

Methods: A total of 106 patients were performed total thyroidectomy. Rotuine oral calcium supplementation was given to group 1 and no treatment to group 2 according to randomization. Serum calcium and PTH level of patients in group 2 at postoperative 6, 12 and 24 h and patients in both groups at postoperative day 7 were evaluated. Patients were compared according to age, sex, operation findings, serum calcium and PTH levels and symptomatic hypocalcemia.

Results: Half of the patients (50%) were in group 1. Most of the patients were female (83%). The most common etiology of thyroid disease was multinodular goiter (64.1%). Oral calcium supplementation was given to 18 (33.9%) patients in group 2. Symptomatic hypocalcemia for group 1 and 2 was found to be 1.9 and 33.9% respectively ($p < 0.05$). No statistical difference can be observed regarding the timing of serum biomarkers.

Conclusion: Serum PTH levels at postoperative 12 and 24 h can predict early post-thyroidectomy hypocalcemia. Prophylactic oral calcium supplementation therapy can prevent early post-thyroidectomy hypocalcemia with advantages of being cost effective and safe.

1. Introduction

Postoperative hypocalcemia is the most common complication after total thyroidectomy. The incidence of hypocalcemia after total thyroidectomy ranges between 5 and 60% [1,2]. Devascularization or excision of parathyroid glands during thyroidectomy result in

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hypocalcemia. Hypocalcemia can be asymptomatic when there is mild decrease in serum calcium (Ca) levels or symptomatic when the patient has Chvostek's and Trousseau's signs and muscle spasms. Hypocalcemia typically occurs 24–48 h after the operation [3]. Most of the cases are transient however permanent hypocalcemia also can be seen.

Many protocols have been described to prevent or determine postoperative hypocalcemia such as; routine Ca supplementation, serial Ca and parathyroid hormone (PTH) monitoring [4–6]. Ca monitoring 48 h postoperatively is the widely accepted model. But it prolongs hospital stay and increases cost. Recently, there is a trend towards decreasing hospital stay and encouraging early discharge for thyroidectomy patients. Even some authors declared that same-day thyroidectomy can be performed safely and have low complication rates in the hands of experienced surgeons [7]. Therefore Ca monitoring and discharging patient 48 h postoperatively is being abandoned.

PTH monitoring was also evaluated by many studies. PTH monitoring 1, 6, 12 or 24 h postoperatively was investigated but there is no consensus on the timing of PTH monitoring [8–10]. Even some authors measured PTH level after skin closure [11]. All these efforts are for discharging patients earlier and determining which patient will have hypocalcemia.

Routine Ca supplementation is found to be effective and also have both advantages of discharging patients earlier and preventing symptoms of hypocalcemia [4,12]. The aim of this current study is to evaluate efficacy of routine oral calcium supplementation and determine which parathyroid hormone level monitoring best predicts postoperative hypocalcemia.

2. Materials and methods

A total of 136 patients were performed total thyroidectomy operation in Baskent University Adana Teaching and Research Center between August 2015 and January 2016. Of these patients 106 were eligible for our study. Patients between 18 and 65 years were included. Patients performed subtotal thyroidectomy or thyroid lobectomy and patients with preoperative abnormal serum calcium, parathyroid hormone, 25-OH vitamin D and albumin level were excluded. Data were prospectively collected and informed consent was taken. Random number table was used as simple randomization method in study cluster distribution. Website link "http://stattrek.com/statistics/random-number-generator.aspx" was used to create table. Patients were divided into two groups; routine Ca supplementation group (Group 1) and no supplementation group (Group 2). Preoperative serum albumin, calcium, parathyroid hormone, 25-OH vitamin D, hemoglobin, free-T3, free-T4 and TSH level were noted. Age, sex, body mass index, American Society of Anesthesiologist (ASA) score, etiology, thyroid fine needle aspiration (TFNA), presence of drain, blood loss, number of intraoperative preserved parathyroid hormone, operation time, pathology, complications, presence of hypocalcemia, intravenous and oral calcium supplementation were compared between groups. Total thyroidectomy was performed for all patients. 24 h after the operation, patients in Group 1 received routine oral calcium supplementation whereas patients in group 2 received none if symptomatic hypocalcemia was not observed. 7 days postoperatively serum calcium and parathyroid hormone level of all patients were collected. Postoperative 6, 12 and 24 h serum calcium and parathyroid hormone level of patients in group 2 were noted. If asymptomatic hypocalcemia or normal calcium level was present in these patients, they were discharged and controlled on postoperative day 7 at outpatient clinic. Oral or intravenous calcium supplementation was given in case of symptomatic hypocalcemia and serum calcium and parathyroid hormone level on postoperative day 7 was neglected. Symptomatic hypocalcemia was defined as; perioral or extremity paresthesia, muscle aches or cramps at any time postoperatively, symptoms persistent after postoperative day 3 or hospital readmission with hypocalcemia symptoms.

This study was approved by Baskent University Institutional Review Board (Project No: KA15/206) and supported by Baskent University Research Fund.

2.1. Surgical technique

Under general anesthesia the patient was positioned supine in 135° angle between legs and trunk. A sandbag was placed between the scapulae. The head was placed on a donut cushion, and the neck was hyper-extended. A Kocher transverse collar skin incision 4–6 cm in length was made 3 cm above suprastrenal notch. Subcutaneous tisse and the platysma muscles were incised and subplatysmal flap was created superiorly to the thyroid cartilage level and inferiorly to the suprasternal notch. The strap muscles were divided in the midline untill the thyroid was visible. Right or left side was approached first depending to the decision of the surgeon. The strap muscles were retracted by blunt and sharp dissection and the middle thyroid veins were ligated and divided. The upper pole was mobilized and vessels of the upper pole were ligated and divided individually. External branch of the superior laryngeal nerve injury was avoided at this point. Then lower pole of the thyroid was dissected. The inferior thyroid vessels were ligated and divided individually close to thyroid gland in order to minimize devascularization of parathyroid glands. Thyroid gland was retracted medially and superior parathyroid glands and recurrent laryngeal nerve were isolated. At this point caution was given to prevent injury to the nerve and devascularization of parathyroid glands. After that thyroid lobe was dissected above trachea and the same procedure was performed for the other lobe. The pyramidal lobe was also dissected and en-bloc dissection with both lobes was done. Mini negative pressure suction drain was placed according to the decision of the surgeon. In case of devascularized parathyroid glands after fragmentation into 1 mm pieces, re-implantation was done into the strap or sternocleidomastoid muscles of the ipsilateral side. After hemostasis the midline was closed with absorbable sutures. Subcutaneous tissue was closed with interrupted absorbable sutures and the skin with subcuticular absorbable sutures.

2.2. Serum calcium and parathyroid hormone assay

Postoperative day 7 serum calcium and parathyroid hormone level blood samples were collected from all patients in both groups. Patients in group 2 were evaluated for postoperative 6, 12 and 24 h serum calcium and parathyroid hormone level to determine which value best predicts hypocalcemia. All blood samples were kept under cold chain. Serum intact parathyroid hormone (i-PTH) and total calcium levels were calculated. ADVIA Centaur XP Immunoassay System® (Siemens Healthcare GmbH, Erlangen, Germany) was used for blood sample analysis. Normal serum calcium level was 8.4–10.2 mg/dL. Normal serum PTH level was 14–72 pg/mL.

2.3. Oral calcium supplementation therapy

Routine oral calcium supplementation was given to all patients in group 1 and patients with symptomatic hypocalcemia in group 2. Patients in group 2 without symptomatic hypocalcemia were warned for hypocalcemia symptoms. Calcimax D3® (Basel, Istanbul) including 2500 mg calcium carbonate and 880 IU vitamin D3 combination (Total 1000 mg iodized calcium) was prescribed to the patients in group 1 and symptomatic patients in group 2. Dosage