

Original Research Article

Timing of hypocalcemia after total or near total thyroidectomy: a prospective observational study

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ABSTRACT

Background: Hypocalcemia after thyroidectomy is the most common metabolic complication that prolongs the hospital stay. The aim of this study was to determine timing of hypocalcemia postoperatively and determine the safest day to discharge post-total or near-total thyroidectomy patients based on serum calcium level.

Methods: From October 2012 to January 2017, the medical records of 117 consecutive patients who underwent a total or near-total, completion or redo thyroidectomy for benign and malignant thyroid diseases in two university hospitals were prospectively analyzed. The serum calcium was measured preoperatively, on the morning on the first, second, third and fourth postoperative days and the postoperative day on which hypocalcemia developed was identified.

Results: Of the 117 patients who underwent a total or near thyroidectomy, 36 (30.7%) developed hypocalcemia, which was transient in 34 (29%) and permanent in two (1.7%) patients. The postoperative hypocalcemia was mild in 10 (8.5%) patients, and 26 (22.2%) patients developed significant postoperative hypocalcemia. Of the 36 patients who developed hypocalcemia postoperatively, the peak incidence of hypocalcemia (72.2%) was on the first postoperative day, and by the third day serum calcium measurement detected 97.3% of patients who developed hypocalcemia.

Conclusions: Postoperative serial serum calcium levels may be useful for identifying patients suitable for early discharge following total/near total thyroid surgery in hospitals that lack the facilities. Hypocalcemia peaked on the first postoperative day. However, based on serum calcium levels alone, the third postoperative day is the crucial day for deciding whether to discharge the patients.

Keywords: Hypocalcemia, Serum calcium, Thyroidectomy

INTRODUCTION

Hypocalcemia after thyroidectomy is the most common metabolic complication that prolongs the hospital stay.¹ In order to avoid prolonged hospital stay and allow a safe

early discharge, fast parathyroid hormone (PTH) assay is used as early as 10 minutes after surgery completion with or without serum calcium measurement to predict early postoperative hypocalcemia.¹ However, the fast PTH assay is not available in the majority of the hospitals in

low resource countries. Measurement of serum calcium in the morning after the surgery is considered a fast and low-cost method to assess parathyroid function in the early post-operative period.² The aim of this study was to determine timing of hypocalcemia postoperatively and determine the safest day to discharge post-total/near-total thyroidectomy patients based on serum calcium level.

METHODS

From October 2012 to January 2017, the medical records of 117 consecutive patients who underwent a total or near-total, completion or redo thyroidectomy for benign and malignant thyroid diseases at department of general surgery, in two university hospitals (Benghazi Medical Centre and Al-Jala Hospital) in Benghazi, Libya, were prospectively analyzed. Patients were excluded if they have pre-operative calcium or PTH levels outside the reference normal range of 8.4-10.2 mg/dl and 9.5-75 pg/ml respectively, renal insufficiency or are on pre-operative calcium replacement.

Patient details such as age, sex, and histopathological diagnosis were recorded. In addition, the following parameters were assessed:

- The serum calcium is measured pre-operatively, on the morning on the first, second, third and fourth postoperative days.
- Postoperative signs and symptoms of hypocalcemia,
- Postoperative day on which hypocalcemia develop and
- The length of postoperative hospital stay.

Mild hypocalcemia is defined as postoperative serum calcium level of less than 8.4 mg/dl but no value of less than 8.0 mg/dl. Significant hypocalcemia is defined as of less than 8.0 mg/dl or if there is clinical symptoms and signs of hypocalcemia (diffuse perioral or fingertip paresthesias, tetany, or a positive Chvostek sign).

Transient hypocalcemia was considered the drop in blood calcium levels below the normal range (reference value: 8.4-10.2 mg/dl) and lasting up to 6 months. Permanent hypoparathyroidism was defined as persistent hypocalcemia for more than 6 months of operation, requiring treatment with calcium.

Mild hypocalcemia is treated with oral calcium carbonate supplementation with or without calcitriol and patients with significant or symptomatic hypocalcemia receive intravenous calcium gluconate infusion according to local protocols. Parathyroid auto-graft in the ipsilateral sternocleidomastoid muscle was only performed in cases of endangered vascular supply or inadvertent excision.

All patients who developed postoperative hypocalcemia were followed up as an outpatient for at least 6 months after surgery and depending on postoperative endocrine status, each patient was instructed to follow a variable

follow up program by the endocrinologist in the endocrine clinic.

Statistical analysis

All statistical analyses were performed by using the Statistical Package for the Social Sciences (SPSS Inc.; Chicago, IL, USA), version 18.0 software program. The data was analyzed using the Chi-square test.

RESULTS

The study included 117 patients (83.3% female) with a mean age of 42.7 years (range, 17-75 years). Of the 117 patients who underwent a total or near-total thyroidectomy, 36 (30.7%) developed hypocalcemia, which was transient in 34 (29%) and permanent in two (1.7%) patients.

Table 1: The characteristics and histopathological diagnosis of patients (n=117).

Variables	Hypocalcaemia group (n=36)	Normocalcaemia group (n=81)
Mean age	42.5	42.8
Gender		
Male	2 (5.6)	14 (17.3)
Female	34 (94.4)	67 (82.7)
Type of operation		
Total or near total	33 (91.7)	71 (87.6)
Completion	2 (5.5)	6 (7.4)
Redo surgery	1 (2.8)	4 (5)
Indication of surgery		
Malignant	4 (11.1)	12 (14.8)
Benign	32 (88.9)	69 (85.2)
Histopathological diagnosis		
Papillary carcinoma	3 (8.3)	11 (13.6)
Follicular carcinoma	1 (2.8)	0
Hurthle cell carcinoma	0	1 (1.2)
Follicular adenoma	1 (2.8)	2 (2.5)
Hurthle cell adenoma	0	1 (1.2)
Grave's disease	0	5 (6.2)
Hashimoto thyroiditis	5 (13.9)	7 (8.6)
Multinodular Goiter	26 (72.7)	54 (66.7)
Parathyroid auto-transplantation	1 (2.8)	2 (2.5)

Data are presented as n (%); n = number; mean age

The postoperative hypocalcemia was mild in 10 (8.5%) patients, and 26 (22.2%) patients developed significant postoperative hypocalcemia. Two patients with a large multinodular goiter developed permanent postoperative hypocalcemia. Table 1 shows the patient characteristics and histopathological diagnoses.

Table 2: Timing of hypocalcaemia who developed mild or significant hypocalcaemia (n=36).

Appearance of hypocalcaemia	Number (%) of patients with hypocalcaemia	Mild N (%)	Significant N (%)
First day	26 (72.2)	8 (22.2)	18 (50)
Second day	3 (8.3)	1 (2.7)	2 (5.6)
Third day	6 (16.6)	1 (2.7)	5 (13.9)
Fourth day	1 (2.7)	0	1 (2.7)

Data are presented as n (%); n= number.

Of the 16 patients who underwent thyroidectomy for a suspected malignant neoplasm, four (25%) developed postoperative hypocalcemia, which was mild in one (6.25%) case and significant in three (18.75%) cases. Of the 101 patients who underwent thyroidectomy for benign disease, 32 (31.7%) developed postoperative hypocalcemia, which was mild in nine (8.9%) patients and significant in 23 (22.8%) patients.

Of the 36 patients who developed hypocalcemia after total/near-total thyroidectomy, hypocalcemia peaked on the first postoperative day in 26 patients (72.2%), on the second postoperative day in three patients (8.3%), on the third postoperative day in six patients (16.6%), and on the fourth postoperative day in one patient (2.7%, Table 2). The average postoperative hospital stay was 4.5 days, ranging from 4 to 9 days.

DISCUSSION

Hypocalcemia is the most common postoperative complication of total thyroidectomy. It varies from asymptomatic in majority of patients to symptomatic and potentially life-threatening in few patients which contributes to the length of hospital stay.³ Postoperative hypocalcemia is the result of transient or permanent hypoparathyroidism due to either from injury to or devascularization of one or more parathyroid glands.³ There is still controversy regarding the best method and time to predict postoperative transient or permanent hypoparathyroidism.⁴

Several retrospective and prospective studies have shown that postoperative serum iPTH measurement is an accurate predictor of postoperative hypocalcemia in patients who underwent total thyroidectomy.⁵⁻⁸ However, the high cost of monitoring and the lack of this facility in some hospitals, require identifying another method to predict both the patients at high risk of developing significant hypocalcemia, who need early treatment, and patients at low risk who are suitable for early discharge.

Serial measurement of serum calcium level postoperatively is a rapid and low-cost, that is available in every hospital. Some hospital protocols measure serum calcium daily for several days to detect rising levels before discharging the patient. Other protocols discharge the patients early on prophylactic calcium and vitamin D supplementation without the need of prolonged serum calcium monitoring.⁹ However, this routine calcium and vitamin D supplementation for every post-thyroidectomy patient is expensive and may expose the patient unnecessarily to side effects of calcium and vitamin D.³ Furthermore, early discharge of these patients might lead to readmission. Delbridge et al reported a 12% readmission rate for hypocalcemia in thyroidectomized patients who had undergone routine supplementation.¹⁰

Hypocalcemia usually manifests in the first or second postoperative day. Hence, monitoring of serum calcium postoperatively may miss patients with hypocalcemia if the patients are getting discharged on the first or second day after the surgery.¹¹ In the present study, serial measurement of serum calcium level was performed daily on the first, second, third and fourth postoperative days. It was found that in the 36 patients who developed hypocalcemia postoperatively, the peak incidence of hypocalcemia (72.2%) was on the 1st postoperative day, and by the 3rd day serum calcium measurement detected 97.3% of patients who developed hypocalcemia (Table 2).

In a prospective study by Sperlongano et al, hypocalcemia was found in 27 out of 180 patients following total thyroidectomy with 40.7%, 22.2%, 29.6%, 3.7% and 3.7% of patients developing hypocalcemia on the first, second, third, fourth and fifth postoperative days respectively.¹²

In another prospective study of 102 total thyroidectomy patients by Pasquale et al, 18 patients developed hypocalcemia, 38.8% of them in the first postoperative day, 22.2% in the second postoperative day, 33.3% in the third postoperative day, and 5.5% in the fourth postoperative day.¹³ Tredici et al reported a frequency rate of 50% of postoperative hypocalcemia in patients undergoing total thyroidectomy with 8% of patients developing hypocalcemia in the first postoperative day, 46% on the second day, 22% on the third day, and the remainder developed hypocalcemia on the 4th and 5th postoperative days.⁹

Asari et al conducted a study to determine whether measuring serum calcium on postoperative days 1 to 4 can predict hypoparathyroidism.⁴ They found that measuring serum calcium on the third postoperative day has the highest sensitivity (72.1%) for hypoparathyroidism compared with the first (18.6%), second (62.8%) and fourth (32.6%) post-operative days.⁴

The study results are consistent with the studies of Sperlongano et al and Pasquale et al in that the peak of

hypocalcemia was in the first postoperative day.^{12,13} However, it is noted that about 16.6-33.3% of patients developed hypocalcemia appeared in 3rd postoperative day. This account for a significant number of patients would be missed if they were discharged earlier on the first or second postoperative days. Based on measurement of serum calcium only, the 3rd postoperative day is the crucial day for deciding whether to discharge the patient or not.

It was recommended that, in hospitals that lack the facilities of fast iPTH testing, in all patients undergoing a total or near thyroidectomy to measure serum calcium on morning of first, second and third postoperative days. On third postoperative day, if the patient is hypocalcemic, start treatment; if not, discharge immediately. The patient instructed to measure serum calcium 24 hours after discharge (laboratory near patient's home), if hypocalcaemic, he should contact the clinician immediately.

CONCLUSION

Postoperative serial serum calcium level measurement may be useful in identifying patients suitable for early discharge following total/near-total thyroid surgery in hospitals that lack the facilities. The peak of hypocalcemia was in the first postoperative day. However, based on measurement of serum calcium only, the 3rd postoperative day is the crucial day for deciding whether to discharge the patient or not.

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