



Measurement of Intact Serum Parathormone and Corrected Serum Calcium after Thyroid Surgery

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Abstract

Postoperative hypocalcemia is an important complication of thyroid surgery. The present study was undertaken to measure the serum levels of intact parathormone (iPTH) and corrected serum calcium (CSC) in the immediate postoperative period and then sequentially till 1 month after thyroid surgery. A total of 36 patients undergoing total thyroidectomy and 44 undergoing hemithyroidectomy had measurement of the level of iPTH and CSC at 1 hour, 1 day, 1 week, and 1 month after surgery. A mean drop of 9.3% in CSC, 40% in iPTH, and 10% in ionic calcium levels was noted 1 hour after total thyroidectomy. All the patients recovered to near preoperative levels at the 1-month follow-up. Among hemithyroidectomy patients, significant postsurgery drop in levels was not observed. The importance of the study is early recognition of a hypoparathyroid state at 1 hour after surgery and institution of calcium replacement, thereby sparing the patient from unpleasant symptoms of hypocalcemia. Furthermore, patients with a drop in the iPTH levels below the defined hypoparathyroidism levels should have careful evaluation of their thyroidectomy specimen for identification and possible autotransplantation of the parathyroid gland intraoperatively or in the immediate postoperative time frame.

Keywords

- ▶ corrected serum calcium
- ▶ serum parathormone
- ▶ thyroid surgery

Neurological injuries and hypocalcemia are the most common complications that can occur after thyroid surgery. Although the incidence of these complications has been steadily declining over the years, when they occur they can lead to serious morbidity and occasional mortality as well.

Postoperative hypocalcemia is secondary to inadvertent removal of the parathyroid glands or their devascularization

during dissection. The incidence of hypoparathyroidism after thyroid surgery has been reported to vary from 14 to 60% for temporary hypoparathyroidism and 1.5 to 11% for permanent hypoparathyroidism.¹ Clinical manifestations of hypocalcemia may vary from perioral, hand, and foot numbness to muscle spasm, depression, hallucination, weak and brittle nails and easily fracturing bones. Furthermore, there are several

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confounding factors such as age, gender, vitamin D status, pH of blood, thyroid function status, and pathology (benign vs. malignant), which can affect postoperative calcium status besides the inadvertent damage to the parathyroids.

The present study was undertaken to evaluate the serum levels of intact parathormone (iPTH) and corrected serum calcium (CSC) in the immediate postsurgery period and in the follow-up period up to 1 month after thyroid surgery.

Patients and Methods

This prospective observational study was conducted over a 3-year period from April 2017 to March 2020, during which 80 patients requiring thyroid surgery were recruited. Out of these, 44 patients underwent hemithyroidectomy and 36 were subjected to total thyroidectomy. The exclusion criteria for patient data accrual for this study were the following:

- Preoperative abnormal serum iPTH (<15 or >51 pg/mL).
- Preoperative abnormal CSC level (<8.5 or >10.5 mg/dL).
- Patient on calcium supplement.
- Patient with abnormal thyroid function, renal function, and hypoalbuminemia.

The intent of including patients undergoing hemithyroidectomy was to demonstrate that there were no extraneous factors, such as anesthetic agents or perioperative medication, that could have influenced the iPTH and CSC levels.

The diagnosis of goiter was confirmed on the basis of clinical evaluation, thyroid ultrasound, thyroid function test, and fine-needle aspiration cytology (FNAC). All the patients had a preoperative measurement of the serum level of intact parathormone (iPTH), CSC, and ionized serum calcium. Repeat evaluation of these parameters was done 1 hour, 1 day, 1 week, and 1 month after surgery.

For iPTH measurement, 2 mL of blood was collected in ice-cooled ethylenediaminetetraacetic acid (EDTA) vial using an overnight ice-cooled syringe. The sample was immediately centrifuged in a refrigerated centrifuge at 4°C and the lab estimation by chemiluminescence method was done as quickly as possible. For ionic calcium, 1 mL of arterial blood was collected in a heparinized syringe free of air. The ionic calcium estimation was done by the ion-selective electrode (ISE) method used for arterial blood gas estimations. CSC was estimated by the following formula: $CSC = \text{patient serum calcium (mg/dL)} + 0.8 (4 - \text{patient serum albumin in g/dL})$.

The normal lab reference range of the three parameters were the following:

- CSC: 8.5 to 10.5 mg/dL.
- iPTH: 15 to 51 pg/mL.
- Ionic calcium: 1.0 to 1.30 mmol/L.

Evaluation for clinical features of hypocalcemia was done by (1) asking patients about the perioral and acral paresthesia, tingling, or numbness, (2) Trousseau's sign of latent tetany, (3) Chvostek's sign, and (4) evidence of spontaneous carpedal spasm or generalized tetany. Trousseau's sign was elicited by inflating the blood pressure cuff to pressure greater than systolic blood pressure and holding it for

3 minutes. Spasm of muscles of the hand and forearm indicated a positive sign. Chvostek's sign was elicited by tapping in front of the ear. Ipsilateral facial muscle spasm indicated a positive sign.

The end point of the study was 1 month after the thyroid surgery at which time CSC, iPTH, and ionic calcium levels were measured again. Values less than the lower limit of reference range were considered hypocalcemic (<8.5 mg/dL of CSC or <1.0 mmol/L of ionic calcium) or hypoparathyroid (<15 pg/mL of iPTH).

Observations

A total of 80 patients who underwent hemithyroidectomy (44) or total thyroidectomy (36) over a 3-year period were included in the study. The mean age of the patients was 43 years (range: 22–68 years) and the gender distribution was 19 males to 61 females (M:F::1:3.2). All patients had a goiter and the preoperative diagnosis were the following: (1) solitary thyroid nodule ($n = 44$); (2) multinodular goiter ($n = 27$); (3) well-differentiated thyroid cancer ($n = 5$), and (4) chronic lymphocytic thyroiditis ($n = 4$).

All patients underwent surgery under general anesthesia with muscle relaxation. The salient features of the operative procedure were the following:

- Capsular ligation of the branches of the inferior thyroid artery.
- Routine attempt at identification of at least one or two parathyroid glands prior to vessel ligation.

Among the 36 patients undergoing total thyroidectomy, we could reliably identify 1 or 2 parathyroid glands in 28 patients. On examination of the resected total thyroidectomy specimen, we could identify one or two parathyroid glands in three specimens. However, autotransplantation was not done in any of the patients because intraoperative preservation of at least one parathyroid gland was demonstrated in the thyroid bed.

Among the 44 patients who underwent hemithyroidectomy, the mean baseline (preoperative) iPTH levels were 35.6 ± 11.6 pg/mL. One hour after hemithyroidectomy, the mean iPTH was 33.4 ± 10.2 pg/mL, which was a 6% drop over the baseline value. At 1 day after surgery, the iPTH rebounded to 43.8 ± 9.8 pg/mL, it was 41.5 ± 10.4 pg/mL at 1 week, and stabilized at 38.4 ± 9.1 pg/mL at 1 month after hemithyroidectomy (► **Table 1**).

Among the 36 patients who underwent total thyroidectomy, the mean baseline (preoperative) iPTH was 39.4 ± 11.9 pg/mL, which dropped by 40% to 23.4 ± 17.5 pg/mL 1 hour after surgery and gradually recovered to 28.6 ± 17.8 pg/mL at 1 day, 30.2 ± 16.2 pg/mL at 1 week, and stabilized at 36.1 ± 13.0 pg/mL 1 month after total thyroidectomy (► **Table 1**, ► **Fig. 1**).

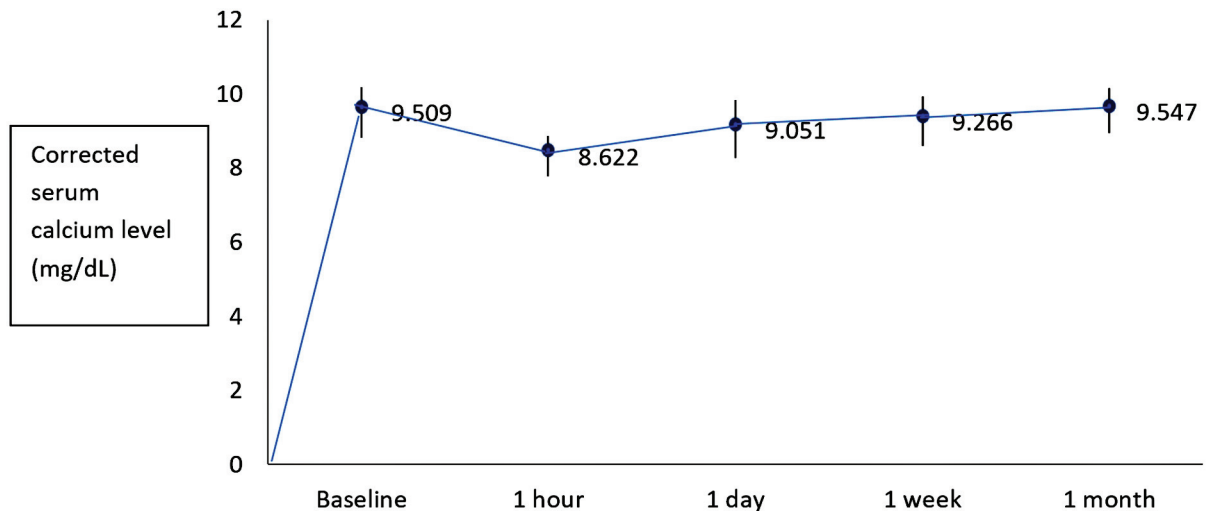
The mean value of CSC in the two groups followed a similar pattern. In the hemithyroidectomy patients, the mean baseline CSC was 9.55 ± 0.77 mg/dL, which dropped by 2.8% 1 hour after surgery and recovered to normal levels at 1 day postoperatively. Among total thyroidectomy patients, the mean baseline CSC was 9.5 ± 0.68 mg/dL, which dropped

Table 1 Serum iPTH levels at baseline and at 1 hour, 1 day, 1 week, and 1 month after surgery

	Hemithyroidectomy (n = 44)	Total thyroidectomy (n = 36)
iPTH baseline (pg/mL)	35.598 ± 11.6320	39.348 ± 11.9700
iPTH 1 h after surgery (pg/mL)	33.427 ± 10.2710 (-6%)	23.416 ± 17.5015 (-40%)
iPTH after 1 d (pg/mL)	43.883 ± 9.8528 (+23%)	28.615 ± 17.8183 (-27%)
iPTH after 1 wk (pg/mL)	41.598 ± 10.4965 (+17%)	30.275 ± 16.2366 (-23%)
iPTH after 1 mo (pg/mL)	38.445 ± 9.1708 (+8%)	36.133 ± 13.0558 (-8%)

Abbreviation: iPTH, intact parathormone.

Note: Values in bracket represent percentage change over base line values.

**Fig. 1** Sequential values of corrected serum calcium (CSC) after total thyroidectomy (n = 36) at baseline, 1 hour, 1 day, 1 week, and 1 month after surgery.**Table 2** Corrected serum (CS) calcium levels at baseline and at 1 hour, 1 day, 1 week, and 1 month after surgery

	Hemithyroidectomy (n = 44)	Total thyroidectomy (n = 36)
CS calcium baseline (mg/dL)	9.550 ± 0.7793	9.509 ± 0.6827
CS calcium 1 h after surgery (mg/dL)	9.283 ± 0.8031 (-2.8%)	8.622 ± 0.5533 (-9.3%)
CS calcium after 1 d	9.694 ± 0.5536 (+1.5%)	9.051 ± 0.7858 (-4.8%)
CS calcium after 1 wk (mg/dL)	9.886 ± 0.4084 (+3.5%)	9.266 ± 0.6676 (-2.6%)
CS calcium after 1 mo (mg/dL)	9.939 ± 0.3711 (+4.1%)	9.547 ± 0.6025 (+0.4%)

Note: Values in bracket are percentage change over the baseline values.

by 9.3% 1 hour after surgery and remained below the baseline value by 2.6% at 1 week after surgery. Stabilization of the CSC level was seen at 1 month after total thyroidectomy compared to 1 day after hemithyroidectomy (►Table 2, ►Fig. 2).

At 1 hour post total thyroidectomy, the CSC level was found to be less than 8.5 mg/dL in 12 patients (33%), which is our defined lower limit for normal CSC range. At 1 month of follow-up, none of the patients had CSC value less than the normal range (►Table 3).

On clinical evaluation on the evening of surgery, of the 36 patients who underwent total thyroidectomy, occult clinical

evidence of hypocalcemia such as perioral or acral tingling or numbness, Trousseau's sign and Chvostek's sign could be evoked by subtle questions or sign elicitation technique in 6 patients. Among these three patients had CSC <8.5 mg/dL and three had CSC >8.5 mg/dL. None of the patients developed spontaneous carpedal spasm or generalized tetany. All patients had recovery of their clinical signs within 2 to 4 days of surgery. Only 1 of 44 hemithyroidectomy patients complained of perioral paresthesia on enquiry.

In none of the hemithyroidectomy patients did the iPTH level fall to <15 pg/mL, which is the usually accepted

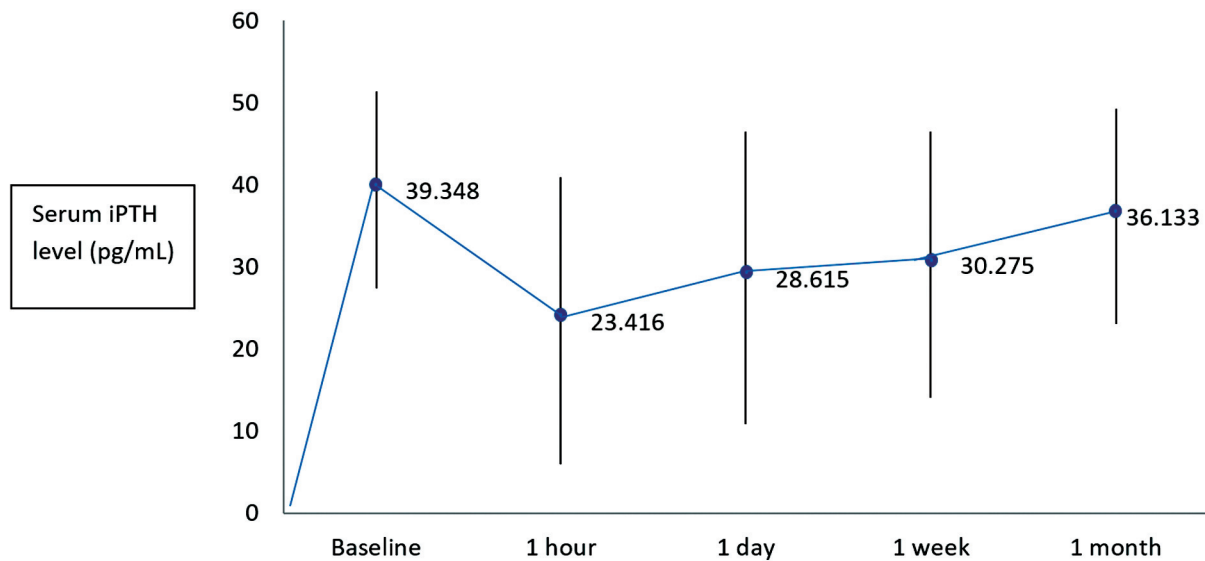


Fig. 2 Sequential values of iPTH after total thyroidectomy ($n=36$) at baseline, 1 hour, 1 day, 1 week and 1 month after surgery.

Table 3 Follow-up of total thyroidectomy patients ($n=36$) whose immediate postoperative iPTH level fell to less than 15 pg/mL and CSC level below 8.5 mg/dL

	At 1 h postoperative	At 1 mo postoperative
iPTH <15 pg/mL + CSC <8.5 mg/dL at 1 h postoperatively (both less than normal range values)	4 (11%)	Nil
Only CSC <8.5 mg/dL (normal iPTH)	8 (22%)	Nil
Only iPTH <15 mg/dL (normal CSC)	1 (3%)	Nil

Abbreviation: CSC, corrected serum calcium, iPTH, intact parathormone.

definition for hypoparathyroidism. Among the 36 total thyroidectomy patients, the iPTH level fell to <15 pg/mL in 5 patients (14%) immediately after surgery although it showed a gradual recovery to near baseline levels in 3 patients. In the remaining two patients, it was 22 and 25 pg/mL at 1 month postoperatively (→ **Table 3**).

Discussion

Hypocalcemia is an important potential complication after thyroid surgery. It is almost exclusively seen after total thyroidectomy specially when central neck node dissection (level VI cervical lymph nodes) is combined with thyroid surgery.² The reported incidence of post thyroidectomy hypocalcemia varies widely from 1 to 50%.³ In the present study, none of the patients who underwent hemithyroidectomy ($n=44$) experienced significant immediate postoperative hypocalcemia, while there was an average drop of 9.3% in CSC and 40% drop in the iPTH level at 1 hour after total thyroidectomy ($n=36$). This is only to be expected because during hemithyroidectomy there can be possible damage to a maximum of two parathyroid glands, while during total thyroidectomy, all four parathyroid glands are at risk of

unintentional removal, devascularization, or surgical stunning due to manipulation.

An important observation in our study was the finding that biochemical hypocalcemia did not demonstrate a linear association with symptoms of hypocalcemia or their severity. None of our patients exhibited obvious clinical signs of hypocalcemia such as spontaneous carpopedal spasm or generalized tetany. However, occult symptoms or signs were evident on day 1 postoperatively in 6 (of 36) patients who underwent total thyroidectomy and 1 (of 44) patient who underwent hemithyroidectomy. These occult manifestations were perioral and acral tingling or numbness, Trousseau's sign, or Chvostek's sign, all of which needed to be elicited by subtle questions or drawn out by the appropriate sign elicitation technique (→ **Table 4**).

Out of 12 patients of total thyroidectomy who had CSC <8.5 mg/dL at 1 hour postoperatively, 3 (25%) exhibited occult clinical features of hypocalcemia. Among the 24 patients who had CSC >8.5 mg/dL, 3 (12.5%) also exhibited occult clinical features of hypocalcemia. In none of these six patients, the signs of occult hypocalcemia could be demonstrated beyond 4 days. It is well known that symptoms of hypocalcemia depend on several other factors besides the

Table 4 Clinical features suggestive of hypocalcemia after thyroid surgery

	Hemithyroidectomy (n = 44)	Total thyroidectomy (n = 36)	
		With CSC <8.5 mg/dL (n = 12) at 1 h post-op	With CSC >8.5 mg/dL (n = 24) at 1 h post-op
Occult symptoms and signs of hypocalcemia (perioral and acral paresthesia, tingling or numbness, Trousseau's or Chvostek's sign)	1 (2.2%)	3 (25%)	3 (12.5%)
Obvious symptoms or signs of hypocalcemia (carpopedal spasm, generalized tetany)	Nil	Nil	Nil

Abbreviation: CSC, corrected serum calcium.

absolute serum calcium values. These factors are (1) fraction of ionic serum calcium, (2) pH of blood, (3) patient receiving calcium supplementation in diet or medication, (4) hydration status, and (5) serum magnesium levels. An additional scenario could be patients who have been chronically calcium deficient and have therefore become acclimatized to low serum calcium levels.⁴

Postsurgical hypoparathyroidism is defined as reduction of the serum iPTH level below 15 pg/mL or decline of CSC <8.5 mg/dL or ionized calcium below 4.4 mg/dL or 1.05 mmol/L with or without symptoms of hypocalcemia.⁵ Transient hypoparathyroidism is defined as resolution of hypocalcemia without treatment within 6 to 12 months. Permanent hypocalcemia has been reported to occur between 0 and 43%. This large variation is due to heterogeneity among reports as to the definition and duration of hypocalcemia.⁶

The half-life of parathyroid hormone in circulation is about 5 minutes or less.⁷ Therefore, intraoperative or very early postoperative measurement of serum iPTH can be a reliable indicator of the status of parathyroid during thyroid surgery. This property of iPTH is also utilized by surgeons for intraoperative assessment of adequacy of parathyroid tumor removal during surgery for hyperparathyroidism. For the purpose of this study, we utilized this attribute of iPTH for parathyroid status assessment even 1 hour after surgery.

The present study has demonstrated that none of our post thyroidectomy patients including the 36 who underwent total thyroidectomy had persistent hypocalcemia at 1 month after surgery. However, there was a drop of 9.3% in the CSC level, 40% in the iPTH level, and 10% in the iCa level at 1 hour after total thyroidectomy. This was followed by a very rapid recovery and the CSC levels improved to -4.8% below the lower baseline at 1 day, -2.6% at 1 week, and +0.4% at 1 month after total thyroidectomy. Similarly the corresponding values for iPTH at 1 day, 1 week, and 1 month were -27%, -23%, and -8% (► **Figs. 1, 2 and 3**). A total of 12 patients attained the defined level of hypocalcemia at 1 hour after surgery. Importantly, only occult clinical features could be elicited in only three of them as well as three who had a CSC level of >8.5 mg/dL. The immediate postoperative drop in the

iPTH and CSC levels could be attributed to one of the following three hypotheses:

- Inadvertent removal of two or three of the parathyroid glands.
- Devascularization of the parathyroids during thyroid lobe mobilization.
- Stunning effect of dissection around the parathyroid glands.

The parathyroid glands are regarded as the “calcium thermostat” of the body. It is pertinent to note that calcitonin-producing cells in the thyroid are removed completely during total thyroidectomy. The normal homeostasis of serum calcium levels is maintained by a fine interplay between iPTH and calcitonin. How this balance of hormones with antagonistic functions is affected after total thyroidectomy has not been satisfactorily explained.

The present study has demonstrated that immediate post-thyroidectomy measurement of iPTH can be a reliable method to assess the possible damage or removal of the parathyroid gland after total thyroidectomy. Identification of such patients can be important for early institution of calcium supplementation therapy and sparing the patients from unpleasant symptoms. Such patients can be monitored till recovery of CSC, which is likely to occur in a few weeks' time.

Another important inference from this study is that patients who demonstrate a fall in iPTH at one hour after total thyroidectomy should have a very careful examination of their thyroidectomy specimen before it is dipped in formalin to look for inadvertently removed parathyroid glands. If found then auto transplantation of one or two of the identified glands can be done under local anesthesia in the brachioradialis muscle immediately thus sparing patient from potential permanent hypo-parathyroid state. For the purpose of intra-operative iPTH level estimation the rapid immunochemiluminescence assay should be performed. This can be completed within 8 to 20 minutes allowing the surgeon to make intra-operative decisions. The intra-operative iPTH assay can be performed in or close to the operating room to avoid delay caused by sample transport.

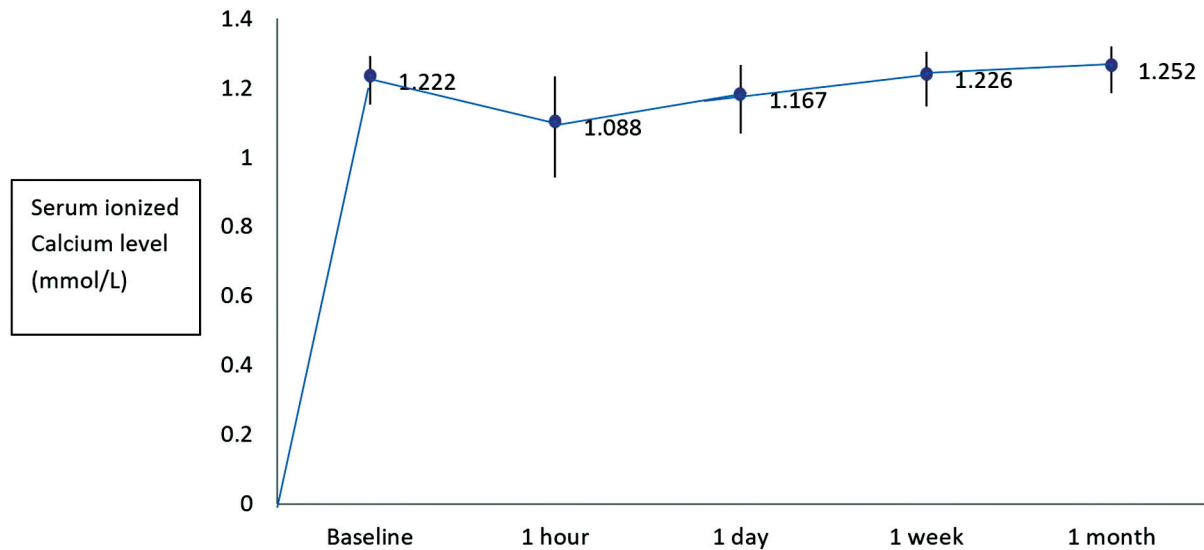


Fig. 3 Sequential values of ionic calcium after total thyroidectomy ($n = 36$) at baseline, 1 hour, 1 day, 1 week and 1 month after surgery.

Conclusion

We observed a 9.3% drop in CSC, 40% drop in iPTH, and 10% drop in ionic calcium levels at 1 hour after total thyroidectomy. The values returned to near-normal levels at 1 month postoperatively in all patients. Although occult symptoms or signs of hypocalcemia could be evoked in first 4 days after surgery in six patients (16%) undergoing total thyroidectomy, obvious clinical features did not appear in any of our patients. As per expectations, drop in serum calcium or iPTH was not observed among hemithyroidectomy patients. Early institution of calcium replacement may be started on the basis of 1 hour post-thyroidectomy iPTH levels to spare the patients from unpleasant symptoms of hypocalcemia. Furthermore, effort should be made to identify the parathyroid glands in the thyroidectomy specimen and consider it for autotransplantation if the 1-hour iPTH falls to below defined hypoparathyroidism levels.

Ethical Approval Statement

The study was a part of MS (surgery) thesis protocol of Dr. Sweety Kumari and was duly approved by the institutional ethics committee and the PG medical board.

Conflict of Interest

None declared.

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