Parathyroid Gland Injuries Post Total Thyroidectomy

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Abstract: Background: Postoperative hypocalcaemia is observed in total thyroidectomy patients and it is the most common complication. It is usually transient, and the incidence of permanent hyperparathyroidism is 3% or less. Despite being self-limiting in most patients, symptomatic hypocalcaemia is of particular concern because of a delay in its manifestation and the consequent need for prolonged patient hospitalization or readmission. **Objective:** The aim is to evaluate the risk of hypocalcaemia (transient or permanent) after total thyroidectomy for goiter, the frequency and impact of unintentional parathyroidectomy. **Patient and Methods:** In this randomized prospective study, we surveyed 50 patients who were admitted in the General Surgery Department, Ain-shams University Hospital, during the period from December 2017 and December 2018 with benign thyroid diseases such as simple multinodular goiter, secondary toxic goiter, diffuse toxic goiter relapsing after full medical treatment, selected cases of thyroiditis (Hashimoto's thyroiditis) and thyroid cancer. **Results:** We found ten cases with transient hypocalcaemia with multinodulargoiter, secondary toxic goiter and papillary carcinoma, whereas no selected cases of permenant hypocalcemia. The typical signs and symptoms associated with hypocalcaemia are neuromuscular irritability, including perioral or acralparesthesia, muscle cramps that may progress to carpopedal spasm, laryngospasm, bronchospasm or even tetany. Treatment is based on the severity of symptoms. Symptomatic hypocalcemic patients were treated with IV calcium supplementations intravenous calcium (10 ml 10% calcium gluconate in 100 ml of normal saline IV over 10 min) till the patients become asymptomatic followed with maintenance therapy of 1-3 mg of calcium gluconate/kg/h usually over the first 24 to 48 h postoperatively and shift to oral calcium (1.5 gm / day) and Vit D (Calcitriol 1.5 ug/day) supplements, the infusion rate is titrated to keep the serum calcium level in the low normal range. **Conclusion:** Transient hypocalcemia is a frequent complication of total thyroidectomy despite careful and meticulous surgical technique. Unintentional parathyroidectomy is uncommon complication of total thyroidectomy and there is no significant relation between histopathological nature of thyroid and unintentional parathyroidectomy and no statistical relation between unintentional parathyroidectomy and transient hypocalcemia.

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1. Introduction

Surgical destruction of the parathyroid glands is the most common cause of hypoparathyroidism. Hypoparathyroidism can occur after any surgical procedure that involves the anterior neck, but it is most commonly seen as a complication of parathyroid surgery or thyroid surgery or after extensive resection for head and neck cancer. Trauma to the parathyroid vascular pedicles or inadvertent removal of the glands leads to either transient or permanent hyperparathyroidism (**Clark et al., 2005).**

Hypocalcaemia is the most common complication of thyroidectomy. The incidence of transient hypocalcaemia ranges from 10% to 50%, and permanent hypocalcaemia usually occurs in 0%–2% of patients according to different definitions. It is known that not all patients with hypocalcaemia will have associated symptoms such as numbness and spasm. Some surgeons advocated prolonged stays that are not cost-effective nowadays. Meanwhile, when most of the surgeons' discharge patients within 24 hours, more emergency room visits or emergency calcium intravenous infusions would also occur. With the increasing preference for shorter stays, identifying patients at high risk is essential for their timely and safe discharge **(Noordzij et al., 2009).**

Several anatomical considerations must be considered during thyroid surgery, the arteries and veins of the thyroid gland; the position of the parathyroid glands and the position of the laryngeal nerves. The most significant complication is recurrent laryngeal nerve palsy, which can cause severe dysphonia and dysphagia, with serious social repercussions. However, permanent hypoparathyroidism is another serious complication which can sometimes be difficult to manage (**Sasson, Pingpank, 2011).**

In recent years, multiple retrospective studies have approved that the absolute value of postoperative serum parathyroid hormone (PTH) is an accurate predictor of hypocalcaemia in postoperative patients (**Vescan et al., 2005).**

Iatrogenic injury of the parathyroid glands is an unintended consequence of total thyroidectomy. Measuring the serum parathyroid hormone (PTH) immediately after surgery is a sensitive and specific method of assessing the function of the parathyroid glands and for identifying patients at risk for hypocalcaemia. If the postoperative PTH level is low, then administering calcium and activated vitamin D (calcitriol) can reduce the incidence of symptomatic hypocalcaemia, the incidence of a low postoperative PTH after total thyroidectomy has been highly variable in the literature, ranging between 7% and 37%. Part of this variability is related to the variety of methods used to define this complication (**Edafe et al., 2014).**

Traditional methods for detecting hypocalcaemia during the postoperative period after total thyroidectomy include frequent monitoring of Ca and ionized Ca (iCa), as well as close clinical monitoring for hypocalcaemia symptoms. These traditional methods can take 24 hours to reveal hypocalcaemia, which prolongs hospitalization. Many endocrine surgeons are interested in predicting hypocalcemia early to prevent serious complications and begin early treatment to hasten hospital discharge. Intraoperative or early postoperative intact parathyroid hormone (iPTH) levels are reliable for predicting postoperative hypocalcemia.15-24 Thus; an early PTH assay can facilitate early discharge, and prospectively treat symptomatic hypocalcaemia (**Dıez et al., 2009).**

A careful surgical technique, including peripheral ligation of the thyroid arteries and meticulous dissection of the parathyroid glands, remains the best approach to preventing hypocalcaemia after total thyroidectomy (**Erwin et al., 2017).**

Aim of the Work

To evaluate the risk of hypocalcaemia (transient or permanent) after total thyroidectomy for goiter, the frequency and impact of unintentional parathyroidectomy.

2. Patients and Methods

We conducted a prospective study by collecting data from 50 patients who were admitted to the General Surgery Department, Ain-shams University Hospital, during the period from December 2017 and December 2018.

Inclusion criteria

All the patients presented with thyroid diseases including simple multinodular goiter, diffuse toxic goiter relapsing after full medical treatment, selected cases of thyroiditis (Hashimoto's thyroiditis) and thyroid cancer.

All patients were subjected to the following:

Preoperative assessment

History taking

History taking included the age, the sex, the marital status and special habits. Symptoms evaluated included neck swelling, pressure symptoms and toxic manifestations.

Clinical examination

Both general and local function tests were performed systematically.

Laboratory investigations

Laboratory tests included thyroid function tests (T3, T4, thyroid-stimulating hormone) and serum calcium before and after the surgery.

Imaging techniques

Imaging techniques performed included ultrasound ± computed tomography ± thyroid scans.

Indirect laryngoscopy was performed before and after the surgery.

All surgical specimens were subjected to histopathology routinely. Postoperative serum calcium levels and serum intact PTH levels were estimated routinely after 24 h of surgery and then subsequently as required. An assessment of symptom relief, recurrent laryngeal nerve (RLN) injury, transient hypocalcaemia and permanent hyperparathyroidism was noted. Postoperative hypocalcaemia was defined as serum calcium levels less than 8.5 mg/dl (normal range 8.5-10.5 mg/dl) in our laboratory. Hormonal replacement therapy was started postoperatively. A standard dose of 100 µg was administered to both the groups, and thyroid function tests were monitored in an interval of 3 months. On the basis of the reports, titration of the dosage of l-thyroxin was carried out.

Serum calcium levels were measured preoperatively, on the day of the surgery, on postoperative days 1 and 6 months postoperatively in the surgical outpatient clinic. Also serum of intact PTH levels were measured 24 h postoperative. Hypocalcaemic patients were followed up for at least 6 months in the outpatient clinic to determine whether the hypocalcaemia was transient or permanent. Results were recorded and tabulated.

Postoperative hypoparathyroidism was assumed when calcium and/or vitamin D was required to treat the clinical symptoms of hypocalcaemia and it was considered permanent when calcium or vitamin D supplementation exceeded 6 months postoperatively to treat the clinical symptoms of hypocalcaemia. In our study no cases selected for permenant hypoparathyroidism.

Total thyroidectomy techniques

Positioning of the patient

Under general anaesthesia, the patient was placed in the supine position on the operating table, placing a sand bag between the shoulders and a ring under the head so that the patient's neck is extended.

The skin is prepared with antiseptic solution (povidone iodine).

Skin incision and creation of skin flaps

The skin incision is performed two finger breadths above the clavicle and the suprasternal notch parallel to the skin crease. The incision extends between the posterior border of the sternocleidomastoid muscles. The subcutaneous tissue is cut in the same line as the skin incision and the platysma is cut slightly above the line of skin incision.

The superior skin flap is raised by applying two allis forceps on the platysma and pulling them vertically by the assistant to demonstrate the space between the platysma and the strap muscles by dissecting the superficial to the deep cervical fascia and the anterior jugular vein using the counter traction to facilitate the dissection (just above the junction between the upper flap and the underlying deep cervical fascia). Usually, we do not divide the anterior jugular vein unless it is enlarged and is interfering with dissection or the gland is huge.

We use both blunt and sharp dissection with diathermy for ligating any blood vessels in the way. This is continued till the thyroid cartilage is recognized by its palpable notch.

The strap muscles are retracted laterally and upwards by two Langenbeck retractors and the lobe is pulled medially, and the space between them is developed using a pledget till the middle thyroid vein is identified (if present), which is then ligated by 3/0 synthetic absorbable ligature (Vicryl) and divided; this allows the lobe to be mobilized more medially and anteriorly.

Handling of the parathyroid glands

The superior parathyroid gland, 'untouched' with its intact supply, is dissected from the trachea; after that, the inferior thyroid within the thyroid capsule is ligated to avoid postoperative hypoparathyroidism; the parathyroid glands are preserved in situ. This is accomplished by dissecting the parathyroid glands downward away from the thyroid capsule. The vascular branches to the thyroid gland are ligated and divided close to the capsule to preserve the blood supply to the parathyroid glands.

Truncal ligation of the inferior thyroid artery should be avoided to preserve the small arterial branches to the parathyroid glands. If necessary, a small remnant of the normal thyroid tissue can be left in place to help preserve a parathyroid gland in situ.

Closure is performed by approximation of the strap muscles using interrupted or continuous Vicryl 3/0 after insertion of a rubber or tube drain in the space of the thyroid gland. The platysma is then approximated by interrupted inverted simple sutures using Vicryl 3/0 and the skin is closed by 3/0 polypropylene subcuticular sutures.

The neurovascular intersection (where the inferior thyroid artery crosses the recurrent laryngeal nerve) is identified, and a loop is placed around the trunk of the inferior thyroid artery. Slight tension applied to this loop facilitates further gentle dissection around the recurrent laryngeal nerve. This loop should be removed when the dissection has been completed. The inferior thyroid artery should be ligated not truncally, but peripherally on the capsule of the thyroid gland to preserve the vascular supply to the parathyroid glands.

In some patients, it is impossible to dissect the parathyroid gland free from the thyroid capsule with an adequate vascular supply. Such glands should be removed, cut into small pieces with a microsurgical knife, confirmed histologically, implanted into an adjacent muscle and marked by a nonabsorbable suture. In the case of an aggressive tumor with the potential for recurrence, the parathyroid gland should be autotransplanted.

The surgical outcome

All surgical specimens were subjected to histopathology routinely. During total thyroidectomy, the parathyroid glands were identified.

Postoperative serum calcium levels were estimated routinely after 24 h of surgery and then subsequently as required. An assessment of symptom relief, RLN injury, transient hypocalcaemia and permanent hypoparathyroidism was made. Postoperative hypocalcaemia was defined as a serum calcium level less than 8.5 mg/dl (normal range 8.5-10.5 mg/dl) in our laboratory.

Bleeding during surgery was variable in both the groups as some of the glands were very vascular. Meticulous dissection was used to minimize the blood loss.

Ten patients (20%) suffered from complications: All suffered from transient hypoparathyroidism as there was no post-operative complication as (stridor, post-operative hemorrhage or change of voice).

Hypocalcaemia is a common occurrence after thyroidectomy. The incidence of temporary hypocalcaemia was reported to be between 6.9 and 25% [11] .

The symptoms and signs of hypoparathyroidism are mainly due to hypocalcaemia; however, cataract has been reported in as many as 70-80% of the patients with permanent hypoparathyroidism despite laboratory evidence of normocalcaemia [12] .

All our specimens showed adequate free margins, and all our cases showed no local recurrences, but this

might also be due to the relatively short time of follow-up.

3. Results

Pre-operative physical and medical characteristics:

Table (1): Demographic data

		No.	%
Sex	Female	44	88.0%
	Male	6	12.0%
Age	Mean ±SD	44.14 ± 9.80	
	Range	25 - 58	

This table shows that 88% of patients were female, mean of age 44.14 with range from 25 to 58 years.

Table (2): Pre-operative serum calcium level

Pre-operative serum calcium level	minimum	8.5
	maximum	10.8
	Mean ±SD	9.44 ± 0.57
	Range	8.5 - 10.5

This table shows the normal serum calcium level 8.5 – 10.5 mg/dl.

Table (3): Pre-operative PTH

	Min	Max	Mean	SD
Pre-operative PTH	32	56	45.20	5.70

This table shows the normal range of serum PTH level 10 – 55 pg/dl

Table (4): Pre-operative provisional diagnosis

	No. of cases	No. of cases%
Papillary carcinoma	12	24.0%
Simple nodular goiter	31	62.0%
Toxic goiter	7	14.0%

Post-operative data:

Table (5): Post-operative histopathological diagnosis

	Number	% of cases
Benign	38	76.0%
Malignant	12	24.0%

Table (1): Post-operative serum Calcium 24 hours (transient hypocalcemia)

		No.	%
Post-operative calcium 24 hours	Range	6.6 - 10.3	
	Mean ±SD	8.70 ± 0.87	
	Transient hypocalcemia	10	20.0%
	Normal	40	80.0%

Table (7): post-operative serum calcium 6 months

		No.	%
Post-operative calcium 6 month	Range	9.24 ± 0.44	
	Mean ±SD	8.6 - 10.4	
	Permanent hypocalcemia	0	0%
	Normal	50	100%

This table show that no cases select of permanent hypocalcaemia.

Table (8): Post-operative PTH 24 hours

		No.	%
Post-operative PTH 24h	Range	7-47	
	Mean ±SD	29.76±7.57	
	Transient hypoparathyroidism	10	20%
	Normal	40	80%

Table (9): The unintentional parathyroidectomy

		No.	%
Unintentional parathyroidectomy	No	47	94.0%
	Yes	3	6.0%
	Intracapsular	2	66.7%
	Juxta capsular	1	33.3%

This table show that no of cases of unintentional parathyroidectomy were only three cases (6%) situated intracapsular 2 cases and juxta capsular in 1 case.

Table (10): Relation between histo-pathological diagnosis and unintentional parathyroidectomy

Unintentional parathyroidectomy	Benign	Malignant
	3(7.8%)	0(0%)

This table shows the present of cases among the unintentional parathyroidectomy was 3 benign cases with presents 7.8% while no cases were selected at the malignant.

Table (11): Relation between unintentional parathyroidectomy and transient hypocalcemia

	No unintentional parathyroidectomy		Unintentional parathyroidectomy		Chi square test	
	No.	%	No.	%	X2	P value
Transient hypocalcemia	9	19.1%	1	33.3%	0.355	0.552
Normal	38	80.9%	2	66.7%		

This table show that there was no statistically significant in transient hypocalcaemia according unintentional parathyroidectomy.

Table (12): No. of parathyroid glands removed during unintentional parathyroidectomy and its relation to hypocalcemia

	No. of parathyroid glands removed	Transient hypocalcemia
	1 gland	1 case (2%)

This table shows that there was no statistically significant in transient hypocalcaemia according to number of glands removed during unintentional parathyroidectomy.

Table (13): Relation between histo-pathological diagnosis and transient hypocalcaemia

		Benign (No.=38)		Malignant (No.=12)		Chi square test/ Independent t test	
		No.	%	No.	%	X2/t*	P value
Post-operative serum calcium 24 h	(Transient hypocalcaemia)	8	21.1%	2	16.7%	0.110	0.741
	Normal	30	78.9%	10	83.3%		
	Mean ±SD	8.68 ± 8.68		8.71 ± 0.82		-0.093	0.926

This table show that there was no statistically significant in transient hypocalcaemia according histo-pathological diagnosis.

4. Discussion

We conducted a prospective randomized study in the period between December 2017 and December 2018 in Ain shams university, general surgery department, endocrine surgery unit, Cairo, Egypt. The study was conducted on 50 patients for whom total thyroidectomy was done.

In our study, age ranged from 25 to 58 years with mean of 44.14 ± 9.80. Eighty eight percent of patients were female (44 female) and only 12 % were male (6 male).

In this study, most patients had simple multinodular goiter (31 patients with 62 %) then papillary carcinoma (12 patients with 24 %), finally secondary toxic goiter (7 patients with 14 %) respectively. All the patients were selected with normal serum calcium level ranged from 8.5 – 10.5 mg/dl with mean of 9.44 ± 0.57 and normal serum PTH level ranged from 10- 55 pg/dl with mean of 45.20 ± 5.70.

The time of operation ranged from 60 minutes to 140 minutes with mean of 100 minutes. The amount of intra-operative blood loss ranged from 100 ml to 220 ml with mean of 170 ml. There was no post-operative complication as (stridor, post-operative hemorrhage or change of voice). While in the study done by TM Chang and his colleague 2.3%, hoarseness (recurrent laryngeal nerve (RLN) injury, temporary/permanent). (TM Chang et al., 2015).

Post-operative serum calcium level was collected at day 1 and 6 months and serum intact PTH level at day 1 in order to detect post-operative hypocalcemia whether (transient or permanent) and post-operative hypoparathyroidism.

As regard Post-operative serum intact PTH level minimum 7 pg/dl, maximum 47 pg/dl, mean 29.76±7.57 and 10 cases have transient hypoparathyroidism where all cases are mild descent but within normal level (10-55 pg/dl) except for the 10 cases (20%) developed transient hypocalcemia the serum intact PTH level descend up to 7 pg/dl, half-life of serum intact PTH is 2-4 min so that post-operative day 1 was able to predict parathyroid failure. While in the study of Azadeh A Carr and his colleague of 77 patients, 20 (26%) had a 1-hour PTH <10 pg/mL. (Carr et al., 2014)

As regard post-operative serum calcium level 24 h: minimum 6.6 mg/dl, maximum 10.3 mg/dl, mean 8.70 ± 0.87. In our study, hypocalcemia developed in 10/50 patients (20%) which is similar to many other studies. While in the study of TM Chang and his colleague 3846 cases were retrospectively examined with Seven percent of the patients had immediate postoperative hypocalcemia (mild and severe). (TM Chang et al., 2015).

As regard histo-pathological diagnosis and transient hypocalcemia 8 cases of hypocalcemia were benign (21%) while normocalcemic patients among benign were 30 cases (78.9%), whereas 2 cases of hypocalcemia were malignant (16.7%) while normocalcemic patients among malignant were 10 cases (83.3%). This shows that histopathological diagnosis and transient hypocalcemia is statistically insignificant.

As regard post-operative serum calcium level 6 months: minimum 8.5 mg/dl, maximum 10.4 mg/dl, mean 9.24 ± 0.44. In our study the overall incidence of permanent hypocalcemia among our patients was 0% while in the study done by Claudius Falch and his colleague was present in 160 of 702 patients (22.8%) with 48 patients (6.8%) had a persistent hypocalcemia above six months.

In our study no case of permanent hypoparathyroidism was recorded in our patients While in the study of Cristiana C and her colleague assumed from 162 patients underwent thyroid surgery there were 31 cases of transient hypoparathyroidism (19.1%) and 8 of permanent hypoparathyroidism (5%), meaning that about 26% of the transient hypoparathyroid patients evolved to permanent hypoparathyroidism. (Cristiana C et al., 2017)

Injury, devascularization and incidental parathyroid gland excision of the parathyroid have all been reported as causes of postoperative hypocalcemia. Although other specific factors have been studied, the cause of postoperative hypocalcemia remains multifactorial. (SS Gad, 2015)

In our study the incidence of unintentional parathyroidectomy in only 3 cases with 6% from the whole cases where 2 cases intracapsular and one case juxta-capsular. The 3 cases with unintentional parathyroidectomy were found among benign cases and no malignant case with unintentional parathyroidectomy was found in our study, so there is no relation between unintentional parathyroidectomy and histopathological diagnosis while in other study by Nina J. and his colleague 414 applicable thyroidectomies were performed during this time with 45 (11%) discovered cases of unintentional parathyroidectomy during thyroidectomy. (Nina J. et al., 2009).

Also, in other study by Khairy GA and Al-Saif A. 287 thyroidectomies were performed and 47 (16.4%) patients had incidentally removed parathyroid glands, the factors that did not increase the risk for inadvertent parathyroidectomy whether benign or malignant (Khairy GA, Al-Saif A., 2011).

In our study, as regard transient hypocalcemia and unintentional parathyroidectomy 9 cases of transient hypocalcemia were at the group of non-unintentional parathyroidectomy while only one case of transient hypocalcemia was at the group of patients with unintentional parathyroidectomy P value 0.552. So, there is no relation between transient hypocalcemia and unintentional parathyroidectomy. Similarly, Sasson et al. described 1 (5%) of 21 patients with incidental parathyroidectomy and 8 (7%) of 120 patients without incidental parathyroidectomy had transient hypocalcemia, respectively; the difference was not significant (P=0.99). (Sasson et al., 2001)

In our study only one parathyroid gland was incidentally excised while the other parathyroid were preserved as the impact of unintentional parathyroidectomy on serum calcium levels is minor when only one parathyroid gland is concerned, with the other parathyroid glands being preserved.

In our study only 1 case with unintentional parathyroidectomy developed post-operative hypocalcemia while the 9 cases of transient hypocalcemia were at the group of non-unintentional parathyroidectomy with P value 0.552, so it is statistically insignificant. Lin et al. found that unintentional parathyroidectomy mostly occurred in the context of re-operations and recurrent lymphadenectomy but did not have any impact on post-operative serum calcium. Debryet al. in a series of 588 thyroidectomies (42 per cent of which were total thyroidectomies), found an unintentional parathyroidectomy incidence of only 1 per cent. Also, location of the parathyroid gland whether intracapsular or juxta-capsular have no impact on post-operative hypocalcemia.

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