EARLY POSTOPERATIVE MEASUREMENT OF CALCIUM AND PARATHRMONE LEVELS AS PREDICTORS OF EARLY PARATHYROID INSUFFICIENCY AFTER TOTAL THYROIDECTOMY

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ABSTRACT

Background: Declines in serum calcium or intact parathyroid hormone (iPTH) levels after surgery have been suggested as being reliable predictors of postoperative hypocalcemia. Although measurements of serum calcium or iPTH allow the identification of patients who have no risk of hypocalcemia after total thyroidectomy, it is not always easy to predict which patients can be discharged early from the hospital or to identify those requiring close monitoring of serum calcium levels or those that should receive calcium and vitamin D supplements**. Aim of the work** To evaluate early postoperative parathyroid insufficiency following total thyroidectomy by estimating parathyroid hormone and calcium level in the early postoperative period, and whether we can rely on to start Ca supplement or not. **Patients and methods:** This study was done in General Surgery department, Zagazig University on 50 patients; 10 males (20%)) 40 females (80%) who underwent total thyroidectomy. Serum total Calcium and Parathormone levels were evaluated in all patients 6 h and 24 h in early postoperative period. **Results:** Our results showed highly significant VALUE OF relative decline of serum calcium and parathyroid hormone 6 h and 24 h after total thyroidectomy. The results showed also highly significant positive correlation between serum calcium and parathyroid hormone both preoperative and postoperative and highly significant positive correlation between relative decline in serum calcium and relative decline of serum parathyroid hormone at both 6h and 24 h after total thyroidectomy IN HYPO CALCEMIC PATIENTS. There was no significant relationship between hypocalcemia and any of demographic, clinical, ultrasonographic and pathological data. There is significant relationship between both relative decline of serum calcium and relative decline parathyroid hormone and postoperative hypocalcemia. **Conclusion:** Relative decline of parathyroid hormone 6 h and 24 h after total thyroidecomy is a good predictor of postoperative hypocalcemia and is reliable for allowing safety discharge of patients 24 h after total thyroidectomy.

Key words: Total thyroidectomy, Calcium, Parathyroid hormone

INTRODUCTION

Postoperative hypocalcemia is observed in up to one third of total or completion thryoidectomy patients and is the most common complication [(1)]**.** Hypocalcemia after total thyroidectomy is usually transient, and the incidence of permanent hypoparathyroidism is 3% or less according to the experience of most of the surgical units. Despite being self-limiting in most patients, symptomatic hypocalcemia is of particular concern because of a delay in its manifestation and the consequent need for prolonged patient hospitalization or readmission ***(2).***

Several authors have attempted to identify risk factors in the development of hypocalcemia. Declines in serum calcium or intact parathyroid hormone (iPTH) levels after surgery have been suggested as being reliable predictors of postoperative hypocalcemia. Although measurements of serum calcium or iPTH allow the identification of patients who have no risk of hypocalcemia after total thyroidectomy, it is not always easy to predict which patients can be discharged early from the hospital or to identify those requiring close monitoring of serum calcium levels or those that should receive calcium and vitamin D supplements ***(3).***

Routine oral calcium and vitamin D supplements have been proposed to prevent the development of symptomatic hypocalcemia and to increase the likelihood of early hospital discharge after bilateral surgical treatment of the thyroid gland or exploration of the parathyroid glands. Because symptomatic hypocalcemia usually develops as late as 24 hours to several days after surgery, postoperative treatment with oral calcium and vitamin D may be a useful approach for avoiding the risk of postoperative hypocalcemic crisis ***((2)).***

AIM OF THE WORK

To evaluate early postoperative parathyroid insufficiency following total thyroidectomy by calculating parathyroid hormone and calcium level in the early postoperative period, and whether we can relay on to start Ca supplement or not.

PATIENTS AND METHODS

This is a prospective study of fifty patients who underwent total thyroidectomy. This number included the patients who under went follow up in early post operative period for 24 hours.

All cases were operated upon in the department of General Surgery, Zagazig University Hospitals during the period from June 2009 to June 2013.

METHODS

➢ Pre operative measures:

Each patient was assessed clinically in the form of clinical history, clinical examination, and laboratory investigations.

All patients subjected to the assessment of vocal cord mobility by indirect laryngoscopy.

1) Clinical history and examination:

A detailed history including personal data, presenting symptoms as thyroid swelling, lymph nodes, toxic symptoms, pain, pressure symptoms and, primary or re-surgery, medication for hyper or hypothyroidism.

Full clinical examination including general assessment for signs of hyper or hypothyroidism and fitness for surgery, and local examination of the thyroid gland and neck region for the swelling characters, presence or absence of lymph nodes, fixation to the trachea and to adjacent structures, tracheal shift, retro sternal extension, scar of previous operations for thyroid or central neck.

2) Laboratory and radiological investigations:

- Routine preoperative investigations for all patients as in any major surgery, as CBC, KFT, electrolytes, chest x-ray.
- Thyroid, and neck U/S. done for all cases.
- Thyroid scan (optional) done when indicated in toxic and malignant cases.
- Preoperative thyroid function test (TFT) T4 [Normal range= 12.0-22.0 P mol/L], TSH [normal range= 0.270-4.20 m IU/L].
- Pre operative parathyroid function tests in the form of:

Serum calcium level. [Normal range= 2.22 - 2.6 m mol /L- (9-10.5 mg/dL)]

3) **Fine needle aspiration cytology (FNAC).** Done for all patients.

➢ Operative technique:

All operations were done under general anesthesia in supine neck extension position and all cases were operated for total thyroidectomy.

➢ Postoperative and follow up:

Clinical evaluation for the presence of clinical symptoms or signs of hypocalcaemia (tetany) by doing Chvostek's or Trousseau's tests every 4 hours.

Post operative thyroid function done once for all patients in the form of TSH, T3 and T4, within the 1st week of surgery.

RESULTS

Table (1): Demographic data of patients.

Parameter		N = 50
Age (years)		
$\overline{X}$ ± SD		40.1 ± 11.54
Range		22-70
Gender (N, %)	**N**	**%**
Male	10	20%
Female	40	80%

This table shows that the incidence is higher in female 40 patients (80%) and lower in male 10 patients (20%).

Table (2): Clinical presentation of patients

Clinical presentations	N	%
Swelling	41	82.0
Pressure	14	28.0
Toxic symptoms	14	28.0
Pain	6	12.0
Lymph node enlargement	8	16.0

This table shows that thyroid swelling was the commonest clinical presentation in our patients followed by pressure and toxic symptoms and lastly pain and lymph node enlargement.

Table (3): Ultrasound findings of patients.

	N	%
Solitary cystic mass	2	4.0
Solitary solid mass	14	28.0
Multi nodular goiter	34	68.0
Lymph node enlargement	8	16.0

This table shows that the commonest finding by neck ultrasound is multi nodular goiter followed by solitary solid mass and lastly solitary cystic mass and lymph node enlargement was found in 16% of patients.

Table (4): Fine needle aspiration cytology of thyroid swelling in our patients.

	N	%
Malignant	4	8.0
Benign	45	90.0
Susp.	1	2.0

This table shows that most cases 45 (90%) was benign by FNAC followed by malignant in 4 (8%) and suspicious in one case (2%) of all studied patients.

Table (5): Preoperative and early postoperative serum Calcium levels.

	$\overline{X}$ ± SD (Range)
Preoperative	9.1 ± 0.65 (7.8-10.5)
6 h postoperative	8.5 ± 1.4 (4.8-10.4)
24 h postoperative	8.6 ± 1.3 (5.4-10.4)

Table (6): Preoperative and postoperative serum parathyroid hormone levels.

	$\overline{X}$ ± SD (Range)
Preoperative	29.1 ± 10.1 (12.5-49.8)
6 h postoperative	25.7 ± 13.2 (4.4-50.0)
24 h postoperative	25.6 ± 13.2 (4.3-50.1)

Table (7): Relative decline of serum Calcium after total thyroidectomy in all studied patients

	Mean % of change	Paired	P value
6 h	-6.0 5	2.98	0.004**
24 h	-5.7 %	3.01	0.004**

This table shows that there is highly significant relative decline of serum calcium 6 h and 24 h after total thyroidectomy.

Table (8): Relative decline of serum parathyroid hormone after total thyroidectomy in all studied patients

	Mean % of change	Paired	P value
6 h	-14.4	3.62	<0.001**
24 h	-14.5 %	3.625	<0.001**

This table shows that there is highly significant relative decline of serum parathyroid hormone 6h and 24 h after total thyroidectomy.

Table (9): Prevalence of hypocalcemia in our studied patients

Total	**N = 50**	**100%**
Hypocalcemia	8	16 %
Manifest tetany	5	10%
Latent tetany	3	6.0%

Hypocalcemia was founded in 8 (16%) of our patients after total thyroidectomy it was manifested in 5 (10%) patients and asymptomatic in 3 (6%) patients.

Table (10): Relative decline of serum calcium in patients with hypocalcemia after total thyroidectomy.

	Mean % of change
6 h	-33.8 %
24h	- 30.0

This table shows that the mean change of serum calcium after total thyroidectomy was -33.8 % and -30.0 % after 6 h and 24 h respectively.

Table (11): Relative decline of serum parathyroid hormone in patients with hypocalcemia after total thyroidectomy.

	Mean % of change
6 h	-66.1 %
24h	- 68.24

This table shows that the mean change of serum parathyroid after total thyroidectomy was -66.1 % and -68.24 % after 6 h and 24 h respectively.

Table (12): Correlation between serum Calcium and parathyroid hormone in all studied patients

	r	P	Significant
Pre	0.39	< 0.001	Highly significant
6 h	0.72	< 0.001	Highly significant
24 h	0.73	< 0.001	Highly significant

This table shows that there is highly significant positive correlation between serum calcium and parathyroid hormone both preoperative and postoperative.

Table (13): Correlation between relative decline in serumCalcium and serum parathyroid hormone in all studied patients

	r	P	Significant
6 h	0.92	< 0.001	Highly significant
24 h	0.92	< 0.001	Highly significant

This table shows that there is highly significant positive correlation between relative decline in serum calcium and relative decline of serum parathyroid hormone at both 6h and 24 h after total thyroidectomy.

Table (14): Comparison between patients with and without postoperative hypocaelcemia as regards to demographic, clinical presentation, ultrasonographic findings and pathological findings.

	Normal N = 42		**Hypocalcima N = 8**		**p**
Age (years)					
$\overline{X}$ ± SD	39.1 ± 11.7		45.8 ± 8.9		0.15
	N	**%**	**N**	**%**	
Gender					
Male	10	23.8	0	0.0	0.31
Female	32	16.20	8	100.0	
Clinical presentation					
Swelling	34	81.0	7	87.5	0.95
Pressure symptoms	12	28.6	2	25.0	0.82
Toxic symptoms	14	33.3	0	0.0	0.13
Lymph node enlargement	5	11.9	1	12.5	1.0

Pain	6	14.3	2	25.0	0.59
Ultrasound findings					
Cystic	2	4.8	0	0.0	0.72
Solid	14	33.3	0	0.0	0.09
Multi nodular goiter	26	61.9	8	100.0*	0.04*
Lymph node enlargement	7	16.7	1	12.5	1.0
Pathology					
Malignant	2	4.8	1	12.5	
Benign	39	92.9	6	75.0	
Susp.	1	2.4	0	0.0	

A part from multinodular goitre which has a significant relationship to postoperative hypocalcemia, there was no significant relationship between hypocalcemia and any of demographic, clinical, ultrasonographic and pathological data.

Table (15): Relative decline of serum calcium and parathyroid hormone in patients with and without hypocalcemia.

	Normal	Hypocalcemia	P
Relative decline in calcium			
6 h	0.81	33.6	< 0.001
24 h	1.1	29.9	< 0.001
Relative decline in parathyroid hormone			
6 h	4.6	66.1	< 0.001
24 h	4.3	68.2	< 0.001

There is significant relationship between both relative decline of serum calcium and relative decline parathyroid hormone and postoperative hypocalcemia.

DISCUSSION

The two primary potential complications that must be considered in performing thyroid surgery are RLN injury and hypoparathyroidism. Both can be further stratified into temporary and permanent categories ***(4).***

Postoperative hypocalcemia is observed in up to one third of total or completion thryoidectomy patients and is the most common complication ***(1).*** Hypocalcemia after total thyroidectomy is usually transient, and the incidence of permanent hypoparathyroidism is 3% or less according to the experience of most of surgeons. Despite being self-limiting in most patients, symptomatic hypocalcemia is of particular concern because of a delay in its manifestation and the consequent need for prolonged patient hospitalization or readmission ***(2).***

There are many controversies and many differences in the design of studies on hypocalcemia and PTH after thyroidectomy. Some series have used rapid determination (intraoperative) of PTH, and others have used intact PTH determination ***(5).***

Several authors have attempted to identify risk factors in the development of hypocalcemia. Declines in serum calcium or intact parathyroid hormone (iPTH) levels after surgery have been suggested as being reliable predictors of postoperative hypocalcemia. Although measurements of serum calcium or iPTH allow the identification of patients who have no risk of hypocalcemia after total thyroidectomy, it is not always easy to predict which patients can be discharged early from the hospital or to identify those requiring close monitoring of serum calcium levels or those that should receive calcium and vitamin D supplements ***(3).***

In the modern climate of increasing cost awareness, thyroid surgery has been considered for a 1 day- surgery regime with limiting factors for early discharge being postoperative bleeding (1-2%), bilateral recurrent laryngeal nerve palsy and symptomatic hypocalcemia ***(6.7).***

In our study we aimed to evaluate early postoperative parathyroid insufficiency following total thyroidectomy by calculating parathyroid hormone and calcium level in the early postoperative period, and whether we can relay on to start Ca supplement or not.

In this study, overall incidence of hypocalcemia was 16%. Hypocalcemia was manifest in 10% and asymptomatic in 6%.

This finding is in agreement with most other authors who reported incidence between 20-30% with symptoms ranging from numbness to tetany (Del Rio et al., 2011).

(8), reported higher figures than our study (overall

incidence 28.5%, symptomatic in 14.6% and asymptomatic in 13.9%). The difference in number of patients between their study and our study (137 patients compared to 50 patients may be responsible for this difference.

Apart from multi nodular goitre which had a significant relationship to postoperative hypocalcemia after total thryoidectomy, there was no significant relationship between postoperative hypocalcemia and any of demographic, clinical, ultrasonographic and pathological data.

Our results are matched with those reported by ***(8),*** who found that there was no significant difference between hypocalcemia and normocalcemic patients according o sex, age, type of pathology and neck dissection.

This finding is accepted as surgery for multi nodular goitre carries the two risk factors that cause hylpocalcemia (ischaemia of parathyroid gland or surgical removal).

Our results showed that the mean change of serum calcium after total thyroidectomy was-33.8% and -30.0% after 6 h and 24 h respectively and the mean change of serum parathyroid hormone after total thyroidectomy was -66.1% and -68.24% after 6 h and 24 h respectively (Table 10, 11).

In our study there was highly significant correlation between relative decline in serum calcium and relative decline of serum parathyroid hormone at both 6 h and 24 h after total thyroidectomy (Table 7, 8).

This finding is supported by the findings of many authors. ***(8),*** reported that patients who developed postoperative hypocalcemia had a significantly lower parathyroid hormone after 4 hours of total thyroidectomy and a significantly greater parathyroid hormone decline and they noted that the threshold enabling prediction of hypocalcemia were 19.4 mg/L for parathyroid hormone after 4 h of total thyroidectomy and 68.5% for relative parathyroid hormone decline.

In this study we used estimation of serum calcium and parathyroid hormone 6, 24 h postoperative depending upon the fact that hypocalcemia may occur early postoperative and also may be delayed up to 24h this is supported by findings of may authors ***(9,10).***

In this study, there was a significant correlation between serum calcium and parathyroid hormone in all patients (Table 12). This is explained as the normal physiology. A findings that supports the choice of parathyroid hormone as a predictor of postoperative hypocalcemia this findings is supported by many other studies but these studies vary widely in terms of trial type methodology, measurement technique, timing and threshold maintained ***(11,12).***

(13), suggested that quick parathyroid hormone assay might have a value concerning the studies which investigated the optimal timing of the measurement, they didn't show any difference between measurements taken at 10 minutes, 1,4,6, or 24 hours. Only ***(14)*** found greater precision with measurements taken at 4 and 6 hours.

On the other hand***(15,16),*** concluded that parathyroid hormone serum level didn't accurately predict postoperative hypocalcemia. In an Australian review of 458 patients in 2007, 7% of patients with a normal parathyroid hormone level developed hypocalcemia.

Depending on the threshold maintained, the single measurement of parathyroid hormone conflicts with a lack of sensitivity or specificity. To resolve this threshold problem. We studied the relative parathyroid hormone decline between its preoperative and postoperative values. We found highly significant correlation between relative decline in serum calcium and parathyroid hormone (table 13).

(17) in analysis of observational studies relevant to PTH decline, investigators found that with a threshold of parathyroid hormone decline (after 6h) of 65% sensitivity and specificity values were respectively 46.4% and 91.4 %. With a threshold decline of 70% sensitivity and specificity were 93.3% and 88% respectively.

This is supported by the work of many authors, and the threshold of parathyroid hormone decline was found in different publications vary from 62.5-75.7% ***(18,11).***

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