

Retrospective Comparative Study of the Incidence of Hypocalcaemia in Total Thyroidectomy between Ain-Shams University as a Referral Center and Damanhour Medical National Institute

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Abstract

Background: Post-operative hypocalcaemia is one of the most serious complications of total thyroidectomy with variable degrees of morbidity.

Aim of Study: The aim of this study was to compare the incidence and to examine several preoperative and immediate post-operative factors for development of hypocalcaemia after total thyroidectomy in patients who underwent total thyroidectomy in Ain-Shams University and Damanhour Medical National Institute.

Patients and Methods: This retrospective study was conducted in Ain-Shams University Hospital and Damanhour Medical National Institute in the period between December 2015 and December 2019. It included 62 patients who underwent total thyroidectomy. The data was collected from patients' files in the Record Department.

Results: There were 52 female and 10 male patients. The mean age was 38 years. Multi-nodular goiter was the most common indication of total thyroidectomy. The mean pre-operative serum Ca was 8.1mg/dl in group A and 8.3mg/dl in group B. 3 (9.7%) patients in group A and 7 (22.5%) in group B developed post-operative hypocalcaemia. The highest frequency of transient hypocalcaemia was on 2nd post-operative day in group A and on 0 day in group B. There was only one patient 3.2% who required calcium and vitamin D supplement for more than six months.

Conclusion: Hypocalcaemia is one of the major concerns following total thyroidectomy that can be prevented by meticulous surgical technique, identification and preservation of parathyroid glands and its vascularity. Post-operative monitoring of serum calcium & early treatment can prevent significant morbidity.

Key Words: Hypocalcaemia – Parathyroid glands – Total thyroidectomy.

Introduction

TOTAL thyroidectomy is one of the most common modalities of treatment of thyroid disorders. One of the most common complications of thyroid surgery is post-operative hypocalcaemia which is defined as a serum calcium level below 8.5mg/dl (2.1 to 2.6mmol/L) [1].

Thyroid cancer, previous thyroid surgery, huge goitre, retrosternal extension and damage or inadvertent removal of the parathyroid glands with the thyroid specimen are important risk factors of this complication. Lateral ligation of inferior thyroid artery devascularizes the parathyroid gland is a strong determinant of hypocalcaemia [2].

Post-operative hypocalcaemia usually manifests itself in the first 24 hours post-operatively or within the 2-3 days after operation. Post-operative hypocalcaemia may be transient, resolving within a few months, or permanent, requiring lifelong oral calcium and vitamin D supplementation. In most patients it is transient and resolve spontaneously [3].

Patients can complain symptoms varying from perioral tingling and numbness to carpopedal spasms and tetany (symptomatic hypocalcaemia) or they can be asymptomatic (when only low calcium serum levels are found, defined as laboratory hypocalcaemia). Even if hypocalcaemia usually recovers in most patients within few months (transient hypoparathyroidism) [1].

Asymptomatic hypocalcaemia does not require calcium supplementation, while in patient with

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severe disturbances or symptoms of hypocalcaemia, intravenous supplementation should be implemented and patients should be released with oral calcium and vitamin D regimen until the hypoparathyroidism resolves. Intravenous calcium gluconate can be given 10-20ml of 10% solution slowly until the symptoms disappear, then 50ml of 10% calcium gluconate can be added to 500ml of 5% dextrose solution and administered by intravenous drip at a rate of 1ml/kg/h [4].

Routine oral calcium and vitamin D supplements have been proposed to prevent the development of symptomatic hypocalcaemia and to increase the likelihood of early hospital discharge after total thyroidectomy [5].

The aim of this study was to compare the incidence of development of hypocalcaemia after total thyroidectomy in patients who underwent total thyroidectomy in Ain-Shams University and Damanhour Medical National Institute.

Patients and Methods

This retrospective study was done in Ain-Shams University Hospital and Damanhour Medical National Institute on a sample of 62 patients who underwent total thyroidectomy and satisfied the inclusion and exclusion criteria to be enrolled in the study during the period December 2015 and December 2019. The data was collected from patients' files in the Record Department under supervision of thesis supervisors. Approval was obtained from the Ethical Committee of the Department of General Surgery, Faculty of Medicine, Ain Shams University. In addition, the medical directors' offices of the hospital granted permission to use the patients' data for this study. All data had no personal identifiers and were kept confidential and therefore did not require informed consent.

Enrollment of patients:

A total number of 62 patients were finally enrolled with criteria as follows: Patients underwent total thyroidectomy without central neck dissection regardless of the thyroid disorder.

Patients were enrolled with exclusion criteria as follows:

- 1- Patients had hypocalcemia, abnormal parathyroid function or renal function before the surgery.
- 2- Patients had a history of thyroid or other neck surgery.

- 3- Patients undergoing thyroid resection other than total thyroidectomy as subtotal thyroidectomy or nodal dissection.

- 4- Patients younger than 15 years old and older than 65 years old.

Patients will be divided into two equal groups (A & B):

- *Group (A):* 31 patients underwent total thyroidectomy in Ain-Shams University Hospital.
- *Group (B):* 31 patients underwent total thyroidectomy in Damanhour Medical National Institute.

During surgery, all thyroid tissue was removed, including the posterior capsule and pyramidal lobe, varying upon patient condition. Total thyroidectomy was performed according to the in house standards with conventional knot tying technique. Visual monitoring of the recurrent laryngeal nerve was routinely applied. All parathyroid glands were identified. The viable parathyroids were identified and if possible preserved on an intact vascular pedicle, and those that appeared nonviable or could not be preserved were removed, autotransplanted to a muscle bed in the sternocleidomastoid.

Collection of clinicopathological parameters and study protocol:

Demographic, pathologic, and laboratory data of all enrolled patients were collected from electronic medical records. Clinicopathological data collected encompassed age, gender, and pre-operative and post-operative serum calcium and Thyroid profile. In addition, information on the type of operation, operative time, and intraoperative management of the parathyroid gland was obtained from the surgical records.

Post-operative assessment:

- The serum calcium was tested on 1st and 2nd post-operative day to predict post thyroidectomy hypocalcaemia, respectively.
- The duration of surgery estimated in minutes from skin incision to skin closure.
- Size of the specimen: Assessment of dimensions by centimetre of the specimen.
- Result of histopathological examination of specimen.
- The presence of parathyroid glands at histological specimen.

All patients were routinely supplemented with oral calcium, and dose adjustment of calcium and appropriate amounts of vitamin D was managed based on clinical symptoms.

Results

There were statistically insignificant differences between both groups regarding age, sex as p -value >0.05 . There were 52 female and 10 male patients. The mean age was (38.26 ± 11.7) years in group A and (38.23 ± 12.5) years in group B (Table 1).

There were statistically insignificant differences between both groups regarding the cause of thyroidectomy as p -value=0.25¹. Multi-nodular goiter was the most common cause in both groups followed by solitary thyroid nodule (Table 2).

Table (1): Patients' demographic data.

	Group A N=31	Group B N=31	p -value
Age (years):			
Mean \pm SD	38.26 \pm 11.7	38.23 \pm 12.5	0.992 ¹
Sex (n, %):			
Male	2 (6.5%)	8 (25.8%)	0.081 ²
Female	29 (93.5%)	23 (74.2%)	
Working status (n, %):			
Working	29 (93.5%)	25 (80.6%)	0.143 ²
Not working	2 (6.5%)	6 (19.4%)	

1: Independent t -test used.
2: Fisher exact test used.
*: Statistically significant as $p < 0.05$.

Table (2): Causes of thyroidectomy among both groups.

Causes	Group A N=31	Group B N=31	p -value
Multi-nodular goiter	23 (74.1%)	20 (64.5%)	0.251 ¹
Solitary thyroid nodule	2 (6.5%)	7 (22.6%)	
Cancer thyroid	2 (6.5%)	3 (9.7%)	
Histopathological surprise	1 (3.2%)	1 (3.2%)	
Hemi thyroidectomy	3 (9.7%)	0 (0%)	

1: Fisher exact test used.
*: Statistically significant as $p < 0.05$.

Some pre-operative data about serum Ca was recorded. There was statistically insignificant differences between both groups regarding the pre-operative serum Ca as p -value=0.928 (Table 3).

Table (3): Pre-operative data among both groups.

Serum Ca (mg/dl)	Group A N=31	Group B N=31	p -value
Mean \pm SD	8.1 \pm 0.2	8.3 \pm 1.2	0.928 ¹

1: Independent t -test used.
*: Statistically significant as $p < 0.05$.

This was no data about intraoperative PTH assay in both groups. The duration of surgery showed insignificant differences between both groups. Only one case in group B had intraoperative bleeding (Table 4).

Table (4): Intra-operative data among both groups.

	Group A N=31	Group B N=31	p -value
Intraoperative PTH assay	0 (0%)	0 (0%)	
Duration of surgery (hrs)	2.4 \pm 0.5	2.6 \pm 0.4	0.143 ¹
Bleeding	0 (0%)	1 (3.2%)	0.524 ²

1: Independent t -test used.
2: Fisher exact test used.
*: Statistically significant as $p < 0.05$.

Out of 62 patients 3 (9.7%) patients in group A and 7 (22.5%) in group B developed hypocalcemia with insignificant difference ($p=0.172$) Fig. (1).

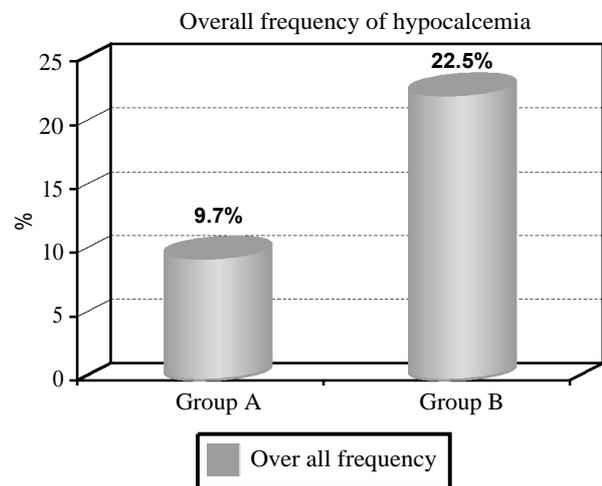


Fig. (1): Overall frequency of hypocalcaemia in both groups.

The highest frequency of transient hypocalcaemia was on 2nd post-operative day in group A and on 0 day in group B. There was only one patient 3.2% who required calcium and vitamin D supplement for more than six months post-operatively in both groups Fig. (2).

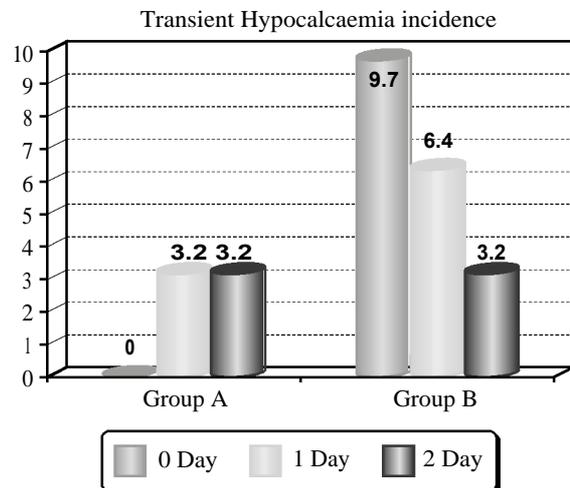


Fig. (2): Transient hypocalcaemia in both groups.

Discussion

Hypocalcaemia is one of the most common complications following total thyroidectomy. It can be either transient or permanent [6].

Symptomatic hypocalcaemia is an extremely unpleasant sequel, it prolongs hospital stay. The symptoms include cramps, tingling sensation, paraesthesia, tetanic contractions, seizures, muscle spasms, and prolong QT interval prolongation on electrocardiogram [7].

The most common cause of post-thyroidectomy hypocalcaemia is injury to parathyroid gland. This may be due to injury, inadvertent removal, or devascularization of the parathyroid glands. Other mechanisms suggested for post-thyroidectomy hypocalcaemia comprises hungry bone syndrome in which there is rapid transfer of calcium into bones following surgical treatment of patients with pre-operative thyrotoxicosis and intraoperative haemodilution [8].

Our objective was to determine the frequency of post-operative hypocalcaemia in patients undergoing total thyroidectomy. This retrospective study included a total 62 patients underwent total thyroidectomy. Patients were divided into two equal groups (A & B): Group (A) included 31 patients underwent total thyroidectomy in Ain-Shams University Hospital and group (B) included 31 patients underwent total thyroidectomy in Damanhour Medical National Institute.

In our study a total of 62 patients' medical records were analyzed. 52 cases were females and 10 were males. The mean age was (38.26 ± 11.7) years in group A and (38.23 ± 12.5) years in group B.

In Baloch et al. study (2019), a total of 854 patients' medical records were analyzed. There were 670 female (78.45%) and 184 (21.54%) male patients. The mean age was 42.1 years (range 14-76 years). Among the patients included, 47.3% (n=404) underwent total thyroidectomy and 52.69% (n=450) underwent completion thyroidectomy. Among these 87.58% (n=748) were malignant and 12.41% (n=106) were benign [9].

Our study found statistical insignificant differences between both groups regarding the cause of thyroidectomy. Multi-nodular goiter was the most common cause in both groups followed by solitary thyroid nodule.

Regarding pre-operative data about serum Ca, there was statistical insignificant difference between

both groups in pre-operative data about serum Ca ranging from 8.1 to 8.3mg/dl.

In this study the duration of surgery showed insignificant differences between both groups. Only one case had intra-operative bleeding. All patients in both groups subjected to ligation and diathermy.

Patients who have total thyroidectomy are routinely supplemented with calcium and vitamin D by many surgeons. However, this practice can reduce the number of symptomatic patients, but it can be inconvenient as treatment is expensive and poorly tolerated. It can distort the incidence rate of post-operative hypocalcaemia especially when definitions are based on serum calcium levels [10].

The ideal way is to predict which patient will develop hypocalcaemia. By this approach we can only treat patients who truly need replacement therapy. The intraoperative Parathyroid Hormone (PTH) assay (quick PTH) has been used as a reliable and rapid method to detect hypoparathyroidism. However, its high cost has often limited its applicability [11].

In our study, we evaluated the serum calcium on 1st and 2nd post-operative day to predict post thyroidectomy hypocalcaemia. Out of 62 patients 3 (9.7%) patients in Ain-Shams University and 7 (22.5%) in Damanhour Medical National Institute developed hypocalcaemia with insignificant difference ($p=0.172$). The highest frequency of transient hypocalcaemia was on 2nd post-operative day in Ain-Shams University and on 0 day in Damanhour Medical National Institute. There was only one patient 3.2% who required calcium and Vitamin D supplement for more than six months post-operatively in both groups.

In Baloch et al., (2019) study, post-operative hypocalcaemia was observed in 7% of 854 patients undergoing total and completion thyroidectomy [9].

Esimontas et al., (2018) reported the highest incidence of transient hypocalcaemia (64.2%) in 257 patients [12]. In previous local study transient hypocalcaemia was 21.62% in 74 patients which is higher than our results. However, different studies used different definitions and are not comparable [13].

Edafe et al., (2017) reported 5.5% rate of permanent hypocalcaemia in 220 patients [8]. Mehanna et al., (2010) reported hypocalcaemia after total

thyroidectomy to occur in 0.33 to 65% of cases [14]. Asari et al., (2008) reported an incidence of 1.6% to 50% [15].

Following thyroid surgery the range of post-operative hypocalcaemia reported in literature varies widely. There are various factors which accounts for these differences in literature such as definition of hypocalcaemia, type of thyroid disease, and surgical technique for thyroidectomy. Patient who had total thyroidectomy with central lymph node dissection had an increased risk of temporary hypocalcaemia [8].

Asari et al., (2008) found that total serum calcium levels alone; measured during the first 2 post-operative days, cannot predict transient hypoparathyroidism correctly. They agreed that day one post-operative PTH measurements may be considered as the most reliable predictor for determining transient or permanent hypoparathyroidism [15].

Asari et al., (2008) commented on intraoperative monitoring of PTH levels recommending that levels that were less below the normal range at the end of or immediately after the operation were highly correlative with post-operative hypoparathyroidism and seemed to allow for early prediction, with a sensitivity and specificity ranging from 71 % to 100% [15].

Falch et al., (2018) founded that patients with a surgery time \geq 189min had significantly more often a post-operative hypocalcemia than those with shorter surgery time (18.3% vs. 28.3%, $p=0.002$). Patients with parathyroid gland reimplantation also had a significant higher rate of initial post-operative biochemical hypocalcemia (45% vs. 21.5%, $p=0.001$). In a multivariate logistic regression analysis, only surgery time, a female gender and parathyroid gland reimplantation were the significant independent predictors for initial post-operative biochemical hypocalcemia [16].

Conclusion:

Hypocalcaemia is one of the major concerns following total thyroidectomy. Meticulous surgical technique, identification and preservation of parathyroid glands and its vascularity is essential in preventing post-operative hypocalcaemia following total thyroidectomy. Post-operative monitoring of serum calcium & early treatment can prevent significant morbidity. These findings were important for guiding surgeons to prevent the occurrence of hypocalcemia and hypoparathyroidism.

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دراسة مقارنة بأثر رجعي لحدوث نقص الكالسيوم بالدم فى الإستئصال الكلى للغدة الدرقية بين مستشفيات جامعة عين شمس كمركز للإحالة والمعهد الطبى القومى بدمنهور

أمراض الغدة الدرقية هى أمراض شائعة مع أسباب متنوعة. إستئصال الغدة الدرقية الكلى هو أحد طرق علاج اضطرابات الغدة الدرقية. بالإضافة إلى أنها من أكثر العمليات الجراحية التى يتم إجرائها. يعد نقص الكالسيوم بالدم بعد الجراحة من أكثر مضاعفات جراحة الغدة الدرقية.

الهدف من الدراسة: هو مقارنة معدلات الإصابة بنقص الكالسيوم فى الدم بعد إستئصال الغدة الدرقية الكلى فى المرضى الذين خضعوا لعملية إستئصال الغدة الدرقية الكلى فى جامعة عين شمس والمعهد الطبى القومى بدمنهور.

المرضى وطرق البحث: تضمنت هذه الدراسة فحص البيانات بأثر رجعى التى تم جمعها من ديسمبر ٢٠١٩ إلى ديسمبر ٢٠١٥ من الملفات السابقة من مستشفيات جامعة عين شمس ومعهد دمنهور الطبى القومى. إشمطت الدراسة على إثنين وستين مريضاً خضعوا للإستئصال الكلى للغدة الدرقية. وقد تم إستبعاد المرضى غير القادرين على الجراحة من الدراسة، وكان عمرهم: أقل من ١٥ عاماً وأكبر من ٦٥ عاماً، المرضى الذين أجروا إستئصلاً كلياً للغدة الدرقية مع تشريح الرقبة وإستئصال العقد الليمفاوية أو خضعوا لجراحة أخرى فى الرقبة سابقاً، وكان لديهم مستوى غير طبيعى من الكالسيوم بالدم قبل الجراحة أو وظائف الكلى غير الطبيعية. تم تقسيم المرضى إلى مجموعتين متساويتين (أ & ب): المجموعة (أ) ضمن ٣١ مريضاً خضعوا لعملية إستئصال الغدة الدرقية فى مستشفيات جامعة عين شمس والمجموعة (ب) ضمن ٣١ مريضاً خضعوا لعملية إستئصال الغدة الدرقية الكلية فى المعهد الطبى القومى بدمنهور. وقد تم بحث البيانات التى تم جمعها من الملفات السابقة فيما يتعلق بالتقييم قبل وبعد الجراحة ومستوى الكالسيوم فى الدم مساء يوم الجراحة وصباح اليوم الأول، ثم كل ٢٤ ساعة حتى خروج المريض.

الخلاصة: يعتبر نقص الكالسيوم بالدم أحد المضاعفات الرئيسية بعد الإستئصال الكلى للغدة الدرقية. تعتبر التقنية الجراحية الدقيقة، والتعرف على الغدد الجار درقية والمحافظة عليها وعلى أوعيتها الدموية أمراً ضرورياً فى الوقاية من نقص الكالسيوم بالدم بعد جراحة الإستئصال الكلى للغدة الدرقية.