Significance of Thyrotoxicosis in Postthyroidectomy Hypocalcaemia

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Abstract

Background: Postoperative hypocalcaemia is one of the most common complications of thyroid surgery.
Objective: To evaluate the significance of thyrotoxicosis in developing hypocalcaemia after thyroid surgery.
Patients and Methods: A prospective study for patients whom submitted to bilateral subtotal thyroidectomy in AL-Kadhimiya Teaching Hospital in the period from Mars 2006-Mars 2011 were included in this study. Patients were divided into two groups; in group A the patients had toxic goiter, while in group B, the patients had euthyroid goiter. Both groups are nearly identical for age, sex, size of the goiter, and the size of the removed thyroid tissue. All the operations were done by the same surgeon and same technique. At least 2 parathyroid glands are identified and carefully preserved in every patient. Serum calcium was measured before and after operation. Patients with malignant thyroid and those underwent lobectomy were excluded from this study.
Results: The total number was 97 patients. Group A, include 24 patients, 10(41.6%) of them had transient hypocalcaemia and 5(20.8%) patients had permanent hypocalcaemia. One patient (4.1%) died eighteen months after the operation due to cardiomyopathy and heart failure.GroupB, include 73patients, 5(6.8%) of them had transient hypocalcemia.The relative risk of hypocalcaemia in toxic goiter is 3.53 (confidence interval 95%) in comparison with euthyroid goiter; P value <0.001which is very significant**.**
Conclusion: Thyrotoxicosis is a significant risk factor in developing hypocalcaemia after thyroid surgery.
Keywords: hypocalcaemia, Thyroidectomy, Thyrotoxicosis, euthyroid.

الخلاصة

خلفية الدراسة: يعتبر نقصان الكالسيوم بالدم بعد عمليات استئصال الغدة الدرقية من المضاعفات الشائعة.مصطلح(تسمم) الغدة الدرقية يستعمل في الوقت الحاضربدلا من زيادة إفراز الغدة الدرقية لان المرض لايقتصر على زيادة إفرازاتالغدة الدرقية فقط.احتمال حدوث.متلازمة جوع العظم هي نقصان الكالسيوم بعد استئصال الغدة الدرقية السامة وترسب الكالسيوم بالعظام

الهدف من الدراسة:تقييم عامل الغدة الدرقية السامة كسبب مؤثر في نقصان الكالسيوم بالدم بعد عمليات استئصال الغدة الدرقية

المرضى وأسلوب العمل:دراسة مستقبلية للمرضى الذين تجرى لهم عمليات استئصال الغدة الدرقية تحت الكامل في مستشفى الكاظمية التعليمي للفترة من آذار 2006 ولغاية آذار 2011. تم تقسيم المرضى إلى مجموعتين المجموعة أ وتضم مرضى الغدة الدرقية السامة والمجموعة ب وتضم مرضى الغدة الدرقية الغير سامة. المرضى في المجموعتين تقريبا

متطابقين من ناحية العمر والجنس وحجم الغدة الدرقية قبل العملية ووزن الغدة الدرقية المستأصلة.العمليات الجراحية للمرضى بالمجموعتين قد أجريت بنفس الطريقة وبواسطة نفس الجراح. على الأقل اثنان من الغددالحول الدرقية تم تمييزها والمحافظة عليها في كل مريض ولم يتم ربط وعقد شريان الغدة الدرقية الأسفل في كل المرضى. لم تشمل الدراسة مرضى سرطان الغدة الدرقية ولامرضى استئصال فص واحد من الغدة الدرقية

النتائج: المجموع الكلي للمرضى هو 97 مريضا . المجموعة أ تشمل 24 مريضا منهم 10(41,6%) مرضى عانوامن نقصان الكالسيوم المؤقت بالدم بعد العملية و5 (20,8) مرضى عانوا من نقصان الكالسيوم الدائمي بعد العملية.وللأسف مريض واحد(4,1%) مات بعد سنة ونصف من العملية بسبب عجز القلب. المجموعة ب تشمل 73 مريضا منهم 5 (6,8%)عانوا من نقصان الكلسيوم المؤقت بالدم بعد العملية. الخطر النسبي للغدة الدرقية السامة في حدوث نقصان الكالسيوم هو5 3, 3 بالمقارنة مع الغدة الدرقية الغير سامة وهو مؤثر إحصائيا بصورة كبيرة (P value <0.001)

الاستنتاج: تسمم الغدة الدرقية هو عامل مؤثر في حدوث نقصان الكالسيوم بعد عمليات استئصال الغدة الدرقية

مفاتيح الكلمات: نقصان الكالسيوم . عملية استئصال الغدة الدرقية.سامة .غير السامة

Introduction

Hypocalcaemia is caused by loss of calcium from or insufficient entry of calcium into the circulation. The clinical manifestation varies from an asymptomatic biochemical abnormality to a life-threatening disorder (tetany, laryngeal spasms, bronchial spasm, dyspnea, wheezing cardiomyopathy and congestive heart failure) depending on the duration, severity, and rapidity of development [(1)].

Hypoparathyroidism is the most common cause of hypocalcemia [(2)].Parathyroid insufficiency, as a complication of thyroidectomy is due to removal of the parathyroid glands or infarction through damage to the parathyroid end artery; often, both factors occur together. Vascular injury is probably far more important than inadvertent removal. Most cases present dramatically 2-5 days after operation; however, very rarely the onset is delayed for 2-3 weeks or a patient with marked hypocalcaemia is asymptomatic. [(3)]

Hypoparathyroidism after thyroidectomy is a debilitating morbid condition with an incidence ranging from 1 to 32%. In recent years, however, attention has been paid to the fact that even milder hypopara-thyroidism with normal or slightly reduced serum calcium can be the cause of fatigue, mental and neuromuscular symptoms and ectodermal changes.[(4)]

Metabolic bone disease, "hungry bones syndrome", results in the rapid influx of serum calcium into bones, particularly if preoperative preparation has been with β-blockade rather than normalization of the serum thyroid hormone level [(3)].

Truncal ligation of the inferior thyroid arteries may increase the risk of parathyroid insufficiency after bilateral subtotal thyroidectomy, but a recent article stated that truncal ligation of the inferior thyroid arteries has no effect on the incidence of postoperative hypocalcaemia. [(5)]

Hypocalcaemia after thyroid surgery may also be secondary to postoperative reversal of thyrotoxic osteodystrophy, calcitonin release due to operative manipulation of the thyroid glands or reactive hypoparathyroidism due to relative hypercalcaemia in thyrotoxic patients [(1)].

Hungry bone syndrome is hypocalcaemia after thyroidectomy for hyperthyroidism. On the other hand, some believe that it was doubted, based on the fact that most thyrotoxic patients undergoing thyroidec-tomy became euthyroid before operation, thus reversing the osteodystrophy. Similarly, the relative hypercalcaemia would have been reversed before surgery [(6)].

Clinical management of patients with hypocalcaemia is costly and can be challenging because the therapeutic window for vitamin D (often a required component of therapy) is narrow. Even

short-term vitamin D intoxication, which may be asymptomatic, can cause nephrolithiasis and obstructive uropathy, resulting in permanent kidney damage. [7]

Patients and Methods

A prospective study for patients whom underwent bilateral subtotal thyroidectomy in AL-Kadhimiya Teaching Hospital in the period from Mars2006- Mars2011.The total number was 97 patients, divided into two groups according to the thyroid hormone levels; group A had toxic goiter and include 24 patients, while group B (the control group) had non toxicgoiter (euthyroid) and include73 patients. Both groups are nearly identical for age, sex, size of the goiter, and the size of the removed thyroid tissue. In each patient, bilateral subtotal thyroidectomy was performed leaving an equal remnant of thyroid tissue posteriorly.Atleast two parathyroid glands were identified and carefully preserved in each patient. Inferior thyroid artery was not ligated in both sides in all the patients. All the operations were done by the same surgeon and by the same technique. Patients with malignant goiter requiring more radical surgery, and patients with lobectomy and those with recurrent goiter were excluded.

Thyrotoxic patients were controlled with antithyroid drugs carbimazole and βblockers propranolol, rendering them euthyroid for at least four weeks before surgery. Serum calcium was measured in all patients in both groups preoperatively for baseline evaluation, and in the1st,2nd,3rd,10th,postoperative day; also it was measured one month, three months, and six months after the operation. Biochemical hypocalcaemia was defined as a serum calcium concentration less than 2.1 mmol/L (normal serum calcium is 2.1-2.6 mmol/L) and clinical hypocalcaemia by the presence of one or more of the symptoms and signs of hypocalcaemia (circumoral and digital numbness and paraesthesia;tetanic symptoms with carpopedalor laryngeal spasms or positive Chvostek'sorTrousseau's signs) .

All the thyroid glands specimens which were removed from the patients were dissected on the couch "bench surgery" for any parathyroid gland which was inadverantly removed from the patient; and if any of them was found it then reimplanted again in the sternocleid-omastoid muscle of the patient after slicing it into small fragments (and one of these small fragments was sent for histopatholo-gical examination to prove that it is parathyroid gland). All the histopatholo-gical reports of the examined thyroid specimens in the laboratory were not containing parathyroid tissue. In cases of hypocalcaemia, the patients required prolonged hospitalization and were treated with slowly intravenous calcium (10 ml of 10% calcium gluconate) and/or oral calcium therapy (1 g three or four times daily) supplemented by vitamin D when necessary according to the severity of hypocalcaemia.

Transient hypocalcaemia considered when serum calcium is corrected to normal state in period less than 6 months. While permanent hypocalcaemia is considered when it is prolonged more than 6 months.

Data were analyzed using SPSS 16 (Statistical Package for Social Sciences) and Microsoft office Excel 2007. Numerical variables were presented as mean ± SE, while discrete variables were presented as number and percentage.

Chi-square test was used to compare discrete variables. P-value less than 0.05 were considered significant.

Results

The total number was 97 patients. Group A include 21(87.5%) female and 3(12.5%) male patients, their age ranges from 20-45 years (mean age = 30.25±8.71 years); while group B include 65 (89%) female and 8 (11%) male patients, their age ranges from 21-48 years (mean age =31.86±5.73 years).The weight of the

resected thyroid gland in group A ranged from 41-233 grams with mean weight (72.12 ± 3.15) and in (group B) it ranged from 52-275 grams with mean weight (81.75 ± 5.11) and it was comparable in both groups with no significant statistical difference between them(P value = 0.08). Serum calcium for all the patients in both groups was normal before the operation.

In (group B) there were 5 (6.8%) patients develop transient hypocalcaemia the onset of which was on the 2nd postoperative day and recovered in the 1st postoperative month.

In group A, 15 (62.5%) patients develop hypocalcaemia; the onset of which was in the first postoperative day. Transient hypocalcaemia was observed in 10 (41.6%) of them. The other 5 (20.8%) patients had permanent hypocalcaemia.

The relative risk of hypocalcaemia in toxic goiter was 3.53 (confidence interval 95%) in comparison with euthyroid goiter. P value <0.001 which is very significant. Table (1) shows the incidence of hypocalcaemia in each group and their significance.

Unfortunately one patient (4.16%) in group A with permanent hypocalcaemia was died eighteen months after the operation due to sever hypoxia. The incidence of mortality was very low and not significant (P value> 0.05).

Inadvertent removal of one of the parathyroid glands(which is reimplanted again in the sternomastoid muscle of the patient after slicing it into small fragments) was occur in one patients in group A and two patients in group B. Those three patients who underwent autotransplantation of parathyroid gland had normal postoperative serum calcium. Table (2) shows Incidence of hypocalcaemia in the patients with and without autotrans-plantation of parathyroid glands.

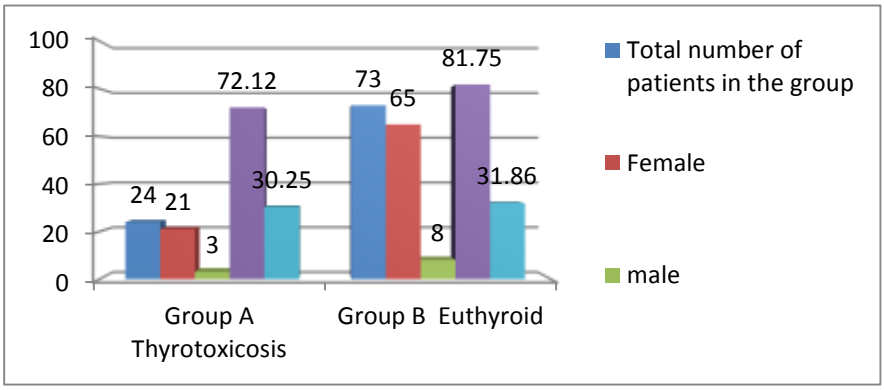

Figure 1. Shows the number of the patients, their mean age, sex incidence; and the mean weight of the resected thyroid gland in both groups which was nearly identical and comparable. There was no significant difference between both groups (P>0.05).

Table 1. The incidence of hypocalcaemia in thyrotoxic patients (Group A) in comparison with euthyroid patients (Group B) and their significance.

	Transient hypocalcaemia	Permanent hypocalcaemia	Normal serum calcium	total
Group A Thyrotoxicosis	**10 (41.66%)**	**5 (20.83%)**	**9 (37.50%)**	**24**
Group B Euthyroid patients	**5(6.84%)**	**0**	**68(93.15%)**	**73**
Total	**15**	**5**	**77**	**97**

Relative risk of hypocalcaemia in toxic goiter is 3.53 (confidence interval 95%) in comparison with euthyroid goiter. P value <0.001 which is very significant.

Table 2. Incidence of hypocalcaemia in the patients with and without autotransplantation of parathyroid glands

	Number of patients	Hypocalcaemia	Normal serum calcium
Autotransplantation of parathyroid gland	**3**	**0**	**3(100%)**
Patients without autotransplantation of parathyroid gland	**94**	**20(21.27%)**	**74(78.73%)**
Total	**97**	**20**	77

Discussion

Hypocalcaemia is more common after surgery for thyrotoxic goiter than after surgery for euthyroid goiter. (1)

Recalcification that occurs in bones postoperatively, (after removal of thyrotoxic goiter) is referred to as "hungry bones syndrome", due to a rapid increase in bone remodeling. If the stimulus is removed (thyroid hormone or parathyroid hormone), there is a dramatic increase in bone formation. Hypocalcaemia can occur if the rate of skeletal mineralization exceeds the rate of osteoclast-mediated bone resorption. This syndrome can be associated with severe and diffuse bone pain. (1)

In group B there were 5 (6.8%) patients who develop clinical and biochemical hypocalcaemia which was transient and occurred in the second postoperative day and recovered in the first postoperative month; it may be due to manipulation of the big goiter. In group A there were 15 (62.5%) patients who develop clinical and biochemical hypocalcaemia which was occurred in the first postoperative day; 10 (41.6%) of them were transient and 5 (20.8%) patients were permanent; in spite of that all the patients in both groups, at least two parathyroid glands were preserved at operation, and that both inferior thyroid arteries were not ligated and the parathyroid glands were not detected histopathologically in the removed specimens.

In this study, the incidence of hypocalcaemia was significantly higher in thyrotoxic patients. Relative risk of hypocalcaemia in toxic goiter was 3.53 (confidence interval 95%) in comparison with euthyroid goiter. P value <0.001 which is very significant.

The explanation of this high incidence of hypocalcaemia after thyroidectomy for thyrotoxic goiter may be due to an increase in bone catabolism in thyrotoxicosis "hungry bones syndrome", and the degree of thyrotoxic osteodystrophy increases proportionately with the severity of thyrotoxicosis.

Although preoperative preparation by antithyroid drugs should reverse osteodystrophy, this reversal takes up to 20 weeks, whereas most surgical patients are prepared for a much shorter period (6–10 weeks) The 'hungry bones syndrome' could be considered as a cause of postthyroidectomy hypocalcaemia particularly in toxic patients.(5)

Unfortunately one patient in group A with permanent hypocalcaemia was died eighteen months after the operation due to sever hypoxia.The patient was 20 years old female with Gravies disease. She had large size goiter and her thyrotoxicosis was controlled with great difficulty by carbimazol and propranolol. She develop hypocalcaemia in the first ostoperative day and treated by intravenous calcium gluconate and vitamin D supplement and she was stayed in the hospital for fourteen days and discharged well from the hospital and put on oral calcium (1 g three times daily)and vitamin D supplement "one alpha tablets 0.01 microgram daily". She was poor patient and not educated and not took her drugs properly (may be due to its

cost) so the patient's follow up was irregular. She was presented one and a half year postoperatively with severe anemia (her serum hemoglobin was 7 grams) complaining of dyspnoea and on examination there was heart murmur on auscultation and pulmonary repitation. The patient was admitted to the hospital for resuscitation as an emergency case but unfortunately she died in the day of admission at the emergency room. The postmortem report in the forensic medicine mentions that the cause of death was cardiomyopathy and congestive heart failure. The explanation of her dyspnoea and heart failure causing her death may be due to severe anemia(nutritional anemia due to poverty) but also it may be due to prolonged hypocalcaemia which is inadequately treated (prolonged hypocalcaemia may cause congestive heart failure and cardiomyopathy).[1]

Some studies show that patients who underwent routine parathyroid autotransplantation had significantly less risk of developing permanent hypoparathyroidism and postoperative hypocalcaemia compared with patients who did not undergo routine parathyroid autotransplantation[4].In this study the three patients who underwent autotransplantation of the inadvertently removed parathyroid gland were not develop postoperative hypocalcaemia.

Investigators who adopted a policy of selective parathyroid autotransplantation for inadvertently removed or devascularized parathyroid glands during thyroidectomy reported an incidence of permanent hypoparathyroidism of less than 6% (0-4.4%).[8]On the other hand, the incidence of permanent hypopara-thyroidism has been reported to be 0% after routine parathyroid transplantation following thyroidectomy.[9]. However there are only occasional reports of parathyroid autotransplantation following bilateral thyroid surgery for benign thyroid disease.[10][11] Studies conducted in the past have shown that unnecessary dissection to identify all the parathyroids should be avoided to reduce the incidence of ischemic injury [12].The same principle has been followed in the present study.

Most of the authors have shown their preference for autotransplanting parathyroid glands in the exposed sternocleidomastoid muscle. [13]The same principle has been followed in the present study because of the convenience of the procedure.

Conclusion

Thyrotoxicosis is a risk factor in developing hypocalcaemia after thyroid surgery. So that the patients with thyrotoxicosis should be aware about this risk and serum calcium should be monitored carefully before and after thyroidectomy

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