Original Article

ESTIMATION OF IONIZED CALCIUM LEVELS AFTER THYROIDECTOMY AT KING ABDUL AZIZ UNIVERSITY HOSPITAL (Jeddah)

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ABSTRACT

Aim: To determine the incidence of hypocalcaemia and the need for calcium supplementation after thyroid surgery in 120 cases.

Methods: A retrospective study of 120 patients who underwent thyroidectomy at King Abdul Aziz University Hospital between January 1999 to September 2003 to determine the incidence of hypocalcaemia by measuring ionized calcium level. The data included pre operative and post operative ionized calcium level, albumin, free thyroxine, thyrotopin and alkaline phosphatase. The medical notes were reviewed for age, gender, type of thyroidectomy and pathological characteristics of resected thyroid tissue and aoutotransplantion of parathyroid gland. Treatment of post operative hypocalcaemia and duration of treatment was recorded.

Results: Hypocalcaemia occurred in (15 %)18 patients from total of 120 patients who underwent total thyroidectomy, had a significant lower calcium level of 1.78+/-0.054 mmol/L compared to 102 (85 %) patients with normal calcium level. Sixteen patients required calcium supplementation with or without oral vitamin D3. Three patients developed hyperparathyroidism with PTH level of 23 pg/L. Two patients developed laryngeal stridor and were treated initially by intravenous infusion of calcium gluconate.

Conclusion: Measuring or calculating ionized calcium level post thyroidectom, to avoid unnecessary calcium supplementation resulting from diagnosing hypocalcaemia from measuring total calcium level alone is more accurate and more appropriate.

KEY WORDS: Post thyroidectomy , hypocalcaemia, ionized serum calcium

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INTRODUCTION

Post operative hypocalcaemia is one of the complications of thyroidectomy. It occurs more frequently after total thyroidectomy than after other more conservative thyroidectomies. The reported incidence of transient hypocalcaemia ranges from 1.6% to 9.3% after subtotal thyroidectomy and from 6.9% to 42 % after total thyroidectomy[1,2]. In contrast, permanent hypocalcaemia has been reported in 0.2% to 3% of patients after subtotal thyroidectomy and in 0.4% to 29% of patients after total

thyroidectomy[3]. The pathogenesis of hypocalcaemia after thyroidectomy is not completely understood. Hypocalcaemia after thyroidectomy has been most commonly attributed to parathyroid insufficiency related to injury, revascularization, or in advertent excision of the parathyroid glands. Other causative mechanisms that have been implicated in the pathophysiology of post-thyroidectomy hypocalcaemia include calcium uptake by bone in patients with thyrotoxic osteodystrophy, parathyroid suppression from increased calcium restored from the bone of patients with hyperthyroidism, transient preoperative haemodilution with increased renal excretion of calcium, increased release of calcitonin as a result of thyroid manipulation, and autoimmune-related fibrosis of the blood supply to parathyroid glands[4]. This study aims to determine the incidence of hypocalcaemia by calculating ionized calcium level from total calcium and albumin level. We also report the cause of hypocalcaemia after thyroidectomy and calcium supplementation as treatment of hypocalcaemia.

METHODS

King Abdul Aziz University Hospital (KAUH) is a teaching government hospital providing health care to a multinational population of mixed socioeconomic status. All patients undergoing thyroidectomy from January 1999 to September 2003 were included to determine the incidence and treatment of post-thyroidectomy hypocalcaemia. Patients with hyperparathyroidism were excluded from the study.

Medical records were reviewed for the following data; age, gender, nationality, thyroid function status; type of thyroidectomy either unilateral lobectomy for benign nodule of thyroid gland, subtotal thyroidectomy for multinodular goiter or total thyroidectomy for carcinoma of thyroid or multi-nodular goiter. The pathological characteristics of resected thyroid tissue were reported as well.

Hypocalcaemia was defined by an ionized corrected calcium level (Ca) less than 2 mmol/L. Ionized calcium represents 50% of the total; this is the biologically important fraction, so it's highly regulated. The level of protein – bound calcium is variable, but estimated to be approximately 40% of the total. The remaining fraction (10%) circulate as complex with anion such as citrate, sulphate, or phosphate. Thus hypoaluminemia will also lower the serum calcium concentration by (0.2 mol/l for every 1.0 g/dL reduction in serum albumin). Ionized calcium level corrected to a PH of 7.4 was measured by a dialysis equibilium method. The formula for corrected ionized calcium calculation is as follows:

Ionized calcium = (40 - measured albumin in g/L) x 0.02 + measured calcium level[5]

Permanent hyperparathyroidism was defined by the requirement for 1, 25 dihydroxy cholecefrol (vitamin D) with calcium supplement for more than 6 months after thyroidectomy to maintain adequate calcium level.

Ionized Ca level, albumin, phosphate, alkaline phosphatase were reported both pre and post operatively, while FT4, Free thyroxin, TSH thyriotropin, were recorded pre-operatively. In few cases with severe hypocalcaemia magnesium level, parathyroid hormone (PTH) level were also tested. The normal range of serum levels are as follows:

Ionized Ca, 2.1- 2.6 mmol/L, albumin 35-50 g/L, magnesium 0.5-0.85 mmol/L, phosphate 0.8-1.4 mmol/L, and alkaline phosphatase 35-105 IU/L. FT4 12-22 p mol/L, TSH 0.27-4.2 uIu/L, PTH was measured by a sensitive specific two – site immunoradiometric assay with normal range 10-65 pg/ml

Data was divided in two groups. Group (1) with normal ionized calcium level post operatively. Group (2) patients with low calcium level after thyroidectomy. Results were expressed as a mean ± SD (standard deviation).

Relationship between hypocalcaemia and patient characteristics were examined by t-test for continuous variables. Results were considered significant if the p value is less than 0.005. All analyses were performed with excel computer program.

RESULTS

Total of 120 patients underwent thyroidectomy at King Abdul Aziz University Hospital during the period of three years from January 1999 to September 2003, all were included in the study. Eighty five patients were females and thirty five were males, with Female: Male ratio of 2.4:1. 102(85%) patients were in group 1 with normal ionized calcium level post-thyroidectomy, 18(15%) patients were in group 2 with hypocalcaemia post-thyroidectomy. Mean age group for all the patients was 39.35±13.97. There was no statistically significant difference in age between the two groups (Table-I).

Fifty patients were Saudi, 70 patients were expatriate with Saudi: expatriate ratio of 0.7:1. However in hypocalcaemia group the ratio was 0.2:1 (Table-I).

A standard thyroid lobectomy was performed in 33 (27.5%) patients and subtotal thyroidectomy in 38 (31.7%) patients and near total thyroidectomy in 49 (40.8%) patients. However total thyroidectomy was done in 55.6% in group (1) with hypocalcaemia when compared to 38.2% in normo-calcemic group (2) (table-II). The pathological diseases of resected thyroid included multinodular goiter in 62 (51.7%). Thyroid cancer in 37 (30.8%), hashitoxicosis (thyroiditis) in 13 (10.3%) and Graves disease in 8 (6.7%) cases. There was no significant difference in the pathology of resected thyroid gland between the two groups (Table-II).

Six patients with Grave's disease were treated with thionamide and beta-blockers, initially; however they did not respond to medical treatment and additionally they had large goiter. So they were subjected to thyroidectomy to control hyperthyroidism. Two patients underwent thyroidectomy without receiving antithyroid medication or a beta-blocker.

The mean post-operative ionized Ca level of all patients was 1.98±0.8 However Ca level was 2.2± 0.142 in group (1), 1.78±0.054 in group (2). There is statistically significant difference in post operative Ca level between the two groups (Table-III).

The most common clinical manifestation of post operative hypocalcaemia was acral numbness and paraesthesia , which occurred in all patients. Other symptoms which were variably present included oral paraesthesia and genaralized muscle cramps. Positive Chovestek's sign[6] and Trousseau's sign[7] was reported in 8 patients and carpo-pedal spasm in 5 patients. Only two patients had laryngeal stridor, one of them needed admission to intensive care unit for respiratory assistance. This patient was admitted several times with severe hypocalcaemia, caropedal spasm and laryngeal stridor because of permanent hypoparathyroidism and also poor compliance to her medications (calcium supplement and vitamin-D[8,9].

Three patients developed severe hypocalcaemia with calcium level of ≤1.4 mmol/L. They were treated by intravenous infusion of calcium gluconate (1 mg/ Kg/hr). Patients simultaneously were started on oral calcium carbonate (1000 mg of element calcium twice a day and 1, 25- dihdroxy vitamin D3 (0.25- 0.5 mg twice a day). Intravenous calcium infusion was discontinued when calcium level was greater than 1.8 -2 mmol/L.16. Patients with Ca level between 1.7 –1.9 mmol/l were treated with oral calcium with or without oral vitamin D3 for duration of 3- 6 months.

Oral calcium and vitamin-D were then tapered on an out patient basis. 3 (16.7%) patients had permanent hypocalcaemia and needed life long calcium with oral vitamin-D3. There was severe hypomagnesaemia with a level 0.4 mmol/L in 2 (11.1%) patients. PTH hormone level was measured in three patients with a very low calcium level with an average level of 15 pg /L.

Table-I: Characteristics of individual patients

Variable	*Number*	*Group (1) Normocalcaemic*	*Group (2) Hypocalcaemia*	*p value*
Patients No	120	102	18	
Females	85	72	13	
Males	35	30	5	
F:M ratio	2.4:1	2.4:1	2.6:1	
Age (mean± SD)	39.35± 13.97	40± 11.4	35.3±13.12	0.1900
Nationality (Saudi)	50	47	3	
Non Saudi	70	55	15	
Saudi: Non Saudi ratio	0.7:1	0.85:1	0.2:1	

Table-II: Pathological resected of thyroid and type of thyroidectomy

Diagnosis	*Total number of patients (%)*	*Group (1) Normocalcaemic (%)*	*Group (2) Hypocalcaemic (%)*
Pathology			
Multinodular goiter	62 (51.7)	52 (51)	10 (55.6)
Cancer	37 (30.8)	32 (31.4)	5 (27.8)
Hashitoxicosis	13 (10.8)	11 (10.8)	2 (11.1)
Grave's disease	8 (6.7)	7 (6.8)	1 (5.5)
Total	120 (100)	102 (100)	18 (100)
Operation			
Lobectomy	33 (27.5)	31 (30.4)	2 (11.1)
Subtotal thyroidectomy	38 (31.7)	32 (31.4)	6 (33.3)
Total thyroidectomy	49 (40.8)	39 (38.2)	10 (55.6)
Total	120 (100)	102 (100)	18 (100)

Table-III: Pre and post thyroidectomy laboratory investigations

Variable Lab Test (mean ±SD)	*All patients*	*Normocalcaemic*	*Hypocalcaemic*	*p value*
Pre- operative				
Ionized Ca	2.04±0.8	2.21±0.147	2.27±0.127	0.06
Albumin	32.1±15.2	35.75±6.37	30±2.87	0.109
PO4	1.089±0.26	1.086±0.27	1.22±0.47	0.046
Alkaline phosphate	92.5±15.44	89.6±13.9	104±22.4	0.5
FT4	16.9±10.73	18.05±1.27	93.3± 77.21	0.02
TSH	2.006±2.07	2.02±0.22	1.44±0.368	0.01
Post operative				
Ionized Ca	1.98±0.8	2.2± 0.142	1.78±0.054	‹ 0.005
PO4	1.266±0.27	1.087±0.29	1.11±0.25	0.329
Albumin	32.1±15.2	32.15±4.65	30±2.28	0.5
Alkaline phosphatase	89.6±12.88	89±12.88	104±20.5	0.49

DISCUSSION

Postoperative hypocalcaemia is sometimes encountered after thyroidectomy and is known as a major cause of postoperative morbidity in patients who have undergone thyroidectomy. The result of our retrospective study showed that transient hypocalcaemia occurred in 15% only, which is lower than reported in pervious studies significantly as 40-49%. However permanent hypocalcaemia due to hypoparathyroidism in 3 (2.5%) of our patients is lower than reported by Wingert et al 4% of 221 consecutive patients who under went thyroidectomy[10]. The low incidence of transient post operative hypocalcaemia in our study compared to other studies could be due to autotransplantaion of parathyroid gland, into a pocket of the sternocleidomastoid muscle[11].

Ionized calcium levels dropped significantly after total thyroidectomy. This decrease in ionized calcium level might have resulted from hypoparathyroidism due to the removal and or the ischemia of parathyroid tissue. The permanent hypoparathyroidism in our study can be explained by the fact that two of our patients required extensive surgery. One with thyroid carcinoma who underwent neck dissection to remove lymph nodes and other patient had large multi nodular goiter with retrosternal extension.[12,13]

Tetany and paraesthesia such as tingling around the mouth and in the distal extremities are commonly seen in hypocalcaemia. The appearance of these symptoms is thought to be related to the degree or speed of decrease in calcium levels after thyroidectomy. These symptoms were mainly reported in 15% of patients after sub- total thyroidectomy and 75%, of patients after total thyroidectomy, with no case reported after lobectomy[14]. These symptoms seemed to be related to the extent of surgical procedure. Other factors that determine the variation in frequency and severity of symptoms include acid-base status and hypomagnesaemia[15].

Tetany and parathesiesa might have been caused by the simple consequence of anxiety or hysterical reaction as well as by true hypocalcaemia especially that 75% of patients with post operative hypocalcaemia were females[16]. Post-operative short- term calcium supplementation was given to 16 (88.9%) and 1, 25-dihdroxy vitamin-D3 in 9 (50%) patient, for a duration of three to six months. Long- term supplementation of vitamin-D3 may have been unnecessary except in three patients who had permanent hypoparathyroidism[17]. Unnecessary supplementation may cause hypercalcaemia and hypercalciuria which could result in renal failure[18]. The evaluation of free calcium level seems to be important in treating patients with calcium and vitamin-D3 supplementation. Although the serum total calcium is routinely measured in a clinical setting, we advise to do corrected ionized calcium in order to check the parathyroid function after thyridectomy and to ovoid unnecessary calcium supplementation, because the fall in the serum total protein level due to haemodiluation. This fall is associated with the stress of surgery which may cause decrease in serum total calcium level unrelated to parathyroid function[19,20].

CONCLUSION

We recommend to measure or calculate ionized calcium level post thyroidectomy as wrong diagnosis can be made of hypoparathyroidism on the basis of total serum calcium level. This would avoid unnecessary long term medications.

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