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The incidence of post-thyroidectomy hypocalcemia in Al-Diwaniyah Teaching Hospital, Iraq

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ABSTRACT

Hypocalcemia, which is mainly transitory, is one of the high frequent complications after complete resection of the thyroid gland. Thus, the aim of the present study is to determine related factors with an increased risk of hypocalcemia due to hypoparathyroidism in related to etiology and surgical procedure. A total of 100 total thyroidectomies were studied for the incidence of hypocalcemia whether transitory or permanent and discuss the relation with surgical procedures. The results of this study revealed that postoperative hypocalcemia was noticed in 35 cases (35%), asymptomatic one was shown in 16 cases (45.7%) while symptomatic one was shown in 19 cases (54.3%). Hypocalcemia in the postoperative period was less in patients with complete surgery after subtotal thyroidectomy than in those that with total thyroidectomy in a single operation. Patients are suffering from Graves-disease shows a high incidence of hypocalcemia in *15*% of the cases. The return function of parathyroid glands was 4.5 months in mean, with 70% of the patients showing recovery within 6 months. Hypocalcemia of transient type after total thyroidectomy is a frequent complication, but the permanent one is rare. Patients with Graves- disease have a more risk to develop postoperative hypocalcemia, and it should have specific follow up. Measurement of calcium at postoperative period has little benefit for early detection of patients predisposing for hypocalcemia.

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INTRODUCTION

Hypocalcemia in the transient picture that may result from accidental injury to the parathyroid gland or compromising vascular supply during surgery has been founded in about half of cases, while permanent type occurs <2% of the time. Postoperative hypocalcemia is more likely in patients who undergo concomitant thyroidectomy with neck dissection and in patients with Graves' disease (Falk, 2009, Rosato *et al.,* 2004). There are multiple explanations about the cause of transient hypocalcemia rather than vascular injuries, likes hypothermia and secretion of endothelin-1. Endothelin-1 is an acute-phase reactant which suppresses PTH production. Another hypothesis is—secretion of calcitonin and bone-hungry syndrome. Calcitonin is produced by the C cells of the thyroid gland which decrease bone destruction and increase renal calcium excretion (opposite of PTH) (Rosato *et al.,* 2004, Testini *et al.,* 2007). The major signs and symptoms of hypocalcemia are a direct consequence of the reduction in plasma levels of ionized calcium, which increases the excitation of the neuromuscular system. The earliest signs and symptoms are circumoral paresthesia, tingling in fingers, and toes. Mental symptoms are also common.

Patients become anxious, depressed, and occasionally confused. Tetany may develop, characterized by carpopedal spasm, tonic-clonic convulsions, and laryngeal stridor. The magnitude of symptoms at any given plasma concentration of ionized calcium varies from patient to patient (Testini *et al.,* 2007, Pfleiderer *et al.,* 2009). On clinical examination, twitching of the facial muscles that stimulated by tapping one cm in front of the ear, (Chvostek's sign), although this sign may be present in 10% of normal patients. Trousseau's sign is also positive and is manifest by the cuff of sphignomonameter inflate at forearm for about 4 min. The development of carpal spasm indicates hypocalcemia, although the test is unpleasant and clinically impractical (Sitges-Serra *et al.,* 2010). Most patients with postoperative hypocalcemia easy to treat with oral calcium. While more severe symptoms will indicate the use of intravenous calcium (Sitges-Serra *et al.,* 2010), the normal parathyroid glands are flat, ovoid, and red-brown to yellow. They are weighing between 30 and 50 mg each. The lower glands are usually larger than the upper glands. The superior glands usually found within the fat on the back surface of the superior thyroid lobe close to the point of entrance of recurrent laryngeal nerve into the larynx (Schaffler, 2010). The arterial supply to both the superior and inferior parathyroid glands is usually from the inferior thyroid artery, although it may arise from the superior thyroid or thyroid ima arteries or the rich anastomosis of vessels supplying the larynx, trachea, and esophagus (Schaffler, 2010, Glinoer *et al.,* 2000). It is sometimes difficult to differentiate between thyroid, fat and parathyroid gland during surgery and inadvertent damage can occur to the gland (Page *et al.,* 2009, Walker Harris *et al.,* 2004). The incidence of permanent hypoparathyroidism post total thyroidectomy should be below (approximately 0.5% to 2%) and the majority of cases show symptoms within 3–5 days' post-surgery but, low percent, there is delay onset for 2–4 weeks (Prim *et al.,* 2001). The purpose of this retrospective, observational study was to elicit the occurrence of hypocalcemia post total thyroidectomy, studying its relationship with surgical procedure and factors which may be the cause that leads to increased risk.

PATIENTS AND METHODS

Total numbers of 100 patients with thyroid disease were undergone total thyroidectomy in Al-Diwaniyah Teaching Hospital, Iraq. Of them 39 were male, and 61 were females. Graves' disease cases were 30, thyroid malignancy was 20, completion surgery for thyroid malignancy cases 30 and multinodular goiter cases were 20.

All patients underwent full preoperative investigations include measuring the level of calcium in serum 12 and 48 h post-surgery. Calcium level lower than 8.5 mg/dl was regarded as postoperative hypocalcemia in spite of the absence of clinical symptoms.

The localisation of parathyroid glands during surgery and careful dissection was taken place at the time of surgery. Replacement therapy was begun in the postoperative period when the clinical manifestation of acute hypocalcemia (tingling, carpal spasm) or when calcium levels below 7.5 mg/dl. Permanent hypocalcemia was defined when we need to maintain oral calcium therapy, may use calcitriol, for more than 12 months postoperatively. The study was approved by the Ethical Approval Committee (EAC) of the College of Medicine, University of Al-Qadisiyah, Iraq. Verbal consent was taken from each woman after explaining the aim and the method of the current study.

Statistical analysis

Statistical analysis was carried out using statistical package for social sciences (SPSS) version 23. Numeric variables were expressed as mean and standard deviation while categorical variables were expressed as number and percentage. Student t-test was used to compare differences in mean values between control and study groups. A p-value > 0.05 was considered as non-significant while a value of ≤ 0.05 was considered as statistically significant.

RESULTS

The study includes 100 patients with multiple thyroid pathologies that end with total thyroidectomy. Of them 39 was male, and 61 was females, showing a higher incidence of thyroid problems in females with a p-value < 0.001, as shown in Table 1. Thyroid diseases that required total thyroidectomy in this study include: Grave's disease 30 cases (30%), primary malignancy cases include 20 cases (20%), completion surgery cases include 30 cases (30%) and multinodular goiter cases include 20 cases (20%), as shown in Table 1. Postoperative hypocalcemia was noticed in 35 cases (35%), asymptomatic one was shown in 16 cases (45.7%) while symptomatic one was shown in 19 cases (54.3%), as shown in Table 2. Grave's disease shows the higher incidence of postoperative hypocalcemia, 15 cases (15%) of the 10 cases was symptomatic with acute manifestations and 5 cases presented as asymptomatic hypocalcemia (laboratory findings only), p-value < 0.001. Malignancy cases were 8 (8%), of the 5 cases presented as symptomatic hypocalcemia and 3 cases as asymptomatic hypocalcemia (3%). Completion surgery after excisional biopsy for malignancy include 5 cases (5%),

Table 1: No. of cases in the study

Disease	No.	Male	Female
Graves' disease	30	6	24
Primary malignancy	20	11	9
Completion surgery	30	17	13
MNG	20	5	15
total	100	39	61

Table 2: postoperative hypocalcaemia

Disease	Asymptomatic hypocalcaemia	%	Symptomatic hypocalcaemia	%	Total
Graves' disease	5	5%	10	10%	15
Malignancy	3	3%	5	5%	8
Completion surgery	3	3%	2	2%	5
Mng	5	5%	2	2%	7
Total	16		19		35

Table 3: symptomatic hypocalcaemia

Disease	Transient	%	Permanent	%
Graves' disease	7	7%	3	3%
Malignancy	4	4%	1	1%
Completion surgery	2	2%	-	-
Mng	2	2%	-	-
Total	15		4	

of the 2 cases were symptomatic hypocalcemia (2%) and 3 cases were asymptomatic. While the MNG cases include 7 cases (7%), of the 2 were symptomatic, and the others were asymptomatic, as shown in Table 2. Permanent hypocalcemia was found in 3 cases of Grave's disease (3%) and one case in malignancy (1%). Transient hypocalcemia was found in other cases and as follow: in Grave's disease 7 cases (7%), primary malignancy 4 cases (4%), completion surgery 2 cases (2%) and in MNG 2 cases (2%), as shown in Table 3.

DISCUSSION

Postoperative hypocalcemia is one of the significant complication post total thyroidectomies; its incidences differ in related to the features used to define it (McGregor *et al.,* 2012). Serum calcium levels do not always indicate symptoms even when they below normal (Gac *et al.,* 2007). The parathyroid glands showing the increased risk of injury due to the fact that they are often found within the thyroid sheath or in some cases may be discovered in the thyroid tissue itself. The blood supply for both superior and inferior glands from the inferior thyroid artery and its anastomotic branch. Blood supply is through an end arterial branch (Proye *et al.,* 1982). As in the study by Prim *et al.,* (1997), they discussed the post-surgical hypocalcaemia to occurs more frequently in those patients that undergoing primary total thyroidectomies than among completion surgery when hemithyroidectomy done for them in first surgery or due to growth of the remaining part of gland post-surgery (Walsh *et al.,* 2007). Hypocalcemia is more common and significant after surgery for Graves' disease than other thyroid conditions. This may explain because of ''hungry bones'' as well as the due to interference with blood supply of parathyroid glands by excessive manipulation (Pattou *et al.,* 1998). Hungry bone syndrome, it found mainly in those with high thyroid hormones and those with signs of thyrotoxicosis for a long period before surgery (Mezher *et al.,* 2017). This condition will cause stimulation of breakdown of bone by the effect of high thyroid hormones. Post-surgery of total thyroidectomy the thyroid hormones showing rapid declines and the triggering of bone breakdown will be gone. (Dakhil, 2017). The bones are now "hungry" for calcium, and will depend on plasma calcium causing a rapid decrease in serum calcium and symptoms will be elicited. Hypocalcemia, hypophosphatemia, hypomagnesemia, and hyperkalemia are four typical features in these patients (Yamashita *et al.,* 2001, Pisanu *et al.,* 2003). In these cases, the use of calcium supplementations with vitamin D products is preferred in the preoperative period mainly in those cases who have deficient in vitamin D and have a high level of alkaline phosphatase (Pisanu *et al.,* 2003). A single parathyroid gland may be capable for maintain calcium level so trying for preserve at least one gland at the time of surgery while some authors do not recommend the searching for parathyroid gland due to the risk of compromising their arterial supply (Lee *et al.,* 1999). The need to keeping healthy and good vascularized parathyroid tissue at the

time of surgery in the thyroid gland is a cornerstone point that surgeon should be kept in mind when performing thyroid surgery. Normal parathyroid tissue is not easy to be detected on gross view (Dakhil, 2017). It may be recognized from the close fatty tissue by some changes in color and the presence of delicate blood vessels which is not shown in the near fat and thymus gland tissue (Han *et al.,* 2007). During surgery, and a parathyroid gland that appears to be devascularized should be autoimplanted after frozen section confirmation (Pattou *et al.,* 1998). This is recognized by a gland that becomes dusky or even black throughout surgery or a gland that accompanies the thyroid specimen as the latter is removed. Hypoparathyroidism is a significant problem for patients after bilateral thyroidectomy. Calcium and, occasionally, vitamin D are required several times a day with careful monitoring. Rates of temporary hypoparathyroidism (usually defined as less than 8.0 mg/dL within 6 months after thyroidectomy) occur in 17% to 40% of patients undergoing total thyroidectomy (Shoback, 2008, Hirai *et al.,* 2001). Permanent hypoparathyroidism rates after total thyroidectomy in expert hands range from 1.2% to 6.5% (Hirai *et al.,* 2001). In an American College of Surgeons survey, which reviewed 24,108 thyroid surgeries, Foster noted a permanent hypoparathyroidism rate of 8% (Payne *et al.,* 2005). Mazzaferri has noted a 13% incidence of permanent hypoparathyroidism after total thyroidectomy in the community setting (Payne *et al.,* 2005). Even in selected tertiary care settings, rates of 29% to 48% have been described. Thomusch found parathyroid injury was associated with the extent of resection, surgery for recurrent disease, advanced age, female sex, and surgery for Graves' disease (Edis *et al.,* 2013). The risk of hypoparathyroidism increases with invasive cancers and when lymph node dissection is performed with thyroidectomy. The risk of hypoparathyroidism is also vitally linked to the experience of the surgeon (Nahas *et al.,* 2006). In the study, 4 patients only were showing a delay in recovery of parathyroid function up to 6 months. A review measurement of PTH level in immediate postoperative period may be effective as early detection for the occurrence of, minutes or hours after the surgery (Roh and Park, 2006). But this test is so expensive, and we can't do it for all patient. The measurement of serum calcium between 6 and 24 h postoperatively may be helpful in early detection of a patient who at risk of developing hypocalcemia symptoms (Al-Hajjiah and Almkhadree, 2018). Administration of calcium supplements and vitamin D as prophylaxis for 14 days' duration is advisable for the prevention of hypocalcemia symptoms (Roh and Park, 2006).

The signs and symptoms of hypocalcemia can be subtle and include perioral or digital paresthesias, muscle cramping, or anxiety. Furthermore, Chvostek sign, facial twitching when the facial nerve is tapped, and Trousseau sign, ischemia-induced carpal spasm (i.e., from a sphygmomanometer), highlight the state neuromuscular excitability during hypocalcemia. Importantly, Chvostek sign may be positive in up to 20% of normocalcemic individuals (Al-Hajjiah *et al.,* 2018). More overt and alarming signs and symptoms include tetany, altered mental status, seizures, prolonged QT interval, heart failure, bronchospasm, and laryngospasm (Roh and Park, 2006, Lecerf *et al.,* 2012). Treatment for hypocalcemia relates to its degree and duration. The goal is to maintain a low-normal calcium level, thereby controlling symptoms while avoiding any toxicity (Dakhil *et al.,* 2018). Acute symptomatic hypocalcemia is treated with intravenous calcium gluconate when a peripheral intravenous catheter is used to avoid tissue necrosis, should intravenous fluid extravasation occur (Kebebew *et al.,* 2000). Magnesium should be given in the oral form when the clinical picture is not improving, or there is a low serum level of magnesium also can be given as parenteral route when symptoms are severe. Calcitriol can be started simultaneously when oral calcium supplementation is initiated (Alsanea and Clark, 2000).

CONCLUSIONS

Post-thyroidectomy hypocalcemia is one of the common complications that developed in the postoperative period. Temporary hypocalcemia usually resolves within 4 weeks of surgery but may last longer. Interval calcium and parathyroid hormone levels should be checked to monitor for recovery. Permanent hypocalcemia is defined as those who require continued calcium and vitamin D supplementation at 1 year postoperatively. Graves' disease has a high risk for postoperative hypocalcemia due to ''hungry bone'' syndrome. There are different regimens to deal with calcium and PTH in the immediate postoperative period that lead to detect those cases with a high possibility to have symptomatic hypocalcemia and them who in need for treatment as replacement therapy.

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