

The Incidence of Transient and Permanent Hypocalcaemia After Total Thyroidectomy for Thyroid Cancer

Sokouti M^a, Montazeri V^a, Golzari S^b

^a Department of Thoracic Surgery and ^b Department of Anesthesiology, Imam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, I.R. Iran

Hypocalcaemia is one of the more acute complications of total thyroidectomy and occurs after parathyroid injury during surgery. The aim of this study is to assess the incidence rate and risk factors of transient and permanent hypocalcaemia in patients who had undergone total thyroidectomy, due to malignant thyroid diseases and to determine the value of parathyroid gland autotransplantation in thyroid cancer surgeries.

Materials and Methods: Sixty-five patients, diagnosed with thyroid malignancy, who were treated by total thyroidectomy with or without radical neck dissection between 2002 and 2006, were studied retrospectively. Of patients 60% were female (mean age 39.59±10.24 years) and 40% were male (mean age 42.11± 11.93 years). Complications of total thyroidectomy, permanent and transient hypocalcaemia in particular, were studied. In eleven patients, parathyroids were transplanted within fibers of sternocleidomastoid and deltoid muscles. **Results:** Transient hypocalcaemia occurred in 18 patients and was treated by intravenous and oral calcium supplements. None of patients progressed to permanent hypocalcaemia. Temporary recurrent laryngeal nerve paresis occurred in 2% of patients but there was no case of paralysis. There was a significant difference in hypocalcaemia occurrence between patients, who had just total thyroidectomy and those who underwent thyroidectomy with neck dissection (p=0.01).

Conclusion: Hypocalcaemia after total thyroidectomy is a serious and dangerous complication, requiring prompt diagnosis and proper treatment. Parathyroid gland transplantation for an injured or incidentally removed parathyroid, between fibers of sternocleidomastoid or deltoid muscles, can prevent the occurrence of permanent hypocalcaemia

Key Words: Hypocalcaemia, Parathyroid autotransplantation, Total thyroidectomy

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Introduction

Total thyroidectomy is the first choice of initial treatment for thyroid cancer¹. Removal of both pathologic and normal thyroids is needed in total thyroidectomy, which is associated with minimal damage to surrounding structures especially parathyroid and their vessels². A frequent postoperative complication of total thyroidectomy, especially related to the parathyroid and its associated vessels is hypocalcaemia³. The occurrence of such complications has been attributed to the surgical techniques, reoperations, neck dissection and experience of the surgical team^{4,5}. The primary and secondary goal of this study is to evaluate the incidence rate and risk factors of transient and permanent

Correspondence: Mohsen Sokouti, Department of Thoracic Surgery, Tabriz University of Medical Sciences, Imam Reza Hospital, Tabriz, Iran
E-mail: Sokouti.mohsen@yahoo.com

hypocalcaemia in patients, who had undergone total thyroidectomies for thyroid cancer, both with or without radical neck dissections. The aim of study is to evaluate the efficiency of parathyroid autotransplantation of glands in preventing hypocalcaemia.

Materials and Methods

In this retrospective study, we evaluated the medical records of 83 patients, who underwent thyroid cancer surgery in referral center of Imam Reza Hospital, affiliated to the Tabriz University of Medical Sciences, over a four year period (2002-2006). The incidences of transient and permanent hypocalcaemia were studied. Fourteen patients were excluded from the study as malignant thyroid disease was not proved in the final pathologic diagnosis and another four because of lapses in the follow up period. Data of the sixty-five remaining patients (mean age 40.60 ± 10.82 years) was used in the study; there were 26 (40%) male patients (mean age 42.11 ± 11.93 years) and 39 (60%) female patients (mean age 39.59 ± 10.24 years). Preoperative work up included medical history and physical examination, thyroid function tests, thyroid ultrasound, fine needle aspiration (FNA), biopsies and chest x-rays. Presenting signs of the patients are given in Table 1.

Table 1. Presenting sign and symptom in 65 patients diagnosed with carcinoma of the thyroid

Clinical presentation	Frequency (%)
Neck mass	53 (83)
Dysphonia	5 (7.7)
Dysphasia	3 (4.6)
Dyspnea	1 (1.5)
Weight loss	1 (1.5)
Hyperthyroidism	1 (1.5)
Cervical lymphadenopathy	5 (7.7)

Surgical procedures performed were total thyroidectomy in 58 patients (89%) and completion of previous thyroidectomy in

seven (11%) patients. Radical neck dissection was performed in 31 patients who had clinically diagnosable lymph nodes or metastatic lymph nodes found during the operation. Unilateral dissections were performed in 29 patients, bilateral dissection in two patients, modified radical dissection in 23 and classic radical neck dissection in 5 patients. Paratracheal lymph node dissections were performed in 12 patients (9 unilateral and 3 bilateral). Parathyroids and recurrent laryngeal nerves were routinely identified before ligation of inferior thyroid and parathyroid vessels. In 11 patients, auto transplantation of parathyroid was performed in the deltoid or sternocleidomastoid muscles, due to vascular injury or removal of glands. Surgical drains, Penrose drains from incision or hemovac-type closed drainage were used. We routinely performed indirect laryngoscopy at the end of anesthesia. Transient hypocalcaemia was considered whenever there was a need for exogenous calcium supplements to maintain normal serum levels (8-10.4 mg/dl) or to correct the clinical signs and symptoms of hypocalcaemia. After 6 months persistent hypocalcaemia was considered permanent.

Statistical analysis:

Data are presented as the Mean \pm SD and frequency (%). Comparisons and normality were performed using the independent samples t and Chi square tests. Fisher exact test was used to assess nominal and ordinal variable. Analyses were conducted using SPSS 16 and P-value < 0.05 was considered statistically significant.

Results

A total of 65 patients diagnosed with thyroid carcinoma and having undergone total thyroidectomy were included in our study. No statistically significant difference was found between men and women, in terms of age. Presenting signs and symptoms of patients are shown in Table 1. Neck mass was the initial presenting symptom in the

majority of the patients (83%). The frequency of tumor types was as following: 64.5 % papillary, 15.5 % follicular, 7.7% anaplastic, 4.5% medullary, and 7.7% Hurtle cell carcinoma as illustrated in Table 2.

Table 2. Distribution of tumors by sex and histological type (n=65)

Histological Type	Male		Female	
	n	(%)	n	(%)
Papillary & Follicular	17	26.0	25	38.5
Hurthle cell	6	9.2	9	13.9
Anaplastic	2	3.0	2	4.5
Medullary	1	1.5	2	3.0

The frequency rates of metastasis were found during clinical exams in 24.6% and surgically in 52% of the patients. Thyroid scan reports were available in 47 patients. Masses reported were hot nodules in two patients and cold in the other 45 patients. In six patients, FNA was not performed and their thyroid malignancy was not diagnosed before surgery. FNA and final pathologic reports are shown in table 3. All the slides were reviewed for confirming diagnosis.

Transient hypocalcaemia was seen in 18 patients (27.7%) whereas permanent hypocalcaemia was not seen in any of our patients (Table 4). Mean time for transient hypocalcaemia correction was two weeks.

Table 3. Comparison of fine needle aspiration and pathological results (n=65)

	Papillary	Follicular	Medullary	Anaplastic	Hurtle cell
FNA	29	13	3	2	6
Pathology	46	9	3	2	5

Table 4. Comparison of hypocalcaemia after total thyroidectomy and total thyroidectomy together with radical neck dissection in carcinoma of the thyroid

Surgery	Patients n (%)	Hypocalcaemia	Normocalcaemia
Total thyroidectomy	27(41.5)	3	24*
Total thyroidectomy With radical neck dissection	38(58.5%)	15	23

*P=0.01

Total thyroidectomy accompanied by neck or paratracheal lymph node dissection was significantly associated with the risk of transient hypocalcaemia. In the group of patients who underwent total thyroidectomy, the incidence of hypocalcaemia was significantly lower than those who had thyroidectomy with neck dissection (Table 4). Autotransplantation of parathyroids was performed in 11 patients (17 %); although these patients progressed to symptoms and signs of transient hypocalcaemia, none of them showed permanent hypocalcaemia.

Discussion

Numerous factors produce hypoparathyroidism after total thyroidectomy. During thyroidectomy, and exploration of thyroid lobes and their blood supply vessels, parathyroids may be injured or accidentally removed. Knowledge of the anatomy and physiology of thyroid and parathyroids and technical skills of the surgeons may play a major role in preventing damage to the parathyroids. Trying to preserve these parathyroids or autotransplantation of accidentally resected glands markedly reduce the incidence of hypocalcaemia⁶.

Permanent hypocalcaemia is a debilitating morbidity following thyroidectomy. Apart

from meticulous dissection to preserve parathyroid gland and their blood supplies, parathyroid auto transplantation has been increasingly used to preserve parathyroid functions. The adoption of parathyroid autotransplantation during thyroidectomy has been reported to be associated with a low incidence of permanent hypocalcaemia. The clearest indication for parathyroid auto transplantation is the patient with radical operation on the thyroid gland or other head and neck organs, where the parathyroids were damaged⁷.

Permanent hypocalcaemia can be avoided by keeping the plane of dissection near the capsule of thyroid gland to prevent, if possible, removal of parathyroid glands. Ligation of the inferior thyroid artery branches in the thyroid capsule should be favored over central ligation to preserve vascular supply to the parathyroids. Surgeons should look in the thyroid specimen for parathyroid glands that may have been removed and re-implant them^{6,8}.

Hypocalcaemia following thyroidectomy is usually temporary and its incidence is reported to 4-42%. A low incidence ranging between 0 to 8% has been reported for permanent hypocalcaemia in currently available literature⁹. In some centers, the incidence for total thyroidectomy is reported to be 2% or less. Halsted and Evans described an end-artery to each parathyroid and they believed it is best to avoid its disruption. If an end-artery is damaged, autotransplantation must be performed¹⁰. If a parathyroid gland appears congested or ischemic at the end of surgery, an incision must be performed on the capsule to liberate venous and arterial blood flow. If the color of parathyroid is satisfying, the gland should be preserved; if not, auto transplantation must be performed in an appropriate location¹¹. The incidence of incidental parathyroidectomy in thyroid surgery ranges between 8 to 19%. According to Turnali, permanent hypocalcaemia is referred to when

patients need calcium and vitamin D supplements six months after operation¹².

Zendenius et al found that in 100 patients with total thyroidectomy, after transplantation of one parathyroid gland in the sternocleidomastoid muscle there was no permanent hypocalcaemia¹³. In the Low and Lam study, among 98 patients with total thyroidectomy, transitory hypocalcaemia occurred in 21.4%, and none of the cases progressed to permanent hypocalcaemia; in their overall series of 271 patients, permanent hypocalcaemia occurred only in patients, on whom parathyroid transplantation was not performed¹⁴. In 20% of Mozzaffary's patients whom underwent total thyroidectomy along with radical neck dissection, without parathyroid transplantation, a 2.5% incidence rate of permanent hypocalcaemia was reported¹⁵. Chow et al reported 16% permanent hypocalcaemia after total thyroidectomy, an incidence, which reached to 30% when patients had thyroid cancers¹. In 310 patients with total thyroidectomy in the Chaudhary series, 17 patients (5.48%) had hypocalcaemia, 12 patients transient, and 5 had permanent hypocalcaemia¹⁶. In the Ganecalves series of total thyroidectomy for thyroid cancer, transient hypocalcaemia was reported in 25.5% of cases and permanent hypocalcaemia in 5.1%; when radical neck dissection was added to total thyroidectomies, these rates increased⁹. In the Vayesberg study, skill and experience of surgeons in performing total thyroidectomies were evaluated and hypocalcaemia was observed in 6.3% of the patients¹⁷.

To prevent postoperative hypocalcaemia following total thyroidectomy, Kihara recommended preservation of the parathyroids in situ, so that they could be autotransplanted for resected or devascularized glands¹⁸.

Lo CY recommended meticulous dissection to preserve parathyroid glands and their blood supply and parathyroid autotransplantation to preserve parathyroid functions during thyroidectomy; he reported a low

incidence of permanent hypocalcaemia in his study⁷.

Strunski studied 351 surgical patients who had undergone total thyroidectomy for bilateral goiters and found 5.2% unintentional parathyroidectomy; parathyroid gland autotransplantation had been performed in 7% of patients during surgery; he suggested parathyroid gland auto transplantation did not affect serum calcium levels³.

Steily performed routine calcium and vitamin D administration and routine autotransplantation of parathyroid gland in 223 patients to prevent permanent hypocalcaemia after total thyroidectomy. Postoperative hypocalcaemia occurred in 17% and no patient developed permanent hypocalcaemia during the follow up period¹⁹.

Assay of intraoperative parathyroid hormone (PTH) has been suggested to be valuable in predicting the development of postoperative hypocalcaemia after thyroid surgery. The objective of the Barezynski study was to evaluate the applicability of intraoperative PTH in guiding the surgeon to selective parathyroid transplantation during total thyroidectomy. Study results indicated that selective intra-operative PTH assay guided to parathyroid auto transplantation significantly decreases the incidence of transient postoperative hypocalcaemia²⁰.

In our study 18 patients showed transient hypocalcaemia and performing parathyroid auto transplantation was found to be markedly beneficial in the prevention of permanent hypocalcaemia.

This retrospective study had acceptable results of morbidity with hypocalcaemia, but it had its limitations because it was not a case-control study.

Parathyroid tissue can be successfully auto transplanted and used as a prophylaxis of parathyroid insufficiency in thyroid cancer surgeries. The secretion of parathyroid hormone from the grafted parathyroid tissue can be shown to progressively increase with time in the postoperative period^{18, 21}.

Some revised data suggest the following thyroid cancer guidelines may benefit surgeons:

A. When primary tumor has extended beyond the thyroid capsule and involved cervical lymph nodes; completeness of surgical resection is an important determinant of outcome, while residual metastatic lymph nodes represent the most common site of disease persistence and recurrence.

B. To minimize treatment-related morbidity, the extent of surgery and the experience of the surgeon both play important roles in determining the risk of surgical complications.

C. To permit accurate staging of the disease, because disease staging can assist with initial prognostication, disease management and follow-up strategies, accurate postoperative staging is a crucial element in the management of patients with differentiated thyroid carcinomas.

D. For patients undergoing Radioactive Iodine (RAI) treatment, remnant ablation or RAI treatment of residual or metastatic disease, removal of all normal thyroid tissue is an important part of initial therapy. Near total or total thyroidectomy may reduce the risk of recurrence.

E. For reducing recurrence, both RAI whole body scanning and measurement of serum Thyroglobulin are affected by residual normal thyroid tissue. In these patients near total or total thyroidectomy is required.

F. Adequate surgery is the most important treatment, while radioactive iodine treatment, thyroid stimulating hormone (TSH) suppression, and external beam irradiation, each play adjunctive roles in at least some patients.

Recommendations D and C of thyroid cancer guidelines focused on expert opinion of surgeons and recommendation A and B is based on good evidence that the service and intervention can improve health outcomes⁵.

To conclude, high risk procedures, such as total thyroidectomy require special surgical training and expertise and when

parathyroids are incidentally removed, or the tumor invades the capsule and end artery of parathyroid, hypocalcaemia is expected to be seen^{5,8}. Autotransplantation of parathyroid between the fibers of deltoid or sternocleidomastoid muscles seems to prevent occurrence of permanent hypocalcaemia.

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