

Iatrogenic hypoparathyroidism after surgery for retrosternal goitre. A single centre retrospective analysis

G. Damiano, G. Cocchiara, V. D. Palumbo, F. Fatica, F. Caternicchia, A. I. Lo Monte, M. Cajozzo

Department of Surgical, Oncological and Stomatological Sciences, University of Palermo, Italy

Abstract

Aim. The aim of this study is to assess, retrospectively, the incidence of secondary hypoparathyroidism after total thyroidectomy in patients with retrosternal goitre.

Materials and methods. From January 2009 to September 2015, 622 patients who undergone total thyroidectomy for goitre, were retrospectively observed. The patients were divided into two groups: Group A, including 58 patients with retrosternal goitre and Group B, including 562 patients with in situ goitre. Those patients with diseases of the parathyroid glands, assumption of drugs modifying calcium metabolism and who received blood transfusions before or after surgery, were excluded from the study. In both groups, a total thyroidectomy was performed under general anaesthesia. The upper and lower parathyroid glands in both groups were observed in situ as well. All surgical specimens underwent histological examination.

Results. Transient hypocalcaemia was observed in a higher percentage in group A (15% vs 7%, $P < 0.05$). The mean hospital stay was greater in group A ($P < 0.05$). There were no statistically differences between the two groups in terms of permanent hypocalcaemia and post-operative blood ionized calcium (72 hours and 1 month).

Conclusions. Many efforts should be made to respect parathyroids during total thyroidectomy in retrosternal goitre; greater attention should be given to inferior parathyroid glands that should be displayed, respecting the vasculature and performing a terminal lower thyroid artery ligation in order to reduce the risk of transient hypocalcaemia and – as a consequence – the average hospital stay. *Clin Ter 2018; 169(2):e67-70. doi: 10.7417/CT.2018.2056*

Key words: goitre, hypocalcaemia, hypoparathyroidism, retrosternal goitre, thyroid gland, and thyroidectomy

Introduction

Goiter is a common condition due to the increase of thyroid gland; retrosternal (or substernal) extension of thyroid was described for the first time by Haller (1). There is unanimous agreement on the definition of retrosternal goiter (RG) (2, 3). Some authors distinguish primitive RG derived from ectopic thyroid tissue (1%) (4, 5) and secondary RG characterized by a descent towards the mediastinum of the

normal tissue of the thyroid gland (5,6) when the thyroid gland extends 3 cm below the sternal incision or below the fourth thoracic vertebra (7,8). According to other authors there are three types of RG: type I (85% of cases) when goiter occupies the anterior mediastinum, type II (15%) the posterior mediastinum and type III (1%) if located entirely within the mediastinum (9).

The incidence of reported RG varies from 20 to 30% among patients undergoing thyroidectomy (10, 11); the risk reported for cancer is ranging from 4 to 22% (12, 13). Transient hypoparathyroidism is a complication of total thyroidectomy that appears in 13-45% of cases (14-18), while permanent hypoparathyroidism after total thyroidectomy varies from 0.3 to 3.5% (15-16, 19-21).

Upper parathyroid glands are localized in the posterior surface of thyroid gland at level of its third middle close to the point where recurrent laryngeal nerve penetrates in larynx; inferior parathyroid glands are located in 60% of cases, in the lower pole of the gland, and 1-2 cm below the lower pole in 20% of cases (22).

The objective of this study was going to assess, retrospectively, in a group of patients who underwent total thyroidectomy for RG, the incidence of secondary hypoparathyroidism.

Materials and methods

From January 2009 to September 2015 they were retrospectively observed 622 patients undergone total thyroidectomy for goiter. The patients were divided into two groups: Group A of 58 patients (20 male, 38 female - average age 61 years) with RG; Group B of 562 patients with in situ goiter (179 men, 383 women - average age 55 yo). The 91% of RG of Group A was extending in anterior mediastinum, 9% in posterior mediastinum. From general population of patients were excluded from the study those patients presenting primitive diseases of the parathyroid, assumption of drugs modifying calcium metabolism and who received blood transfusions before or after the surgery.

Preoperative diagnosis was made by physical examination, ultrasonography of the neck (ETG), chest X-ray,

fT3, fT4 and TSH dosage. In patients for whom there was physical examination and ETG highly suspicious for RG a chest CT scan was performed. Indications for surgery were: compressions and/or tracheal deviation, suspect neoplastic degeneration of thyroid from fine needle aspiration biopsy, compressive symptoms as dysphagia and/or dysphonia, and hyperthyroidism.

In both groups a total thyroidectomy was performed under general anaesthesia and following the direct view and respect in place (no touch technique) of bilateral recurrent nerves. The upper and lower parathyroid glands in both groups were observed in situ as well (14).

58 patients from group A (98%) were operated via the transcervical approach; in 2 cases a median sternotomy was performed.

All surgical specimens underwent histological examination.

In the post operative, for each patient of both groups, it was determined the blood ionized calcium, and phosphorus at 24, 48, 72 hours (post-operative) and at 1 month following surgery (Nova analyser - Nova biomedical, Darmstadt, Germany; coefficient of variation 3.5% per $x=1.19$ mmol/l). Serum ionized calcium was considered normal between 1.16-1.32 mmol/l. Patients were clinically evaluated at 24, 48, 72 hours and 30 days for evoking Chvostek and Trousseau signs and symptoms of hypocalcaemia, such as numbness in the limbs and/or perioral region, convulsions and laryngospasm. Hypocalcaemia was defined transient in presence of ionized calcium <1.16 mmol/l and signs and symptoms needed medical treatment for less than 6 months, conversely permanent if hypocalcaemia lasted more than 6 months. The postoperative treatment with calcium associated to oral calcitriol was only initiated if serum calcium levels were <1.16 mmol/l and appeared if signs and symptoms of hypocalcaemia. It was also evaluated the mean hospitalization stay for each patient, the mean serum calcium (at 24, 48 and 72 hours), and the percentage of transient and permanent hypocalcaemia in both groups. For all patients it was performed a clinical and blood test follow-up at 5 and 8 months after surgery to assess the impact of definitive hypocalcaemia.

Data were collected and elaborated by Graph Pad (GraphPad Software, Inc). Age of patients, average length of stay in hospital and post-operative serum calcium levels at 24, 48 and 72 hours were evaluated by comparing the means of two samples with different size, with a level of significance of 5%; χ^2 test was used to evaluate the sex, the transient and permanent hypocalcaemia incidence, and the percentage of upper and lower parathyroid displayed and left in situ.

Results

No statistically significant differences were observed regarding sex and age in the two groups.

The average weight of thyroid was 257 g for group A and 35 g in Group B.

Final histological examination of sub-sternal thyroids (group A) showed: 36 cases (62%) of colloid cystic macro- and microfollicular goiters, 13 cases (22%) of papillary microcarcinomas, 4 (6.8%) Hurtle adenomas, 2 (3.4%) papillary carcinomas, 2 (3.4%) follicular carcinomas, 1 (1.7%) medullary carcinoma. Final histological examination for group B showed: 381 (67.8%) of colloidcystic goiters, 78 (13.9%) papillary microcarcinomas, 41 (7.3%) autoimmune thyroiditis, 24 (4.3%) hurtle cells adenomas, 18 (3.2%) papillary carcinomas, 16 (2.8%) follicular carcinomas, 4 (0.7%), medullary carcinomas.

There was a lesser number of superior parathyroid glands displayed during surgery in Group A compared to B (96% vs 99%), and a lower percentage of inferior parathyroid glands displayed in group A than in group B (82% vs. 98%) $p < 0.0001$ (Table 1).

Final histological examination has not found greater percentage of upper parathyroid removed with thyroid between the two groups (97% vs. 99%). While the percentage of lower parathyroids found in surgical specimen (therefore a lesser number of parathyroids in situ) at histology was significantly higher than group B ($p < 0.0001$) (Tab. 2). It was not found statistical difference between the upper and lower parathyroid displayed and those left in situ (96% vs. 97%) and (99% vs. 99%) in group A (82% vs 84%) and (99 vs 98%) respectively.

The values of mean serum calcium in the postoperative period at 24 and 48 hours, were 1.23 ± 0.081 mmol/l and 1.20 ± 0.080 mmol/l in patients in group A and 1.26 ± 0.079 mmol/l and 1.24 ± 0.079 mmol/l in group B ($p < 0.0001$); while there was no statistically significant difference in the controls at 72 hours between the two groups, and 30 days after surgery (Tab. 3).

Tab 1. Displayed parathyroid glands

	Upper Parathyroid glands	Lower Parathyroid glands
Group A	112/116 (96%)	96/116 (82%)
Group B	1110/1124 (99%)	1110/1124 (99%)
p-value	$p=0.02$	$p<0.0001$

Tab 2. In situ left parathyroids at histology

	Upper Parathyroid glands	Lower Parathyroid glands
Group A	113/116 (97%)	98/116 (84%)
Group B	1113/1124 (99%)	1109/1124 (99%)
p-value	$p=0.1240$	$p<0.0001$

Tab 3. Average values of ionized serum calcium post-intervention

	24 h	48 h	72 h	30 days
Group A	1.23 ± 0.081	1.20 ± 0.080	1.24 ± 0.080	1.25 ± 0.081
Group B	1.26 ± 0.079	1.24 ± 0.079	1.26 ± 0.079	1.26 ± 0.079
p-value	$p<0.0001$	$p=0.0003$	$p=0.0672$	$p=0.3602$

The transient hypocalcaemia was clinically manifested in a higher percentage of patients in group A (16% vs 7%, $p < 0.05$) (Table 4).

In such patients, clinical manifestations observed were: perioral paraesthesia and/or at the hands and/or the positive Trousseau sign and serum ionized calcium was < 1.09 mmol/l.

In these patients it was administered calcium gluconate (1 mg/kgbw/hour for 48 hours) with the disappearance of the symptomatology.

Permanent hypocalcaemia was reported in 2.4% of patients in group A and in 0.7% of the 2 patients (no statistically significant difference between the two groups). The mean length of stay in hospital was greater in group A ($p < 0.0001$) (Tab. 5).

Discussion

Surgery is the treatment of choice for symptomatic patients with goitre or substernal malignant tumors of the thyroid (1,23,24); although associated with a low rate of mortality and morbidity, the role of surgery in asymptomatic patients is controversial (25). Transient and/or permanent hypoparathyroidism may occur following total, sub-total or near total (whenever justified (26)) thyroidectomy due to a combination of factors: excision of the parathyroid (including partial reduction of the number of them), their devascularization, hampered by a venous outflow (14,27-30).

A recent prospective longitudinal study of Puzziello et al. shows that the main factors of influencing transient hypocalcaemia in patients who underwent thyroidectomy are: thyroid cancer, lymph node excision, and female sex; the authors conclude further that the display and respect of parathyroid influences the incidence of transient hypoparathyroidism, thus having an impact on hospital inpatient time (31).

Few studies have focused on the possibility of preserving the parathyroid glands in situ during total thyroidectomy for RG (22). Since inferior parathyroids are localized near the lower pole, in substernal goitre the volume increase of the lower pole that migrates to the mediastinum may render more

difficult identifying and respecting the lower parathyroid glands (22,32). Heineman et al. report in fact that inferior parathyroid glands can be identified, but with lower efficacy in patients with substernal goiter, compared to those with no substernal goiter (22). An analysis of the findings from our retrospective study shows that there was a greater likelihood of view and respect in situ of inferior parathyroids in patients with substernal goiter than in patients with goiter confined in the neck and therefore, in the first group of patients we had a higher incidence of transient hypoparathyroidism, related to a mean serum calcium at 24 and 48 hours after surgery, significantly lower in patients with RG. Therefore, in this last group of patients, the average length of stay in hospital, was significantly higher. The higher incidence of transient hypoparathyroidism in group A we think could be related to a lower number of parathyroid remained in situ compared to group B and moreover from the increased surgical manipulation in patients with substernal goiter that could be the cause of a greater likelihood of altering inferior parathyroid glands blood flow. Normalization of serum calcium at 72 and 30 days after surgery is probably due, instead, to the establishment of collateral circulation between the anastomotic tissue thyroid-thymic and parathyroid lower and the connective tissue that separates the thyroid and parathyroid lobes (20,33); for this reason a terminal inferior thyroid artery ligation should be performed.

We evaluated, also, that there was no statistically significant difference between the number of upper and lower inferior parathyroid glands visualized during surgery and those actually left in situ (verified by the absence of parathyroidal tissues on specimens at histological examination) in both groups, without the need to performing an intraoperative histological examination as reported by Heineman et al. (22).

Many efforts should be made to respect parathyroids in situ during total thyroidectomy; greater attention should be given to the inferior parathyroid glands that are to be displayed, respecting the vasculature and performing a terminal lower thyroid artery ligation (14) in order to reduce the risk of transient hypocalcaemia and - as a consequence- the average length of stay in hospital.

Table 4. Transient and permanent hypocalcaemia incidence

	Transient hypocalcaemia	Permanent hypocalcaemia
Group A	9/58 (16%)	1/58 (1.7%)
Group B	40/562 (7%)	3/562 (0.5%)
p-value	$p = 0.0153$	$p = 0.3808$

Table 5. Average length of stay in hospital

Group A	86 h \pm 13.39
Group B	45 h \pm 13.42
p-value	$p < 0.0001$

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