



Original/Cáncer

Transient hyperthyroidism after total laryngectomy for laryngeal cancer

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Abstract

Introduction: Thyroid damage is a complication of total laryngectomy (TL) and may be caused by manipulation of the gland. There are isolated descriptions in the literature related to transient hyperthyroidism (HT) post-head and neck surgery. The aim of this study was to determine the frequency of HT after TL and to evaluate its relationship with the surgical procedure.

Methods: Retrospective cohort study. Forty-four patients were included and stratified in Group 1 (TL + pharyngectomy), and Group 2 (TL + neck dissection). Post-op thyroid function was measured in all patients. Results were analyzed with chi square plus Yates and OR ($p<0.05$).

Results: Twenty-four patients (54.6%) developed HT, with a mean TSH 0.11 ± 0.09 μ U/ml and a median FT4 1.5 ng/dl (1.2-1.8, IQR 0.30). Four patients (16.6%) required a pharmacological approach, because of their clinical course. Patients in Group 1 showed significantly more hyperthyroidism compared to Group 2 ($p=0.04$, OR 4, CI 95% CI, 1.03-15.53). All became euthyroid before discharge.

Conclusion: We found a high prevalence of HT after TL, and it was related indeed to the surgical procedure. All patients became euthyroid before discharge. We suggest to check thyroid function in routine lab tests in this setting. The hypothetical repercussion of these findings on resting energy expenditure and haemodynamics requires further studies.

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Keywords: *Transient hyperthyroidism. Total laryngectomy. Laryngeal cancer.*

HIPERTIROIDISMO TRANSITORIO TRAS LARINGECTOMÍA TOTAL POR CÁNCER LARÍNGEO

Resumen

Introducción: La tiroiditis postquirúrgica es una complicación de la laringectomía total (TL) y pueden ser causada por manipulación de la glándula. Existen descripciones aisladas en la literatura referentes a hipertiroidismo transitorio (HT) en el postoperatorio de cirugía de cabeza y cuello. El objetivo del presente estudio es relacionar la frecuencia de HT tras TL y evaluar su relación con el procedimiento quirúrgico.

Métodos: Estudio de cohorte retrospectiva. Se incluyeron 44 pacientes y se estratificaron en Grupo 1 (TL y faringectomía), y grupo 2 (TL y disección cervical). Se midió la función tiroidea postoperatoria a todos los pacientes. Los resultados fueron analizados con el test de chi cuadrado con corrección de Yates y OR ($p<0.05$).

Resultados: Cuarenta y cuatro pacientes (54.6%) presentaron HT, con TSH promedio de 0.11 ± 0.09 μ U/ml y mediana de FT4 1.5 ng/dl (1.2-1.8, IQR 0.30). Cuatro pacientes (16.6%) requirieron tratamiento médico, debido a su curso clínico. Los pacientes del Grupo 1 mostraron significativamente mayor hipertiroidismo comparados con el Grupo 2 ($p=0.04$, OR 4, CI 95% CI, 1.03-15.53). Todos los pacientes fueron dados de alta eutiroideos.

Conclusión: Encontramos una alta prevalencia de HT tras TL, la cual se relacionó con el procedimiento quirúrgico. Todos los pacientes fueron dados de alta eutiroideos. Sugerimos medir la función tiroidea en la analítica de rutina de estos pacientes. Las repercusiones hipotéticas de estos hallazgos en el gasto energético en reposo y hemodinámico requieren mayores estudios.

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Palabras clave: *Hipertiroidismo transitorio. Laringectomía total. Cáncer laríngeo.*

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Introduction

Transient hyperthyroidism is defined as elevated FT4 levels with TSH suppression, self-limited, with no evidence of previous disease¹. It may be related to immune mechanisms by increasing circulating antibodies, such as postpartum hyperthyroidism, or manipulation of the thyroid gland after surgery (also called post-surgical thyroiditis). There is a third mechanism, where the release of thyroid autoantigens during parathyroidectomy may trigger reactivation of autoimmune thyroid disease in a predisposed individual, with a similar pathophysiology to postpartum hyperthyroidism².

In transient hyperthyroidism secondary to post-surgical thyroiditis a typically thyrotoxic phase occurs during the first two weeks after surgery, and remission occurs in 4 to 6 weeks. Before making a diagnosis of post-surgical thyroiditis, other causes of hyperthyroidism must be excluded¹. Most patients are asymptomatic³, and in those with symptoms, the most common ones are sweating, palpitations, chest pain, heat intolerance, weight loss, anxiety; all of them self-limited^{4,5}. Its pathogenesis has been suggested as a transient thyroiditis caused by manipulation of the thyroid or neck dissection during the course of surgery or other procedures, which causes the release of thyroid hormones^{1,2,4,6,7}.

There are few reports of transient hyperthyroidism after needle aspiration of solid thyroid nodules⁸, seat-belt thyroiditis⁹, parathyroidectomy for primary^{7,10}, secondary¹¹, tertiary¹² hyperparathyroidism, and resection of parathyroid adenoma², with a varying incidence between 1-77%, onset of 1-2 weeks, and resolution between 3-4 weeks.

There are isolated descriptions in the literature related to transient hyperthyroidism post-head and neck cancer surgery^{13,14,15}, mainly related to development of atrial fibrillation. These articles refer to the paucity of literature on the topic. The relationship between surgical treatment of laryngeal cancer and hypothyroidism is well documented in previous studies, especially its relationship with radiotherapy^{22,23}, thus the assessment of thyroid function is recommended in the preoperative evaluation of patients with laryngeal cancer. However, we have found very few reports in the literature about transient hyperthyroidism after laryngectomy, which is a surgery that often includes thyroid mobilization, and even its section^{16,17,18,19,20,21}.

The objective of this study was to determine the incidence of hyperthyroidism after total laryngectomy for laryngeal cancer, and whether it was self-limited or not. We also defined demographic characteristics, risk factors and treatment of those patients, and evaluate the association between type of surgery and development of transient hyperthyroidism.

Material and methods

Population: Patients undergoing total laryngectomy (TL) for laryngeal cancer in the Burgos Universi-

ty Hospital during the period January 2009 - August 2011. We excluded patients with incomplete data, preoperative thyroid medication, previous thyroid disease, neck surgery, or radiotherapy.

Design: Retrospective cohort study. We reviewed medical records of the study population and relevant information was entered into the data collection notebook consigning: age, sex, history of smoking and alcohol abuse, type of surgery, laboratory tests including thyroid hormones and their follow-up until the resolution of hyperthyroidism, if indicated. We considered hyperthyroidism as a TSH lower than 0.3 μ U/ml. FT4 levels were checked to stratify into clinical or sub-clinical hyperthyroidism. Reference values of thyroid hormones were: TSH 0.3-5.0 μ U/ml, FT4 0.8-1.7 ng/dl, measured using Cobas® e-602 (Roche) equipment using an electro-chemiluminescence immunoassay (ECLIA) with ruthenium technique.

Statistical analysis: We stratified the study population into Group 1 (TL + pharyngectomy) and Group 2 (TL + neck dissection). Post-op TSH and FT4 was measured in all patients. Numerical data were expressed as mean \pm SD according to normal distribution, and as median and interquartile range if not. Frequency analyses were measured for qualitative variables and compared using the chi square test, and Yates correction if needed. Odds ratio (95% CI) between variables was determined. Statistical significance was reached at $p < 0.05$. Data were analyzed with SPSS 21.0. Ethics: All patient data were anonymized. The project was approved by the Clinical Research Ethics Committee of the Health Area of Burgos and Soria.

Results

Fifty-six TL were performed, 54 (96%) males and 2 (4%) females. Twelve patients were excluded from the analysis, six because they did not have complete data, one had laryngeal stenosis, and five due to lack of postoperative thyroid hormones. The final sample was $n=44$ patients, 42 (96%) males and 2 (4%) females, all with squamous laryngeal cell cancer. Regarding risk factors, 41 (93.2%) had a previous smoking history, 21 (47.7%) alcohol abuse, and 21 (47.7%) both.

The study population was distributed depending on TNM staging as: 0 (0%) Stage I; 5 (11.36%) Stage II, 8 (18.19%) Stage III, and 31 (70.45%) Stage IV; and were distributed according to type of surgery performed: Group 1 (TL plus pharyngectomy) 16 (36.36%) and Group 2 (TL + neck dissection) 28 (63.64%).

Twenty-four patients (54.6%) developed transient hyperthyroidism within two weeks of the intervention, with a mean value of TSH 0.11 ± 0.09 μ U/ml (range 0.01-0.29) and a median value of FT4 1.5 ng/dl (1.2-1.8, IQR 0.300). All thyroid hormone levels returned to normal before discharge (range 7-60 days), with a mean value of TSH 1.39 ± 0.71 μ U/ml (range 0.46-2.89) and a median value of FT4 1.1 ng/dl (1-1.2, IQR

Table I
Mean values of thyroid hormones

	<i>TSH (range, SD)</i>	<i>FT4 (median, IQR)</i>
HT (n=24) at diagnosis	0.11±0.09 uU/ml (0.01-0.29)	1.5 ng/dl (1.2-1.8, 0.30)
HT (n=24) at discharge	1.39±0.71 uU/ml (0.46- 2.89)	1.1 ng/dl (1-1.2, 0.09)
HT with clinical course (n=4)* At diagnosis	0.14±0.09 uU/ml (0.01-0.25)	1.75 ng/dl (1.45-9.3, 2.42)
HT with clinical course (n=4)* At discharge	1.79±0.47 uU/ml (1.1-2.39)	0.95 ng/dl (0.85-1.1, 0.13)

* Four patients from the HT group.

0.09) (Table I). Patients in Group 1 showed significantly more hyperthyroidism compared to Group 2 ($p=0.04$, OR 4, CI 95% CI, 1.03-15.53) (Table II).

Only 4 out of 24 patients that developed transient hyperthyroidism showed a clinical course, with a mean TSH 0.14 ± 0.09 uU/ml (range 0.01-0.25) and a median FT4 1.75 ng/dl (1.45-9.3, IQR 2.42), and required medical treatment, two with propranolol and two with methimazole. All became euthyroid at discharge, with a mean TSH 1.79 ± 0.47 uU/ml (range 1.1-2.39) and a median FT4 0.95 ng/dl (0.85-1.1, IQR 0.125).

Discussion

Laryngeal cancer has a frequency of 2% of all malignancies, and it is the most common malignancy of the upper aerodigestive tract in Europe, with an estimated annual incidence of 25 cases per 100,000 inhabitants in Spain. There are important factors associated confirmed in the present study, such as alcohol abuse and smoking^{24,25}. It is often diagnosed in advanced stages, and treatment is mainly surgical, involving total laryngectomy with neck dissection, and even pharyngectomy.

There are a paucity of case reports regarding to patients who developed transient hyperthyroidism after total laryngectomy, and no clinical series were found after literature review^{13,14}. Our study shows a very high incidence (over 50%) of transient hyperthyroidism after total laryngectomy. Although its pathophysiology has not been clearly defined, we postulate that it may be due to thyroid manipulation.

Kobayashi et al compared two series of patients who had thyroid puncture and needle aspiration for thyroid nodules cysts, after which one of the patients developed transient hyperthyroidism, concluding that the emergence of this phenomenon has an incidence of less than 1% in this setting⁸. Leckie et al described a case with onset of thyroiditis, demonstrated by decreased uptake of Tc-99m in the left lobe of thyroid gland, with normal thyroid hormones in a 64 year-old patient after chronic trauma in the left side of the neck due to car seat-belt use, the thyroiditis was resolved one month after changing the seat-belt⁹.

The occurrence of transient hyperthyroidism has an incidence of 20% in post-parathyroidectomy patients as primary,⁶ and up to 77% as secondary hyperparathyroidism¹¹. Total laryngectomy usually involves thyroid isthmus section for mobilization of the larynx, and in some cases hemi-thyroidectomy; thus it seems reasonable to relate the mobilization of the gland with development of transient hyperthyroidism. Moreover, the more aggressive surgery, the higher the risk that transient hyperthyroidism appears, as was shown in our study.

Given the self-limited and subclinical course of hyperthyroidism, in most patients drug treatment is not indicated. Beta blockers can be given if there are marked symptoms or in patients with coronary disease^{1,3,16}. Methimazole takes 1-2 weeks to take effect, so it is not indicated in this setting.

Conclusions

A high incidence of self-limited hyperthyroidism was found after total laryngectomy for laryngeal cancer, with all TSH values returning to normal at discharge. A more aggressive type of surgery is clinically and statistically associated with a higher incidence of transient hyperthyroidism. Given the subclinical course of this condition, most patients do not require treatment other than monitoring during their hospital stay; thus we recommend checking thyroid hormones in the postoperative period of these patients. The hypothetical repercussion of these findings on resting and haemodynamic energy expenditure requires further studies.

Table II
Frequency of hyperthyroidism (HT) according to surgical procedure

	<i>Group 1 (n,%)</i>	<i>Group 2 (n, %)</i>	
HT (+)	12 (75%)	12 (42,86%)	24 (54,54%)
HT (-)	4 (25%)	16 (57,14%)	20 (45,46%)
Total	16 (100%)	28 (100%)	44 (100%)

$p=0.04$, OR 4, CI 95% CI, 1.03-15.53.

Group 1 = Total laryngectomy + pharyngectomy.

Group 2 = Total laryngectomy + neck dissection.

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