

ONCOLOGY

Parathyroid function study in patients submitted to laryngeal surgery for squamous cell carcinoma

Studio della funzione paratiroidea in pazienti sottoposti a chirurgia laringea per carcimoni squamocellulari

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SUMMARY

Aim of this study was to investigate any eventual quantitative variations in the serological concentration of parathormone in a homogenous sample of patients suffering from laryngeal squamous cell carcinoma who underwent only surgery. A total of 12 patients (2 female, 10 male), aged between 58 and 76 years, were treated between June 2002 and June 2003. The patients were all affected by T2-T3 laryngeal squamous cell carcinoma. Serum intact parathyroid hormone and calcaemia were measured pre- and post-operatively. Of these patients, 2 underwent total laryngectomy (including thyroid isthmectomy), 5 patients received partial supraglottic laryngectomy, while the remaining 5 were submitted to supracricoid laryngectomy. Results showed a progressive regression of parathyroid hormone level, in only one case and was not, however, below normal limits. Contrary to data reported in the literature, this study indicated that the incidence of hypoparathyroidism following laryngeal surgery, even in radical surgical approaches, proved to be closer to zero.

KEY WORDS: Parathyroid hormone, Squamous Cell Carcinoma, Larynx, Laryngeal surgery

RIASSUNTO

Questo studio si propone di ricercare variazioni quantitative della concentrazione sierologica di paratormone in un campione omogeneo di pazienti affetti da neoplasia squamocellulare laringea sottoposti a trattamento chirurgico elettivo ed esclusivo. 12 pazienti (2 donne, 10 uomini) di età compresa fra 58 e 76 anni, sono stati trattati dal giugno 2002 al giugno 2003. Tutti i pazienti, affetti da neoplasie squamocellulari maligne in stadio T2 o T3, sono stati sottoposti ad un follow-up comprendente dosaggio sierico di paratormone intatto e calcemia, dopo 3, 6, 12 mesi dall'intervento chirurgico. Di questi pazienti 2 sono stati sottoposti a laringectomia totale (comprendente istmectomia tiroidea), 5 a laringectomia sub-totale sopraglottica e 5 a laringectomia sopracricoidica. In un solo caso si è riscontrata una diminuzione progressiva della paratormonemia, pur non al di sotto dei limiti di norma. A differenza di quanto riportato in letteratura, l'incidenza di ipoparatiroidismo post chirurgia laringea, pur comprendendo approcci chirurgici più o meno demolitivi, è parsa essere prossima allo zero.

PAROLE CHIAVE: Paratormone, Carcinoma squamocellulare, Laringe, Chirurgia laringea

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Introduction

In laryngeal surgery, dissection or closure of the vascular peduncles of the thyroid ¹, is performed, the common embryological origin of the parathyroid and thyroid glands being reflected in the same vascular anatomy. The close anatomic relationship of these glands with the laryngeal structures exposes patients who have undergone surgery for laryngeal squamous cell carcinoma (SCC) to the risks of hypothyroidism and hypoparathyroidism ². Hypothyroidism related to surgery and radiotherapy for laryngeal SCC is widely acknowledged ^{3,4}. This incidence is reported to be between 65% and 95% ⁵⁻⁷. Hypoparathyroidism can be found in 50%-73% of patients after having undergone total pharyngolaryngectomy ^{8,9}; furthermore, it is related to surgery on the thyroid in 3%-32% of cases depending on the extent of the treatment ¹⁰.

With regard to laryngectomy combined with partial thyroidectomy, hypoparathyroidism is estimated to occur in between 12% and 31% of cases ¹¹.

Only one study linked the exposure to radiation to the onset of hyperparathyroidism ¹².

Material and methods

A series of patients treated for laryngeal SCC, from June 2002 to June 2003, were included in this research. An Ethics Committee is not available in our Institution, albeit valid consent was obtained from the patients with a personal permission document, in keeping with the mandate of the Declaration of Helsinki.

Age, at the time of treatment, ranged from 58 to 78 years (mean 66.7). Selection criteria included: absence of thyroid

or parathyroid disease before the diagnosis of SCC, absence of other malignancies, states of hyponutrition, metabolic osseous diseases, presence of T2-T3 laryngeal SCC and, most important, surgical treatment alone.

Only two of the patients underwent total laryngectomy with thyroid isthmectomy. Five patients were submitted to horizontal supraglottic laryngectomy and five to supracricoid laryngectomy with crico-hyoido-pexy or crico-hyoido-epiglottis-pexy. In all these cases, except one, patients underwent bilateral functional neck dissection. In all cases, the surgical technique of total and partial laryngectomy involves dissection of the superior and inferior laryngeal peduncles, accompanied, in specific cases, by their closure. However, this technique does not include ipsilateral thyroid lobectomy on the side of the lesion in the absence of any extralaryngeal involvement. Nonetheless, it does involve thyroid isthmectomy, except in the case of total laryngectomy. It is not normal practice to search for the parathyroid glands. In all cases, functional neck dissection involves closure of the venous laryngo-thyroid efferents to the internal jugular veins.

Serum levels of intact parathyroid hormone (PTH), calcaemia and albuminaemia were measured pre-operatively and, thereafter, at 3, 6 and 12 months post-operatively, with a mean follow-up of 7 months. For the diagnosis of hypoparathyroidism, the following reference intervals were used: intact PTH 9-75 pg/ml, Ca^{++} 4.4-5.2 mEq/l. Since none of the patients displayed conditions of pre- or post-operative hypo- or hyper-albuminaemia, it was not considered necessary to correct the values of calcaemia due to the proteic concentration by applying the following formula: $Ca^{++} \times (40 - Alb) \times 0.025$. The study used the immunoradiometric measurement method for PTH level. Immediately after surgery, we investigated and remained alert for the typical signs and symptoms of acute hypocalcaemia. Then 3, 6 and 12 months after surgery, the values of PTH and calcaemia were compared. The eventual symptoms were associated with hypoparathyroidism, such as convulsions, psychotic states or cataracts, with the aim of diagnosing hypoparathyroidism¹³.

Results

None of the post-operative results revealed states of hyponutrition, however, normal means of alimentation were recuperated after differing periods of time, depending on the individual patient and compatibility with recovery of natural deglutition. There were no cases of post-operative death or relapse of the disorder during follow-up. None of

the patients presented signs or symptoms of acute hypocalcaemia immediately after surgery, or complained of typical symptoms of hypoparathyroidism during follow-up¹³. No patients demonstrated values of albuminaemia < 3200 mg/dl during follow-up. In one case, the pre-operative value of PTH was above normal, but was associated with normal calcaemia level. This was possibly due to a reduced intake of Ca^{++} in the patient's diet. The same finding was observed in 2 post-operative controls of the same patient (after 6 and 12 months) but was always associated with normal values of calcaemia.

None of the patients presented calcaemia values below normal in the post-operative evaluations.

Discussion

Reports in the literature have, for some time, emphasized the vulnerability of the parathyroid glands due to lack of anastomosis at vascularization level¹⁴. Data regarding hypoparathyroidism following laryngeal surgery is, to say the least, non-homogeneous, varying from 12% of patients treated with laryngectomy and partial thyroidectomy to 73% in patients treated for total pharyngolaryngectomy and total thyroidectomy. Subclinical hypoparathyroidism can become manifest even years after surgical intervention, and can reach levels of up to 63% of the patients treated¹⁵. In our study, protection of the thyroid gland during laryngectomy led to preservation of thyroid function, bearing in mind a period of observation limited to one year. Dissection of the thyroid peduncles and closure of the laryngeal vessels has not clinically modified functioning of the parathyroid glands, not even in the two cases of total laryngectomy in which a thyroid isthmectomy was performed. The increase of PTH values associated with normal calcaemia highlights the capacity of the glands to compensate in conditions of stress (reduced contribution or increased re-absorption of Ca^{++}), thus confirming adequate vascularization. Despite the fact that in 91.6% of cases, bilateral functional neck dissection was performed (including closure of the glandular venous efferents), no cases of parathyroid hypofunctioning were observed, thus demonstrating an adequate possibility of redistribution of venous flow through preserved anatomical ways. In our opinion, therefore, based upon personal data, despite being limited and contrary to earlier findings regarding thyroid function, it does not seem appropriate to propose careful monitoring of parathyroid function in patients affected by laryngeal SCC treated only with surgery¹⁶.

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