

## Hypoparathyroidism after the treatment of laryngopharyngeal carcinoma

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### Abstract

Thirty patients with squamous cell carcinoma of the laryngopharynx were treated with surgery (total laryngectomy and hemithyroidectomy) and radiotherapy. Group 1 (n = 7) patients had surgery only; Group 2 (n = 7) had radiotherapy followed by salvage surgery while Group 3 (n = 16) had surgery followed by radiotherapy.

Parathyroid hormone and calcium levels were measured pre- and post-operatively and post-radiotherapy. In Group 1 no patients were hypoparathyroid. In Group 2, 29 per cent of patients pre-operatively and 57 per cent post-operatively, were hypoparathyroid. In Group 3, no patients were hypoparathyroid pre-operatively, while 25 per cent were hypoparathyroid post-operatively and post-radiotherapy. Parathyroid hormone and calcium levels were averaged and compared within and between each group. There was no significant difference within each group, when comparing levels post-operatively and post-radiotherapy from those of pre-operatively. There was no significant difference in levels between each of Groups 1, 2 or 3 ( $p > 0.05$ ).

**Key words:** Hypoparathyroidism, Radiotherapy, Surgery, operative; Laryngectomy

### Introduction

Parathyroid hormone is critical for calcium homeostasis and its function is well documented (Van Middlesworth, 1993). While 95 per cent of parathyroid tissue is in the thyroid compartment, active tissue may be found anywhere between the hyoid and the pericardium, including paratracheal, retropharyngeal and mediastinal (Isaacson *et al.*, 1977).

Total laryngectomy, with or without partial pharyngeal surgery, for advanced squamous carcinoma of the laryngopharynx, includes removal of anterior neck and pretracheal tissues; and hemithyroidectomy with mobilization of the contralateral side. In addition, the blood supply to the preserved thyroid and parathyroids may be disturbed with mobilization (or ligation) of the superior and inferior thyroid vessels (Stell and Maran, 1993; Gregor, 1997).

Buchanan *et al.* (1975) studied six patients who had undergone total pharyngolaryngectomies and total thyroidectomy for carcinoma. They showed that while all patients had evidence of parathyroid gland function, in three cases this function was insufficient to maintain normocalcaemia. Osborne and Jones (1968), evaluated parathyroid function in patients who had undergone surgery for carcinoma of the laryngopharynx, including hemithyroidect-

omy. In an 11-year follow-up, while no patients had parathyroid insufficiency, five of 16 patients showed evidence of reduced parathyroid reserve.

Radiotherapy to the head and neck in therapeutic doses, along with destruction of tissues and reduction in blood supply of the tissues of the neck, may compromise function of endocrine tissue (Hancock *et al.*, 1991; Ledger, 1994). Fujiwara *et al.* (1994) showed that parathyroid hormone levels increased with radiation exposure, the aetiology being unclear.

Chronic alcoholism is an associated risk factor for squamous carcinoma of the laryngopharynx (Sasaki and Carlson, 1993). It is also associated with chronic malnutrition states, in which the patient is at risk for hypocalcaemia (Graham, 1981; Hermans *et al.*, 1996), therefore the further insult of surgery and possibly radiotherapy would potentially increase the risk for hypoparathyroidism and hypocalcaemia.

The aim of this study was to assess if patients with laryngopharyngeal carcinoma, treated with surgery and radiotherapy were at risk for chronic hypoparathyroidism and hypocalcaemia.

### Patients and methods

This prospective study was performed over a 12 month period on patients admitted to the Groote

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TABLE I  
PATIENT GROUP ACCORDING TO TREATMENT MODALITY

Patient groups	Treatment modality	Number	Males: Females	Average age (yrs)
Group 1	Surgery only	7	6:1	61.0 ± 6.6
Group 2	Pre-operative radiotherapy + surgery	7	5:2	58.3 ± 11.3
Group 3	Surgery + post-operative radiotherapy	16	15:1	58.8 ± 11.1
Total		30	25:5	59.2 ± 10.0

Schuur Hospital, Cape Town. Patients included in the study were those diagnosed as having squamous carcinoma of the laryngopharynx, assessed as requiring surgical excision of their tumour. Patients who had had previous neck surgery were excluded from the study. Patients who had non-squamous cell carcinoma were excluded from the study. Patients who died within two weeks of surgery were removed from the study.

Serum was taken for determination of parathyroid hormone, total serum calcium and albumin levels pre-operatively, 14 days post-operatively and if the patient had radiotherapy, at one month post-radiotherapy.

Corrected calcium levels were determined by the following formula:  $(40 - (\text{serum albumin})) \times 0.025 + \text{uncorrected calcium}$ . Normal ranges as determined by the hospital laboratory were used; that is, calcium 2.1-2.6 mg/dl and parathyroid hormone 12-72 pg/ml.

Patients were divided into three groups according to their modality of treatment. Group 1 had surgery only; Group 2 had pre-operative radiotherapy with subsequent salvage surgery and Group 3 had surgery followed by radiotherapy within six weeks of surgery.

Radiotherapy, using a Cobalt 60 source was a 60 Gray tumour dose given by lateral parallel, opposed fields.

## Results

Thirty patients were included in the study, consisting of 25 males and five females with an average age of  $59.2 \pm 10$  years. Table I shows the patient data for each of the three groups.

All patients had a total laryngectomy, with hemithyroidectomy on the side of the lesion, with preservation of the contralateral lobe, ligation of the superior thyroid vessels and mobilization of the inferior thyroid vessels. In addition, two patients in Group 2 and nine patients in Group 3 had partial pharyngeal resection.

The average parathyroid hormone levels measured pre- and post-operatively in each of the groups and post-radiotherapy in Group 3 are detailed in Table II, with the number of hypoparathyroid patients at each stage in Table III.

TABLE II  
PARATHYROID HORMONE LEVELS

Patient group	Pre-operative	Post-operative	Post-radiotherapy
Group 1	32.0 ± 10.7	28.7 ± 7.8	
Group 2	18.0 ± 9.4	22.5 ± 16.8	
Group 3	26.9 ± 18.0	25.7 ± 21.8	24.5 ± 17.2

Calcium levels for each of the three groups are listed in Table IV, with the number of hypocalcaemic patients in Table V.

## Statistics

Using a two way Analysis of Variance, *p* values were calculated, comparing the average calcium values and parathyroid hormone values between Groups 1, 2 and 3 and within the three groups (pre-operatively, post-operatively and post-radiotherapy). Significance was measured as a *p* value  $\leq 0.01$ . There was no significant difference within each group, when comparing calcium and parathyroid hormone levels post-operatively and post-radiotherapy from those of pre-operatively. There was no significant difference in calcium levels between each of Groups 1, 2 or 3.

## Discussion

There was no significant difference between any of the groups or within any of the groups across time, for either parathyroid hormone or calcium levels. There were however, individual patients who had abnormally low parathyroid hormone levels. These patients were in Groups 2 and 3, with no hypoparathyroidism detected in the surgery only group (Group 1). In the surgery and pre-operative radiotherapy group, two of seven patients (29 per cent) pre-operatively and four of seven (57 per cent) post-operatively, were hypoparathyroid. In the surgery with post-operative radiotherapy group, no patients were hypoparathyroid pre-operatively while four of 16 (25 per cent) were hypoparathyroid post-operatively and post-radiotherapy.

Group 1 patients had less extensive surgery than those in Groups 2 and 3, some of whom had partial pharyngeal surgery. This may account for the 25 per cent of patients in Group 3 versus no patients in Group 1 developing hypoparathyroidism. This is supported by Krespi *et al.* (1985), who showed that hypoparathyroidism and requirements for post-operative calcium supplementation was related to the extent of laryngopharyngeal surgery. In our study however, the contralateral hemithyroid gland was preserved in every patient. One would expect the preserved parathyroid gland/s to maintain para-

TABLE III  
NUMBER OF HYPOPARATHYROID PATIENTS

Patient group	Pre-operative	Post-operative	Post-radiotherapy
Group 1	0	0	
Group 2	2	4	
Group 3	0	4	4

TABLE IV  
CORRECTED CALCIUM LEVELS

Patient group	Pre-operative	Post-operative	Post-radiotherapy
Group 1	2.35 ± 0.16	2.39 ± 0.18	
Group 2	2.31 ± 0.14	2.36 ± 0.09	
Group 3	2.33 ± 0.11	2.36 ± 0.11	2.33 ± 0.18

thyroid function. This study suggests that the combined modality of surgery and radiotherapy places the patient at risk for hypoparathyroidism. The effect of radiotherapy on parathyroid hormone function pre-operatively is possibly greater than post-operatively, in that 57 per cent in Group 2 versus 25 per cent in Group 3 after their combined modality treatment had reduced parathyroid function. The reason for this being unclear. No studies were found in the English literature to support this finding.

One patient in Group 2 post-operatively and one in Group 3 post-operatively and post-radiotherapy were hypocalcaemic. This shows that not all patients with hypoparathyroidism in the immediate post-operative or post-radiotherapy period develop hypocalcaemia. These hypoparathyroid patients' calcium levels now recognized as at risk patients, should be monitored in the longer term (a shortfall in this study).

The symptoms of chronic hypoparathyroidism and hypocalcaemia are behavioural abnormalities, mental slowing, dementia, psychotic states, weakness, fatigue and cataract formation (Isaacson, 1980; Ledger, 1994). Convulsions (Lehman and Leidy, 1994) and cardiomyopathy are also reported (Kudoh *et al.*, 1992) although these complications are rare. The neurological and ophthalmologic signs are not uncommonly associated with patients who have had surgery and radiotherapy for head and neck malignancies (Isaacson, 1980), and thus not necessarily identified as potential complications of chronic hypoparathyroidism. These symptoms are also similar to the symptoms of chronic alcoholism (Fink *et al.*, 1996). The cause of these neurological symptoms may go unrecognized for years before the diagnosis of chronic hypoparathyroidism is made (Bellamy and Kendall-Taylor, 1995).

In summary patients who have surgery and radiotherapy for squamous carcinoma of the laryngopharynx, even with partial parathyroid gland preservation, are at risk for developing chronic hypoparathyroidism. The symptoms of chronic hypoparathyroidism can go unrecognized or confused with the psychoneurosis associated with patients treated for head and neck cancers.

TABLE V  
NUMBER OF HYPOCALCAEMIC PATIENTS

Patient group	Pre-operative	Post-operative	Post-radiotherapy
Group 1	0	0	
Group 2	0	1	
Group 3	0	1	1

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