

PARATHORMONE, CALCIUM AND PHOSPHORUS IN AUTOTRANSPLANTED PARATHYROID, TOTAL THYROIDECTOMIZED PATIENTS

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مستوى هورمون الغدة الجاردرقية بعد زرعها في حالات استئصال الغدة الدرقية
المصابة بالسرطان وكذا مستوى الكالسيوم والفوسفور في نفس المرضى

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من أربعة عشرة حالة استئصال للغدة الدرقية المصابة بالسرطان . تم بنجاح زراعة الغدد الجاردرقية
المأخوذة من نفس المرضى في غدد ثلاثة عشرة حالة من المرضى المترددين على معهد الأورام القومي
في خلال الثلاث سنوات الماضية . في عدد أربع حالات تم زراعة أربعة غدد جاردرقية ، وفي باقي
الحالات تم زراعة من اثنين إلى ثلاث غدد .

وتم متابعة جميع الحالات يومياً بقياس مستوى الكالسيوم والفوسفور وتم تعويض المرضى الذين
أصابهم نقص في مستوى الكالسيوم ، بإعطائهم حقن كالسيوم أو كالسيوم عن طريق الفم . وفي
خلال ٤٥ يوم بعد العملية وصلت نسبة هرمون الباراثورمون في الدم إلى النسبة الطبيعية (٠,٠٥ -
٠,٣ نغ/مل) . وفي نهاية الشهرين بعد العملية كان متوسط مستوى هرمون الباراثورمون (٠,٢٣ ±
٠,٠٤ نغ/مل) والكالسيوم (١,١٠ ± ٩,٤٠ مج %) والفوسفور (٠,٩٣ ± ٣,٦١ مج %) وهذه كلها نسب
طبيعية .

وهذا إن دل إنما يدل على نجاح عملية الزرع وأن الغدد الجاردرقية المزروعة قد بدأت في أداء
وظيفتها .

Key Words: Parathormone, Total thyroidectomy, Thyroid tumour, Autotransplanted parathyroid

ABSTRACT

The success of parathyroid autotransplantation was indicated by the postoperative assay of serum parathormone in thirteen out of fourteen patients to whom total thyroidectomy was carried out because of thyroid cancer during the past three years. Four glands were auto-transplanted in four patients and from two to three glands were transplanted in the remaining nine patients. All patients were followed up with daily calcium and phosphate determinations. Patients with low Ca^{++} level and with hypocalcemic manifestations were given oral and i.v. Ca^{++} supplementation. Postoperatively, seven patients developed hypocalcemia ($x 5.7 \pm 1.12$ mg.%) All patients were successively tapered from all supplementation within one to two months from thyroidectomy. The parathormone reached the normal value within 45 days. All have a normal level of serum calcium ($x 9.4 \pm 1.40$ mg.%), phosphorus ($x 3.61 \pm 0.93$ mg.%) and parathormone ($x 0.23 \pm 0.04$ ng./ml).

INTRODUCTION

Thyroid cancer as a pathological entity and its treatment have been the subjects of controversy for many years.

With more precise histopathological classification and the recognition of the influence of age and sex among other factors, on the clinical and biological characteristics of carcinoma of the thyroid as emphasized by Eisenberg [1] and

Franssila[2]. It is now clear that these neoplasms comprise some of the slowest growing tumours as well as some of the most virulent malignant neoplasms with a large intermediate group composed primarily of the mixed papillary follicular and medullary variants.

Five and ten years survival rates for the papillary and follicular varieties have shown significant increase in the recent decades [1]. This has been attributed to more effective extensive operative excision [3] cobalt therapy [4] and utilization of radioactive iodine and TSH suppression with thyroxin administration [3].

The principle controversy regarding the operative management of carcinomas of the thyroid revolves around the extent on the side contralateral to that harbouring the palpable tumour. The advocates of total thyroidectomy point to the reported high incidence of multicentricity and bilaterality in carcinoma of the thyroid as emphasized by Clark et al., [5]. Difficulties in subsequent completion of the thyroidectomy, and recurrence in the neck as the principal cause of death from these tumours as reported by Fazill and Foote [6]. The proponents of lobectomy or lobectomy with contralateral subtotal lobectomy agree with the logical treatment for carcinoma of the thyroid which would be total removal of the gland if it could be done without injury to the vital structures i.e. recurrent laryngeal nerve and the parathyroid glands. The possibility of recurrent nerve injury plus hypoparathyroidism is too high a price to pay for the treatment of such tumours, especially since the consequences of inadequate resection do not manifest themselves for 10-20 years or more [7].

The incidence of permanent hypoparathyroidism subsequent to total thyroidectomy has been reported to be as high as 24-29% according to Tollefsen et al [8] and Wilson et al [9] respectively. The application of technical refinement has reduced this figure to 2% [10]. This last incidence was achieved by painstaking dissection and preservation of parathyroids in situ with their precarious blood supply is a technical feat for which Thompson and associates should receive credit, but which cannot be expected from most surgeons. Even with their interest and experience in the surgical treatment of thyroid and parathyroid diseases, Paloyan et al., [11] could not reduce the incidence of hypoparathyroidism below 3 percent in 64 consecutive total thyroidectomies prior to the use of parathyroid gland autotransplantation. With autotransplantation of the parathyroid the incidence of permanent hypoparathyroidism in 54 total thyroidectomies was reduced to zero [11].

Saxe [12] described successful parathyroid autotransplantation in dogs. These animals became hypocalcemic upon removal of the autotransplanted parathyroid tissue. However, it is only during the past 20 years that this simple and effective method of preserving parathyroid function is being used by an increasing number of surgeons.

The aim of this study is to determine the clinical status of patients with thyroid carcinoma undergoing total thyroidectomy and parathyroid autotransplantation with respect to the incidence of hypocalcemia.

The ultimate objective was to determine the necessity and duration of medical management of hypocalcemia and to ensure that the autotransplanted parathyroid glands are functioning properly through the measurement of the parathyroid hormone i.e. parathormone.

MATERIAL AND METHODS

Fourteen patients had a completely total thyroidectomy during a period of three years (1992-1994) at the NCI, Cairo University. At the time of operation the youngest patient was 22 years and the oldest was 64 years with a mean age of 33.4 years. There were nine females and five males. Total thyroidectomy and functional block dissection were done for eight patients who presented with enlarged cervical lymph nodes and proved to be metastatic thyroid carcinoma by lymph node biopsy. In five patients carcinoma was diagnosed after lobectomy and contralateral exploration. These patients presented clinically by a large solitary thyroid nodules. Thyroid scanning showed a solitary cold nodule. A completion of total thyroidectomy was performed later. In one patient completion of total thyroidectomy was done after subtotal thyroidectomy for multinodular goiter outside the NCI. On histological examination carcinoma was detected. The identified parathyroid glands were autotransplanted according to the techniques described by Kaplan [14].

All patients are followed with daily calcium and phosphate determination in the immediate postoperative period. Patients with symptoms including generalized weakness, tingling, perioral numbness or clinical signs including a positive chvostek's sign, positive trousseau's sign carpopedal spasm were given oral calcium supplementations, calciferol and 0.373 mg dihydrotachysterol every 6 hours. Their hypocalcemic state was confirmed by the low level of their serum calcium. Serum calcium and phosphate levels were monitored until resolution of symptoms which usually occurred within 24 - 48 hours at which time the patient was discharged on varying combinations of oral calcium and vitamin D. Calcium and phosphate were determined according to the kits of the Boehringer Mannheim Co.

Follow up consisted of a visit every month for patients with normal serum calcium and no requirement of supplementation. Patients requiring calcium and/or vitamin D supplementation were followed initially weekly with serum calcium and phosphate determination. Supplementation were gradually reduced according to the maintenance of a normal serum calcium and absence of symptoms. Parathormone level was determined from day 40 to day 52 postoperative till the normal plasma level was reached. Parathormone was determined by radioimmunoassay kit from INCSTAR Laboratories., Minnesota, USA.

RESULTS

Postoperatively, seven patients (54.6%) developed hypocalcemia (\bar{x} 5.7±1.12 mg%). The incidence of hypocalcemia was 100 percent in the four patients in whom the four parathyroid glands were autotransplanted and 33.3 (three out of nine) in patients in whom 2-3 glands were autotransplanted.

All patients were gradually tapered of all supplementation within 45 days of thyroidectomy. All have normal level of serum calcium (\bar{x} 9.4 ± 1.4 mg%), phosphorus (\bar{x} 3.61 ± 0.93 mg%) and parathormone (\bar{x} 0.23 ± 0.04 ng/ml). The patient with preservation of the parathyroid gland in situ did not develop hypocalcemia postoperatively.

Table 1 shows the pathological characteristics of the thyroid carcinomas.

Table 2 and Fig. 1 show the gradual normalization of parathormone level of the followed seven patients postoperatively, in which all patients reached the normal plasma parathormone level after about 45 days post operatively.

Table (1)

Histological findings in 14 patients with carcinoma of the thyroid

Histopathological	Number of cases	%
Papillary	9	64.3
Follicular	2	14.3
Mixed	3	12.4
Total	14	100
LN metastasis	8	57.1

Table (2)
Post operative Parathormone level (ng./ml.)

Patient Days	Patient						
	1st. pt.'	2nd. pt.'	3rd pt.'	4th. pt.'	5th. pt.'	6th. pt.'	7th. pt.'
40	0.06	0.01	0.009	0.003	0.008	0.002	0.01
41	0.08	0.01	0.01	0.008	0.009	0.002	0.01
42	0.1	0.02	0.015	0.01	0.01	0.01	0.02
43	0.11	0.03	0.019	0.015	0.02	0.03	0.025
44	0.13	0.03	0.03	0.029	0.023	0.05	0.03
45	0.19	0.05	0.04	0.03	0.027	0.09	0.031
46	0.19	0.08	0.045	0.035	0.029	0.12	0.033
47	0.22	0.1	0.06	0.05	0.04	0.16	0.04
48	0.23	0.12	0.09	0.07	0.1	0.19	0.06
49	0.25	0.15	0.1	0.1	0.13	0.23	0.11
50	0.26	0.18	0.11	0.14	0.19	0.26	0.19
51	0.26	0.2	0.13	0.18	0.22	0.29	0.25
52	0.26			0.2		0.31	0.25
53	0.24						0.26

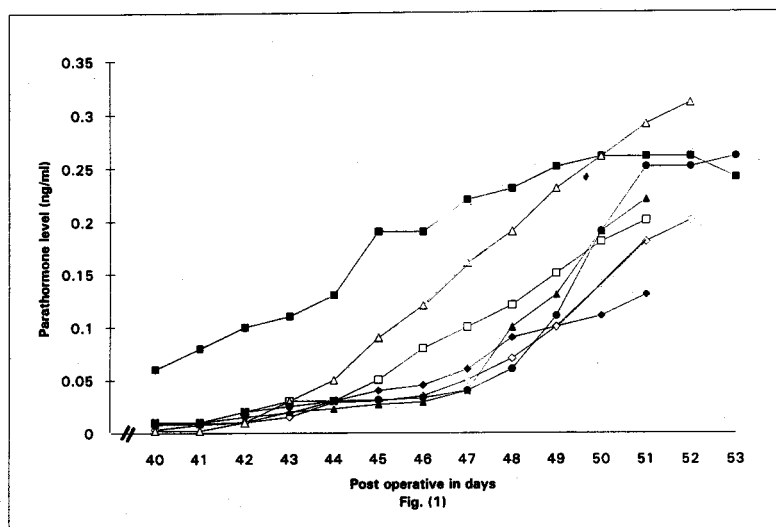


Fig. 1 : Post operative in days

DISCUSSION

Historically, postoperative hypocalcemia with tetany has been a major source of postoperative morbidity and mortality in patients undergoing total thyroidectomy. The incidence has been reported in up to 29% of such patients [10]. These results of direct devascularization of the parathyroid, and removal of parathyroid tissue especially in the presence of intrathyroid parathyroids, may be as a result of wound complications including hematoma, infection or possibly as result of oedema secondary to the trauma of operations in the neck. The incidence of temporary hypoparathyroidism was 100% in patients in whom the four parathyroid glands were transplanted. These results are similar to that reported by Paloyan et al. [11].

Autotransplantation of the parathyroid tissue has become a common practice since the mid 1960's. This was achieved by the ingenious technique of excising all parathyroid tissue from the neck and autotransplanting a portion in the musculature of the forearm. Subsequent determination of the parathormone levels in the blood down from the venous drainage of the transplanted site as compared with those of the contralateral forearm proved that the autotransplanted parathyroid tissue was the principle if not the only source of parathormone in such patients.

In our series no patients developed permanent hypocalcemia. Patients demonstrated normal calcium and phosphate levels and had a normal parathyroid hormone level within 45 days postoperatively without any supplementation.

Experimentally, parathyroid autotransplants have been shown to function within 1-2 weeks [13] Calcium supplementation can be withdrawn by 3-4 weeks following transplantation [14].

Total thyroidectomy for malignant tumours of thyroid should no longer be considered a serious operation with a high incidence of complications. With appropriate and meticulous dissection the incidence of recurrent nerve injury can be reduced to a negligible level. Furthermore, the incidence of permanent hypoparathyroidism can be reduced nearly to zero with a combination of autotransplantation of the parathyroid and preservation of the four glands in situ. Therefore, the preservation of parathyroid function should not longer be considered a valid reason advocating subtotal resection for carcinoma of the thyroid in preference to total excision.

Our results are in agreement with the results of Wells and his associates [15] who proved that autotransplanted parathyroid glands synthesize and secrete parathormone. Takauchi et al. [16] also proved the same results.

In conclusion, we recommend selective parathyroid autotransplantation in patients undergoing total thyroidectomy

because of malignancy, when the viability of the parathyroids is questionable especially if less than four glands have been identified. All patients undergoing total thyroidectomy should have at least one parathyroid gland autotransplantation [9] to prevent permanent hypocalcemia.

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