PARATHYROID HORMONE VS. SERUM CALCIUM AFTER TOTAL THYROIDECTOMY IN EARLY DETECTION OF HYPOPARATHYROIDISM

THESIS

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Aim of the Work

The aim of the study is to establish the accuracy of early postoperative PTH in identifying patients at risk of developing postoperative hypocalcemia and related symptoms.

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Table Of Contents

Topic	Page
INTRODUCTION	
ANATOMY OF THE THYROID AND	
PARATHYROID GLANDS	
Thyroid Gland	3
Developmental Embryology	3
Congenital Abnormalities	5
Anatomy And Surgical Implications	7
Muscular, Fascial, and Airway Relationships	9
Vascular Relationships	11
Neurologic Relationships	13
Lymphatic Relationships	17
Parathyroid Gland	19
Anatomy	19
PHYSIOLOGY OF PARATHYROID	
HORMONE	
Basic Biology Of Calcium Metabolism	
Absorption and Excretion of Calcium and	
Phosphate	
Parathyroid Hormone	31
Actions of Parathyroid Hormone	39
DIAGNOSIS OF HYPOPARATHYROIDISM	49
Clinical Picture	49
Investigation	56
TREATMENT OF HYPOPARATHYROIDISM	58
ROLE OF PTH IN DETECTING	68
HYPOPARATHYROIDISM	

PATIENTS AND METHODS		
Patients	71	
Age and Sex	71	
Inclusion Criteria	71	
Exclusion Criteria		
Assessment		
Preparation		
Operative Technique	73	
Operative Technique Statistical Analysis of the Results	73 75	
	, -	
Statistical Analysis of the Results	75	
Statistical Analysis of the Results	75 77	
Statistical Analysis of the Results RESULTS DISCUSSION	75 77 91	
Statistical Analysis of the Results RESULTS DISCUSSION CONCLUSION	75 77 91 102	

List Of Figures

Figure	Title	Page
Figure 1.1	Thyroid gland – AP view.	8
Figure 1.2	Relations of the thyroid gland – axial section.	10
Figure 1.3	The blood supply of the thyroid gland.	12
Figure 1.4	The standard anatomic relationship.	14
Figure 1.5	Cernea classification of the relationships between the external branch of the superior laryngeal nerve, the superior pole of the thyroid, and the superior thyroid artery.	16
Figure 1.6	Classification scheme for regional lymph node basins in the neck.	18
Figure 1.7	Schematic illustration of the location of the superior and inferior parathyroid glands.	20
Figure 1.8	(A) pharyngeal arches in a 5-week embryo. The corresponding pouches extend from within the pharynx into each arch (B) Schematic representation of the differentiating epithelium of the respective pharyngeal pouches.	22
Figure 1.9	A normal adult parathyroid is composed of about half parenchyma and half fat.	24
Figure 2.1	Overview of calcium exchange between different tissue compartments in a person ingesting 1000 mg of calcium per day.	29
Figure 2.2	Approximate effect of plasma calcium concentration on the plasma concentrations of parathyroid hormone and calcitonin.	33
Figure 2.3	Approximate changes in calcium and phosphate concentrations during the first 5 hours of parathyroid hormone infusion at a moderate rate.	34

Figure 3.1	Hypocalcemic tetany in the hand, called carpopedal spasm.	50
Figure 3.2	Illustration of the facial points.	53
Figure 3.3	Illustration of the elicitation of Trousseau's sign.	55
Figure 7.1	Diagnosis of the cases.	79
Figure 7.2	Clinically manifested hypoparathyroidism.	82
Figure 7.3	Comparison between asymptomatic and clinically manifested patients regarding PTH level.	85
Figure 7.4	Receiver Operating Characteristic curve.	86
Figure 7.5	Comparison between treatment modalities given to patients and PTH level.	89

List Of Tables

Table	Title	Page
Table 3.1	Diagnosis: clinical features of hypocalcemia.	51
Table 4.1	Treatment of Hypoparathyroidism and Monitoring.	66
Table 7.1	Gender description of the cases.	78
Table 7.2	Diagnosis of the cases.	78
Table 7.3	Type of operation.	79
Table 7.4	Post-operative complications.	80
Table 7.5	Post-operative complications (cont.).	80
Table 7.6	Post-operative hypoparathyroidism.	81
Table 7.7	Relation between PTH level, calcium level day 1 & 2 and the clinical manifestation of hypoparathyroidism.	83
Table 7.8	Relation between PTH level and calcium level.	84
Table 7.9	Mode of treatment.	87
Table 7.10	Statistical comparison between treatment modalities given to patients and PTH level, calcium level in day 1 & 2.	88

INTRODUCTION

Thyroid surgery is generally performed with low morbidity and has been performed as a short stay procedure in selected series. Close monitoring of postoperative calcium concentrations is usually recommended after surgery of substernal goiter, recurrent goiter, Grave's disease, and other thyroid operations that include a concomitant lymph node dissection. However, in the literature, little guidance is found on the optimal method of surveillance for the majority of patients subjected to thyroid surgery. (*Thomusch et al.*, 2000)

Transient hypoparathyroidism is a challenging event after total thyroidectomy because of the lack of objective data for verifying intraoperative (IO) viability of parathyroid glands and reliable parameters for predicting postoperative hypocalcemia and related symptoms. In the past few years, close monitoring of serum calcium level, requiring repeated blood sampling, has been recommended to prevent postoperative hypocalcemia. Its actual utility, however, has recently been questioned. (*Quiros et al., 2005*)

Hypocalcaemia from hypoparathyroidism is a well-recognised complication of total thyroidectomy. It might be permanent in up to 10%, and temporary in up to 50%, of patients. It can take up to four days to reach its nadir, and can lengthen a patient's hospital stay considerably. (*Quiros et al.*, 2005)

Early postoperative hypocalcemia may, in fact, be a result of perioperative haemodilution. Furthermore, the lowest calcium level is seldom reached until 24–48 hours after surgery, and this may partially restrict the planning of a safe, early discharge. The option of treating all patients with calcium therapy to reduce postoperative length of stay may not appear to be the proper solution. Only selected cases require replacement therapy, and overtreatment may inhibit parathyroid function. (*Fahmy et al.*, 2004)

Early postoperative PTH monitoring potentially could determine which patients would need more than oral calcium supplements to avoid symptoms of hypocalcemia. The presumed cause of hypocalcemia after thyroidectomy is multifactorial. Some investigators have shown that hypocalcemia is more likely to occur in the setting of bilateral thyroidectomy, procedures requiring parathyroid autotransplantation, thyroid malignancy, and substernal thyroid gland extension. (*Abboud et al.*, 2002)

The physiologic basis of postoperative PTH monitoring is the 2- to 3-minute half-life of the intact PTH molecule. Factors affecting the parathyroid gland during cervical exploration, particularly trauma to the glands or devascularization, have a direct and rapid impact on serum PTH levels. (*Abboud et al.*, 2002)

ANATOMY OF THE THYROID AND PARATHYROID GLANDS

I. THYROID GLAND

Developmental Embryology

As the first endocrine gland to develop, the thyroid is mostly of endodermal origin and originates from the ventral embryologic digestive tract. A midline diverticulum arises in the area of the foramen cecum at the base of the tongue at approximately 4 weeks of gestational age. The rudimentary thyroid tissue descends as the *median thyroid component* (or *anlage*), which ultimately becomes the isthmus (overlying the upper tracheal rings) and most of each lateral lobe. It reaches its final position by gestational week 7 and undergoes histologic differentiation into recognizable follicles between week 8 and 11. (*Moore*, 1993)

The embryology of the median component is fairly well understood. Its initial appearance in evolution seems to be the endostyle, a groove in the pharyngeal floor of the ammocaete larva of sea urchins, which takes up iodine in a fashion similar to the human thyroid. (*Brookes et al., 1998*) The portion associated with the foramen cecum ruptures and resorbs during week 6 of gestational age leaving behind a regressive fibrous tract, which becomes the thyroglossal duct tract (including the portion associated with the central

hyoid bone). The distal end associated with the isthmus persists as a pyramidal thyroid lobe (also known as the ultimobranchial body in some vertebrates) develops on each side from the caudal pharyngeal endoderm (with the contribution of the fourth and fifth branchial pouches). (*Larsen*, 1997)

They arise later in development than the median component. These fuse with the posterior portion of the median component on each side and, with this process, C cells (from neural crest origin) migrate into the superolateral portion of the lobes and eventually secrete calcitonin. The median and lateral thyroid components unite by a complicated mechanism in which the lateral components move anteriorly and cranially and the median component migrates posteriorly and cranially. (*Weller*, 1933)

Only after this point does the unified thyroid begin to differentiate into thyroid follicles. Basic glandular function begins on a cellular level by the third month of gestation when iodine trapping occurs and thyroid hormones are first secreted. The control of descent and fusion of thyroid tissue appears to be influenced by multiple transcription factors such as TTF-1, TTF-2, and Pax-8. (*Sackett et al.*, 2002)

The lateral components become increasingly removed from the pharynx leaving a tapering connection on each side, which eventually detaches and is replaced by mesenchyme. The residual posterolateral projection from the lateral thyroid component toward the pharynx, when present, is known as the tubercle of Zuckerkandl [attributed to Viennese anatomist Emil Zuckerkandl (1849–1910)]. Because of its branchial pouch origin, the lateral thyroid component is closely associated with the superior parathyroid anlage (from fourth pouch). (*Gauger et al.*, 2001)

Congenital Abnormalities

An uncommon developmental malformation is the lingual thyroid gland, which is most often associated with agenesis of thyroid tissue in the standard position. It represents a failure of the median thyroid component to descend from the region of the foramen cecum. The size of a lingual thyroid can often be decreased by using exogenous thyroid hormone to suppress thyroid-stimulating hormone (TSH) or, in some cases, by ¹³¹I ablation. Surgical excision may be required if airway obstruction, obstructive dysphagia, or hemorrhage occurs. Ectopic thyroid tissue can be found in other areas of the central cervical compartment and the mediastinum. These can be sequestered nodules associated with multinodular goiters or they may be embryologic rests of thyroid tissue. Although the concept of lateral aberrant thyroid tissue was originally used to describe the findings of follicular tissue in the carotid sheath or the lateral compartments of the neck, it is now generally agreed that this cannot occur as an embryologic abnormality. If thyroid tissue is found in these areas, it most

likely represents a regional nodal metastasis of an occult thyroid cancer-typically a follicular variant of papillary thyroid cancer, which may have follicular architecture that is similar to normal thyroid tissue. (*Mulholland et al.*, 2006)

Thyroglossal duct cysts occur in the midline of the neck along the path of descent of the median thyroid component. They may occur from the base of the tongue to the low central neck, although most are located just inferior to the hyoid bone. Although they are often discovered during infancy and childhood, it is not uncommon for them not to be evident until adulthood—discovered either because of complaints of mass or evidence of infection. Because the posterior wall of the cyst abuts the flexible anterior pharynx, enlargement of the cyst can cause dysphagia and choking. When examining the patient, elevation of the mass with protrusion of the tongue is very suggestive of a thyroglossal duct cyst. Resection of a thyroglossal duct cyst involves excision of the entire thyroglossal duct on either side of the cyst. The tract is often intimately associated with the central portion of the hyoid bone and, for that reason, excision of this segment of bone is critical to prevent recurrence (known as the Sistrunk procedure). The epithelial lining usually contains some thyroid cells and, thus, thyroid carcinomas (usually of papillary type) can arise primarily in thyroglossal duct cysts. Excision of the cyst and the thyroglossal duct may be