

A study on Tumor Marker Calcitonin (CT) in Thyroid Patients

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الخلاصة

شملت هذه الدراسة فحص 80 ثمانون شخصاً تم تقسيمهم إلى مجموعتين، المجموعة الأولى تضمنت 60 مريضاً من المصابين بوحيدة أو متعددة عقيدات الغدة الدرقية، تتراوح اعمارهم بين (20-60 سنة)، أما المجموعة الثانية فتضمنت 20 عشرون شخصاً من الاصحاء باعتبارهم مجموع سيطرة تتراوح اعمارهم بين (20-60 سنة) ايضاً. تم أخذ العينات من المصابين قبل اجراء عملية استئصال الغدة الدرقية. فحصت جميع العينات بواسطة تقنيات الامتزاز المناعي المرتبط بالأنزيم (الاليزا) للكشف عن الكالسيتونين. بينت النتائج أن ارتفاع معدل تركيز الكالسيتونين في ثلاثة فقط من مرضى متعدد عقيدات الغدة الدرقية (20.69 ± 3.55) مقارنة ببقية المرضى حيث ان معدل تركيز الكالسيتونين (0.07 ± 4.18) أظهرت نتائج الدراسة دور الكالسيتونين في الكشف المبكر عن الإصابة بسرطان الغدة الدرقية النخاعي في مرضى متعدد العقيدات الدرقية، وان هناك علاقة ذات أهمية احصائية في متوسط تركيز الكالسيتونين في مصل هؤلاء المرضى في اول دراسة وصفية وذات نسبة مقارنة لدراسات خارج العراق، كما اوضحت الدراسة ان مستويات هرمونات الغدة الدرقية لا تتأثر عند ارتفاع معدل تركيز الكالسيتونين في الدم.

Abstract:

The study included 60 patients with preoperative single and multiple nodule goiter, their age ranged from (20-60) years. The other group included (20) persons as healthy control with age (20-60) years. Serum samples were tested by using ELISA technique for detection of (CT). Our findings indicated that calcitonin concentration in three patients with multiple nodule goiter had high mean level (20.69±3.55) compared with the other patients (4.18± 0.07). The detection of calcitonin concentration may the first studied descriptive study in Iraq, and the results were compared abroad studies. Lastly the level of thyroid hormone was not affected by the elevated concentration calcitonin.

Introduction:

Thyroid cancer is the most common endocrine related cancer. It occurs when cells in the thyroid undergo genetic changes (mutations), the mutation allow the cells to grow and multiply, 70%-80% of patients with well differentiated carcinoma of the thyroid presented with a thyroid nodule^[1]. Most patients with this disease are women; women have a better prognosis when compared to men with the same pathological entity, while men with a solitary nodule are more likely to have carcinoma than women with a solitary nodule^[2].

Medullary thyroid cancer (MTC), is 5% to 8% of cases of thyroid cancers, it develops from the C- cells of the thyroid gland, sometimes this cancer can spread to lymph nodes, the lungs, or liver even before a thyroid nodule is discovered, these cancers usually release calcitonin and carcinoembryonic antigen (CEA) into the blood, causing high levels of them when checked by blood tests^[3].

Nontoxic multinodular goiter (MNG), occurs in up to 12% of adults MNG is more common in women than men and increases in prevalence with age. It is more common in iodine - deficiency regions but also occurs in regions of iodine sufficiency, reflecting genetic, autoimmune and environmental influences on the pathogenesis^[4].

Cancer cells can sometimes make substances called tumor markers also called biomarkers which are normally present in small amount in the blood or urine, or body tissues. When the amount of these substances rises above normal, the cancer might be present in the body, examples, Thyroglobulin and Calcitonin consider thyroid tumor marker^[5]. Calcitonin (CT) is a hormone known to participate in calcium and phosphorus metabolism.

In mammals, the major source of calcitonin is from the parafollicular or C- cells in the thyroid gland. Calcitonin is a 32 amino acid peptide cleaved from a larger prohormone, it contains a single disulfide bond, which causes the amino terminus to assume the shape of ring^[6].

In normal subject, serum CT levels are low and barely detectable by commonly used assays, increased CT levels are highly suggestive of medullary thyroid carcinoma with medullary thyroid cancer and C cell hyperplasia^[7].

The aim of this study is to detect calcitonin tumor marker in patient with nodule thyroid gland goiter in preoperative.

Materials and Methods:

A prospective study was conducted on the main following groups during the period from August 2010 -April 2011.

This study includes (60) nodular and multinodular goiter patients who were attending the Medical City\Surgery department and Dijlah Private Hospital.

Twenty (20) healthy individuals served as control. The patients were subjected to a personal interview and full history was taken including age, disease history in the family, other associated disease and drug intake. The result of neck scan, analysis of thyroid hormone, clinical feature, was taken from the case sheet. All patients were investigated in teaching laboratory of medical city /immunology department.

Samples collection:

Five ml of venous blood was drawn from each patient. Sera were separated after leaving the sample at room temperature for about 15-30 minutes, then centrifuged at 1500 rpm (revolution per minute) for 5 minute, and then sera dispensed into 4-5 Eppendorf tubes, kept at -20°C until the assessment of (CT). By using enzyme linked immune sorbent assay (ELISA), calcitonin ELISA.

Enzyme immunoassay for the quantitative determination of calcitonin (ELISA) technique.

Calcitonin Immunoassay is a two-site ELISA, for the measurement of the biologically intact 32 amino acid chain of calcitonin. It utilizes two different mouse monoclonal antibodies to human calcitonin specific for well-defined regions on the calcitonin molecule. One antibody binds only to calcitonin 11- 23 and this antibody is biotinylated. The other antibody binds only to calcitonin 21-32 and this antibody is labeled with horseradish peroxidase [HRP] for detection. The reagents are calcitonin ELISA. Demeditec Company, Germany.

Statistical analysis:

Statistical analysis was carried out with the statistical analysis system (SAS) (2004) program, after translated data into codes. Suitable statistical methods were used in order to analyze and assess the results, they include the followings:

* T-test was used to the significant compare between means.

*Chi-square test was used to compare between percentages.

The level of significance considered when P-value less than 0.05 and 0.01

SAS.2004.SAS \STAT Users guide for personal computers .release 7.0 SAS Institute inc. Cray, Nc., USA. (SAS=Statistical analysis system).

Result and discussion:

Calcitonin hormone in single and multiple nodule patients:

A total of sixty newly diagnosed thyroid goiter patients, were included in this study. Forty four patients with multiple nodule aged (22-71), sixteen patients with single nodule aged 23-80years, and twenty healthy aged (20-60 years) as a control group.

Serum (CT) tumor marker in among studied groups:

The number and percentage of goiter thyroid patients whom have CT in their serum are presented in (Table -2) In this study, plasma concentrations of

human calcitonin (hCT) were determined in patients with thyroid multi nodular disease (5.45%). We don't found any CT concentration in nodule thyroid goiter patient.

Serum CT concentration in single and multiple nodule goiter:

(Table-3) demonstrate the mean of serum CT concentration in three patients with elevated CT tumor marker which was (20.69) pg/ml with statistically significant if compared with patient with normal value of serum CT. (P value<0.01)>

CT measurement is routinely performed in patients with a thyroid nodule to detect medullary carcinoma, However, increased calcitonin does not always correlate with medullary carcinoma^[8]. Incidence of medullary cancer in patients with thyroid nodular disease is about 0.5% to 2%^[9]. Testing of CT, which is consider one of the markers to detect medullary thyroid cancer^[10]. All the patients with no nodular thyroid disease had normal basal CT levels. Routine CT determination in patients with thyroid nodules permits early diagnosis. The real aim of CT testing is not just detection of smaller tumors, but rather reduced mortality, which has not been clearly demonstrated^[11]. Patients with basal and \or stimulated plasma CT concentration of more than 100 pg/ml should be must eradicate the thyroid gland, because they run a substantial risk to suffer either medullary thyroid cancer or C-Cell hyperplasia, a potentially precancerous condition, this will increase the chance of timely diagnosis of MTC and provide the chance of curative surgery.

The results agreement with finding obtained by ^[12], in which CT concentration in three patients with multiple nodule goiter had high level and that increased serum concentration of CT is not harmful, it is useful as a marker which can be tested in blood.

Thyroid hormones in single and multiple nodules goiter:

Data elucidated in (Table -4) showed the number of patients with thyroid hormone concentration that above normal on single and multiple nodules goiter patients preoperative to thyroidectomy.

For better understanding the association between thyroid hormones and thyroid cancer, multiple nodule patients, single nodule patients and control were evaluated for these hormones highest frequency of positive cases was observed in within normal concentration of hormones. This study agreed with former study conducted by ^[13], who found that goiter can occur in a gland that is producing too much, too little hormone, or the correct amount of hormone hyperthyroidism, hypothyroidism euthyroidism respectively in a healthy patient a normal thyroid gland secretes all of the circulating T4 (about 90 to 100mcg daily) and about 20% of the total circulating T3 (about 30mcg daily). The T4 made by the thyroid gland circulates throughout the body and is converted into roughly equal amounts of T3 and reverse T3. Normal physiological production ratio of T4 to T3 is 3.3:1. Normal metabolism of T4 requires the production of

the appropriate ratio, or balance, of T3 to rT3. If the proportion of rT3 dominates then it will antagonize T3, thus producing hypothyroid symptoms in spite of sufficient circulating levels of T4 and T3. In comparison with some previous studies, this result is agreed with^[14], who mentioned that the synthesis and secretion of the two thyroid hormones is influenced by a hormone released by the pituitary gland called thyroid-stimulating hormone TSH.

The characteristic Hashimoto's thyroiditis patient would have high TSH values and low T3 and T4 (or Free T3 and Free T4) levels, while Hyperthyroidism can usually be confirmed by use of the TSH, T4 (or Free T4), T3 (or Free T3). This finding was in congruent with the study carried out by^[15] which found that on medullary thyroid cancer when calcitonin in high levels other thyroid tests, such as T4, T3, and TSH, are usually normal while calcitonin levels are elevated.

Groups	No.	Sex and age			
		Male	Age	Female	Age
Patients with multiple nodule	44	5	22-53	39	20-71
Patients with single nodule	16	3	30-61	13	23-80
Control	20	6	20-50	14	22-60

Table-1: The demographic characteristics of the studied group.

	Type of disease	No.	hCT
Patients	Single nodule	16	0
	Multiple nodule	44	3(5.4%)
Control		20	0
Total		80	

Table-2: The normal level of serum hCT in single and multiple nodules patients.

Serum CT among patients	Mean± SE	T- test	x ² value
Elevate calcitonin concentration	20.69±3.55	5.028	0.0048**
Normal calcitonin concentration	4.18±0.07		

Table-3: Serum CT concentration in nodular and multinodular goiter with elevated and within normal group.

** (P<0.01)

Types	Total	Below normal			Within normal			Above normal		
		T3	T4	TSH	T3	T4	TSH	T3	T4	TSH
Multiple nodule	44	8	4	6	34	38	34	2	2	4
Single nodule	16	3	2	1	12	13	11	1	1	4
Control	20	1	1	3	17	18	15	2	1	2

Table-4: Serum level of thyroid hormones in patients with single and multiple nodules goiter patients.

Normal range

T3: n.Mol /L. (1.2-2.285)*0.066

T4: n.Mol /L. (54.1-152.3)*0.077

TSH: U /L. (0.5-5.5)

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