The Effect of Hyperthyroidism on Leptin and Immunoglobuline E Levels in Asthma Patients

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Abstract

This study aimed to explain the relationship between hyperthyroidism and asthma by indicating the effect of thyroid hormones (T3 and T4) on leptin and IgE levels.To determine whether T3 and T4 alters serum leptin and IgE levels, twenty newly diagnosis hyperthyroidism patients,twenty asthma patients, ten asthma with hyperthyroidism patients and ten (healthy) as a control were studied. Serum samples were collected to measure the leptin and IgE levels in addition to T3,T4 and TSH Levels. The results revealed a significant ($p<0.05$) increase in leptin and IgE levels in hyperthyroidism, asthma and hyperthyroidism with asthma patients compared with the control group.These results indicated that elevation in T3 and T4 induced asthma,by affected these hormones on differenation of adipocyte tissue that cause increase of leptin hormone and increase O2 consumes from cells and make immune cell in activated state results increase IgE level.This study concluded there is a relationship between hyperthyroidism and asthma through increase Leptin and IgE.

Key words: hyperthyroidism, asthma, leptin,IgE.

تأثير فرط الغده الدرقيه على مستويات اللبتين والكلوبيولين المناعي اي في مرضى الربو

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الخلاصه:

تهدف هذه الدراسه الى ايجاد العلاقه بين فرط الغده الدرقيه والربو من خلال الاشاره الى تاثير هرمونات الغده الدرقيه (T3 andT4) على مستوى هرمون اللبتين و الكلوبيولين المناعي E ليحدد ما اذا كان (T3 and T4) يغير مستوى اللبتين والكلوبيولين المناعي E في مصل الدم .شملت الدراسة (10) اشخاص غير مصابين استخدمو كمجموعة السيطرة و (20)مريضا مصاب بفرط الغدة الدرقية و (20) مصابا بمرض الربو و(10) مريضا مصاب بفرط الغدة الدرقية والربو وجمعت عينات مصل الدم لقياس مستوى اللبتين والكلوبيولين المناعي E بالاضافه الى مستوى (T3,T4 and TSH). اظهرت النتائج ارتفاع معنوي في تركيز اللبتين والكلوبيولين المناعي E في المرضى المصابين لفرط الغده الدرقيه والمرضى المصابين بالربو والمرضى المصابين بفرط الغده الدرقيه مع الربو مقارنه بمجموعه السيطره .اتضحت من هذه النتائج ان زيادة هرمونات الدرقيه محفز لظهور الربو وهذا قد يكون بسبب تاثير هرمون (T3 and T4) على تمايز الخلايا الدهنيه مسببة انتاج هرمون اللبتين وكذلك زيادة استهلاك الاوكسجين من الخلايا جاعلا الخلايا المناعية في دور

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التنشيط وزيادة مستوى الكلوبيولين المناعي E.نستنتج من هذه الدراسة بان هناك علاقة ماب ين فرط الغدة الدرقية والربو من خلال زيادة هرمون اللبتين والكلوبيولين المناعي E.

الكلمات المفتاحيه : فرط الغده الدرقيه والربو واللبتين والكلوبيولين المناعي اي

Introduction:

Thyroid gland is the first endocrine gland to develop in the embryo around 3rd week of intrauterine life and is the largest endocrine gland in the body [1]; Disorder of thyroid gland a hyperthyroidism, a pathological syndrome in which tissue is exposed to excessive amounts of circulating thyroid hormones **,** its easily diagnosed by a high serum level of thyroxine (T4) and triiodothyronine (T3) and a low serum level of thyroid stimulating hormone (TSH) [2]. Thyroid hormones are involved in numerous physiological processes, such as development, growth and the metabolism of lipids and carbohydrates. While it is believed thyroid hormones are not critical to the development of a normal immune response, they are thought to be involved in the maintenance of immune function in response to environmental stimuli and stress-mediated immunosuppression [3]The immune system and endocrine system are respectively , to defend the body against infection and to regulate physiologic activities of the body [4]. Thyroid hormones are correlated with a series of endocrine parameters such as leptin, glucocorticoids ,insulin,testosterone[5]. Hyperthyroidism patients are a risk of developing asthma and its possible that the reactive oxygen species may be contriburting factor in exacerbating wheezing in our thyroid patients so thyroid and lung disease (asthma) occasionally together and thyroid hormone especially T3 causes asthma [6].

Materials and methods:

Subjects

Twenty patients with newly diagnoses hyperthyroidism ,twenty patients with asthma , ten patients asthma with hyperthyroidism and ten healthy serve as control group were studied.The Patients were recruited from the AL-Kadmia Hospital /Baghdad and from Allergy and Asthma Institute.

Blood samples collection

Blood samples were collected from the patients and the control subjects.About 10 ml of blood were obtained by venepuncture using a 10ml disposable syringe. Blood samples were collected after 12-14 hour fasting between (9.00-11.00) a.m.The blood was allowed to clot in plain tubes at room temperature. The serum was separated after centrifugation at 3000 rpm for 10 minutes. Then serum was divided into aliquots in eppendroff tubes and stored at -20 C until used.

Measurement of serum leptin

The DRG leptin ELISA kit (DRG instruments Gmbh, Germany) was based on the Sandwich principle. The microtiter wells were coated with a monoclonalantibody was directed towards a unique antigenic site on a leptin molecule**.** An aliquot of patient sample containing endogenous leptin was incubated in the coated well with a specific rabbit anti leptin antibody (a sandwich complex was formed). After incubation the unbound mat erial was washed off and anti rabbit peroxidase conjugate was added for detection of the bound leptin. Having added the substrate solution, the intensity of colour was developed proportional to the concentration of leptin in the patients and the control samples.The absorbance (OD) of each well was determined at 450 nm with a microtiter plate reader (ELISA,DRG,Germany).

Measurement of serum Immunoglobulne E

The DRG IgE Quantitative Test is a solid phase enzyme-linked immunosorbent assay (ELISA) based on sandwich principle.

1-The test specimen (serum) is added to the IgE monoclonal antibodies immobilized on polystyrene microtiter wells (solid phase).

2- It is incubated with zero buffer .If the IgE in the specimen, it will be combine with antibodies on the well.

3-The well is then washed to remove any residual test specimen and goat anti-IgE in antibody-enzyme (horseradish peroxidase).

4-The conjugate reagent is added.It will bind immunologically to the IgE on the well,resulting in the IgE molecule being sandwiched between the solid phase and enzyme –linked antibody.

5-After incubation at room temperature ,the solid phase is washed with water to remove unbound labelet anti body.
6-A solution of 3,3,5,5-tetramethylbenzidin (TMB) is added and incubated for 20 minutes, resulting in the development of a blue color.
7-The color development is stopped and the resulting yellow color is measured spectrophotometrically at 450nm. (ELISA,DRG,Germany).

Thyroid hormones measurment

Serum concentration of thyroid hormones (T3and T4) and TSH were measured by using mini-VIDAS (VIDAS,Biometrix,France). Through an enzyme linked fluorescent assay (ELFA) technique.

Results

All the results of this study are shown in Table-1 and Figure-1, showing that there was a significant ($p<0.05$) increase in serum leptin level in asthma patients (28.49 ± 2.70)U/L and in hyperthyroidism with asthma (16.16± 3.22)U/L when compared with the control group(5.08±0.58**)** U/L and hyperthyroidism group(10.94± 0.41**) .**Also the result showed a significant($p<0.05$) increase IgE level in hyperthyroidism group (18.23±1.08) U/L when compared with the control group(9.06± 1.45)U/L and a significant increase ($p<0.05$) in asthma group (373.63± 29.46) U/L and hyperthyroidism whith asthma group (112.59±12.07) U/L when compared with control and hyperthyroidism group.(Figure 2) While The results revealed a significant ($p<0.05$) increase in T3 in hyperthyroidism group (2.43±0.17) nmol/L and hyperthyroidism with asthma group (4.20±0.83)nmol/L when compared with asthma (1.15 ±0.09) nmol/L and control group (0.963±0.03) and a significant ($p<0.05$) increase in serum T4 level in hyperthyroidism group (88.78± 13.58)nmol/L and hyperthyroidism with asthma group (56.21±15.70) when compared with asthma (8.89±0.37) nmol/L and control group(8.02±0.42) nmol/L Also the statistical analysis of the results showed that there was a significant increase TSH level in hyperthyroidism group (7.15±2.35)nmol and hyperthyroidism with asthma group (6.35±1.92)nmol when compared with asthma(1.77±0.13) nmol/L and control group(1.78±0.34) and decrease TSH level when compared with T3 and T4 level.

Table 1- The concentration of thyroid hormones (T3,T4 and TSH) in hyperthyroidism ,asthma and hyperthyroidism with asthma patients

Group	T3(nmol/L)	T4 (nmol/L)	TSH (nmol/L)
Control	0.963±0.03 c	8.02±0.42 c	1.78±0.34 b
Hyperthyriodism	2.43±0.17 b	88.78±13.58 a	7.15±2.35 a
Asthma	1.15±0.09 c	8.89 ±0.37 c	1.77±0.13 b
Hyperthyriodism with asthma	4.20±0.83 a	56.21±15.70 b	6.35±1.92 a

- Values are Mean ± SE.
- Similar letter indicated there is no significant difference while different letters indicated there is significant difference**.**

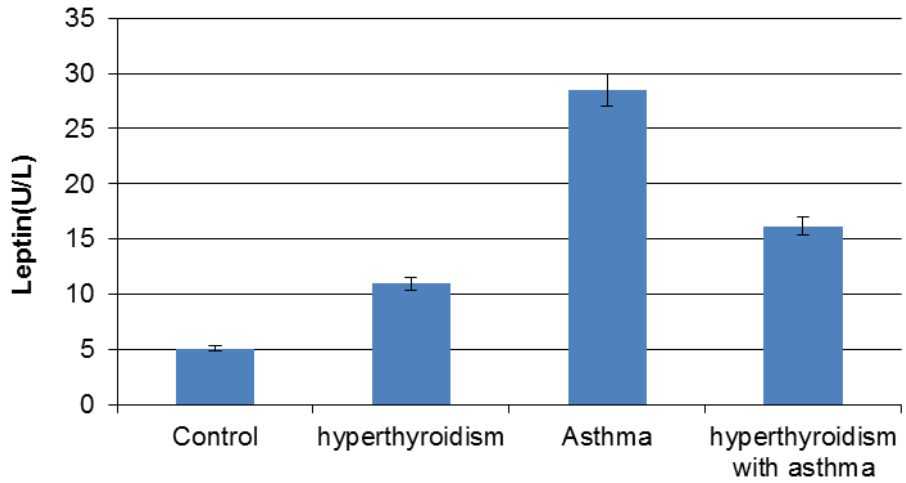

Figure 1-Effect of hyperthyroidism, asthma and hyperthyroidism with asthma on Leptin level

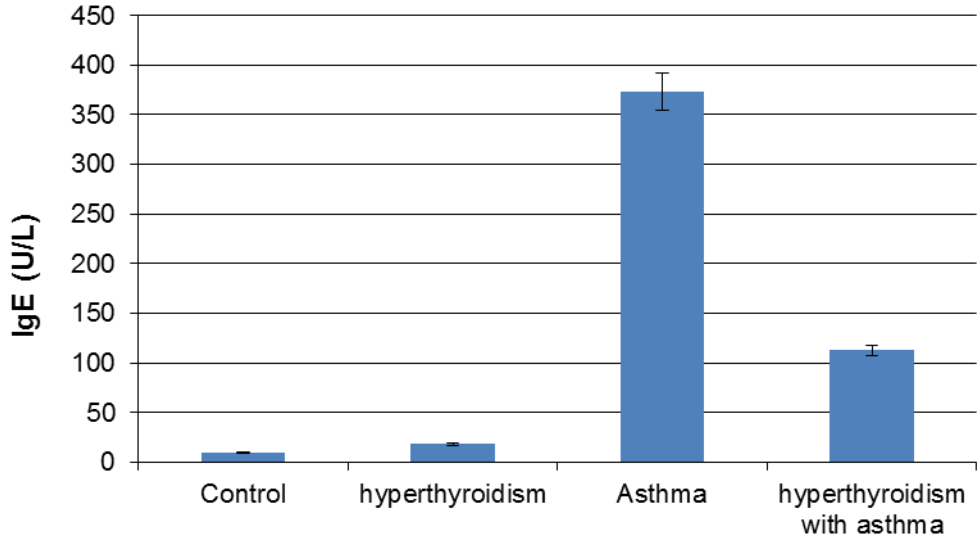

Figure 2-Effect of hyperthyroidism, asthma and asthma with hyperthyroidism on lgE level

Discussion

The study revealed that there was a significant increase in the level of leptin hormone and IgE in the serum taken from patients with hyperthyroidism compared with the control and asignificant increase in hyperthyroidism with asthma compared with hyperthyroidism and control that agreement with [7] who found that T3 can affected on leptin mRNA and secretion of leptin hormones that occure when T3 hormone interfer directly on receptors of T3 on adipocytes tissue and suggest that thyroid hormones (THS) may regulated the genes of human adipocyte.This result also agreement with [8] who explained that T3 affected directly on diffrenation of adipocyte and lipid droplit formation and leptin secretion. Increase thyroid hormone causes modulation of immune system by increase the relase of oxygen (O2) from the cells [9].There is a possative relation between immune cell and leptin secretion by effect leptin on the thymocyte leading to increase immune cell proliferation rates,so increase or decrease in leptin level affect on physiological work of the body [10].T-cell was important to secret excess of IL-13 to stimulation B-cell in order of synthesis IgE so humeral immune response modulated. IgE has an important role in immune pathogensis of allergic disease, It was showed that IgE make the patients with hyperthyroidism and asthma more worsing and also increase asthma symptoms;because IgE production from B-lymphocyte is strongly regulated by cytokine secrete from T-cell that activated by leptin hormone.Also T3,T4 that binding on the receptors of activating cell [11,12]. An increase secretion of thyroid hormone in asthmatic patients with hyperthyroidism lead to increase production O2 from neutrophil and make it in activated state and increase IgE and increase airway contraction [13,6]**.** While Leptin was decreased in this group when compared with asthma group because of the effect of TSH hormone that binding to TSH receptors on adipocyte tissue that make leptin secretion less than other group because of interaction between TSH and T3 with adipocyte tissue [14],so the increase in serum leptin level in patients with hypersensitive asthma may be due to the leptin affected by allergic reaction in the airway and play a role in asthma prevelance [15].Leptin links the neuroendocrine and immune system that causes modulation of immune response and inflammation.The increase in leptin production that occure during inflammation strongly suggest that leptin is apart of immune system and cytokine network, which governs the inflammentory – immune response and host defence mechanism so increase in IgE level[16].This study concluded there is a relationship between hyperthyroidism and asthma through increase Leptin and IgE

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