Effect of thyroid disorders on insulin secretion in Iraqi patients

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ABSTRACT

Thyroid hormones (T_3, T_4) are important hormones affecting body metabolism. Any change in their levels results in appearance of many complications including changes in blood sugar levels. In this study we determined blood sugar level in cases of hyper, hypo and euthyroidism. It was found that there was highly significant elevation in blood sugar level in case of hyperthyroidism ($p<0.01$). There is obvious correlation (r=-0.237) between blood sugar level and TSH value in patients with hypothyroidism.

تأثير اختلال هرمونات الغدة الدرقية على إفراز الانسولين للمرضى العراقيين

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الخلاصة

تعد هرمونات الغدة الدرقية (T_3, T_4) من الهرمونات المهمة ولها تأثير كبير على فعاليات الجسم الحيوية، وان اي اختلاف عن مستوياتها الطبيعية يؤدي الى ظهور مضاعفات ومنها اختلاف مستوى السكر في الدم ومن خلال هذه الدراسة تم تعيين مستويات السكر في حالات ارتفاع وانخفاض والحالة الطبيعية للغدة الدرقية حيث تبين من خلالها ارتفاع معنوي واضح للسكر عن مستواه الطبيعي في حالة فرط افراز الغدة الدرقية، وعند تعيين الترابط بين مستوى السكر في الدم عند مرضى انخفاض افراز الدرقية وقيم TSH اتضح ان هناك ترابط واضح بينهما.

Introduction

The thyroid hormones, thyroxine (T4, tetraiodothyronine) and triiodotyronine (T3) are iodinated compounds, synthesized by the thyroid gland. The pituitary thyroid stimulating hormone (TSH) stimulates T3 and T4 secretion, the iodinated thyroglobulins in thyrocolloid are reabsorbed by the cells via endocytosis (15). T3 is 3–8 times more biologically active than T4 and acts more rapidly (half-life of T3 is 1 day, that of T4 7 days). Only 20% of all circulating T3 originate from the thyroid; the other 80% are produced by the liver, kidneys, and other target cells that cleave iodide from T4. The conversion of T4 to T3 is catalyzed by microsomal 5-deiodase. T3 is therefore the more potent hormone,while T4 is mainly ascribed a storage function in plasma(15; 3). These hormones are essential for cellular metabolism and for normal central nervous system development (4), also thyroid hormone stimulates cellular oxygen consumption and is considered to be a major regulator of mitochondrial activities (7), stimulating mitochondrial fatty acid oxidation (16).

Diseases of thyroid gland are manifested by alteration in the thyroid hormones secretion .Hypothyroidism occurs when TSH-driven thyroid enlargement is no longer able to compensate for the T3/T4 deficiency (hypothyroid goiter). This type of goiter can also occur due to acongenital disturbance of T3/T4 synthesis or thyroid inflammation (15). Hyperthyroidism occurs when a thyroid tumor or diffuse Struma (e.g., in Grave's disease) results in the overproduction of T3/T4, independent of TSH. In the latter case, an autoantibody against the TSH receptor binds to the TSH receptor. Its effects mimic those of TSH, i.e., it stimulates T3/T4 synthesis and secretion. Thyroid hormone level increase physiologically in response to stress (14).

Glucose is a complex organic molecule; contain much potential energy because of their high degree of structural order. The concentration of blood glucose in most mammals is maintained between 4.5 and 5.5 mmol/L. After the ingestion of a carbohydrate meal, it may rise to 6.5–7.2 mmol/L, and in starvation, it may fall to 3.3–3.9 mmol/L. Glucose is also formed from liver glycogen by glycogenolysis .The maintenance of stable levels of glucose in the blood is one of the most finely regulated of all homeostatic mechanisms, involving the liver, extrahepatic tissues, and several hormones(15). The hormone insulin plays a central role in regulating

blood glucose and the anterior pituitary gland secretes hormones (growth hormone and adrenocoricotrophic hormone) that tend to elevate the blood glucose and therefore antagonize the action of insulin (10). Accordingly this study has been designed to overview the effect of disturbance in thyroid gland secretion like changes in blood glucose level which not due to diabetes mellitus.

Materials and methods

Control and patient subjects:

Control samples were obtained from twenty healthy subjects, aged 20-45 years (29.04±10.51). Twenty five hyperthyroid patients, aged 20-45 years (30.57±8.3) and twenty one hypothyroid patients aged 20-45 year (31.9±7.72) were involved in this study. The history of patients subjects were obtained, they have no other medical diseases other than thyroid disorder and they do not take other medication except that for treatment of thyroid disorders which is under supervision of specialist physician. The samples were obtained from Al-yarmok Teaching Hospital/Department of nuclear medicine / Baghdad. The diagnosis was confirmed by the clinical features of hyperthyroidism and hypothyroidism (by physician) and thyroid function test (serum thyroxin and triiodothyronine), most of patients were previously diagnosed and they take their medication by specialist doctors.

Blood sampling:

Venous blood samples (3ml) were withdrawn from subjects after overnight fasting before test. Samples then transferred to centrifuge tubes. Blood samples were left to clot for one hour, then centrifuged at 1000×g for 10 min. using Janetzki K_{23} centrifuge.

Determination of serum T_3 , T_4 and TSH:

Using mini VIDAS, Biomérieux (France), No.ITV129084, serum total T_3 and T_4 concentration were determined for patients and controls according to the manufacturer recommended procedure, by using Biomérieux T_3 and T_4 kit.

Determination of serum glucose levels:

Using spectrophotometer (Cecil Ce 1011 Cambridge England), serum glucose concentration was determined for patients according and controls to the manufacture recommended procedure, by using Linear Chemicals Kit (Spain).

Statistical Analysis:

Statistical Analysis were done using student T-test. The statistical significance and strength of linear correlation between two continuous variable was assessed by Pearson's correlation coefficient. P value less than 0.01 and 0.05 was considered statistically significant.

Results and Discussion

Results:

Serum thyroid hormones levels (T3, T4 and TSH) were measured for Hyperthyroid, Hypothyroid patients and for control groups, results shown in the (Table, 1).

Table (1): Thyroid hormones level and TSH in patients and control group.

Condition / Hormones	Hyperthyroidism means ± SD* n= 25	Control means ± SD n= 20	Hypothyroidism means ± SD n= 21
T_3 nmol/l	4.246 ± 2.560	1.625± 0.353	0.911 ± 0.601
T_4 nmol/l	183.333 ±74.528	81.692 ± 10.047	28.457 ± 19.485
TSH mIu/l	0.108±0.058	2.016±1.205	7.737±1.486

* **SD: Standard deviation:**

There is highly significant elevation of serum glucose level in hyperthyroid patients while its level decrease but not significantly in hypothyroid patient compared with control group, although there is negative correlation between serum glucose level and TSH value in hypothyrdism (r=-0.237) as shown in (Figure, 1).

Table (2): Serum glucose level in patients and control group.

Condition	Hyperthyroidism means ± SD♦	Control means ± SD	Hypothyroidism means ± SD
Serum glucose (mmol/l)	*6.307 ± 1.079	5.373 ± 0.801	5.066 ± 0.783

* p<0.01 compared with control.
♦SD: Standard deviation.

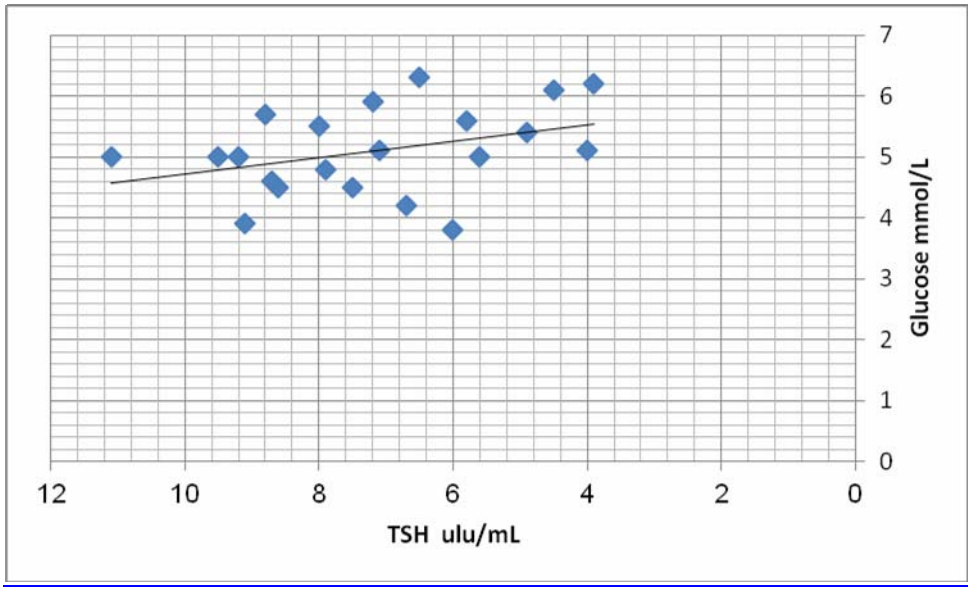

Figure (1): Correlation between serum glucose level and TSH value in hypothyrdism (r=-0.237)

Discussion:

Insulin produced by the B cells of the islets of Langerhans in the pancreas plays a central role in regulating blood glucose through its stimulation of glucose uptake in response to hyperglycemia (2). Liver cells are freely permeable to glucose whereas cells of extrahepatic tissues (apart from pancreatic B islets) are relatively impermeable, and their glucose transporters are regulated by insulin (10).

The concentrations of T_3 may play a role in the regulation of insulin secretion (11). It should, however, be noted that Riis, etal.

recorded 25% lower circulating insulin concentrations in the thyrotoxic patients (13). This is in all probability due to increased insulin clearance this lead to increase blood glucose level as reported by some authors (5; 12).

In hyperthyroidism glucose uptake are resistant to insulin (6), also the insulin receptor number was increased by 70% in hypothyroidism and decreased by 40% in hyperthyroidism. The sensitivities of the effects of insulin on glucose oxidation were increased fourfold in hypothyroidism and decreased fivefold in hyperthyroidism (1).

Hypokalemia (potassium deficiency) (9) is attributable to large shifts of potassium from the extra cellular to the intracellular compartment that are presumably caused by increased Na/K ATPase pump activity associated with the hyperthyroid state (17; 8). Carbohydrate metabolism are dependent upon potassium, which is assists in the conversion of glucose to the form that can be stored in the liver as glycogen (9). So decrease body potassium results in increase glucose in blood.

The above causes explain results that show significant increase in serum glucose level in hyperthyroid patient and decrease its level but not significantly in hypothyroid patients although there is negative correlation between serum glucose level and TSH in hypothyroidism (depending in the correlation on TSH since it stimulates T_3 and T_4 secretion "feedback mechanism", therefore TSH consider as a good factor for determining thyroid disorders) `(10).

References

1. Arner, P.; Bolinder, J.; Wennlund, A. and Ostman, g. (1984). Influence of thyroid hormone level on insulin action in human adipose tissue. Diabetes. 33(4): 369-375.
2. Baron, A. (1994). Hemodynamic actions of insulin. Am. J. Physiol. 267: 187-202
3. Bianco, C. A. and Kim, B. W. (2006). Deiodinases: implications of the local control of thyroid hormone action. J. Clin. Invest. 116(10): 2571-2579.
4. Chan, S. and Kilby, M. D. (2000). Thyroid hormone and central nervous system development J. Endocrinol. 165: 1-8.
5. Cohen, P.; Barzilai, N.; Barzilai, D. and Karnieli, E. (1986). Correlation between insulin clearance and insulin responsiveness: studies in normal, obese, hyperthyroid, and Cushing's syndrome patients. Metabolism. 35: 744-749.
6. George, D.; Panayota, M.; Vaia, L.; Eleni, B.; Eirini, M.; Efi, K.; Marinela, T.; Nikolaos, T. and Sotirios, A. (2006). Glucose and Lipid Fluxes in the Adipose Tissue after Meal Ingestion in Hyperthyroidism. J. Clin. Endocrinol. Metab. 91(3): 1112-1118.
7. Goglia, F.; Silvestri, E. and Lanni, A. (2002). Thyroid hormones and mitochondria. Biosci Rep. 4: 456-465.
8. Kung, A. W. (2006). Thyrotoxic periodic paralysis: a diagnostic challenge. J. Clin. Endocrinol. Metab. 91: 2490-2495.
9. Linda, R. (1992). Healthy Healing, London Text Press. 254.
10. Murray, R. K.; Granner, D. K.; Mayes, P. A. and Rodwell, V. W. (2003). Harper's Illustrated Biochemistry. 26th ed., McGraw-Hill Companies. 160.
11. Ortega, E.; Koska, J.; Pannacciulli, N.; Bunt, J. and Jonathan, J. (2008). Free triiodothyronine plasma concentrations are positively associated with insulin secretion in euthyroid individuals. European Journal of Endocrinology. 158(2): 217-221.
12. Randin, J. P.; Tappy, L.; Scazziga, B.; Jequier, E. and Felber, J. P. (1986). Insulin sensitivity and exogenous insulin clearance in Graves disease. Measurement by the glucose clamp technique and continuous indirect calorimetry. Diabetes. 35: 178-181.
13. Riis. A. L.; Gravholt, C. H.; Djurhuus, C. B.; Norrelund, H.; Lunde J. O.; Weeke, J. and Moller, N. (2002). Elevated Regional Lipolysis in Hyperthyroidism. Clinical Endocrinology and Metabolism. 87(10): 4747-4753

14. Saeb, M.; Baghshani, H.; Nazifi, S. and Saeb, S. (2009). Physiological response of dromedary camels to road transportation in relation to circulating levels of cortisol, thyroid hormones and some serum biochemical parameters. Tropical Animal Health and Production. 10(1007): 9385-9389.

15. Silbernagl, S. (2003). Color Atlas of Physiology. 5th ed., Thieme. 288.

16. Yamauchi, M.; Kambe, F.; Cao, X.; Lu, X.; Kozaki, Y.; Oiso, Y. and Seo, H. (2008). Thyroid Hormone Activates Adenosine 5'-Monophosphate-Activated Protein Kinase via Intracellular Calcium Mobilization and Activation of Calcium/Calmodulin-Dependent Protein Kinase Kinase-β. Molecular Endocrinology. 22(4): 893-903

17. Zachary, D. and Goldberger, M. D. (2007). An electrocardiogram triad in thyrotoxic hypokalemic periodic paralysis. Circulation. 115: 179-180.