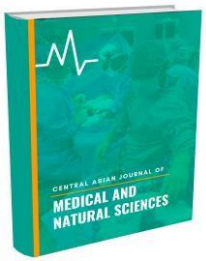

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Article

The Role of Annexin A1, Copeptin, Cholesterol Concentration and AST Activity in Serum of Primary Hypothyroidism Women Obese Patients

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Abstract: Thyroid hormones, plays an a major important and essential functions in metabolic processes. Hypothyroidism is caused by inadequate thyroid hormone synthesis or activity in target tissues. Annexin A1 (AnxA1), is a key factor that have a role in the defense against inflammation and it is considered as endogenous agent that effects on the some types of steroid hormones (glucocorticoids). Copeptin is a small molecule that has a leucine-rich sequence, discovered by Holwerda et al. have a leucine repeats. It is share the precursor molecule with vasopressin - neurophysin II. The eighty women patients suffering have primary hypothyroidism women were participated, their ages ranged from 30 to 45 years. There a significant decrease (P>0.05) in T3 and T4 levels, a highly significant increase (<0.01) in TSH, AnxA1 and cholesterol, a significant increase (p<0.05) in the serum levels of Copeptin and AST activity in women patients group when compared to women control group.

Keywords: AnxA1, primary, Copeptin, AST

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1. Introduction

Hypothyroidism according to pathology type in the thyroid glands, is classified as primary, central or peripheral. The most common type is acquired hypothyroidism, which is usually primary and often caused by severity decline in iodine levels. There is a large variation in clinical signs and the presence of hypothyroid symptoms, especially in women pregnancy and in children. The clinical signs were very variation particularly in children and women [1], [2], [3].

Also referred to as lipocortin-1, annexin A1 (AnxA1) is a mediator of the anti-inflammatory effects of glucocorticoids and is essential to the resolution of inflammation [4]. Under normal circumstances, innate immune cells express it widely. AnxA1 exhibit a variety of antiphlogistic response in experimental settings, including fast posttranslational effects and transcriptional alterations. Glucocorticoids cause isolated monocytes/macrophages or peripheral blood mononuclear cells to synthesize AnxA1 from scratch and to translocate it to the cell surface. The AnxA1 expression may serve in circulating immune cells as a sign of anti-inflammatory response and sensitivity to glucocorticoid [5]. Annexin A1 is a protein that binding to calcium. This annexins protein family is have some functions including proliferation, differentiation, and cellular apoptosis. Also, it can bind phospholipids [6].

Arginine Vasopressin (AVP) is one of the important key hormones in the body. AVP is clinically important because it maintains vascular tone and balance of body fluid. Copeptin, the C-terminal of the precursor of AVP (Pro-AVP), that released in levels that equal with AVP, which making it a sensitive sign of AVP release. Copeptin have a lot of concern as a novel indicator. The important function of copeptin as a clinical signs, especially in the earliest recognizing a disease and in diseases prognosis [7]. Copeptin is a glycopeptide consist of 39-amino-acids, making it an active strong marker for release of AVP [8], Copeptin, was discover by Holwerda et al. in 1972, as a small molecule that have a leucine-rich repeat sequence [9].

Dyslipidemia refers to a lack of balance in lipids profile. This disorder is considered as a risk factor for the buildup of plaque in the coronary, peripheral or carotid arteries as coronary heart disease, ischemic cerebrovascular disease, and peripheral vascular disease [10].

Liver healthy closely related with the glucose regulation in blood and with impaired insulin sensitivity. The enzymes of liver are responsible for the gluconeogenesis pathway. Aspartate aminotransferase (AST) is found in: brain, kidneys, liver, muscle, and lungs [11].

The aim of current study is to find out if plasma Anax A1, Copeptin, cholesterol levels, and AST activity may have role in primary hypothyroidism.

2. Materials and Methods

Eighty women patients suffering from primary hypothyroidism were participated, their ages ranged from 30 to 42 years. All patients were diagnosed by a specialist physician. Patients were grouped in to two categories; 50 from healthy subjects (control) whose age ranged between 27 to 40 years, and 30 from patients. Biochemical measurements of hormones; triiodothyronine (T3), thyroxine (T4), thyroid-stimulating hormone (TSH) levels by AFIAS-10. Anax A1, Copeptin measured by kits from Sun Long Biotech – China, and cholesterol and AST activity measured by DRI-CHEM NX600. Results data were analyzed by Excel XLSTATE statistical software. A statistic used are Student's t-test.

3. Results and Discussion

3.1. Thyroids hormones

The mean (±SD) of T3, T4, TSH ng/ml in serum of women control and primary hypothyroidism women patients groups according to BMI are illustrated in Table 1. T3 and T4 were a significantly decline in women hypothyroidism compared to women control and no differences in BMI groups. A highly significant increase (<0.01) in TSH level in women patients group compared to women control group, a highly significant increase (<0.01) in T3, TSH between A1 and A2 women patients groups, a highly significant increase (<0.01) between A1 women control group and A1 women patient groups, and a highly significant increase (<0.01) between A2 women control group and A2 women patient groups in T3, T4, TSH.

Table 1. The mean of thyroids hormones for studied groups

Parameters/Groups		Mean ± SD	
		Control	Patients
T3 nmol/L	Total	3.04± 0.25	1.22± 0.67
	A1 (BMI =23-25)	3.11± 0.13	1.56± 0.28
	A2 (BMI=25-30)	3.00± 0.43	1.24± 0.52
T4 nmol/L	Total	133.1± 14.11	55.2± 6.20
	A1 (BMI =23-25)	138.1± 13.23	56.7± 6.24
	A2 (BMI=25-30)	139.1± 11.11	52.6± 6.33
TSH μIU/ml	Total	1.31± 0.11	7.44± 0.63
	A1 (BMI =23-25)	1.30± 0.09	6.53± 0.50
	A2 (BMI=25-30)	1.33± 0.12	7.91± 0.72

P value

Parameters	Control/ Patients	A1 Control /A2 Control	A1 Patients /A2 Patients	A1 Control /A1 Patients	A2 Control /A2 Patients
T3	≤ 0.001	>0.05	<0.01	≤ 0.001	≤ 0.001
T4	≤ 0.001	>0.05	>0.05	≤ 0.001	≤ 0.001
TSH	≤ 0.001	>0.05	<0.01	≤ 0.001	≤ 0.001

Due to elevated TSH pituitary in primary hypothyroidism, there was a downsecretion in T4 and T3. The level of TSH in the blood is used to detect primary hypothyroidism in most patients. The level of TSH in the blood is used to detect primary hypothyroidism in most patients. Women have 3.5% a lifetime risk and men have 1.0% a risk of obtain undisguised hypothyroidism. The most common signs, are tiredness, being sensitive to cold, weight gain, and constipation [12]. Hypothyroidism effects on many organs in all age categories and on ability to function on a routine basis. Consult endocrinology is recommended in preconception, pregnancy, hypothyroidism in infants and children, treatment failure, thyroxine malabsorption, co-existing disorders like cardiac or other defect endocrine, interpretation in thyroid report, and medications which help or induced hypothyroidism [13], [14]. Nearly 14% of adult women affected by thyroid disorders and are one of the most prevalent disease of an endocrine gland in women of childbearing age. Sex is a predictor for thyroid dysfunction, as women are three to five times susceptible to treatment for thyroid disturbance than in men [15], [16], [17]. Thyroid disease common in individuals who have BMI higher than 25 kg/m^{2}or people in East Asia [18]. Thyroid imbalances established as a one of causes of a weak in female reproduction which is a polymorphic, with impacts on hypothalamic-pituitary-ovarian axis [15].

3.2. Annexin A1

The mean (±SD) of AnxA1 (ng/ml) concentration in serum of control group and primary hypothyroidism women patients group according to BMI are in Table 2. A significant increase ($p<0.05$) in the levels of AnxA1 in women primary hypothyroidism compared with women control, and a highly increase ($p<0.001$) in serum AnxA1 levels in A2 women patients compared with A2 women control.

Table 2. The mean of AnxA1 (ng/ml)

Groups	Mean ± SD of AnxA1 (ng/ml)	
	Control	Patients
Total	3.59±0.33	3.98±0.29
A1 (BMI =24-25.5)	3.99±0.24	4.08±0.29
A2 (BMI=25.6-30)	3.29±0.30	3.87±0.29

P value				
Control/ Patients	A1 Control /A2 Control	A1 Patients /A2 Patients	A1 Control /A1 Patients	A2 Control /A2 Patients
<0.05	>0.05	>0.05	>0.05	<0.001

AnxA1 plays a critical role in disease like joint inflammation and obstructed airflow from the lungs. AnxA1 was increased in type 1 diabetes without impairment in renal function [19], [20], [21]. Apparently, ANXA1 may make different regulatory signs on different pathways which either activation or inhibition cell division (proliferation), beside important functions [20], [21], [22]. ANXA1 promotes anti-inflammatory immunosuppressive and antipyretic response in the condition of normal function (physiological conditions), specifically strengthen the macrophage differentiation. ANXA1 is considered a mediator of the action of glucocorticoids, thus regulating its expression/secretion. Also, ANXA1 may act as an Inducible endogenous inhibitor that reacts to anti-inflammatory substances [23], [24].

3.3. Copeptin

The mean (±SD) of copeptin (pg/ml) concentration in serum of women control group and primary hypothyroidism women patients group according to BMI are illustrated in Table 3.

Table 3. Mean ± SD of copeptin (pg/ml) concentration

Groups	Mean ± SD of Copeptin (pg/ml)	
	Control	Patients
Total	77.03± 0.85	127.4±11.1
A1 (BMI =24-25.5)	74.8± 0.92	109.6±12.3
A2 (BMI=25.6-30)	80.1± 0.69	145.01±11.1

P value				
Control/ Patients	A1 Control /A2 Control	A1 Patients /A2 Patients	A1 Control /A1 Patients	A2 Control /A2 Patients
≤0.001	>0.05	≤0.001	≤0.001	≤0.001

There are a highly increase ($p<0.001$) in women primary hypothyroidism compared with women control, a highly increase ($p\leq 0.001$) in A1 patients compared with A2 patients, A1 control / patients and in A2 control / A2 patients groups.

Results were agreement with Skowsky and Kikuchi [25]. Also agreement with others who reported that patients with hypothyroidism showed low levels of sodium and AVP

without volume depletion. Clinical and biochemical test were a like to increased secretion of antidiuretic hormone. Results indicate that In hypothyroid patients, hormonal imbalances are linked to elevated oxidative stress state [26], [27]. In both human adult and animal models, the relationship between copeptin, obesity and metabolic have been previously investigated. Evidence about positively correlation between copeptin levels in children, metabolic syndrome, and obese [28], [29], [30].

Increased plasma AVP may have a critical role in: diabetes, insulin resistance syndrome, chronic kidney diseases and heart and blood vessel diseases. High copeptin levels in circulating plasma were associated with abdominal obesity, insulin resistance, impaired glucose tolerance, higher insulin levels, hypertension, and lipoprotein disorder [31].

3.4. Cholesterol

The mean (±SD) of cholesterol mg/dl concentration in serum cholesterol of women control group and primary hypothyroidism women patients group according to BMI are illustrated in Table 4. A significant difference ($p \leq 0.01$) in the levels between primary hypothyroidism when compared with control, and between A1 Patients compared with A2 Patients, A1 Control compared with A1 Patients, A2 Control compared with A2 Patients.

Table 4. Mean ±SD of cholesterol mg/dl concentration

Groups	**Mean ± SD of cholesterol (mg/dl)**	
	Control	Patients
Total	134 ± 15.1	221 ± 17.6
A1 (BMI =24-25.5)	129 ± 13.3	200 ± 18.1
A2 (BMI=25.6-30)	138 ± 14.9	239 ± 17.0

P value

Control /Patients	A1 Control /A2 Control	A1 Patients / A2 Patients	A1 Control /A1 Patients	A2 Control /A2 Patients
≤0.01	>0.05	≤0.05	≤0.001	≤0.001

Thyroid hormone effect on lipid metabolism including biosynthesis and catabolism, and increases the enzymes activity receptors of lipoproteins and scavenger. Insufficient concentration of thyroid hormones can be associated with dyslipidemia [32]. The dyslipidemia is increased biosynthesis, lead to increased levels of total cholesterol and low-density lipoproteins in overt hypothyroidism [33]. Current study agree with Tarboush, F.et al., were showed a significant elevated in cholesterol levels in patients with hypothyroidism [34].

3.5. AST

The mean (±SD) of AST activity IU/L concentration in serum of control group and primary hypothyroidism women patients group according to BMI were illustrated in Table 5. A significant difference (<0.05) in the AST activity IU/L in primary hypothyroidism group when compared with control group, a highly difference (<0.001) between A1 / A2 patients, and between A2 control / A2 patients.

Table 5. Mean ±SD of AST activity IU/L concentration

Groups	Mean ± SD of AST activity IU/L	
	Control	Patients
Total	38.4 ± 5.01	45.2 ± 5.3
A1 (BMI =24-25.5)	37.1 ± 4.2	40.4 ± 4.95
A2 (BMI=25.6-30)	39.98 ± 4.97	53.0 ± 5.12

P value

Control /Patients	A1 Control /A2 Control	A1 Patients /A2 Patients	A1 Control /A1 Patients	A2 Control /A2 Patients
<0.05	>0.05	≤0.001	>0.05	≤0.001

Serum liver enzymes interconnected TSH levels and thyroid hormones. Thyroid abnormalities in hepatic diseases has been mentioned in a number of studies [35], [36], [37], [38]. Hepatic functions and thyroid activities interact with each other. The liver have a significant function in activation, transportation, and metabolism of thyroid hormone [39]. Studies have established that non-alcoholic fatty liver disease is one of the several liver conditions caused by interference with the cellular thyroid hormone transmission [40], [41]. The dysregulation of metabolism in thyroid disorders lead to elevated aminotransferase. Upnormal metabolism and pathways within the hepatocytes may be happen by disturbances of thyroid hormones, and lead to increase synthesis of liver enzymes [37].

3.6. Relationships between parameters

The results obtained in Table 6 revealed a significant related between parameters. There are positive correlation between AnxA1, TSH and AST, while there was negative correlation between AnxA1, T3, T4 and cholesterol.

Table 6. Correlation of parameters between patients

Parameters	AnxA1	Copeptin
T3	-0.41	0.001
T4	-0.45	0.10
TSH	0.64	0.39
Cholesterol	-0.59	0.12
AST	0.42	0.39

4. Conclusion

AnxA1 and Copeptin levels might be useful as an early marker to detect metabolic disorders in hypothyroid subjects.

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