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Study on the Changes of Serum Vaspin Level and its Regulatory Mechanism in Patients with Thyroid Dysfunction

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Abstract: ***Objective:*** To study the changes of serum vaspin levels in hyperthyroidism and hypothyroidism, and the correlation between serum vaspin and FT3, FT4, TSH and HOMA-IR. ***Methods:*** According to the diagnostic criteria of hyperthyroidism and hypothyroidism published in the 8th edition of internal medicine, the patients were divided into hyperthyroidism group (n=47), male 14, female 33, average age (35±9) years; hypothyroidism group: 23 hypothyroidism patients, 7 males and 16 females, with an average age of (38±10) years. The blood pressure, height and weight of all the participants were measured by a specially assigned person, and the body mass index (BMI=weight (kg) /height (M^2) and ankle brachial index (ABI) were calculated. Venous blood samples were drawn from all subjects after fasting for 8 hours in the morning to determine biochemical indexes. Fasting insulin (fins) was measured by chemiluminescence method, insulin resistance index (HOMA-IR, HOMA-IR=FPG×fins/22.5) was calculated by homeostasis model assessment (HOMA-IR), and HbA1c was determined by high-pressure liquid chromatography. The levels of FT3, FT4 and TSH were detected by radioimmunoassay. Serum vaspin levels were measured by ELISA. ***Results:*** The level of BMI in hypothyroidism group was significantly higher than that in hyperthyroidism group and control group (P<0.01), BMI level in hyperthyroidism group was significantly lower than that in control group (P<0.05), FT3 and FT4 levels in hyperthyroidism group were significantly higher than those in hypothyroidism group and control group (P<0.01), TSH level in hypothyroidism group was significantly higher than that in control group and hyperthyroidism group (P<0.01). The level of FPG in hyperthyroidism group was significantly higher than that in control group (P<0.01), but there was no significant difference between hyperthyroidism group and hypothyroidism group, and fins level in hypothyroidism group was significantly higher than that in control group and hyperthyroidism group (P<0.01). The level of HOMA-IR in hyperthyroidism and hypothyroidism group was significantly higher than that in control group (P<0.01). Compared with the control group and the control group, the blood lipid indexes (TC, LDL-C) in the hyperthyroidism group were lower than those in the control group and hypothyroidism group (P<0.01), and all the blood lipid indexes in the hypothyroidism group were significantly different from those in the control group (P<0.01). The vaspin level of hyperthyroidism group was significantly higher than that of control group and hypothyroidism group, and the latter two groups showed that the level of vaspin in hypothyroidism group was significantly lower than that of control group (P<0.05). Correlation analysis showed that serum vaspin was positively correlated with FT3 and FT4 (r=0.255, P=0.005; r=0.327, P=0.001), and negatively correlated with BMI, TC and HDL (r=-0.250, P=0.006; r=-0.244, P=0.007; r=-0.258, P=0.004).). ***Conclusion:*** Serum vaspin level is related to thyroid function. The level of serum vaspin increases in hyperthyroidism and decreases in hypothyroidism. Abnormal changes of fat factor vaspin are associated with thyroid dysfunction.

Key words: Hyperthyroidism; Hypothyroidism; Vaspin
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Thyroid hormone is an important metabolic hormone in human body, which participates in various physiological processes including fat and carbohydrate metabolism. The main manifestations of thyroid dysfunction are hyperthyroidism and hypothyroidism, which have the characteristics of high prevalence, young onset age, rapid progress of disease, and multiple organ functions are easy to be affected at the same time, but the specific mechanism of its occurrence has not been fully clarified. It has been one of the frontier fields in life science research to explore the pathogenesis of thyroid diseases and find effective intervention targets[1].

In recent years, the endocrine function of adipose tissue and its role in diseases have attracted much attention. In the past decade, it has been recognized that in addition to energy storage, adipose tissue can secrete many cytokines, including vaspin, and play a role in a series of metabolic abnormalities characterized by central obesity, dyslipidemia, type 2 diabetes, hypertension and cardiovascular disease[2]. Abnormal thyroid hormone levels caused by thyroid dysfunction often lead to metabolic abnormalities such as dyslipidemia, impaired glucose tolerance, insulin resistance and accelerated atherosclerosis.

Both thyroid hormone and vaspin are involved in the regulation of metabolism. Whether adipokines act as pathogenic or protective factors in the process of thyroid dysfunction is still unclear.

Vaspin is a new type of adipokines closely related to insulin resistance and obesity. At present, there are few studies on the changes of serum vaspin level in patients with thyroid dysfunction and the correlation between vaspin and thyroid dysfunction. We compared the serum vaspin levels of normal people, hyperthyroidism patients and hypothyroidism patients to explore the correlation between vaspin and thyroid dysfunction[3].

1 Data and methods

1.1 Clinical data

Patients in our hospital from January 2017 to June 2020. According to the diagnostic criteria of hyperthyroidism and hypothyroidism (8th edition of internal medicine), the patients were divided into hyperthyroidism group (n=47, male 14, female 33, mean age (35±9) years); hypothyroidism group: 23 patients with hypothyroidism, 7 males and 16 females, with an average age of (38±10) years. Exclusion criteria: (1) patients with severe heart and brain diseases; (2) diabetes; (3) patients with moderate and severe liver and kidney dysfunction; (4) patients with hereditary hyperlipidemia; (5) patients with acute and chronic infectious diseases; (6) patients with malignant tumors; (7) drug addicts and alcoholics; (8) pregnant women and lactating women. In addition, 50 healthy people were taken as control group. There were 16 males and 34 females with an average age of (36±11) years. Diabetes mellitus, coronary heart disease and other endocrine and metabolic diseases were excluded according to the WHO 1999 diabetes diagnostic criteria, 1997 WHO-ISH hypertension diagnostic criteria, clinical manifestations and electrocardiogram. The study protocol was approved by the hospital research ethics committee, and all patients signed written informed consent.

1.2 Research methods

The blood pressure, height and weight of all the participants were measured by specially assigned person, and the body mass index (BMI=weight (kg) /height $(m)^2$) and ankle brachial index (ABI) were calculated. Venous blood samples were drawn from all subjects after fasting for 8 hours in the morning to determine biochemical indexes. Methods: TC, TG, HDL, LDL, FPG were measured, fasting insulin (fins) was measured by chemiluminescence method, insulin resistance index (HOMA-IR, HOMA-IR=FPG×fins/22.5) was calculated by homeostasis model assessment (HOMA-IR), and HbA1c was determined by high-pressure liquid chromatography. Test tubes without pyrogen and endotoxin were used. After collecting the blood, the serum and red blood cells were separated rapidly and carefully by centrifuging at 1000×g for 10 minutes. Serum FT3, FT4, TSH and vaspin levels were determined.

The levels of FT3, FT4 and TSH were detected by radioimmunoassay. The radioimmunoassay was provided by Beijing atomic energy Reagent Co., Ltd. The intra assay CV was less than 2.5%, and the inter

assay CV was less than 3.0%.

Serum vaspin level was measured by ELISA. The reagents were purchased from Shanghai enzyme linked Biotechnology Co., Ltd., and the CV of both in plate and between plate were less than 10%.

The data were analyzed by SPSS 13.0. The measurement data are expressed as mean ± standard deviation, and the non normal distribution variables are converted to normal distribution first. One way ANOVA was used for statistical analysis, and LSD test was used for pairwise comparison between multiple means. The relationship between variables was analyzed by partial correlation analysis and logistic regression analysis. $P<0.05$ was statistically significant.

2 Results

2.1 Comparison of clinical data and biochemical indexes in each group

There was no difference in gender and age among the three groups. The level of BMI in hypothyroidism group was significantly higher than that in hyperthyroidism group and control group ($P<0.01$), BMI level in hyperthyroidism group was significantly lower than that in control group ($P<0.05$), FT3 and FT4 levels in hyperthyroidism group were significantly higher than those in hypothyroidism group and control group ($P<0.01$), TSH level in hypothyroidism group was significantly higher than that in control group and hyperthyroidism group ($P<0.01$). The level of FPG in hyperthyroidism group was significantly higher than that in control group ($P<0.01$), but there was no significant difference between hyperthyroidism group and hypothyroidism group, and fins level in hypothyroidism group was significantly higher than that in control group and hyperthyroidism group ($P<0.01$). HOMA-IR of hyperthyroidism and hypothyroidism group was significantly higher than that of control group ($P<0.01$). Compared with the control group and the control group, the blood lipid indexes (TC, LDL-C) in the hyperthyroidism group were lower than those in the control group and hypothyroidism group ($P<0.01$), and all the blood lipid indexes in the hypothyroidism group were significantly different from those in the control group ($P<0.01$). See Table 1 for details.

2.2 Comparison of serum vaspin in each group

The vaspin level of hyperthyroidism group was significantly higher than that of control group and hypothyroidism group, and the latter two groups showed that the level of vaspin in hypothyroidism group was significantly lower than that of control group ($P<0.05$). See Table 2.

2.3 Correlation analysis of serum vaspin and clinical and biochemical indexes

Correlation analysis showed that serum vaspin was positively correlated with FT3 and FT4 (r=0.255, P=0.005; r=0.327, P=0.001), and negatively correlated with BMI, TC and HDL (r=-0.250, P=0.006; r=-0.244, P=0.007; r=-0.258, P=0.004).

Table 1. Comparison of clinical and biochemical indexes of each group ($\bar{x} \pm s$)

Group	Age(yr)	BMI(kg/m^2)	FT3(pmol/L)	FT4(pmol/L)	TSH(μIU/ml)	FPG(mmol/L)
Control(n=50)	54.46±8.15	23.23±2.45	4.93±1.31	15.68±2.94	2.86±1.28	5.06±0.64
Hyperthyroidism group (n=47)	58.68±10.90	22.35±1.77*	10.30±3.37**	27.96±7.20**	0.09±0.07	6.36±0.83**
Hypothyroidism group (n=23)	52.87±10.37	25.78±1.33$^{**\Delta\Delta}$	2.42±0.82$^{**\Delta\Delta}$	9.85±3.46$^{**\Delta\Delta}$	21.65±16.80$^{**\Delta\Delta}$	5.92±1.38**

Group	HbA1c (%)	Fins (μU/ml)	HOMA-IR	TC (mmol/L)	TG (mmol/L)	HDL (mmol/L)	LDL (mmol/L)
Control(n=50)	5.16±0.70	10.24±3.32	2.30±0.82	4.67±0.71	1.38±0.70	1.23±0.28	2.95±0.62
Hyperthyroidism group (n=47)	5.72±0.91**	10.09±3.64	2.84±1.03**	3.68±0.93**	1.70±0.60	1.03±0.25**	2.49±0.72**
Hypothyroidism group (n=23)	5.51±1.31	12.42±2.66$^{*\Delta\Delta}$	3.34±1.25**	6.17±1.16$^{**\Delta\Delta}$	2.56±1.15$^{**\Delta\Delta}$	1.03±0.16**	3.99±1.23$^{**\Delta\Delta}$

$^{*}P<0.05$, $^{**}P<0.01$ vs control group; $^{\Delta}P<0.05$, $^{\Delta\Delta}P<0.01$ vs hyperthyroidism group

Table 2. Comparison of serum vaspin levels among group($\bar{x} \pm s$)

Group	n	Vaspin (ng/mL)
Control	50	0.52±0.21
Hyperthyroidism group	47	0.61±0.21*
hypothyroidism group	23	0.42±0.16*$^{\Delta\Delta}$

$^{**}P < 0.01$ vs control group, $^{\Delta\Delta}P<0.01$ vs hyperthyroidism group

3 Discussion

Adipose tissue secretes a variety of bioactive substances, called adipocytokines, which play a role in autocrine, paracrine and endocrine ways. They play a role in controlling appetite, thermogenesis, thyroid and reproductive function. All of these molecules may cause local and systemic inflammation and mediate metabolic related vascular diseases, including hypertension, diabetes, atherosclerosis and insulin resistance. Thyroid dysfunction is associated with changes in body weight, heat production and energy consumption. The relationship between cardiovascular risk factors such as dyslipidemia, impaired glucose tolerance, insulin resistance, atherosclerosis and thyroid dysfunction has been reported. In the abnormal state of thyroid function, adipocytokines may play an inducing or protective role in the development of these diseases. In hypothyroidism and hyperthyroidism, the reports of abnormal levels of adipocytokines (adiponectin, leptin, resistin, angiotensin and visfatin) are controversial.

Both thyroid hormone and vaspin are involved in the regulation of metabolism. Whether vaspin is a pathogenic or protective factor in the process of thyroid dysfunction is still unclear. Little is known about the regulatory relationship between them. Some studies have shown that hypothyroidism inhibits the expression of vaspin. Other studies have shown that compared with normal thyroid function rats, the expression of vaspin mRNA in hyperthyroidism rats is significantly lower than that in hypothyroid rats, although their blood glucose and insulin levels did not change, it suggested that thyroid dysfunction might affect vaspin expression[4-6]. Some scholars have studied the relationship between TSH and vaspin levels before and after weight loss. TSH level decreased significantly, which was positively correlated with vaspin level. However, there is no clear conclusion on whether vaspin causes TSH level reduction and whether thyroid function changes affect serum vaspin level. Another clinical study showed that there was no significant difference in vaspin level between patients with normal thyroid function and hypothyroidism, and there was no significant change in vaspin level after thyroid hormone level was normal[7]. This seems to indicate that thyroid hormone status does not affect serum vaspin levels. More research is needed to understand the relationship between vaspin and thyroid hormones.

Our study showed that vaspin level in hyperthyroidism group was significantly higher than that in control group and hypothyroidism group, and the comparison between the latter two groups showed that the serum vaspin level was significantly lower than that of the control group; correlation analysis showed that serum vaspin was positively correlated with FT3 and FT4, and negatively correlated with BMI, TC and HDL. The results suggest that serum vaspin level is related to thyroid function. The serum vaspin level increases in hyperthyroidism and decreases in hypothyroidism. Abnormal changes of fat factor vaspin were found in patients with thyroid dysfunction.

Some studies have shown that the use of levothyroxine sodium in the treatment of hypothyroidism can achieve normal thyroid function through replacement therapy, which can increase the level of adiponectin and reduce the level of leptin, independent of the change of body fat mass[8]. This suggests that thyroid function may affect the regulation level of adipokines.

Whether vaspin can protect or promote thyroid function remains to be further studied.

4 Declaration of interest

The authors declare that there is no conflict of interest that would prejudice the impartiality of this scientific work.

5 Acknowledgments

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