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Original Article

Insulin resistance and its correlation with chemerin and visfatin in Saudi patients with hyperthyroidism

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ABSTRACT

Objective: This study aimed to assess the relationship between chemerin and visfatin concentrations and insulin resistance in Saudi women with hyperthyroidism.

Materials and Methods: Seventy healthy participants and 70 participants with hyperthyroidism were recruited for the study. Concentrations of chemerin, visfatin, thyroid profile, fasting glucose, insulin, and homeostatic model assessment of insulin resistance (HOMA-IR) were measured.

Results: Hyperthyroid patients showed significantly higher concentrations of fasting glucose and insulin ($P < 0.001$) and significant increases in HOMA-IR values than the control group. Spearman's correlation coefficient analysis showed that thyroid-stimulating hormone was negatively correlated with glucose, insulin, and HOMA-IR, while free triiodothyronine was positively correlated with the same parameters. Total triiodothyronine and total thyroxine also showed a significant positive correlation with glucose, and the levels of thyroglobulin were also positively correlated with insulin and HOMA-IR. Furthermore, chemerin levels correlated positively with glucose, insulin, and HOMA-IR. Inversely, visfatin was negatively correlated with insulin and HOMA-IR.

Conclusion: A significant relationship was observed between adipokines and thyroid profile, glucose, insulin, and insulin resistance in hyperthyroid patients. This suggests that visfatin and chemerin levels might affect insulin sensitivity in conjunction with thyroid hormones and thus may alter the metabolism of glucose and leads to insulin resistance.

Keywords: Adipokines, chemerin, hyperthyroidism, insulin resistance, thyroid hormones, visfatin

Introduction

Thyroid hormones regulate a wide range of metabolic processes essential for normal growth and development as well as regulating carbohydrate and lipid metabolism.[1,2] Hyperthyroidism is a pathological disorder that occurs due to the excessive production of thyroid hormones; thyroxin (T4) and triiodothyronine (T3), and insufficient levels of thyroid-stimulating hormone (TSH).[3,4]

Adipokines, such as leptin, adiponectin, and resistin, are biologically active substances secreted by adipose tissue with different physiological functions. They play essential roles in the regulation of energy homeostasis, insulin sensitivity, and lipid/carbohydrate metabolism.[5-7] There are conflicting data about the associations between the thyroid hormones and adipokine levels in general. Alteration in adipokines secretion has been reported in patients with hyperthyroidism in different studies. For example, serum levels of resistin as well as adiponectin have shown positive correlation with thyroid hormones,[8-11] whereas serum levels of leptin were negatively correlated with thyroid hormones.[10-12]

Over the past decades, the view of adipose tissue has undergone a dramatic change and an increasing number of adipokines such as chemerin, visfatin, and omentin have been described in literature. Therefore, the authors aimed in a previous study to focus on studying some of these recent recognized adipokines including chemerin, visfatin, and omentin, to investigate the potential influence of hyperthyroidism on their levels. Our previous results showed that visfatin concentrations were significantly decreased in hyperthyroid patients. In addition, a novel association between hyperthyroidism and chemerin concentrations was also observed.[13] Since adipokines and thyroid hormones share some physiological effects on energy expenditure and are involved in the regulation of glucose

and lipid metabolism, it is suggested that hyperthyroidism may influence the action of adipose tissue, which, in turn, contributes to other metabolic disorders. However, limited studies have investigated this relationship. Therefore, the aim of the current study is to assess the relationship between insulin resistance and the concentrations of chemerin and visfatin in Saudi female with hyperthyroidism.

Materials and Methods

Study subjects

In this case–control study, a total of 140 Saudi women between the age of 20 and 45 years were recruited from different hospitals in Jeddah, Saudi Arabia (King Abdulaziz University Hospital, King Fahd Armed Forces Hospital, and King Fahd Hospital) from December 2016 to December 2017. Hyperthyroidism was diagnosed by elevated T3 and T4 concentrations and reduced concentration of TSH. Accordingly, participants were grouped into two groups, the euthyroid control group ($n = 70$) and the hyperthyroid group ($n = 70$). Biochemical analyses were performed at King Fahd Medical Research Center and King Abdulaziz University Hospital. The exclusion criteria were the presence of any other disease including diabetes and hypertension and pregnancy. In addition, patients treated with either radioactive iodine therapy or thyroidectomy were excluded from the study. The study was approved by the ethical committee, Faculty of Medicine, King Abdulaziz University (ref. no. 418–6) and the health affairs of Jeddah city (ref. no. 412). All participants have signed an informed consent form before participating in the study.

Biochemical measurements

After an overnight fast (12–14 h), blood samples were collected from all participants. The separated serum was stored immediately at −80°C until assayed. An enzyme-linked immunosorbent assay kit (ab155430-Chemerin Human ELISA kit) was used to quantitatively determine serum chemerin according to the manufacturer's protocol (Abcam, USA). Serum visfatin was measured quantitatively using human visfatin ELISA kit (cat no. SG-10381, SinoGeneclon biotech Co., Ltd).

Thyroid hormones including TSH, total triiodothyronine (TT3), total thyroxine (TT4), free triiodothyronine (FT3), FT4, and thyroglobulin were all measured by the electrochemiluminescence immunoassay "ECLIA" method using COBAS e 411 automated machine analyzer (Roche Company, USA).

Concentrations of glucose and insulin were measured by enzymatic methods that are automatically performed by Dimension Vista® system (Siemens, Germany). Insulin resistance was estimated with homeostatic model assessment of insulin resistance (HOMA-IR), which was calculated as fasting serum insulin (μU/ml) × fasting plasma glucose (mmol/l)/22.5.[14]

Statistical analysis

Statistical analysis was performed using GraphPad Prism 7. Mean ± standard error of the mean was used for descriptive data analysis of the study sample. The independent sample *t*-test was used to evaluate the difference in serum glucose and insulin concentrations and HOMA-IR between the two groups. Spearman's correlation coefficients were used to evaluate the association between serum thyroid hormones concentration and glucose, insulin, and HOMA-IR in hyperthyroid patients. The same approach was used to investigate the relationship between serum adipokines and glucose, insulin, and HOMA-IR. $P < 0.05$ was considered statistically significant.

Results

The results showed that hyperthyroid patients exhibited highly significant increases in the concentrations of fasting glucose and insulin ($P < 0.001$) and significant increases in HOMA-IR level ($P < 0.05$), compared to the control group [Figure 1].

Spearman's correlation [Table 1] showed a significant correlation between chemerin and visfatin and fasting glucose, insulin, and HOMA-IR. The analysis showed that chemerin levels correlated positively with HOMA-IR, as well as fasting glucose and insulin concentrations. On the other hand, a significant inverse correlation was observed between visfatin and fasting insulin levels and HOMA-IR. In addition, the results revealed that TSH values were negatively correlated with glucose, insulin, and HOMA-IR, whereas FT3 levels showed a significant positive correlation with the same parameters. TT3 and TT4 values also showed a significant positive correlation with glucose while thyroglobulin levels were positively correlated with insulin values and HOMA-IR.

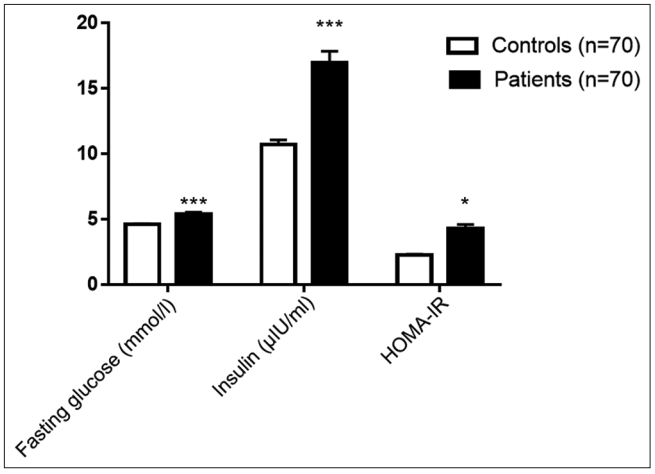

Figure 1: Mean serum concentrations of glucose, insulin, and homeostatic model assessment of insulin resistance in the control and the hyperthyroidism groups. Values are presented as means ± standard error of the mean. *$P < 0.05$, ***$P < 0.001$

Table 1: Spearman correlation between adipokines and thyroid profile and glucose, insulin, and HOMA-IR

Variables (*n*=140)	Glucose	Insulin	HOMA-IR
Chemerin	0.30***	0.31 **	0.31***
Visfatin	−0.11	−0.39***	−0.30**
Thyroid-stimulating hormone	−0.33***	−0.18*	−0.21*
Total triiodothyronine	0.39****	0.10	0.17
Total thyroxine	0.33***	0.012	0.16
Free triiodothyronine	0.40****	0.19*	0.25**
Free thyroxine	0.06	−0.04	−0.03
Thyroglobulin	0.07	0.19*	0.20*

HOMA-IR: Homeostatic model assessment of insulin resistance. *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001

Discussion

In this study, we aimed to examine the correlation between insulin resistance and serum concentrations of chemerin and visfatin in Saudi female patients with hyperthyroidism. According to different studies, thyroid hormones have shown a significant effect on glucose metabolism and the development of insulin resistance.[15-17] Mechanistic studies have been focusing on elucidating this relationship. In overall, it has been reported that the elevated plasma glucose levels in this condition were explained by the increase in the rate of glycogenolysis and gluconeogenesis.[18-20] In addition, it has been suggested that may adipokines which are regulated by thyroid hormones play a role in the development of insulin resistance in hyperthyroidism. The results from our previous study have supported this hypothesis and have showed significant decrease in serum concentrations of visfatin and significant increase in serum concentrations of chemerin in hyperthyroid group than control group.[13] Moreover, our current study has shown significant negative correlation between HOMA-IR and visfatin and significant positive correlation between HOMA-IR and chemerin.

It has been suggested by different studies that visfatin is a beneficial adipokine with insulin-mimicking/-sensitizing effects.[21,22] Several lines of evidence indicate that it binds to and activates the insulin receptor.[23] Accordingly, we hypothesized that the excess of thyroid hormones can affect the functions of adipose tissue and its visfatin secretion. The decrease effect on visfatin level can consequently reason insulin receptors inactivation that can contribute to insulin resistance. However, other studies have showed different results. Chu *et al*.[24] reported that although hyperthyroid group had significantly higher visfatin concentrations and HOMA-IR than the control group, visfatin did not correlate with insulin and HOMA-IR levels. In addition, Caixàs *et al*.[25] study has showed an increased level of circulating visfatin in hyperthyroid patients without association with insulin resistance.

To the best of our knowledge, this study is the first to examine the correlation between chemerin and insulin resistance in hyperthyroid patients. Conflicting data exist regarding the effect of chemerin on insulin signaling. However, Becker *et al*.[26] and Sell *et al*.[27] have concluded that chemerin is involved in the cross-talk between liver, adipose tissue, and skeletal muscle and induces insulin resistance.

Conclusion

Our findings proved that insulin, glucose, and insulin resistance levels were higher in hyperthyroid patients than the controls. In addition, a significant correlation was observed between adipokines and thyroid profile, glucose, insulin, and insulin resistance. This suggests that visfatin and chemerin levels might affect insulin sensitivity in conjunction with thyroid hormones and, thus, alters the metabolism of glucose and energy homeostasis and leads to insulin resistance.

Recommendations

Future prospective studies are needed to explore the mechanistic links between adipokines and insulin resistance in hyperthyroid patients.

Limitations

The study has some limitations. Due to the small sample sizes, hyperthyroid patients were not subgrouped according to the cause of the disease. Moreover, the results did not include treated patients to compare their results with the untreated patients with hyperthyroidism.

Conflicts of Interest

All the authors declare that they have no conflicts of interest.

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