Study the relationship between adiponectin with thyroid hormones and cortisol in Type 2 diabetic patients (NIDDM)

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ABSTRACT

Thyroid hormones has profound effects of lipid metabolism and carbohydrate homeostasis. Abnormalities in serum lipids and lipoproteins are frequent findings in thyroid dysfunction, mainly in hypothyroidism. Impaired glucose tolerance and insulin resistance have been documented in patients with thyroid dysfunction. In addition, thyroid hormones are remarkable regulators of energy metabolism, being the adipose tissue the largest fuel storage compartment. Furthermore, thyroid hormones share some physiological actions with adiponectin, such as reduction of body fat by increasing thermogenesis and lipid oxidation. However, a few number of studies have found low adiponectin levels in hypothyroid subjects (Díez and Iglesias, 2009). Cortisol excess in man is characterized by abdominal obesity, hypertension, glucose intolerance or diabetes and dyslipidemia. All these features share a state of insulin resistance, and contribute to high cardiovascular risk typical of this condition. Glucocorticoids negatively regulate adiponectin mRNA in human visceral adipose tissue. Cortisol counteracts the action of insulin at multiple sites, and increases hepatic gluconeogenetic efficiency (Falloon et al., 2004). Study the relationship between adiponectin with thyroid hormones and cortisol for both gender and for both control and diabetic groups also in diabetic patients according to duration of disease. This study was conducted between November 2010- November 2012 and, it was carried out at the diabetic Centre / Merjan Teaching Hospital in Babel Province by taking 120 diabetic patients (Type II DM) (60 male and 60 female) with disease duration (0-5), (>5-10) and (>10) years, with age average (30-65 year) and most of them were on oral hypoglycemic drugs. While the study included 40 people apparently healthy that included 20 male and 20 female with age average (30-65 year).

Introduction

The classical perception of adipose tissue as a storage place of fatty acids has been replaced over the last years by the notion that adipocytes and adipose tissue produce a wide range of hormones and cytokines involved in glucose metabolism (e.g. adiponectin, resistin), lipid metabolism (e.g. cholesteryl ester transfer protein, CETP), inflammation (e.g. TNF-a, IL-6), coagulation (PAI-1), blood pressure (e.g. angiotensinogen, angiotensin II), and feeding behaviour (leptin), thus affecting metabolism and function of many organs and tissues including muscle, liver, vasculature, and brain. Plasma adipocytokine levels rise with an increase in adipose tissue and adipocyte volume, except for plasma adiponectin which is lower in obesity. These adipocyte products acting in autocrine, paracrine and endocrine ways, are capable of influencing not only local adipocyte physiology, but also the function of different organ systems (Hajer et al., 2008; Díez and Iglesias, 2009).

Adiponectin encoded by gene APM1 which has been mapped to chromosome 3 q 27, consist from 244 amino acid, abundantly synthesized and secreted by the adipose tissue, and has structural homology to complement factor C1q and collagen VIII and X (Nedvidkova et al., 2005). Murine studies show the half-life of circulating adiponectin to be 75 minutes with clearance mediated by the liver (Robinson et al., 2011). Adiponectin was first identified in 1995, circulates at relatively high concentration of 2 to 30 µg/ml in blood, accounting for up to 0.01% of total plasma protein in humans (Daimon et al., 2003; Shimada et al., 2004; Kadowaki et al., 2006; Heidemann et al., 2008).

Thyroid hormones influence many aspects of reproduction, growth, differentiation, and metabolism. Many of these actions occur cooperatively with other hormones, and the thyroid hormones enhance their effectiveness. This cooperative role for thyroid hormones is referred to as permissive action whereby thyroid hormones produce changes in target tissues that “allow” these tissues to be more responsive to another hormone. The importance of thyroid hormones is reflected in the observation that the incidence of thyroid disease in humans is exceeded only by the incidence of diabetes mellitus. Under normal conditions, circulating T4 levels are much greater than T3 levels (Norris, 2007).

Thyroid hormone excess is associated with weight loss, reduction in fat mass, depletion in lipid storage and reduction of some serum lipids. Glucose intolerance and insulin resistance are also frequent findings in patients with thyrotoxicosis. In rats, adiponectin concentrations correlated positively with serum T4.
and T3 and negatively with TSH. A positive correlation between adiponectin and free T4 in patients with hyperthyroidism before and after treatment has also been reported. It has also been suggested that elevated levels of adiponectin in hyperthyroid patients might be the result of stimulating action of thyroid hormones on transcriptional induction of adiponectin through PPARγ pathway, and it could be a cross-talk between PPAR and thyroid hormone signalling pathways (Fernandez-Real et al., 2003).

One postulated mechanism for anti-inflammatory of glucocorticoid is the glucocorticoid-induced inhibition of the kallikreins, enzymes which catalyze formation of kinins from a plasma precursor protein. Kinins induce inflammation by causing release of histamine normally observed following the combination of antigen and antibody. Another suggestion for glucocorticoid anti-inflammatory activity stems from observations of their effects on lysosomes. Glucocorticoids cause stabilization of lysosomal membranes, thereby reducing release of hydrolytic enzymes following cell injury and hence reducing the spread of the inflammatory reaction. Inhibition by glucocorticoids of the cyclooxygenase enzyme necessary for prostaglandin synthesis reduces prostaglandin induction of inflammation. Glucocorticoids also inhibit the synthesis of cytokine agents (e.g., interleukins) that mediate inflammation and cell-mediated immune responses (Norris, 2007).

In a study by Venkatesh et al. (2009) on healthy volunteers, it was observed a significant positive relation between plasma cortisol and adiponectin, particularly in males.

Sundbom et al. (2008) indicated that patients with type 2 diabetes have high intracellular levels of glucocorticoids. Glucocorticoids have been shown to decrease the levels of adiponectin in animal models and in humans.

In a study by Lehrke et al. (2008) it was indicated that increased in cortisol levels causes diabetes because the cortisol increased glucose availability by augmentation of hepatic glucose production via transcriptional and post-transcriptional activation of gluconeogenic enzymes including glucose-6-phosphatase and phosphoenolpyruvate. In addition, cortisol inhibits glucose uptake and utilization by peripheral tissues and cortisol excess impairs glucose tolerance and causes diabetes.

### Materials and Method:

About five milliliters of venous blood were collected from each subject in the study. The blood was separated by centrifugation at (3000 rpm) for 15 min. The sera were used for measurement of lipid profile while the remaining stored frozen at (-20 °C) until assayed.

To determine the serum adiponectin, cortisol, TSH, T3 and T4 the quantitative sandwich enzyme immunoassay technique were used.

### Statistical Analysis:

Analysis were performed using the Statistical Package for Social Sciences (SPSS version 18.0). Data were represented as mean ± SE. Bivariate correlations were performed using the Pearson correlation coefficient. P value (P<0.05) was considered statistically significant.

### Result:

Correlation analysis showed an inverse correlation between adiponectin and cortisol in female diabetic patients (r= -0.36, P= 0.05) while in male diabetic patients there was positive correlation between adiponectin and T4 was found (r= 0.46, P= 0.01). The correlation of TSH and T3 with adiponectin appears no significant correlation for both groups and for both males and females as shown in Table (1), Figure (1) and Figure (2).

### Figures:

- **Figure (1):** The relationship between cortisol (mg/dl) and adiponectin (µg/ml) in males of diabetes group
- **Figure (2):** The relationship between T4 (mg/dl) and adiponectin (µg/ml) in males of diabetes group.
- **Figure (3):** The relationship between cortisol (mg/dl) and adiponectin (µg/ml) in females of diabetes third group (>10 year) duration
- **Figure (4):** The relationship between TSH (mIU/ml) and Adiponectin (µg/ml) in males of diabetic first group (0-5 year) duration
Table(1): Correlation analysis between adiponectin and hormones of control and diabetic patients Type 2.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Adiponectin(µg/ml)</th>
<th>Adiponectin(µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control groups</td>
<td>Diabetes groups</td>
</tr>
<tr>
<td>Indices</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Cortisol(mg/dl)</td>
<td>0.1</td>
<td>0.78</td>
</tr>
<tr>
<td>TSH(mIU/ml)</td>
<td>-0.31</td>
<td>0.4</td>
</tr>
<tr>
<td>T3(ng/ml)</td>
<td>0.38</td>
<td>0.3</td>
</tr>
<tr>
<td>T4(mg/dl)</td>
<td>0.2</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Correlation coefficient (r)

*. Correlation is significant ≤ 0.05 level (2-tailed).

Table(2): The relationship between adiponectin and hormones of diabetic patients Type 2 according to the durations of disease

<table>
<thead>
<tr>
<th>Indices</th>
<th>Adiponectin(µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-5</td>
</tr>
<tr>
<td></td>
<td>Diabetes groups</td>
</tr>
<tr>
<td></td>
<td>Male</td>
</tr>
<tr>
<td>Cortisol (mg/dl)</td>
<td>0.58</td>
</tr>
<tr>
<td>TSH (mIU/ml)</td>
<td>-0.68*</td>
</tr>
<tr>
<td>T3 (ng/ml)</td>
<td>0.02</td>
</tr>
<tr>
<td>T4 (mg/dl)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Correlation coefficient (r)

*. Correlation is significant ≤ 0.05 level (2-tailed).

Figure(5): The relationship between T3(ng/ml) and Adiponectin (µg/ml) in females of diabetic second group (>5-10 year) duration

\[ y = 0.176x + 4.220 \]
\[ r = 0.15 \]
\[ P \text{ value} = 0.04 \]

Figure(6): The relationship between T4(mg/dl) and Adiponectin (µg/ml) in males of diabetic second group (>5-10 year) duration

\[ y = 0.339x + 1.52 \]
\[ r = 0.91 \]
\[ P \text{ value} = 0.001 \]
This study agreement with study of Ferrandez-Real et al. (2005) that found free cortisol correlated negatively with adiponectin only in women but not in men.

While other study found significant positive relation between plasma cortisol and adiponectin has been shown in healthy volunteers, particularly in males. A possible mechanism for the positive relation could be that the promoter region for the adiponectin gene contain consensus sequences for glucocorticoid receptor binding (Venkatesh et al., 2009).

**References:**


