ABSTRACT

Background

Acute hyperglycemia is a frequently encountered condition in the Emergency Department (ED) mostly because it is seen as a complication of diabetes mellitus (DM). In this study we aimed to detect the change in adiponectin levels during acute hyperglycemic state and after normalization of blood glucose with insulin treatment.

Material and Methods

48 patients over the age of 18 years who were admitted to the ED with acute hyperglycemia were included in the study. Serum samples were taken from patients on admission and six hours after the normalization of blood glucose with insulin treatment. Adiponectin levels were measured in both samples.

Results

There were 21 female and 27 male patients with a median age of 58.7±18 years. All patients' blood glucose levels were normalized with insulin treatment according to international recommendations. Serum adiponectin levels decreased significantly after the normalization of blood glucose in the whole group. Adiponectin levels decreased from 28.9±16.5 to 12.1±10.9 µg/ml (p<0.0001) in the whole group. This decrease was independent of diabetes type and body mass index.

Conclusion

Normalization of blood glucose in patients with hyperglycemia caused a decrease in adiponectin levels independent of diabetes type and/or body weight in acute emergency setting. Inhibited upregulation of adiponectin secretion and/or blunted suppressive effect of insulin due to hyperglycemia or exogenous insulin administration may have caused the decrease in adiponectin levels.

Key Words: Hyperglycemia, adiponectin, body mass index
Adiponectin levels decrease independently of body mass index and diabetes type after the normalization of hyperglycemia.

1. Introduction

Diabetes mellitus (DM) prevalence is increasing worldwide [1]. Hyperglycemia is a frequently encountered condition of patients with DM who are admitted to the ED [2].

Adiponectin is an adipokine which was initially thought to be secreted only from adipocytes, but it was later proven that adiponectin is also secreted from osteoblasts, liver parenchymal cells, myocytes, epithelial cells and placental tissue [3, 4]. Adiponectin is a major regulator of glucose metabolism with insulin-sensitizing properties, thus low levels of adiponectin are associated with diabetes [5].

Adiponectin circulates in the concentration range of 3-30 µg/ml in healthy individuals. The clearance of adiponectin is primarily mediated by the liver. It has a surprisingly rapid turnover. The half-life of adiponectin is reported to be between 75-150 minutes. The serum half-life is reduced in patients with Type 2 DM, it may even be shorter in patients with large fat cells and poor diabetes control [6, 7]. Adiponectin levels are positively associated with insulin sensitivity. The glucose-lowering effect of adiponectin is primarily mediated by suppressing gluconeogenesis or glycogenolysis, it may also be mediated by upregulation of PPARα [4].

Adiponectin is also known as an anti-inflammatory hormone [8]. It maintains metabolic homeostasis, higher levels of adiponectin is associated with lower type 2 DM risk [9, 10]. Adiponectin with its an insuling sensitizing, anti-atherogenic, anti-apoptotic and anti-inflammatory effects, administration of adiponectin may play a role in the future therapies of obesity, type 2 diabetes and atherosclerosis [4].
The effect of acute hyperglycemia on adiponectin levels is less studied [3, 11]. We evaluated the effect of the normalization of blood glucose levels on adiponectin in patients admitted to the ED with acute hyperglycemia.

2. Material and Methods

2.1. Patients

This study was approved by the ethical board of Hacettepe University (HEK 09/177-107). Forty-eight adult patients admitted to the ED with hyperglycemia (blood glucose ≥300 mg/dl) were included in the study. Written informed consent forms were obtained from all patients. Demographic features (age, sex), height, weight, and type of diabetes were recorded.

2.2. Methods

All patients were treated according to international recommendations for hyperglycemia, with appropriate amounts of intravenous fluid and intravenous crystalline insulin infusion. Euglycemia was reached within six-twelve hours. Serum samples were taken from the patients on admission and 6 hours (which is chosen as an optimum time for half-life of adiponectin) after normalization of blood glucose to measure adiponectin levels. Adiponectin levels were measured with Biovendor Human Adiponectin Elisa. Results are given as µg/ml.

2.3. Statistical analyses

Statistical analyses were carried out using the SPSS® software package, version 15.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Numerical variables are shown as mean (range) and categorical variables are shown as frequencies and percentages. The Mann-Whitney U test and Kruskal-Wallis test were used to determine differences in numerical variables between groups, and the χ² test was used to determine differences between categorical variables. A P value of ≤0.05 was considered to be statistically significant.
3. Results

The study was included on 48 patients (21 female and 27 male), with a median age of 58.7±18 years. Clinical and laboratory parameters are presented in Table 1.

Thirty-one patients had Type 2 DM, 10 had Type 1 DM, and 7 patients were diagnosed with diabetes at that particular admission.

Serum adiponectin levels decreased significantly after the normalization of blood glucose in the whole group. Adiponectin levels decreased from 28.9±16.5 to 12.1±10.9 µg/ml (p<0.0001) in the whole group. The decrease in adiponectin persisted when evaluated according to BMI and type of DM (Table 2, Table 3).

4. Discussion

The results of the present study demonstrated that adiponectin levels decreased after the normalization of blood glucose in patients with hyperglycemia. This was not dependent on diabetes type and/or body weight. Studies that evaluate the effects of acute hyperglycemia are rare. This is the first study which demonstrated a decrease in adiponectin levels after correction of hyperglycemia.

Aso et al. investigated the effect of acute hyperglycemia after oral glucose load in healthy subjects on total and high molecular weight (HMW) adiponectin. HMW adiponectin decreased significantly at 120 minutes after oral glucose load [12]. In another study after acute glucose load test HMW adiponectin decreased in patients with normal glucose tolerance test and with those who has impaired fasting glucose (fasting blood glucose levels over 100 mg/dL) but there was no change in patients with impaired glucose tolerance (Glucose levels between 140-200 mg/dL 2 hours after glucose challenge) and diabetes (Glucose levels over 200 mg/dL 2 hours after glucose challenge). Percentage change in adiponectin was negatively correlated with serum insulin but not glucose levels. This change is explained with an increase in insulin levels.
which was less prominent with patients with impaired glucose tolerance and diabetes [13].

Koniari et al. reported that glucose loading increased adiponectin levels in healthy and impaired glucose tolerant patients. This response was significantly lower in diabetic patients. They stated that acute hyperglycemia is a stress factor that upregulates adiponectin secretion. The absence of this upregulation in the diabetic group is explained by the presence of lower adiponectin levels in diabetics [14].

In a study by Siervo et al., after oral glucose tolerance tests, adiponectin levels decreased both in healthy patients and in those with metabolic syndrome [15]. Dullaart et al. evaluated the effects of insulin secretion on adiponectin levels in the state of hyperinsulinemic clamp in type 2 diabetic and healthy patients. Insulin lowered adiponectin levels in patients with type 2 DM, however it did not change the levels in normal patients [16]. Insulin receptor dysfunction is associated with increased circulating adiponectin. Insulin directly suppresses adiponectin secretion from marrow’s adipose tissue [17]. In another study, in which the separate and combined effects of hyperglycemia and hyperinsulinemia on different markers were evaluated, adiponectin increased in euinsulinemia-hyperglycemia clamp. Adiponectin decreased in the states of hyperinsulinemia-hyperglycemia, and hyperinsulinemia-euglycemia clamp. Hyperinsulinemia is thought to prevent the effect of hyperglycemia in increasing adiponectin [11].

In this study we demonstrated a decrease in adiponectin levels after correction of hyperglycemia with insulin treatment. This is the first clinical study which demonstrated the effect of correction of acute hyperglycemia on adiponectin levels. Adiponectin is known to inversely correlate with body weight and abdominal obesity [18]. The decrease in adiponectin levels were independent of BMI in our study.
Although visceral obesity which is a main contributor of type 2 diabetes has a major role in the secretion of adipokines, adiponectin levels were also reported to change and affect outcome in those with type 1 DM [19, 20]. The decrease in adiponectin was not affected by diabetes type in our study.

This change may be due to an inhibited upregulation of adiponectin secretion and/or blunted suppressive effect of insulin due to hyperglycemia or exogenous insulin administration may have caused the decrease in adiponectin levels.

The insulin-sensitizing action of adiponectin is primarily due to the decreased hepatic gluconeogenesis and increases glucose transport in the muscle. Adiponectin mediates anti-diabetic effects via direct metabolic actions and by improving insulin sensitivity, and as recently demonstrated an as playing an important role in stimulation of autophagy [21, 22].

Our sample size was limited with patients who have different background disease profile. These might have influenced the adiponectin levels. Scientist still need to do further studies to enlighten the puzzling cross talk between adiponectin and remaining metabolic factors.

5. Conclusion

Adiponectin decreased after the correction of hyperglycemia in an emergency setting. This decrease was independent of diabetes type and/or body weight. Acute hyperglycemia which upregulates adiponectin secretion and/or exogenous insulin administration may have caused the decrease in adiponectin levels. Adiponectin is a promising adipokine in treatment of many diseases, however perplexing factors in both

Declaration of Interest

There is no conflict of interest.


Table 1. The distribution of the patients according to the BMI, gender and previous DM

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Normal (&lt;24.9)</th>
<th>Overweight (25-29.9)</th>
<th>Obese (&gt;30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>16</td>
<td>20</td>
<td>12</td>
</tr>
<tr>
<td>Sex</td>
<td>3 F/13 M</td>
<td>9 F/11 M</td>
<td>9 F/3 M</td>
</tr>
<tr>
<td>Previous DM</td>
<td>11 (68.8%)</td>
<td>19 (95%)</td>
<td>11 (91.75%)</td>
</tr>
</tbody>
</table>

BMI – body mass index; DM – diabetes mellitus Data is presented as n % or mean ±SD.

Table 2. The change in adiponectin levels before and after treatment according to BMI

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Number (n)</th>
<th>Adiponectin µg/ml</th>
<th>Before Treatment</th>
<th>After Treatment</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (&lt;24.9)</td>
<td>16</td>
<td>26.4 ±17.5</td>
<td>13.3±13.0</td>
<td>0.006</td>
<td></td>
</tr>
<tr>
<td>Overweight (25-29.9)</td>
<td>20</td>
<td>34.6±14.2</td>
<td>13.3±11.9</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Obese (&gt;30)</td>
<td>12</td>
<td>24.4±17.1</td>
<td>8.9±5.5</td>
<td>0.005</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. The change in adiponectin levels before and after treatment according to Diabetes Type

<table>
<thead>
<tr>
<th>Diabetes Type</th>
<th>Adiponectin µg/ml</th>
<th>Before Treatment</th>
<th>After Treatment</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>28.8 ±17.3</td>
<td>10.5±8.2</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>Type 2</td>
<td>26.3±18.4</td>
<td>8.7±7</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>