Serum Selenium Status in Patients with Type 2 Diabetes and Control Group

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Received: July 28, 2016   Accepted: September 18, 2016   Online Published: October 18, 2016
doi:10.5539/gjhs.v9n5p234          URL: http://dx.doi.org/10.5539/gjhs.v9n5p234

Abstract

In addition to known risk factors, the role of different micronutrients such as selenium in diabetes incidence has been proposed. Some previous studies have shown an association of selenium deficiency and type 2 diabetes mellitus, while other studies have not confirmed such a relationship. The aim of this study was to evaluate serum level of selenium in patients with Type 2 diabetes compared with the control group. This cross-sectional study was carried out on patients with type 2 diabetes in Zahedan, southeastern Iran. One hundred newly diagnosed type 2 diabetic patients were evaluated for serum selenium level. One hundred subjects from the general population who had normal fasting blood sugar levels were selected as the control group. The control group subjects were matched in pairs with each of patients on the basis of sex, age (± one year), and body mass index (±1). Serum level of selenium was determined by spectrometry method. Results were compared using t-test. The mean serum level of selenium in patients was 94.47±18.07 µg/L whereas in control group was 142.79±23.67 µg/L. The mean serum level of selenium was significantly different between the two groups (P<0.001). Serum levels of selenium in diabetic patients with significant difference statistically were lower than the control group. In order to evaluate serum level of selenium in patients with diabetes, studies with larger sample size are required. Likewise, prospective studies along with selenium supplementation and investigating its effect on incidence of diabetes are accordingly needed.

Keywords: selenium, Type 2 diabetes mellitus

1. Introduction

Type 2 diabetes mellitus accounts for about 90% of all diagnosed cases of diabetes and is characterized by hyperglycemia, insulin resistance and relative decline in insulin secretion. Type 2 diabetes is a debilitating and progressive disease whose prevalence has increased in recent decades (Engelgau et al., 2004). According to previous studies, Iran is facing an increasing prevalence of diabetes; therefore, the prevalence of disease in Iran population reaches to 7% (Esteghamati et al., 2008). Type 2 diabetes is characterized by varying degrees of insulin resistance in peripheral tissue such as muscle, liver and adipose tissue as well as relative decrease in insulin secretion by beta cells that genetic and environmental factors are involved in each of these factors (Stumvoll, Goldstein, & van Haeften, 2005; Li et al., 2004). The most important risk factors for type 2 diabetes are high energy intake, aging, sedentary lifestyle and obesity. In addition to these known risk factors, the role of different micronutrients such as selenium in incidence of diabetes has also been proposed.

Selenium is an essential mineral and micronutrient, with antioxidant properties which is able to change immune and inflammatory response. Selenium is an essential component of glutathione peroxidase enzyme that plays a role in the detoxification of free oxygen radicals and other toxic oxygen derivatives. Functional defect in glutathione peroxidase can cause damage to cell membranes (Steinbrenner, Speckmann, & Klotz, 2016; Oztürk et al., 2015; Sedighi, Makhlough, Shokrzadeh, & Hooshad, 2014; Rayman, 2000). Selenium induces a decrease in serum levels of glucose in the rats treated with this element. In addition, serum levels of metabolites that cause liver damage and disturbance in lipid metabolism are markedly reduced in these rats (Zou, Qiu, Chen, Dou, & Liang, 2016; Hwang et al., 2007). Diabetes is usually associated with increased free radical production (Sailaja, Baskar, & Saralakumari, 2003; Baynes & Thorpe, 1999) or decreased antioxidant defenses (Maritim, Sanders, & Watkins, 2003). Increased free radicals cause damage to cellular proteins, membranes lipids and nucleic acid and ultimately
cell death. In diabetes, hyperglycemia not only increases the production of free radicals but also decreases the antioxidant defense mechanisms (Saxena, Srivastava, & Baquer, 1993).

Selenium acts like insulin on glucose homeostasis in previous studies (Gouaref, Bellahsene, Zekri, Alamir, & Koceir, 2016; Al-Quraishy, Dkhil, & Abdel Moneim, 2015; Chen, Qiu, Zou, Dou, & Liang, 2015; Becker et al., 1996). Diabetes associated oxidative stress is responsible for secondary complications of diabetes (González de Vega, Fernández-Sánchez, Fernández, Álvarez Menéndez, & Sanz-Medel, 2016; Kahya, Naziroğlu, & Övey, 2016). However, other studies have shown that there is a positive correlation between serum level of selenium and diabetes incidence (Laclaustra, Navas-Acien, Stranges, M. Ordovas, & Guallar, 2009; Stranges et al., 2007; Steinbrenner, Speckmann, Pinto, & Sies, 2011; Lu et al., 2016; Thompson et al., 2016; Farrokhian et al., 2016; Rotter et al., 2015; Bleys, Navas-Acien, & Guallar, 2007; Mueller, Mueller, Wolf, & Pallauf, 2009).

The existing literature data regarding the role of serum selenium levels in type 2 diabetes and its complications are controversial, thus we conducted this study in order to investigate whether selenium levels differ in Type 2 diabetic patients and control group.

2. Materials and Methods

The present study was conducted using case-control method on patients with type 2 diabetes referring to Imam Ali Hospital in Zahedan, between October 2015 and February 2016. Patients with type 2 diabetes who were at least 30 years old were continuously enrolled in the study. Patients data such as age, gender, type of diabetes, duration of diabetes, incidence of other diseases, drug history and body mass index were recorded. Diabetes is defined as fasting plasma glucose ≥ 126 mg per deciliter (two times), oral glucose tolerance test ≥ 200 mg per deciliter, glycated hemoglobin ≥ 6.5 and random blood sugar > 200 mg per deciliter in the presence of symptoms. Pregnant patients as well as patients with liver disease, kidney disease, hyper or hypothyroidism, acute coronary syndrome, stroke, cancer or patients who take vitamin supplements were excluded. Finally, 100 patients with type 2 diabetes were enrolled in the study. For each patient in case group one person who was matched in terms of age (± one year), sex and body mass index (± 1) was selected among healthy volunteers of blood donors referred to Zahedan Blood Transfusion Organization as a control group. In the control group, fasting plasma glucose was measured to rule out diabetes, if their fasting blood sugar was less than 100 they were enrolled as controls. Body weight without shoes using a digital scale and height in standing position was measured using a stadiometer. Body mass index was determined using this formula: weight in kilograms was divided by the square of height in meters. All blood samples were collected between 8 and 9 am and after 8 hours fasting and stored frozen at -70 until examination. Selenium using spectrometry method was measured [Graphite furnace atomic absorption spectrometry Varian, Australia (Spectr AA 240fs, 2009)]. Reference range for selenium was 70-150 µg/L. Glucose was measured with glucose oxidase technique (Pars Iran test). Quantitative variables were expressed as mean (and standard deviation) and qualitative variables were expressed as a percentage, t-test and Mann-Whitney U-test were used to compare quantitative variables and Chi-Square was used to compare qualitative variables. Multivariate logistic regression analysis was done with diabetes as the dependent variable and age, body mass index, serum level of selenium as independent variables. All the analysis were performed by software STATA version 12 (Stata Corporation, College Station, TX). Informed written consent was obtained from all subjects. The Research was approved on Ethics Committee of Medical Sciences (ethical code number IR.ZAUMS.REC.1392.56).

3. Results

In this study, 200 patients (100 with diabetes and 100 healthy subjects) who met the inclusion and exclusion criteria were registered. Gender distribution between two groups was equal, as 50 males and 50 females in each case and control group. The subjects in case group were diabetics and participants in control group were healthy subjects. The average age of the participants in the study was 44.32±10.10 years. The average age of study groups was 44.54±10.50 years in the case group and 44.40±10.43 years in the control group. Using Independent sample t-test there was no statistically significant difference between the two groups in terms of age (P=0.8). The mean BMI (body mass index) in case group was 27.05±4.22 kg/ m² and controls 27.11±4.15 kg/ m². Using Independent sample t-test there was no statistically significant difference between BMI of both groups (P= 0.9).
Table 1. Characteristics of subjects in each group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency</th>
<th></th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case</td>
<td>Control</td>
<td>Case</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>female</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Age (years)</td>
<td>&lt;40</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>40-60</td>
<td>61</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>&gt;60</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>&lt;18.5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>18.5-24.9</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>25-29.9</td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>≥30</td>
<td>28</td>
<td>28</td>
</tr>
</tbody>
</table>

As shown in Table 2, the mean serum level of selenium in case group was 94.47±18.07 mcg per liter (µg/L) and in the control group was 142.79±23.67 µg/L. Mean serum level of selenium in both case and control groups showed significant difference (P<0.001).

Table 2. Comparison of selenium serum level in participants in the study based on group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Means±SD</th>
<th>Range</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum selenium</td>
<td>Case</td>
<td>94.47±18.07</td>
<td>56.10-156.40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>levels (mcg per</td>
<td>control</td>
<td>142.79±23.67</td>
<td>79.82-162.40</td>
<td></td>
</tr>
<tr>
<td>dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SD: standard deviation.

Selenium deficiency has been effective in diabetes (P=0.006). Also, people who had higher serum selenium levels, their chance to be non-diabetic was 19.33 times higher (Table 3).

Table 3. Effective factors in diabetes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with diabetes (frequency)</th>
<th>Healthy subject (Frequency)</th>
<th>Total (frequency)</th>
<th>OR</th>
<th>CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
<td>50</td>
<td>50</td>
<td>100</td>
<td>1</td>
<td>0.57-1.74</td>
</tr>
<tr>
<td></td>
<td>female</td>
<td>50</td>
<td>50</td>
<td>100</td>
<td>1</td>
<td>0.57-1.74</td>
</tr>
<tr>
<td>Age (year)</td>
<td>&lt;40</td>
<td>25</td>
<td>24</td>
<td>49</td>
<td>1.05</td>
<td>0.55-2.01</td>
</tr>
<tr>
<td></td>
<td>≥40</td>
<td>75</td>
<td>76</td>
<td>151</td>
<td>1</td>
<td>0.52-1.91</td>
</tr>
<tr>
<td>BMI</td>
<td>&lt;25</td>
<td>24</td>
<td>24</td>
<td>48</td>
<td>1</td>
<td>0.52-1.91</td>
</tr>
<tr>
<td></td>
<td>≥25</td>
<td>76</td>
<td>76</td>
<td>152</td>
<td>1</td>
<td>0.52-1.91</td>
</tr>
<tr>
<td>Selenium Deficiency</td>
<td>Yes</td>
<td>47</td>
<td>22</td>
<td>69</td>
<td>19.33</td>
<td>2.31-161.56</td>
</tr>
<tr>
<td></td>
<td>&lt;60 µg/dl</td>
<td>53</td>
<td>78</td>
<td>131</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>22</td>
<td>78</td>
<td>131</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OR: oddsratio, CI: confidence interval.
4. Discussion
In this descriptive cross sectional study, a total of 200 patients (100 patients with type 2 diabetes and 100 healthy individuals), after applying inclusion and exclusion criteria were enrolled. Mean serum level of selenium in the case and control groups was significantly different.

These results are in accordance with some previous studies (Rajpathak, Rimm, Morris, & Hu, 2005; Kilinc, Guven, Ezer, Ertas, & Coskun, 2008; Yadav et al., 2016; Ubajaka et al., 2015). In a study (Kruse-Jarres & Rukgauer, 2000), serum levels of selenium in both diabetics and non-diabetics control group was measured in three components of plasma, erythrocytes and complete blood that in all three components, selenium concentration was lower in the diabetic group and this decrease is more clearly shown in erythrocytes. Additionally, in another study, serum level of selenium in patients with diabetes mellitus was determined compared with the control group. In the diabetic group that included 150 diabetic patients aged 11 to 60 years, the average concentration of plasma selenium significantly lower than the control group (Ruiz, Alegria, Barbera, Farre, & Lagarda, 1998). Similar to our study, in a study conducted in 2012 in diabetic patients aged 40 to 60 years, serum level of selenium in the diabetic group showed a significant decrease in comparison to the control group (Kumar, 2012).

But, in other studies the increasing serum level of selenium was associated with an increased incidence of diabetes (Wang, Yang, Wei, Lei, & Zeng, 2016; Ogawa-Wong, Berry, & Seale, 2016; Bleys, Navas-Acien, & Guallar, 2007). Concentration and activity of glutathione peroxidase and other selenoproteins increases with increasing selenium intake until dose-response relationship reached an equilibrium state. The maximum rate of this condition in serum levels is 70-90 µg/L. In plasma levels higher than this amount, the selenomethionine entry into albumin and other proteins increases and concentration or activity of glutathione peroxidase does not change (Burk, 2002). Animal studies show that diets containing abundant selenium may stimulate the secretion of glucagon leading to hyperglycemia (Satyanarayana et al., 2006). Selenium enters into the structure of selenoproteins such as selenocysteine. Selenoproteins are responsible for the biological function of selenium and specific selenoproteins such as glutathione peroxidase, selenoprotein P and thioredoxin reductase are important antioxidant enzymes (Rayman, 2000).

In addition to the effect of antioxidant, selenium has anti-diabetic and insulin-like effects (Wang et al., 2016; Gurbanov, Bilgin, & Severcan, 2016; Mueller & Pallauf, 2006). In a study conducted in 2013 serum selenium level was measured in patients with diabetes in different countries. According to this study, in France, China and Italy high concentrations of selenium was associated with an increased incidence of diabetes, but in America increased selenium was associated with reducing the diabetes. In Singapore, no relationship between serum selenium and diabetes was reported (Rayman, 2013). Such different results in different countries may be due to various reasons, including ethnic differences and various confounding factors that need further studies. Also, Diet is the most important source of selenium in most countries (Wei et al., 2015). Soil selenium content is different in various geographical regions which can lead to different serum selenium levels among the various countries. For example, in volcanic regions, low soil selenium causes selenium deficiency in these populations (Thomson, 2004).

The lack of measurement of selenium content in the diet and urine was one of the limitations of this study. Another limitation of this study is its cross-sectional nature, which naturally cannot show the causal relationship. But the sample size is relatively acceptable and matching case and control groups based on gender, age and body mass index as pairs is of the strength of this study. Prospective studies with larger sample size and selenium supplementation and evaluation of its effect on the incidence of diabetes, can be effective to to further clarify the role of this element in the incidence and pathogenesis of diabetes.

5. Conclusion
Serum levels of selenium in diabetic patients with statistically significant difference statistically were lower than the control group. Studies with larger sample size to evaluate serum level of selenium in patients with diabetes are therefore, required. Prospective studies along with selenium supplementation and investigating its effect on incidence of diabetes are also needed.

Acknowledgements
The authors would like to thank the patients who participated in the study. This study was supported by Zahedan University of Medical Sciences.

Competing Interests Statement
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.
References


Turkish women with gestational diabetes mellitus, glucose intolerants, and normal controls. Biological Trace Element Research, 123(1-3), 35-40. http://dx.doi.org/10.1007/s12011-007-8087-2


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