Contents lists available at Science-Gate

International Journal of Advanced and Applied Sciences

Journal homepage: http://www.science-gate.com/IJAAS.html

Serum levels of selenium and copper in an Iranian elderly women diagnosed type-1 diabetes mellitus and correlations with diabetic complications

Elham Bamdadi Kalurazi [1], Mahshid Mohammadian [2], Sadegh Rostaminasab [3], Attabak Toofani Milani [2, *], Sonia Darvishi [6], Shima zeinaly [2], SiamakRashidi [4, 5], Farhad FathiYounesi [5], Farid Javandust [2]

[1]*Department of Biochemistry, Faculty of Basic Sciences, Payamenoor University, Mashhad, Iran*
[2]*Department of Biochemistry, Urmia University of Medical Sciences, Urmia, Iran*
[3]*Department of Biochemistry, Faculty of medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
[4]*Diabetes Clinic, Kurdistan University of Medical Sciences, Sanandaj, Iran*
[5]*Aria Medical Laboratory, Sanandaj, Kurdistan, Iran*
[6]*North Tehran Branch, Islamic Azad University, Tehran, Iran*

ARTICLE INFO

Article history:
Received 10 April 2016
Received in revised form
23 June 2016
Accepted 23 June 2016

Keywords:
Type1 diabetes mellitus
Selenium
Copper

ABSTRACT

Type 1 diabetes mellitus (T1DM) is an autoimmune disease which correlated with various Miscellaneous factors. Environmental and genetic factors and oxidative stress-induced free radicals may have a role in the pathogenesis of this complex disorder. Trace element such as selenium and copper are involved in an antioxidant defense that may play a role in T1DM complications, so in this study we evaluate the two major trace elements (selenium, copper) status in T1DM patients and their probable relationships with diabetic complications. In a case-control study concluded 68 female patients with T1DM in compared with 122 healthy female individuals, Fasting plasma samples were analyzed for fasting blood sugar (FBS), fructose amine, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglyceride (TGs), serum copper and selenium concentrations were measured by flame atomic absorption spectrophotometry. Statistical analysis was performed with SPPS software. Based on our data, in patient group, mean copper and selenium concentration were lower in compared to healthy controls ($p>0.05$) dyslipidemia was found in a significantly higher percentage of women with T1DM compared to that of the non-diabetic control group. Overall in patients group the majority of the dyslipidemia subjects had suboptimal glycemic status and lower level of selenium. Lipid disorders in women with T1DM may be present regardless of their metabolic control that found that poorer glycemic control is related to higher serum lipids levels and lower plasma selenium status. Indeed Dyslipidemia and poorer glycemic status was significantly more frequent among females with selenium deficiency.

1. Introduction

Type one Diabetes mellitus (T1DM) is a chronic heterogeneous group of disorder which affects body metabolism. There is a strong relation between some essential metal elements and T1DM (Ozenc et al., 2015; Mohammadian et al., 2015). Selenium and copper is an important trace element for human health. In pathogenesis of T1DM, Oxidative stress play important role so that reduces insulin secretion and increases diabetes related insulin resistance (Wei et al., 2015; Siva et al., 2013). Selenium, an essential trace element with antioxidant properties, is a component of complex defense system against oxidative stress (selenium-dependent glutathione peroxidases and selenoproteins) (Rayman et al., 2012). Antioxidants are thought to offer some protection against chronic diseases (Steinbrenner et al., 2009) including T1DM, and selenium has become a popular supplement in recent years (Laclaustra et al., 2009). For this reason, it seems selenium acts as preventer agent of diabetes developmental process so, selenite (other kind of selenium), has insulin like activity in experimental models (Navarro-Alarcon et al., 1999). Copper (Cu) is an important part of many essential enzymes involved in a number of vital biological reactions. Copper, participate in oxidation-reduction reactions in energy metabolism. A deficiency in dietary Copper also increases cellular susceptibility to oxidative damage. Indeed Abnormal metabolism of Copper may have role in pathogenesis

* Corresponding Author.
Email Address: Toofani2020@yahoo.com (A. Milani)

of chronic inflammatory disorders including T1DM (Siva et al., 2013). Optimal levels of essential trace elements is urgent for human health conditions and prevent several chronic disorders(Chan et al., 1998). It seems that copper and selenium have main role as important components of antioxidant defense that may be involved in T1DM complications. Different surveys of selenium and copper levels in diabetic patients specially T1DM have led to contradictory findings as the possible relationship between the degree of diabetic control and the changes in mineral contents (Navarro-Alarcon et al., 1999; Ozenc et al., 2015; Laclaustra et al., 2009), so In this presented study we investigated two major trace elements status in T1DM patients and their probable relationships with diabetic complications.

2. Methods and materials

In a case-control study concluded 68 female patients with T1DM in compared with 122 healthy female individuals, were selected from aria medical laboratory, diabetic clinic, Sanandaj, Kurdistan, Iran. The mean age of patients (52.2 ± 2) and healthy controls (49.4 ± 3.2) were matched and didn't have significant differences. For each subjects clinical examination and T1DM criteria diagnosis pattern were performed. Fasting venous blood samples (10 mL) was collected for laboratory examinations. 5ml was poured in to the EDTA containing tube for plasma based examinations. To obtain serum, 5 milliliters was poured in to the non-contained anticoagulant tube. Serum isolation with centrifugation method was done, then serum specimens were stored at −20 °C until use (Mohammadian et al., 2015). Fasting plasma samples were analyzed for fasting blood sugar (FBS) and fructose amine, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), fasting blood sugar (FBS) by using glucose oxidase method, high-density lipoprotein cholesterol (HDL-C), triglyceride (TGs), total cholesterol by cholesterol oxidase–peroxidase method, serum triglycerides (TG) by glycerol kinase-peroxidase method, high density lipoprotein-cholesterol (HDL-C) by enzymatic method and low density lipoprotein-cholesterol with this Friedewald formula calculated: LDL=T.C – (HDL+VLDL); were analyzed. All mentioned kits were obtained from Pars Azmoon Company, Tehran, Iran (based on photometric method). Fructose amine was assessed by Nitro-blue Tetrazulyn. For mineral assay, serum sample were used for copper and selenium assay. For copper concentration measurement, flame atomic absorption spectrophotometry method were used (SOLAAR, Atomic Absorption Spectrophotometer, Thermo Electron, UK). Selenium concentrations were measured using an atomic absorption spectrophotometer GF95 furnace. Analysis is performed in a controlled environment to minimize contamination. Statistical analysis were performed with SPPS software (version 21), and statistical testing contains paired *t* test, two-sample *t* tests, analysis of variance, Pearson Chi-square testing (correlation coefficients), were used. Results data were presented as means and standard deviations (mean± SD). Statistical significance was considered as $p<0.05$.

3. Results

Patient and control groups demographic and biochemical characteristics presented in Table 1.

Table 1: Patients and control groups Demographic and biochemical characteristics

P value	*Controls N=122	*Patients N=68	Parameters
P> 0.05	26 ± 2.4	27.9 ± 3.4	BMI (Kg/m^2)
P> 0.05	69 ± 9.1	73 ± 6.2	Weight (Kg)
P > 0.05	161 ± 7.2	156 ± 8.7	Height (m)
P > 0.05	49.4 ± 3.2	52.2 ± 2	Age (year)

Standard deviation ±meanData presented as**
*Significant level : p <0.05

The mean value of serum selenium, copper, glycemic control parameters (FBS and fructoseamine) and lipid profiles (TC, TG, HDL-C, LDL-C) in two groups including patient and control are shown in Table 2.

Table 2: Biochemical parameters comparison between the two groups of patient and control

P value	*controls N=122	Patients * N=68	Parameters
*P < 0.05	153.01±21.8	122.90±25.1	Selenium (ug/l)
*P < 0.05	1.24±0.23	1.01±0.20	copper (mg/l)
*P < 0.05	78.9±9.1	160.2±4.6	FBS (mg/dl)
*P < 0.05	133.5 ± 40.1	182.1 ±33.2	TG(mg/dl)
*P < 0.05	87.1 ± 21	120.9 ±29.9	LDL-c(mg/dl)
*P > 0.05	52.1 ± 17.2	43 ±20.6	HDL-C(mg/dl)
*P < 0.05	136.2 ± 32.1	182.1 ± 29.8	TC(mg/dl)
*P < 0.05	320±6.1	529.3±28.7	Fructose amine µmol

TC, total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol. FBS: Fasting blood sugar.
Standard deviation ±meanData presented as**
*Significant level : p <0.05

Based on results no difference in age was found between both groups. Mean body mass index (BMI), height, weight haven't significantly differences among groups. Between patients, 27.9% were underweight, 19.4% overweight, and 52.7% had normal weight.in patient group Many alterations in lipid profile were observed. The percentage of diabetic subjects with high total cholesterol levels was 37.2%. About 30.7 % of diabetic subjects were found to have high LDL-C levels. In T1DM patients, statistically significant differences were found in plasma copper and selenium contents between the control subjects and the diabetic patients with medium or poor metabolic control. There are significant difference between diabetic persons and healthy subjects was seen in hypertriglyceridemia (41.3%) low levels of HDL-C was similar between both groups. Mean fasting plasma glucose in diabetic subjects was higher than that of control. In control group Mean fasting plasma copper and selenium levels were found to be higher than that of patients group. In Pearson correlation analysis, plasma copper concentration negatively correlated with age ($p<0.05$). A negative correlation was observed between selenium level with LDL-c, TC, TG and FBS and age ($p<0.05$). In our study selenium seems to correlate with all the components of the T1DM complications.

4. Discussion

Copper, selenium, are engaged in many biochemical reactions supporting healthy life such as cellular respiration, cellular utilization of oxygen, DNA and RNA reproduction, maintenance of cell membrane integrity, and destruction of free radicals. On the other hand, impaired intake of these trace elements leads to disease, so, it seems that natural trace elements balance is important for human body health. Trace element deficient patients usually faced with different complications and may be these deficiency have a role in some metabolic disorder susceptibility or may be these deficiency correlated with metabolic disorders etiology (Wei et al., 2015; Siva et al., 2013; Ozenc et al., 2013). Evaluation of selenium and copper levels in T1DM patients have led to inconsistent findings as the possible relationship between the diabetic control status and the changes in trace elements contents (Ruiz et al., 1998; Ozenc et al., 2013). Furthermore, it is important to differentiate whether trace element deficiency affect the primary cause of the disorder including diabetes, or is secondary to investigate. Probable trace element impaired status due to T1DM. A combination of analyses for multiple trace elements status is important to pinpoint the trace element(s) involved. In this study patients with type 1 diabetes in compared to control group (healthy volunteer) were studied. In T1DM patients, statistically significant differences were found in plasma copper and selenium contents between the control subjects and the diabetic patients with medium or poor metabolic control. In this study, dyslipidemia was found in a significantly higher percentage of women with T1DM compared to that of the non-diabetic control group. Hypertriglyceridemia and hyper cholesterolemia were found to be the most common types of dyslipidemia in T1DM group. Mean duration of T1DM showed no significant difference between the dyslipidemia status among patient group ($p>0.05$). We found that Plasma selenium concentration correlate negatively with lipid concentrations (LDL-c TC, TG), glycemic status (FBS) and age. In the present study, mean copper concentration negatively correlated with age; in this study, the majority of the dyslipidemia group had suboptimal glycemic status and lower level of selenium. Lipid disorders in women with T1DM may be present regardless of their metabolic control that found that poorer glycemic control is related to higher serum lipids levels and lower plasma selenium status. It seems that successful treatment of the primary disorder will lead to complete recovery. Therefore mineral supplements administration for diabetic patient may be having effect on diabetic complications. In the present work trace element deficiency (copper, selenium) and Dyslipidemia in women with type 1 diabetes mellitus (T1DM) was significantly more frequent than healthy women. Dyslipidemia and poorer glycemic status was significantly more frequent among females with selenium deficiency. The most frequent type of dyslipidemia was high TC and TG.

Changes in level of copper may contribute to progression of diabetes mellitus (DM) and development of the complications.

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