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Original Research Article

Evaluation of selected trace elements in the Moroccan type 2 diabetic patients

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ABSTRACT

Background: Several trace elements have been implicated in the etiology of type 2 diabetes, they can influence the onset or pathogenesis of diabetes in various ways including disruption of normal metabolism of glucose and insulin. The purpose of this work is to evaluate the serum status of copper, zinc, selenium, chromium and manganese in Moroccan type 2 diabetics compared to control group.
Methods: Blood samples from 100 type 2 diabetics and 90 control subjects were analyzed for blood glucose, glycated hemoglobin (only for diabetics), lipid status and serum trace elements concentrations.
Results: Glucose and triglyceride values were statistically higher in diabetics; while those of HDL-cholesterol were lower. Concentrations of zinc, selenium, chromium, and manganese were lower in diabetics compared to controls. In contrast, copper concentrations were higher.
Conclusions: The status of trace elements is impaired in type 2 diabetics compared to a control group.

Keywords: Chromium, Copper, Manganese, Selenium, Type 2 diabetes, Zinc

INTRODUCTION

In recent decades, diabetes has become one of the major health problems worldwide. Globally, it is estimated that 422 million adults were living with diabetes in 2014, compared to 108 million in 1980. Diabetes, and especially type 2 diabetes, is related to the change in lifestyle between yesterday and today.[1]

Type 2 Diabetes (T2D) is a multifactorial disease defined by fasting blood glucose ≥1.26 g/l or random blood glucose >2 g/l due to dysfunction of insulin function and/or secretion.[1] For a diabetic, several biological parameters can be altered such as lipid profile, renal function, vitamin or metal profile. Indeed, several trace elements have been implicated in the etiology of T2D, they can, according to several studies influence the onset or pathogenesis of diabetes in various ways including the disruption of normal metabolism of glucose and insulin. Many studies have reported that the status of several trace elements such as zinc, copper, chromium, selenium and manganese is altered in diabetes mellitus and these imbalances can play important roles in the pathogenesis and progress of diabetes.[2,3] On the other hand; the homeostasis of these trace elements is frequently disturbed by diabetes mellitus because of impaired digestive absorption and the increased urinary excretion.[4] Several studies have been published about the relationship between the status of trace elements and diabetes mellitus. In general, these results are not

consistent, this may be because of the difference in ethnics, geography, eating habits and size of sample population. However, there are few reports on the role of trace elements in the pathophysiology of diabetes in Moroccan patients. In 2017, an article was published on the assessment of oxidative stress in the Moroccan T2D; this work showed the imbalance of selected trace elements in diabetics.[5] Thus, the purpose of the present study is to evaluate the serum concentrations of copper (Cu), zinc (Zn), selenium (Se), chromium (Cr) and manganese (Mn) in Moroccan T2D.

METHODS

This is a cross-sectional study, carried out between March and July 2019, conducted according to the principles of the Declaration of Helsinki and approved by the Ethical Committee from the Faculty of Medicine and Pharmacy in Rabat, Morocco.

This study was conducted in 100 patients with T2D who were admitted to the Department of Internal Medicine B; Mohammed V Military Teaching Hospital of Rabat, Morocco. Ninety clinically and biologically healthy volunteers were also recruited as a control group. The subjects were randomly selected, and all accepted the conditions of the study by reading and signing informed consent. All subjects participating in the study were of Moroccan origin.

Inclusion criteria

- Patients with T2D for at least 3 years, diagnosed on the basis of fasting blood glucose greater than or equal to 1.26 g/l and Glycated Hemoglobin (HbA1C) greater than or equal to 6.5%.
- Patients who accepted to participate in the study.

Exclusion criteria

- Type 1 diabetes and gestational diabetes,
- Smoking patients,
- Pregnant or lactating women,
- People receiving dietary supplements
- Patients who refused to participate in the study.

Intervention/ assessment

Blood samples, on tubes with and without anticoagulants, were taken after 12 hours of fasting for both groups. The studied parameters in the two groups were glucose, lipid balance and trace elements; whereas HbA1C has been determined only in diabetics. Glucose, total cholesterol (CT), High Density Lipoprotein (HDL) and triglycerides were determined by conventional automated methods (Cobas Integra 400 plus, Roche Diagnostics, Germany) while low density lipoproteins (LDL) were calculated using the Fried Ewald formula. HbA1C was determined by the liquid chromatographic system (D-10; BIO-RAD), according to the manufacturer's recommendations. Serum concentrations of Cr, Cu, Mn, Se and Zn were determined by atomic absorption spectroscopy (AA-7000; Shimadzu). Cu and Zn were determined by flame mode using an air-acetylene flame and external standards calibration. Cr and Mn levels were measured by graphite furnace atomic absorption after standard addition calibration while serum Se levels were measured by hydride generation- AAS (HVG-1, Shimadzu). ASC-7000 was used as an autosampler. All measurements were performed in duplicate and serum quality controls purchased from Recipe (Munich, Germany) were used during the analysis.

Statistical analysis

Depending on their normal or skewed distribution, data were expressed as Mean±Standard deviation or median and interquartile or full range. The normality of the variables was verified by the distribution parameters and the Kolmogorov Smirnov test. Comparison between variables was performed using the t-test, Wilcoxon's test, or chi-square test. Pearson or Spearman rank correlation analysis was used to evaluate the correlations between variables. All analyses were performed using SPSS 13.0 for Windows (SPSS, Inc., Chicago, IL, USA). Value of $p < 0.05$ was considered statistically significant.

RESULTS

The diabetic and control groups were similar regarding sex, age, and BMI ($p>0.05$). Overall the cases and the controls were in the age of 35-66 years. There were 55 females and 45 males in T2D group and 43 females and 47 males in normal. There was no significant difference found in BMI between the two groups. The median of the diabetes duration was 7 years with extremes between 3 and 12 years. The main characteristics of the studied population are summarized in (Table 1).

Table 1: Characteristics of studied population (diabetic and healthy controls groups).

Variables	Diabetics	Controls	p value
Number sex M/F	100 45/55	90 43/47	- 0.58
Age(years) M±SD	52.7±21.4	51.9±19.8	0.48
BMI(Kg/m^2) M±SD disease duration (years)	24.6±1.6 7 (3-12)	24.1±3.9 -	0.31 -

M /F: male/female; m±SD: mean±standard deviation; BMI: body mass index.

Table 2 shows that fasting values of glucose were significantly higher in T2D compared to normal subjects with an average of 7.9±3.5 % for HbA1C in diabetic group. Triglyceride values were statistically higher in diabetics; while those of HDL-cholesterol were lower compared to the control group ($p<0.001$).

In (Table 2), it was observed that there is a significant decrease (≤0.001) of serum Zn in diabetics in contrast to non-diabetic, also shows a decline of serum Se in diabetics as compared to non-diabetic. Similar results were observed for Cr and Mn whose serum concentrations were lower in the diabetic group. In contrast, a significant increase in serum Cu concentration was observed in the diabetic group compared to controls (p<0.001). No significant difference in concentrations of trace elements was observed between men and women.

Table 2: Results of the studied parameters.

Variables	Diabetics	Controls	p value
Glycemia (g/L)	1.78±0.41	0.92±0.11	<0.001*
HbA1C (%)	7.9±3.5	-	-
Total cholesterol (g/L)	1.93±0.25	1.78±0.26	0.054
Triglycerides (g/L)	1.36±0.11	0.70±0.15	<0.001*
LDL (g/L)	1.38±0.26	1.26±0.22	0.06
HDL (g/L)	0.35±0.20	0.56±0.12	<0.001*
Cr (µg/L)	0.13±0.04	0.35±0.08	<0.001*
Cu (mg/L)	1.68±0.38	1.26±0.21	<0.001*
Mn (µg/L)	1.15±0.13	2.35±0.24	<0.001*
Se (µg/L)	66.5±20.3	95.1±18.8	<0.001*
Zn (mg/L)	0.58±0.17	1.18±0.21	<0.001*

HbA1c: glycated hemoglobin, LDL: low density lipoprotein, HDL: high density lipoprotein
*: Statistically significant.

Correlation studies between trace elements (Cu, Zn, Se, Cr and Mn) and other parameters (BMI, Glucose, CT, HDL, LDL, triglycerides, duration of diabetes and HbA1C) have shown that serum chromium concentrations were negatively correlated with the percentages of HbA1C (r= -0.74, p=0.03, n=100). The other correlation studies were not significant.

DISCUSSION

The presence of a trace element imbalance in diabetic patients has been reported by several studies. Some of these trace elements play a key role in the development and evolution of diabetes. In the present study evaluation of the serum status of Cu, Zn, Se, Cr and Mn in Moroccan T2D. Serum Cu concentrations were higher in diabetic group compared to controls. This result has been reported by other series.[5,6] The increase of serum Cu concentration in diabetics may be explained by the decrease in Cu affinity to ceruloplasmin because of its glycosylation.[7] However; Cu also has insulin-like activity and this deficiency of Cu may be associated with carbohydrate intolerance and insulin resistance.[8,9]

Compared to controls, the concentrations of Zn were significantly lower in diabetics. This agrees with the works done by other researchers.[8] Zn is involved in glucose metabolism; it plays a key role in the storage and the release of insulin and in the regulation of its receptor synthesis.[10] Low concentration of Zn in diabetic patients are explained by several authors by the fact that Zn homoeostasis is mostly affected by hyperglycaemia which results in hyperzincuria or decreased gastrointestinal absorption of Zn or even both.[11]

The significant lower Se level observed in this study also agreed with previous studies.[12,13] The relationship between Se and diabetes is very complex and not yet very clear. Low Se level has been shown to reduce insulin secretion and increase insulin resistance, thereby possibly playing a role in the development and pathogenesis of T2D. Also, Se acts as an antioxidant and peroxynitrite scavenger when incorporated into selenoprotein and can therefore play a key role in oxidative stress in diabetics. This oxidative stress which is known to be associated with the pathogenesis of diabetes mellitus.[14]

Results showed that serum chromium levels are lower in diabetics. Similar results have been found by other studies. Ekmekcioglu et al, reported lower plasma concentrations of Cr in diabetics.[15] Another study showed that plasma levels of Cr were significantly reduced in patients with T2D compared to control subjects of both sexes, but urinary levels of this element were higher in diabetic patients.[2] The low serum Cr concentration could be attributed to hyperglycemia and osmotic diuresis resulting from glycosuria, which increases the excretion of Cr in urine.[15] In addition, a negative correlation was found between Cr serum concentrations and HbA1C. These have also been reported by some studies.[16] Indeed; Chromium deficiency increases glucose concentration because its entry into the cell is impaired.[16] Some authors have even suggested Cr supplementation in diabetics that seems to improve the balance of the diseas.[17]

The decrease in Mn in this study supported data of Kazi et al, and Adewumi et al.[2,18] The decrease of Mn concentration in diabetics might be as a result of the increase of its urinary excretion since some authors reported that urinary Mn excretion was higher in diabetics compared to non-diabetic controls.[19] An appropriate Mn levels seem to be required for development of the normal insulin synthesis and secretion ; in this context, a Mn deficiency can result in a glucose intolerance.[20,21] However; published studies seem to be not conclusive respect to the role of Mn in diabetes.

Results show trace elements imbalance in diabetics patients. These trace elements are playing a key role in glucose metabolism and thus in the pathogenesis of diabetes. However, the published data are inconclusive as to the relationship between trace element status and the development and pathogenesis of diabetes. In order to better understand the role of the trace elements in diabetes, further clinical studies are required enrolling larger number of patients, analyzing several trace elements and using various biological matrices.

CONCLUSION

This study showed that serum levels of Zn, Se, Cr, and Mn were significantly lower in T2D patients than in controls while Cu levels were higher. A significant negative correlation between the serum levels of Cr and HbA1C was also observed. This imbalance may affect the evolution and pathogenesis of diabetes considering the roles of these trace elements in glucose metabolism. Author suggests the determination of selected trace elements in diabetics and advise dietary control and mineral supplementation if needed.

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Ethical approval: The study was approved by the Institutional Ethics Committee from the Faculty of Medicine and Pharmacy in Rabat, Morocco.

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