The Status of Serum Zinc, Magnesium and Calcium in Type 2 Diabetic Patients and Their Correlation with Renal Function.

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Abstract:

Trace elements play significant roles in the metabolism of insulin. The aim of this study is to investigate the level of serum zinc, magnesium and calcium in type 2 diabetes mellitus and relate them with the functionality of kidneys. 200 diabetic individuals and 50 healthy controls were enrolled. For each individual, blood sugar, serum urea and serum creatinine were determined. In addition, serum zinc, magnesium and calcium were determined for each individual via flame atomic absorption spectrometry. Significant differences were found in the level of serum zinc and magnesium between diabetic and healthy control groups. However, there was not any difference in the level of serum calcium between the two groups. It is not certain whether the low level of serum zinc and magnesium cause diabetes or they are the consequence of development of diabetes. The level of serum trace elements did not correlate with the functions of kidneys.

Keywords*: Diabetes mellitus, Trace elements, Zinc, Magnesium, Calcium.*

Introduction:

Diabetes mellitus (DM) is a complex disorder, characterized by hyperglycemia. DM is one of the leading causes of deaths in the world. It is said that disorder in metabolism of trace elements contribute partly in the development of diabetes mellitus (Yahya et al., 2011).

Trace elements can be defined as essential minerals that are needed in small quantities to perform many functions; some act as coenzymes for enzymes that are involved in immune system, gene regulation, chronic disease prevention, and defense by antioxidants (Strachan, 2010). Other trace elements play a major role in redox reactions for energy generation in cells. Moreover, they can also contribute in stabilizing many molecules (Akhuemokhan et al., 2013).

The trace element zinc plays a key role in the synthesis, storage and excretion of insulin. So, studying the link between this element and DM might enhance our knowledge of DM (Yahya, et al., 2011). Furthermore, magnesium has an important role in the oxidative decarboxylation of glucose in the citric acid cycle and in oxidative phosphorylation of glucose in anaerobic metabolism. Magnesium also contributes to the release of insulin from the beta cell of pancreas (Elamin and Tuvemo, 1990). Any defect in the homeostasis of calcium, affect the metabolism of glucose and hence the development of type 2 diabetes(Zaccardi et al., 2015). This occurs, because calcium regulates exocytosis of insulin (Wollheim and Sharp, 1981).

The aims of this research are, (1) to investigate the level of zinc, magnesium and calcium in diabetic patients, (2) to study the correlation of these trace elements with the functionality of kidney since some trace elements act as antioxidant that protect the tissues (Leung, 1998).

Materials and methods:

Collection of samples

The study was carried out at Duhok Diabetes Center in the city of Duhok in Kurdistan Region of Iraq. After taking a written consent, 200 type 2 diabetic patients were recruited as well as 50 health subjects as controls. The recruited subjects were from both genders and aged >30 years. Patients taking supplements, vitamins, thyroid hormones, diuretics, progesterone or antihypertensive drugs were excluded from the study.

About 5 mL of blood was taken from each sample after overnight fasting. Afterwards, the blood samples were centrifuged and serum samples were separated and stored at -20 °C for analysis.

Analysis of samples and statistical analysis

Fasting blood sugar (FBS) was determined via glucose oxidase method. Serum urea and serum creatinine were determined by urease and Jaffe methods respectively (Masood et al., 2009). Before carrying out trace elements measurement, 500 µL serum of each subject was diluted five-fold with de-ionized water. However, lipemic were diluted ten-fold. Determinations of the trace elements were performed by flame atomic absorption

spectrometry (Perkin Elmer) (Masood et al., 2009).

Statistical analysis of the results was evaluated by the program GraphPad Prism 5. The significant difference in the levels of trace elements, fasting blood sugar (FBS), serum urea and serum creatinine between type 2 diabetic patients and the control were tested using t-test analysis. In addition, t-test was also used to find the difference between the trace elements in the groups aged <= 50 years and > 50 years. One-way ANOVA was used to evaluate the difference in the level of the three trace elements with duration of diabetes. The Pearson's correlation analysis was used to find the association of trace elements levels with blood urea and serum creatinine. For both t-test and Pearson's correlation analysis, a probability value (p-value) <0.05 was regarded as statistically significant.

Results:

This study enrolled 200 type 2 diabetic patients and 50 healthy individuals. The general characteristics of both groups are shown in table 1. The mean age of the diabetic groups was 53.38 ± 9.42 vs. 49.64 ± 7.15 for the healthy group and the mean age was statistically similar. The ratio of male to female in each group was approximately 1. However, there was no significant difference in body mass index (BMI) between the two groups. The duration of diabetes for about half of the population of the diabetic group was less than 5 years.

Table 1: General characteristics of diabetic and non-diabetic groups.

Parameter	Non-diabetic (n=50)	Diabetic (n=200)	p-value
Mean age	49.64 ± 7.15	53.38 ± 9.42	> 0.05
Gender			
• Male	24 (48%)	94 (47%)	
• Female	26 (52%)	106 (53%)	
Mean BMI	28.32 ± 4.80	34.02 ± 6.59	> 0.05
Duration of diabetes			
• <5 years	Nil	104 (52%)	
• 6-10 year	Nil	60 (30%)	
• >10 years	Nil	36 (18%)	

There was a highly significant difference in the mean of FBS between diabetic group (213.7 ± 98.4) and non-diabetic group (97.5 ± 18.2) (p-value < 0.0001) (table 2). Regarding kidney function tests, the difference in the mean for serum urea was significant but for serum creatinine, it was not significant. There was significant statistical differences in the level of serum zinc and magnesium in both groups. There were 36% of diabetic patients who were zinc deficient (reference range 0.65-1.24 mg/l (Leung, 1998)). Whereas magnesium deficiency were found in 40% of the diabetic group. However, as for calcium, there was no statistical difference in the mean for the two groups.

Table (2): The mean values of serum FBS (mg/dl), serum urea (mg/dl), creatinine (mg/dl), zinc (mg/l), magnesium (mg/l) and calcium (mg/l) in diabetic and non-diabetic groups.

Results are expressed as mean ± standard deviation.

Parameter	Healthy control (n=50)	Diabetic (n=200)	p-value
Mean FBS	97.5 ± 18.2	213.7 ± 98.4	< 0.0001
Mean serum urea	30.48 ± 9.65	36.88 ± 13.79	0.0414
Mean creatinine	0.72 ± 0.22	0.89 ± 1.84	> 0.05
Mean zinc	0.98 ± 0.16	0.76 ± 0.33	0.0030
Mean magnesium	21.06 ± 3.53	16.72 ± 3.29	0.0105
Mean calcium	113.6 ± 22.36	122.0 ± 18.97	> 0.05

The level of the three trace elements did not differ significantly with duration of diabetes and age (p-value >0.05) (table 3). Furthermore, the three trace elements did not correlate with serum urea and creatinine (table 4).

Table (3): Association of zinc, magnesium and calcium with duration of diabetes and age. Results are expressed as mean ± standard deviation.

Parameter	Zinc	Magnesium	Calcium
Duration of diabetes			
• <5 years	0.76 ± 0.35	17.06 ± 3.71	123.5 ± 26.45
• 6-10 years	0.81 ± 0.32	16.38 ± 3.48	121.2 ± 8.31
• >10 years	0.71 ± 0.36	15.88 ± 2.41	119.1 ± 6.93
• P-value	> 0.05	> 0.05	> 0.05
Age			
• < or = 50 years	0.75	16.9	120.0
• > 50 years	0.77	16.6	123.3
• p-value	> 0.05	> 0.05	> 0.05

Table (4): Correlation value (r) between serum urea, serum creatinine and BMI with serum zinc, magnesium and calcium.

Parameter	Zinc	Magnesium	Calcium
Serum urea	0.168, p-value= 0.168	0.116, p-value= 0.116	- 0.116, p-value= -0.117
Serum creatinine	0.030, p-value= 0.835	0.0207, p-value= 0.886	0.04592, p-value= 0.751
BMI	0.061, p-value= 0.669	-0.073, p-value= 0.610	0.147, p-value= 0.305

Discussion:

Trace elements perform various functions in the living organisms. Of which, stabilizing the structure of many hormones and enzymes such as insulin (Akhuemokhan et al., 2013). In this study, we investigated the level of serum zinc, magnesium and calcium in diabetic and healthy control. We found significant differences in the mean levels of serum zinc and magnesium between diabetic and healthy control (p-value= 0.0030, 0.0105 respectively).

The presence of significant difference in the level of serum zinc and magnesium does not confirm that diabetes might be caused by the deficiency of these trace elements since these deficiencies might be caused by the increased excretion of the trace elements owing to polyuria (Kamal et al., 2009). Further studies are required in order to know whether diabetes causes deficiency of the trace elements or the development of diabetes mellitus is the consequence of deficiencies of zinc and magnesium. However, zinc and magnesium are involved in the metabolism of insulin and glucose (Nriagu, 2007, Ramadass et al., 2015, Jansen et al., 2009). Our finding that serum zinc is significantly low in diabetic population is comparable with Nasli-Esfahani et al. 2011 (Nasli-Esfahani et al., 2011), Walter et al. 1991 (Walter et al., 1991). In addition, our finding of low serum magnesium in diabetic patients is in accordance with those reported in many studies (Akinleye, 2007, Walter et al., 1991, Nsonwu et al., 2006). Our results of not having significant difference in the mean level of serum calcium between diabetic and not-diabetic is also reported by Zaccardi et al. 2015 (Zaccardi et al., 2015).

All trace elements did not decrease significantly with duration of diabetes. In addition, zinc and magnesium excrete mainly in the feces hence, polyuria has little influence on the excretion of trace elements (Davenport, 2014). Furthermore, the level of the three trace elements did not correlate with both serum urea and serum creatinine (p-value= > 0.05). These findings indicates that excretion of these trace elements is not significant in type 2 diabetic patients and the low level of these two trace elements in diabetic patients is evidence that deficiencies of these two trace elements contribute in the development of diabetes mellitus.

In conclusion, there are significant differences in the level of zinc and magnesium between diabetic and healthy control subjects. These differences could be because of lack of trace elements in the diet or excretion of these trace elements. Further studies are required in order to know what causes these differences.

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دیارکرنا برا زینکی، مگنیسیومی و کالسیومی ل نەخوشێن شەکری و پەیوەندیا ڤان توخما دگەل کارکرنا سیهیێ.

کورتیا لێکولینێ:

ئەو توخمین کو لەش پیویستی پی ببرکی کیم، رولەکێ کاریگەر یێ هەی د میتابولیزما ئەنسولینی. ئارمانج ژڤێ لێکولینێ ئەوە زانینا ئاستێ توخمێن (زینك، مەگنیسیوم و کالسیوم) دناف سیریژا خوینێ دا یا نەخوشێن شەکرێ جورێ 2 وگریدانا وان توخمان دگەل ئەرکێ گورچیلی. هژمارا کەسان دڤێ لێکولینێ دا 250 ی کەس بوون، 200 ژوان نەخوشێن شەکرێ هەبوون دگەل 50 کەسێن ساخلەم. بو هەر نەخوشەکی ئەف تێستێن هەنێ هاتنە کرن: ریژا شەکرێ، یوریایێ و کریاتینیێ دناف سیریژا خوینێ دا. هەر ووسا پیڤانا توخمێن زینك، مەگنیسیوم و کالسیوم هاتە کرن بریکا ئامیرێ.

لناف ڤێ لێکولینێ دا جیاوازیەکا گرنگ هاتە دیتن ل دور ریژا توخمێ زینك و مەگنیسیوم دنافبەرا کەسێن ساخلەم و کەسێن نەخوش ب نەخوشیا شەکرێ، لێ دگەل وێ چ گھورین نە هاتنە دیتن ل دور ریژا توخمێ کالسیومی دناف هەردووك جوراندا. هەرووسا نە یا پشتراستە ئەرێ هاتنا خار یا توخمێ زینك و مەگنیسیومی دناف سیریژا خوینێ دا ئەگەری وی ئەوا توشبوونێ ب نەخوشتیا شەکرێ یان خارنا مادیین کو ئەڤ هەردوو توخما ب ریژکا کیم تیدا هەنا، هەرووسا دیار بو کو ئاستێ هەرسی توخمان چ پەیوەندی دگەل ئەرکێ گولچیسکا دا نینە.

تقدير تركيز الزنك و المغنيسيوم و الكالسيوم في مرضى سكر الدم النوع الثاني و علاقة هذة العناصر مع عمل الكلية.

الخلاصة:

بعض العناصر التي يحتاجها جسم الانسان بكميات صغيرة تلعب دورا مهما في ايض الانسولين. الهدف من هذا البحث هي دراسة تركيز الزنك، المغنسيوم و الكالسيوم في مصل الاشخاص المصابين بمرض السكر من النوع الثاني و علاقتها مع وظيفة الكلية. الدراسة تضمنت 200 مريض و 50 اشخاص اصحاء. لكل شخص، تم قياس نسبة السكر و اليوريا و الكرياتينين في مصل الدم بالاضافة الى الزنك، المغنسيوم و الكالسيوم بواسطة مطيافية الامتصاص الذري. كان هناك فرق مهم في مستوى تركيز الزك و المغنسيوم بين المصابين بالسكر و الاصحاء. لم يكن هناك اي فرق مهم بين مستوى تركيز الكالسيوم بين المصابين بالسكر و الاصحاء. قلة مستوى تركيز الزنك والمغنسيوم دليل على ان هذة العناصر تلعب دورا في الاصابة بمرض السكر او ان قلة مستواها، مجرد بسبب كثرة التبول.