Clinical Research

Chrome, Zinc, Copper and Magnesium Levels and Fasting Blood Sugar, Insulin and HbA_{1c} Values in the Plasma and Erythrocytes by Type 2 Diabetes

Elif POLAT[1,a], Yaşar Nuri ŞAHİN[2], Nezahat KURT[3], Akar KARAKOÇ[4], Asuman ÖZKAN[4]

[1]*Erzurum Teknik Üniversitesi, Beslenme ve Diyetetik Anabilim Dalı, Erzurum, Türkiye*
[2]*Kastamonu Üniversitesi, Beslenme ve Diyetetik Anabilim Dalı, Kastamonu, Türkiye*
[3]*Erzincan Binali Yıldırım Üniversitesi, Tıbbi Biyokimya Anabilim Dalı, Erzincan, Türkiye*
[4]*Atatürk Üniversitesi, Sağlık Hizmetleri ve Teknikleri Anabilim Dalı, Erzurum, Türkiye*
[5]*İzmir Katip Çelebi Üniversitesi, Tıbbi Biyokimya Anabilim Dalı, İzmir, Türkiye*

ABSTRACT

Objective: The present study, in patients with type 2 diabetes; It was aimed to analyze fasting blood glucose, insulin and HbA1c values and trace element (zinc, copper, magnesium and chromium) levels.
Material and Method: The study included patients who were 20 patients with type 2 diabetes and 20 healthy controls applied to the Internal Medicine outpatient clinic of Erzurum Regional Training and Research Hospital. The results of the analyzes were calculated with the help of the SPSS (Version 19.0) software package.
Results: Levels of HbA1c, glucose, and insulin in the patient group were significantly higher than in the control group. There was no significant difference among levels of plasma zinc (Zn) and copper (Cu) and erythrocyte Cu in the control group and the patient group. Levels of plasma magnesium (Mg) and chromium (Cr) and erythrocyte Zn, Mg and Cr levels in the control group were significantly higher than in the patient group. Levels of plasma and erythrocyte Mg in people with diabetes were significantly lower than in the control group ($p < 0.005$). The levels of plasma and erythrocyte Cr in the group with type 2 diabetes were significantly lower than in the control group.
Conclusion: To understand the relationship between diabetes and the trace element, well-specified patient samples should be collected. Studies should be carried out using standard methods. More studies should be done to make sense of the changes in trace element levels in diabetes. The necessity of trace element supplementation as a support for treatment should be investigated.

Keywords: *Diabetes, Plasma, Insulin, Trace Elements, Chromium.*

ÖZ

Tip 2 Diyabette Plazma ve Eritrositlerde Krom, Çinko, Bakır ve Magnezyum Seviyeleri ile Açlık Kan Şekeri, Insülin ve HbA_{1c} Değerleri
Amaç: Bu çalışmada Tip 2 Diyabetes Mellitus'lu hastalarda; açlık kan şekeri, insülin ve HbA1c değerleri ile eser element (çinko, bakır, magnezyum ve krom) seviyelerinin incelenmesi amaçlanmıştır.
Gereç ve Yöntem: Çalışmaya Erzurum Bölge Eğitim Araştırma hastanesi Dahiliye polikliniğine başvuran, tip 2 diyabet tanısı almış 20 hasta ve 20 sağlıklı kontrol grubu dahil edilmiştir. Analizlerin sonuçları SPSS (Versiyon 19.0) yazılım paketi yardımı ile hesaplandı.
Bulgular: Hasta grubunda HbA1c, glukoz ve insülin seviyeleri kontrol grubuna göre anlamlı derecede yüksekti. Kontrol grubu ve hasta grubunda plazma çinko (Zn) ve bakır (Cu) ile eritrosit Cu düzeyleri arasında anlamlı bir fark yoktu. Kontrol grubunda plazma magnezyum M(g) ve krom (Cr) seviyeleri ile eritrosit Zn, Mg ve Cr seviyeleri hasta grubuna göre anlamlı derecede yüksekti. Diyabetli kişilerde plazma ve eritrosit Mg seviyeleri kontrol grubuna göre anlamlı derecede düşüktü ($p < 0.005$). Tip 2 diyabetli grupta plazma ve eritrosit Cr seviyeleri kontrol grubuna göre anlamlı derecede düşüktü.
Sonuç: Diyabet ve eser element arasındaki ilişkiyi anlamak için, iyi spesifiye edilmiş hasta örnekleri toplanmalı. Çalışmalar standart yöntemler ile yapılmalı. Diyabette eser element seviyelerindeki değişikliklerin anlamlandırılması için daha çok çalışma yapılmalı. Tedaviye destek olarak eser element takviyesinin gerekliliği araştırılmalıdır.
Anahtar Sözcükler: *Diyabet, Plazma, Insulin, Eser Elementler, Krom.*

Bu makale atıfta nasıl kullanılır: Polat E, Şahin YN, Dr. Kurt N, Dr. Karakoç A, Özkan A. Tip 2 Diyabette Plazma ve Eritrositlerde Krom, Çinko, Bakır ve Magnezyum Seviyeleri ile Açlık Kan Şekeri, Insülin ve HbA_{1c} Değerleri. Fırat Tıp Dergisi 2024; 29(1): 9-12.

How to cite this article: Polat E, Sahin YN, Dr. Kurt N, Dr. Karakoc A, Ozkan A. Chromium, Zinc, Copper and Magnesium Levels and Fasting Blood Glucose, Insulin and HbA1c Values in Plasma and Erythrocytes in Type 2 Diabetes. Firat Med J 2024; 29(1): 9-12.

ORCID IDs: E.P. 0000-0003-0042-4084, Y.N.Ş. 0000-0002-8278-5272, N.K. 0000-0002-1685-5332, A.K. 0000-0002-1222-8091, A.Ö. 0000-0001-8857-3409.

Diabetes Mellitus (DM) is a disease that is seemed most common all over the world most common worldwide and in all age groups. In the modern age, the addition of environmental and cultural factors to genetic characteristics has led to an increase in the prevalence of type 2 diabetes mellitus (1). Type 2 DM occurs together with insulin resistance in adipose tissue, liver, muscle, and beta-cell insulin secretory defect (2,

[a]Yazışma Adresi: Elif POLAT, Erzurum Teknik Üniversitesi, Beslenme ve Diyetetik Anabilim Dalı, Erzurum, Türkiye
Tel: 444 5 388 e-mail: elif.polat@erzurum.edu.tr
Geliş Tarihi/Received: 11.05.2022 Kabul Tarihi/Accepted: 21.11.2022

3).
DM can be diagnosed along with past and laboratory tests. The diagnosis of diabetes is based on the American Diabetes Association (ADA) (2017) criteria (4).

- A1c ≥ 6.5%.
- Fasting plasma glucose (FPG) ≥ 126mg/dL (7.0 mmol/L)
- 2-h plasma glucose ≥ 200mg/dL (11.1mmol/L) during an oral glucose tolerance test (OGTT).
- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1mmol/L)

Trace elements are one of the components of food and essential for optimal health. These metals are essential for the functionality of many enzymes in various biochemical pathways. Zinc plays several vital roles in most cells because it is an essential component of several important enzymes, such as carbonic anhydrase, superoxide dismutase, alcohol dehydrogenase, lactate dehydrogenase, carboxypeptidase, and alkaline phosphatase.
Control of Zn homeostasis is vital for all biological systems. It is observed that zinc homeostasis is impaired in diabetes mellitus. Therefore, the concentration of zinc in the metabolism is strictly regulated (5, 6).
Zn and Cu, are essential components of many enzyme systems. Zn plays storage and secretion of insulin. Insulin is stored in β cells of the pancreas as crystals that contain Zn. Zn has a major impact on insulin activity. Also Cu metabolism changes in diabetic patients. However, the mechanism is not known precisely (7). Mg is a co-factor in biochemical reactions. Mg is involved in various metabolic events such as energy production, regular functioning of muscular systems, maintaining osmotic pressure, lowering blood pressure, carbohydrate metabolism, nervous system, and DNA synthesis (8). Mg^{+2} deficiency can cause insulin resistance, abnormal lipid metabolism, and impaired glucose tolerance. Therefore, type 2 diabetes mellitus develops (9, 10).
Chromium is of great importance in the regulation of protein, lipid and carbohydrate metabolism. Cr increases insulin activity and allows glucose to enter the cell. Studies have reported that the people with type 2 diabetes who have Cr supplements added to their diets the effect of insulin and glucose intolerance has improved (11, 12).

MATERIAL AND METHOD

This study was conducted onward patients and outpatients with Type 2 DM who were admitted for treatment to the hospital. A total of 40 patients, 20 of them diagnosed with diabetes type 2 (age 48.10±8.77) and 20 (age 44.95±13.30) of them as the control group were included in the study. The estimated power (1-beta) test value was calculated as 0.833 with the G-Power program.
HbA1c, insulin, fasting blood glucose (FBG), and plasma and erythrocyte zinc, copper, magnesium and chromium levels were measured by collecting the blood samples from the patients who were included to the study, and from the control group.
HbA1c was measured by turbidimetric inhibition immunoassay method. Insulin, in Dade Behring Dimension RXL analyzer, with Immulite 2000 insulin kit chemiluminescence was measured by immunometric method. And fasting blood glucose was measured by hexokinase method in Modular PP, Roche Auto-analyzer device.
Plasma and erythrocyte levels of zinc, copper, magnesium, and chromium elements were measured by atomic absorption spectrometry. Chrome was analyzed by the electrothermal method, and zinc, copper, and magnesium were analyzed by flame atomization methods.
Variables in the present study show a normal distribution as to the Kolmogorov-Smirnov test, so Independent t-test was applied from parametric tests. As statistical, p <0,005 values was considered significant.

RESULTS

Table 1 shows HbA1c, insulin and glucose levels in the patient and control groups .Levels of HbA1c, glucose, and insulin in the patient group were significantly higher than in the control group (p <0.001).

Table 1. *HbA1c, FBG and insulin values of patient and control groups.*

Parameter	Patient Group (n =20) Mean ± SD	Control Group (n =20) Mean ± SD	
HbA1c %	8.97±2.44	5.58±1.41	0.001*
FBG (mg/dL)	183.95±93.48	96.60±14.84	0.001*
Insulin (mlU/mL)	19.28±11.11	10.45±8.45	0.002*

**: statistically significant.*

Table 2 shows plasma Zn, Cu, Cr and Mg and erythrocyte Zn, Cu, Cr and Mg values in the patient and control groups. There was no significant difference among levels of plasma zinc (Zn) and copper (Cu) and erythrocyte Cu in the control group and the patient group.

Table 2. *Plasma and erythrocyte values of the elements in the patient and control group.*

Parameter	Patient (n =20)	Control (n =20)		Patient (n =20)	Control (n =20)	
	Plasma Mean±SD			Erythrocyte Mean±SD		
Zn (mg/L)	1.83±0.72	1.63±0.70	0.417	11.64±3.74	16.64±6.74	0.012*
Cu (mg/L)	1.77±0.94	1.64±0.46	0.473	2.17±0.65	1.95±0.36	0.180
Mg (mg/L)	17.0±2.59	18.73±2.53	0.044*	63.44±17.07	72.55±11.61	0.037*
Cr (µg/L)	8.10±1.52	12.21±3.40	0.001*	17.54±5.30	26.64±5.35	0.001*

**: statistically significant.*

Levels of plasma magnesium (Mg) and chromium (Cr) and erythrocyte Zn, Mg and Cr levels in the control group were significantly higher than in the patient group. Levels of plasma and erythrocyte Mg in people with diabetes were significantly lower than in the control group ($p < 0.005$). The levels of plasma and erythrocyte Cr in the group with type 2 diabetes were significantly lower than in the control group.

DISCUSSION

Type 2 diabetes pathogenesis is quite complex and is still a matter of debate in many ways (3). It is not entirely clear whether the defect in trace elements is caused by type 2 diabetes or causing type 2 diabetes (13).

When it is considered that insulin synthesis, its releasing and disorders on effect tracts have the main to play a role, in DM pathogenesis, working of Cr^{+3} that increase the efficiency of the hormone with the receptor, in diabetics often took place in the studies. Also, in this study, Cr^{+3} levels in plasma and erythrocyte were found low in diabetics as to non-diabetics according to the literature (14-16).

The glucose level that is high in DM increases the non-enzymatic glycation and thus, many glycosylated proteins that are glycated lose their function gradually. In this study, diabetics' HbA1c value was found significantly higher than non-diabetics. Any correlation was not identified between plasma and erythrocyte Cr^{+3} levels of HbA1c and insulin levels like Kamal et. al.'s similar studies (17).

In this study, plasma and erythrocyte Mg^{++} levels in diabetics were found as significantly lower than plasma and erythrocyte Mg^{++} levels in the control group. In Schnack et al.'s study, as to the literature, it was specified that serum and intra- erythrocytes Mg^{++} level on patients with type 2 DM is significantly lower than control group and inversely proportional to the metabolic control, and hypomagnesemia cause insulin resistance (18). Resnick et al. (19) captured the attention to intracellular Mg deficiency in type 2 DM and specified that serum ionized Mg levels were significantly lower. Keskek et al. (20) Stated in their study that magnesium deficiency was associated with high HbA1c and high glucose levels. Another study found a significant frequency of hypomagnesemia in diabetic patients, and the mean concentration of magnesium in plasma was lower than in the control group (21).

Cu, as an inorganic component of many enzymes is a trace element with the physiological function of metabolism varies plasma concentration with diabetes. In Zargar et al. (22) study, the serum Cu in diabetics was found higher than non-diabetics. Prabodh et al. (23) did not found any significant difference between patient and control groups. Also, in our study, plasma Cu^{++} was high in the patient group. But, there was not any significant difference. When there is not any significant difference between the patient and control group for plasma Cu^{++} levels, there was a significant difference among erythrocyte Cu^{++} levels. Chausmer found erythrocyte Zn^{++} levels as lower in diabetics in his study (24). Also, we found erythrocyte Zn^{++} levels significantly lower for diabetics in our study. Bandeiraa et al. (25) study, both plasma and erythrocyte zinc levels were found to be lower than the control group.

It was identified that plasma and erythrocyte values of Cr^{+3}, Cu^{+2}, Zn^{+2} and Mg^{+2} elements that are important for their roles on carbohydrate metabolism and physiologic functions varied for diabetics when they were compared with non - diabetics, and these variables are correlated with blood glucose, and HbA1c values and these results are compatible with most of the studies that were concluded before, about this subject in this study.

REFERENCES

1. Karadağ S. Tip 2 diabetes mellituslu renal disfonksiyonu olmayan nefropatili hastalarda albuminüri ile serum sistatin C İlişkisi. Uzmanlık Tezi, İstanbul: Sağlık Bakanlığı İstanbul Okmeydanı Eğt. ve Arş. Hastanesi 2006.
2. Onat T, Emerk K, Sözmen E. İnsan Biyokimyası. 2. Baskı, Ankara: Palme Yayıncılık 2006.
3. Durupınar Ü. Sigara alışkanlığının tip 2 diabetiklerde diabet tedavi seyri üzerine etkilerinin irdelenmesi. Uzmanlık Tezi, İstanbul: Şişli Etfal Eğitim ve Araştırma Hastanesi, Aile Hekimliği Koordinatörlüğü 2007.
4. Cefalu W. The journal of clinical and applied research and education. Diabetes Care 2017; 40: 1.
5. Jansen J, Karges W, Rink L. Zinc and diabetes-clinical links and molecular mechanisms. J Nutr Biochem 2009; 20: 399-417.
6. Thomas JH, Gillham B. Wills' biochemical basis of medicine. Elsevier 2013.
7. Kurtul N, Pençe S, Çil MY, Aksoy H, Erman F. Tip 2 Diabetes mellituslularda serum çinko ve bakır değerleri ile cinsiyet ve yaş arasındaki ilişki. Gaziantep Tıp Dergisi 2007; 7-12.
8. Gröber U, Schmidt J, Kisters K. Magnesium in prevention and therapy. Nutrients 2015; 7: 8199-226.
9. Zhang Y, Li Q, Xin Y, Lv W, Ge C. Association between serum magnesium and common complications of diabetes mellitus. Technol Health Care 2018; 26: 379-87.
10. Palacios OM, Kramer M, Maki KC. Diet and prevention of type 2 diabetes mellitus: beyond weight loss and exercise. Expert Rev Endocrinol Metab 2019; 14: 1-12.
11. Havel PJ. A scientific review: the role of chromium in insulin resistance. Diabetes Educ 2004; 30: 1-14.
12. Davì G, Santilli F, Patrono C. Nutraceuticals in diabetes and metabolic syndrome. Cardiovasc Ther 2010; 28: 216-26.
13. Meyer JA, Spence DM. A perspective on the role of metals in diabetes: past findings and possible future directions. Metallomics 2009; 1: 32-41.
14. Hambridge K, Casey C, Krebs N et al. Trace elements in human and animal nutrition. Orlando: Academic Press 1987.
15. Basaki M, Saeb M, Nazifi S, Shamsaei HA. Zinc, copper, iron, and chromium concentrations in young patients with type 2 diabetes mellitus. Biol Trace Elem Res 2012; 148: 161-4.
16. Kazi TG, Afridi HI, Kazi N, et al. Copper, chromium, manganese, iron, nickel, and zinc levels in biological samples of diabetes mellitus patients. Biol Trace Elem Res 2008; 122: 1-18.
17. Kamal M, Salem M, Kholousi N, Ashmawyc K. Evaluation of trace elements and Malondialdehyde levels in type II diabetes mellitus. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2009; 3: 214-8.
18. Schnack C, Bauer I, Pregant P, Schernthaner G. Hypomagnesaemia in type 2 (non-insulin-dependent) diabetes mellitus is not corrected by improvement of long-term metabolic control. Diabetologia 1992; 35: 77-9.
19. Resnick LM, Altura BT, Gupta RK, Laragh JH, Alderman MH, Altura BM. Intracellular and extracellular magnesium depletion in type 2 (non-insulin-dependent) diabetes mellitus. Diabetologia 1993; 36: 767-70.
20. Keşkek ŞÖ, Kırım S, Karaca A, Saler T. Low serum magnesium levels and diabetic foot ulcers. Pak J Med Sci 2013; 29: 1329.
21. Sampaio FA, Feitosa MM, Sales CH, et al. Influence of magnesium on biochemical parameters of iron and oxidative stress in patients with type 2 diabetes. Nutr Hosp 2014; 30: 570-6.
22. Zargar AH, Shah NA, Masoodi SR, et al. Copper, zinc, and magnesium levels in non-insulin dependent diabetes mellitus. Postgrad Med J 1998; 74: 665-8.
23. Prabodh S, Prakash DS, Sudhakar G, Chowdary NV, Desai V, Shekhar R. Status of copper and magnesium levels in diabetic nephropathy cases: a case-control study from South India. Biol Trace Elem Res 2011; 142: 29-35.
24. Chausmer AB. Zinc, insulin and diabetes. J Am Coll Nutr 1998; 17: 109-15.
25. da Silva Bandeira V, Pires LV, Hashimoto LL, et al. Association of reduced zinc status with poor glycemic control in individuals with type 2 diabetes mellitus. J Trace Elem Med Biol 2017; 44: 132-6.