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Review Article

Trace elements and their relation to diabetes mellitus and obesity

Noha EM. Hassanin [1], Maha MS. Elkishki[2], Laila H. Fawzy [2]

[1]Clinical Pathology Department, Damietta specialized hospital, Egypt

[2]Clinical Pathology Department, Medicine Faculty for Girls, Cairo, Al-Azhar University, Egypt

ABSTRACT

Background: The human body is composed of two types of elements, abundant and trace elements. Abundant elements include the major elements that are important constituents of tissues e.g. oxygen, carbon, nitrogen, and hydrogen. Trace elements are micronutrients which are important for the human body, but they are only present in traceable quantities. They are classified into essential, and non-essential elements. Essential trace elements include iron, zinc, copper, cobalt, fluoride, iodide, manganese, molybdenum & selenium. Probably essential trace elements include Nickel, tin, vanadium, silicon, Boron. Non-essential trace elements include aluminum, lead, silver, mercury, rubidium, strontium, titanium, and zirconium. Although trace elements account for only 0.02% of the total body weight, yet they have many functions in the biological process. Some of them like iron, zinc, chromium, copper and iodine act as antioxidants and cofactors for many enzymes affecting the metabolism and insulin action and have great effect on insulin and leptin receptors. Nevertheless, the biochemical functions are well-defined. If the level of these micronutrients decreased or increased, widespread issues in human health occur.

Aim: Some of the trace elements and their role in the pathology and development of obesity and diabetes mellitus are the subject of this article.

Conclusion: This review concludes that deficiency or excess of some trace elements may contribute directly or indirectly to pathogenesis of diabetes mellitus and obesity. Further investigations are needed to complete gaps in our knowledge on trace elements.

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Correspondence Author: Noha Hassanin, **c**linical pathology resident, Damietta specialized hospital, Damietta, Egypt. **Tel:** 01014195519. **E-mail:** dr.a.mahmoud89@gmail.com.

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INTRODUCTION

Trace elements are main micronutrients necessary for normal functions in the body. These elements regulate the physiology of certain functions [1].

Trace elements are necessary to stabilize enzymes and protein and serve as co-factors for a lot of enzymes. Some trace elements control the essential biological processes by binding to the receptor of the cell membrane or changing the receptor shape to prevent the entry of specific molecules into the cell [2].

Micronutrients play a dual role: they sustain the cellular structure normally at their adequate levels; however, their disturbance contributes to various pathways alternation and may cause functional disturbances [3]. These physiological effects of micronutrients are essential and have direct relation with diabetes and obesity. Overall, this analysis validates that deficiencies or excess in trace elements can be directly or indirectly related to oxidative stress that eventually precede insulin dysfunction or diabetes mellitus. Free radical formation in diabetes by non-enzymatic glycation of proteins, glucose oxidation and increased lipid peroxidation leads to damage of enzymes, cellular machinery, and increased insulin resistance due to oxidative stress [4, 5]. The aim of this article was to clarify the role of trace elements in the pathology and development of obesity and diabetes mellitus.

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1. Iron

Iron is one of the most essential trace elements. Total body iron content is 3 to 5gms. About 75% of iron is present in blood. The rest is in liver, bone marrow & muscles. It has a great effect in the metabolism of glucose. Recent studies revealed the bidirectional relationship between glucose homeostasis and iron metabolism [6]. Impaired uptake of iron could affect the consumption and storage of glucose. The serum ferritin concentration may influence insulin sensitivity, vascular strength, viscosity, and oxidative damage. Both serum ferritin and BMI will act as separate predictors in the glucose tolerance test [7].

Increased iron content in the body may cause severe oxidative stress resulting in severe damage to pancreatic cells, promoting beta cells apoptosis. Ultimately affecting insulin production and increasing the risk to insulin resistance. Moreover, weakening of the ability of the liver to use insulin and gluconeogenesis [8].

High levels of body iron can increase Type 2 Diabetes (T2D) and obesity risk [9]. Circulating ferritin levels had a positive association with the amount of computed tomography (CT)-assessed visceral fat, subcutaneous fat and hepatic fat in a previous study. Finally, serum ferritin levels correlated with fat tissue-derived molecules including leptin, interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) and adiponectin [10].

2. Zinc (Zn)

Zinc is the second most abundant trace element in the body. It is the most common catalytic metal ion in cell cytoplasm. It controls the development and neutralizing of protein folding, gene expression, and more than 100 enzymes. Zn plays an important role in cell signals and cellular biology including cell divisions. Low serum zinc levels are linked to apoptosis, diabetes, and insulin resistance. [11].

Zinc acts as an antioxidant and Zn intake decreases development of reactive oxygen species (ROS) that are an important cause in ageing and insulin resistance [12]. Zn is a key element for proper storage, secretion, and action of insulin in mammalian pancreas. Cytokine-induced damage is increased in the autoimmune attack by low serum Zn, which also damages islet cells of Type 1 Diabetes (T1D) patients [13]. It may lead to progression of diabetes by genetic polymorphism in the 8th gene of the zinc carrier and in metallothionein (MT) genes related to T2D [14, 15]. There is complex correlation between diabetes, insulin and zinc. Diabetes affects zinc metabolism and increase Zn urinary loss and decreases zinc overall in the body [16].

Low concentrations of zinc were proved to be associated with higher abdominal fat. Zn-a2-glycoprotein (ZAG) is an adipokine which stimulates energy expenditure in skeletal muscle and brown adipose tissue, resulting in reductions in body weight, glycaemia, triglycerides, and non-esterified fatty acids (NEFAs). Its level is lower in subcutaneous and visceral adipose tissue and livers of obese humans. [17].

3. Copper

Copper is the third largest trace element found in human body after iron and zinc. It acts as a strong enzyme catalyst and a harmful hydroxyl radical reactant generator. Copper normal levels range from 70-140μg / dL (11-22 μmol / L) in the body [18]. Low Copper levels affect glucose metabolism negatively, reduce response to insulin and lead to hypercholesterolemia and atherosclerosis. Copper has insulin-mimetic action and activates lipogenesis [19, 20].

4. Chromium

Chromium plays an important role in glucose homeostasis it is also a necessary component of the glucose tolerance factor and is a crucial cofactor for the action of insulin [21]. It has a great role in increasing glucose tolerance by reducing the resistance of insulin. Some studies have shown that Cr supplemented T2DM patients reduced their blood glucose, dose dependent insulin and levels of cholesterol and HbA1c% [22].

Proper intake of chromium reduces blood triglycerides and cholesterol and improves insulin function [23]. Insulin sensitivity, beta cell sensitivity, insulin internalization, insulin receptors and their enzymes number are also up regulated by chromium [24]. Chromium has garnered interest for use as a weight loss aid, chromium could suppress appetite and stimulate thermogenesis through sensitization of insulin-sensitive glucoreceptors in the brain. Body fat distribution is related to insulin sensitivity; peripheral fat is more insulin sensitive than central fat found in the chest and abdomen [25].

5. Iodine

The total body contains about 20 mg of iodine. Thyroid gland contains 80% of total body iodine. Muscles, salivary glands, and ovaries also contain some amount of iodine. Decreased iodine level leads to decreased synthesis of the thyroid hormone which leads to increased secretion of TSH and affecting thyroid gland functions and size. The cell viability may be diminished and the function of insulin secretion in beta cells may be compromised through inducing pro-apoptotic proteins [26].

Energy metabolism is controlled by thyroid function, but disturbed thyroid functions affects diabetics' blood glucose control. Thyroid disease risk increases in patients with diabetes mellitus [27, 28]. Some findings reported that treating hyperthyroidism controls diabetes in diabetics with hyperthyroidism patients [29].

6. Magnesium

Magnesium was considered as trace element but now it has an essential function as a cation in metabolism. Magnesium is an important cofactor for glucose storage and for the metabolism of carbohydrates. It participates in cellular action of insulin. decreased intake of magnesium increases the risk of diabetes [30].

Magnesium deficiency inactivates cellular defense against oxidative stress effects, which in turn contributes to reduced resistance to diabetes-led oxidative stress, accelerates progression of complications of diabetes. Low levels of Mg may deteriorate T2D, but studies reported that optimum levels of magnesium decrease T2D and metabolic syndrome risk by decreasing resistance to insulin [31–32].

7. Manganese

Manganese is an essential trace element. It has a significant action in carbohydrate, amino acid, and cholesterol metabolism and it is essential for processing and secretion of insulin normally. Manganese has a great function in many physiological processes, and it is an essential component of several enzymes as well as activators of various enzymes including phosphoenolpyruvate carboxykinase (PEPCK) and glutamine synthetase [33]. These enzymes are important for carbohydrates, amino acids, and cholesterol consumption. Manganese activates the metabolism of glucose and essential for normal insulin homeostasis [33]. Some studies have shown that T2D patients have lower serum manganese than control subjects. Manganese is essential for manganese superoxide dismutase for reduction of mitochondrial oxidative stress [34].

CONCLUSION

Trace elements have a great role in regulating body metabolism. Some of them like iron, zinc, chromium, copper and iodine act as antioxidants and cofactors for many enzymes affecting the metabolism and insulin action. Their deficiency or excess may contribute directly or indirectly to pathogenesis of diabetes mellitus and obesity.

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الملخص العربى

العناصر النزرة وعلاقتها بداء السكري و السمنة

نهى السعيد محمود حسنين [1]، مها محمد سليمان الكشكي[2]، ليلي حسين فوزي[2]
[1]قسم الباثولوجيا الاكلينيكية، مستشفى دمياط التخصصي، دمياط، جمهورية مصر العربية
[2]قسم الباثولوجيا الإكلينيكية، كلية طب البنات، القاهرة، جامعة الأزهر، جمهورية مصر العربية

ملخص البحث

الخلفية: تمثل العناصر النزرة مواد طبيعية غير عضوية مطلوبة في الانسان بكميات صغيرة . ومنها الزنك واليود والفلوريد والنحاس والحديد والكروم والسيلينيوم والمنغنيز والموليبدينوم. وتعد هذه العناصر جزء من الإنزيمات والهرمونات والخلايا في الجسم التي .يمكن أن يسبب نقصها أعراض نقص التغذية، وتقاس في الدم بالميكروجرام / لتر. و على الرغم من أن هذه العناصر تمثل فقط 0,02٪ من وزن الجسم، الا ان لديها العديد من الوظائف في العملية البيولوجية .على سبيل المثال، لديهم دور كبير في الاستجابة المناعية والتعبير الجيني مثل الزنك والحديد والنحاس والسيلينيوم، و يلعب بعضهم دورا في ايض الدهون والعظام مثل النحاس والحديد والمنغنيز . ويشارك الحديد في الاستجابة المناعية الخلوية لعمل الخلايا الملتهمة. و يعد الزنك والسيلينيوم من مضادات الأكسدة.

وتنقسم العناصر النزرة الى:

- العناصر النزرة الأساسية كالحديد،الزنك، اليود.
- العناصر النزرة الغيراساسية كالالومنيوم، الباريوم، الرصاص.

وتوجد علاقة في مرض السكري بين وظيفة البنكرياس ومستوى الزنك في الدم و يؤثر الكروم على ايض الجلوكوز ويؤثر المغنيسيوم ايضا على عملية استهلاك الكربوهيدرات و له دور في تطور اعتلال الشبكية السكري.

تترافق السمنة مع أيض غيرطبيعي ونقص المغذيات الدقيقة.و تمثل العناصر النزرة قيمة كبيرة في تنظيم التمثيل الغذائي في الجسم الطبيعي، لأنها تتفاعل مع العديد من الإنزيمات والهرمونات.

وقد تكون تركيزات العناصر النزرة مضطربة في مرضى السمنة المفرطة مع نقص المغنيسيوم والنحاس بالدم اللذان يرتبطان عكسيا مع وزن الجسم ومؤشر كتلة الجسم. ويرتبط اضطراب العناصر النزرة مع متلازمة الأيض.

الهدف: بعض العناصر النزره و دورها فى علم الامراض و تطور السمنه و مرض السكرى .
الخلاصه: تخلص هذه المراجعه الى أن نقص أو زياده بعض العناصر النزره قد يساهم بشكل مباشر أو غير مباشر فى التسبب فى مرض السكرى و السمنه. هناك حاجه الى مزيد من التحقيقات لسد الثغرات فى معرفتنا بالعناصر النزره.
ومما سبق يتضح الأهمية البالغة للعناصر النذرة في الوقاية من مرض السمنة و داء السكري .

كلمات مفتاحية: العناصر النزرة، داء السكري، السمنة

الباحث الرئيسي
الاسم: نهى السعيد محمود حسنين، قسم الباثولوجيا الاكلينيكية، مستشفى دمياط التخصصي، دمياط، جمهورية مصر العربية.
الهاتف: 01014195519
البريد الالكتروني: dr.a.mahmoud89@gmail.com