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OBEZ ÇOCUKLARDA DEPRESYON VE ESER ELEMENT İLİŞKİSİ

ASSOCIATION OF DEPRESSION AND TRACE ELEMENTS IN OBESE CHILDRE

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Öz

Depresyon, anksiyete bozuklukları, öğrenme yetersizliği çocukluk çağında ilgi gerektiren yaygın problemler olup obezite ile bağlantılı oldukları bulunmuştur. Artmış ve azalmış eser element düzeyleri depresyon göstergeleri olabilirler. Bazı elementlerin eksiklik ya da fazlalıkları da, özellikle çocuklarda ve adolesanlarda dünya çapında artış kaydeden bir sağlık problemi olan obeziteye yol açan ağırlık artışlarına neden olabilirler. Bu derlemede pediatrik ve adolesan obezitesinin fiziksel ve akıl sağlığına ilişkin sonuçları eser elementler bakış açısından değerlendirilecektir. Eser elementlerin nörofizyolojik süreçlerle ilgili metabolik yollara katılımlarının, etkileşimlerinin ve kümülatif etkilerinin daha iyi anlaşılması sağlığın ve tedavinin etkilerinin iyileştirilmesine yardımcı olacaktır.

Anahtar kelimeler: Depresyon, Obezite, Çocuklar, Eser Elementler

Abstract

Depression, anxiety disorders, learning disability are common problems requiring pediatric care and found to be associated with obesity. Elevated and reduced levels of trace elements may be indicators of depression. Deficiencies or toxicities of some elements may also cause weight gain leading obesity, which is a health problem increasing worldwide particularly among children and adolescents. In this review, the physical and mental health consequences of pediatric and adolescent obesity will be evaluated from the trace elements point of view. Better understanding of the participation of trace elements in the metabolic pathways related to neurophysiological processes, their interactions and cumulative effects will help to improve health and also the effects of treatment.

Key Words: Depression, Obesity, Children, Trace Elements

Introduction

Trace elements constitute a fascinating world. Currently, they are not in the position they merit[1]. For the ages, they found fields of usage within the scope of many treatment protocols designed for diseases such as preeclampsia, rheumatoid arthritis, Helicobacter pylori infection, type 2 diabetes mellitus, bipolar depression, cancer and Wilson's disease. Obesity and depression are also included in this list (Figure 1).

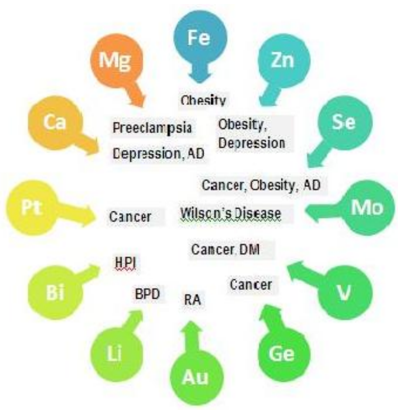

Figure 1. Trace elements in the treatment protocols of diseases. [AD; Alzheimer's Disease, HPI; Helicobacter

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pylori infection, DM; diabetes mellitus, BPD; bipolar depression, RA; rheumatoid arthritis]

A study performed a meta-analysis combining data from multiple studies revealed that obesity increased the risk of depression, while depression was also predictive of developing obesity[2]. Deficiencies and toxicities of some elements may cause weight gain leading obesity, which is increasing worldwide particularly among children and adolescents[3]. In a similar manner, elevated or reduced levels of metals may be indicators of depression. The associations between metals and members of neurotransmitter systems are also involved[4]. Iron, zinc, copper and selenium are essential during growth and development. They are also important during the evaluation of both obesity and depression. In this review, the relationship between childhood obesity and depression in children and adolescence as well as their associations with trace elements are going to be discussed under the light of very recent studies.

Iron

Iron can affect the clinical course of several chronic metabolic diseases such as obesity and associated diseases type 2 diabetes and atherosclerosis[5].

Obesity is associated with a higher prevalence of iron deficiency in children and adolescents. Adiposity may lead to reduced response to oral iron[6].

Iron distribution is altered both at the cellular and tissue levels in obesity. Adipose tissue plays a predominant role in this change. Increased fatty acids may contribute to the changes in iron-rich adipose tissue macrophage phenotype and their reduced capacity to handle iron[7].

The prevalence of obesity and diabetes mellitus in hereditary hemochromatosis may be associated with the degree of iron overload besides various other factors[8].

Systemic iron deficiency and low iron levels are observed in obesity and closely associated with adiposity. However, several other factors may influence the role of iron status in adiposity[9-12]. Where iron deficiency remains prevalent but rates of obesity are high, the use of corrected serum ferritin levels is recommended to assess iron deficiency status [13]. Obese individuals displayed lower iron absorption possibly due to subclinical inflammation associated with obesity[14]. With increasing BMI, the estimated body iron was relatively lower. Iron status in the newborns is impaired by maternal obesity and excessive weight gain during pregnancy[15]. Iron status and inflammation may be improved by weight reduction[16].

Iron status affect cognitive performance in children. Infants with iron deficiency anemia are associated with lower cognitive, motor, social-emotional and neurophysiological development. It is important to protect the developing brain from iron deficiency [4,17,18].

Depression is negatively associated with iron intake[19]. Total iron intake was found to be lower in children with depressive symptoms compared to the children with non-depressive symptoms [20].

Zinc

Zinc supplementation improves zinc indices but excess amounts induce iron deficiency. Depression is negatively associated with zinc intake[19]. Zinc transporters and metallothioneins are important in maintaining zinc homeostasis in the brain. There are very recent evidences supporting the hypothesis that zinc dyshomeostasis may be involved in the pathophysiology of depression [21].

Upon evaluation of school children and adolescents for depression using CDI-score analysis, CDI scores correlated negatively with physical activity and zinc [22].

Zinc is known to have a positive effect as an adjunctive therapy on reducing depressive symptoms. Zinc monotherapy has been reported to improve mood in overweight and obese subjects most likely through increasing brain-derived neurotrophic factor levels [23]. Zinc is proposed as a marker of depression. Zinc supplementation was found to produce antidepressant effects24.

The negative correlations between zinc concentrations and leptin as well as high fat diet support the interrelationship between obesity and zinc metabolism. The prevalence of type 2 diabetes is high in populations having high rates of overweight and obesity. The insulin mimetic actions of zinc as well as its role as a regulator of oxidative stress, inflammation, apoptosis and insulin secretion are known. Zinc has been shown to have beneficial effects on glycemic control by reducing glucose and glycated hemoglobin levels[25].

The association of low zinc concentrations with lipids, inflammation and insulin resistance has been observed in obese and overweight children[26]. Low zinc concentrations as well as a significant negative correlation between serum leptin and zinc levels were reported in obese children[10]. Low zinc levels were observed in obesity due not only to the intake but also to the pattern of zinc distribution altered by body fat composition or some inflammatory processes. As a result of dietary intervention, the redistribution of zinc, which is not affected by zinc intake has been observed with the decrease of body fat in obese adolescents[27].

Zinc finger proteins, one of the largest classes of transcription factors in eukaryotic genomes, have been documented as important functional contributors to the regulation of adipogenesis. They may become promising targets to combat obesity[28]. Replication initiator 1 is characterized as a zinc finger protein involved in DNA binding and bending during initiation of DNA replication. It is highly expressed also in adipose tissue and suggested as a candidate gene for obesity. Its role in adipocyte function suggests its emergence as a promising therapeutic target in obesity[29]. A transiently responsive zinc finger protein, ZNF395, coordinate the transcriptional regulatory pathway with peroxisome proliferator-acivated receptor gamma 2 obesogene, which may stimulate lipid uptake and adipogenesis by fat cells[30].

Zinc-α_2-glycoprotein is an adipokine with the potential as a therapeutic agent in the treatment of obesity and type 2 diabetes. Its oral administration increases serum levels through interaction with β-adrenergic receptors

[31]. This adipokine reduces body fat by increasing lipolysis. It may participate in depletion of adipose tissue. Due to its involvement in fat wasting mechanisms, it may be useful in the development of new therapeutic agents related to the matter[32].

Copper

The obese children may be at a great risk of developing unbalanced essential trace element status, which may play roles in the pathogenesis of obesity. These are generally in the forms of deficiencies, particularly for iron, zinc and selenium. Copper exhibits an extraordinary pattern among those. Significantly higher copper levels were detected in obese children[10, 33].

High copper concentrations are correlated with higher LDL/HDL ratio in children and adolescents (34). Copper deficiency results in alterations in lipid metabolism, which may contribute to the deposition of lipids in myocardium and the concomitant body leanness[35].

Copper is a component of some antioxidant enzymes. Increased copper-zinc superoxide dismutase activity, total circulating copper as well as plasma copper concentrations were reported in obese children[36-39].

Reactions between copper and serotonin may contribute to the development of depression because copper may cause alterations in dopamine and norepinephrine levels[4,40].

There are enhanced demands in serotoninergic and dopaminergic signaling for their reward system that may lead to increased motivation for food consumption in overweight subjects [41].

When children and adolescents were evaluated with CDI-score analysis for depression, scores correlated positively with BMI and copper concentrations [22].

Selenium

Diets enriched with organic forms of selenium may cause positive changes in obesity, psychoemotional state of patients with cardiovascular disease, adaptive capacity. Selenium can also influence cognitive outcomes and protection of the brain from oxidative stress[18]. It increases activity, improves health and cognitive functions, mood stabilization, reduces anxiety and emotional lability[42]. Selenium deficient children had lower scores on all cognitive tests than normal children[18]. By this means, selenium supplementation was reported to produce antidepressant effects [24].

Selenium, as an essential trace element important to neurotransmission, is toxic at high levels. A doubling of the selenium level was found to be associated with 56 % higher odds of having depressive symptoms[43].

Obesity-related complications are related to chronic inflammation and oxidative stress. Trace element levels in obese children may vary due to poor nutritional habits. Serum paraoxonase (PON1) activities are reported to be lower in obese children. Also, a positive correlation between selenium levels and PON1 activities is detected. This may be the indicator of a relation between selenium and antioxidant system in obese children[33].

In another recent study performed on the obese children, lower selenium levels are reported[10]. Low selenium and glutathione peroxidase levels, associated with increased cancer rates, are also the indicators of increased oxidative stress among the obese/overweight children[44].

With its anti-inflammatory and anti-oxidative nature, selenium may lead to alterations in obesity-related or mood disorders. Selenium compounds are suggested as promising approaches during the treatment of obesity and depression, both associated with inflammation[45].

Issues related to bariatric surgery

Obesity is a worldwide epidemic associated with diseases such as diabetes mellitus, metabolic syndrome and cardiovascular diseases. Since current methods for weight loss are not very effective, surgical therapy may be recommended particularly for those with morbid obesity [46,47].

There are problems related to the trace element concentrations following bariatric surgery[46,47]. In a recent report, decreased blood copper and zinc as well as increased iron levels were observed regardless of the type of surgery[46]. Mineral malnutrition following bariatric surgery was noted. Malnutrition in essential minerals including calcium, zinc, copper and iron commonly occurs following bariatric procedures. If left untreated these may lead to devastating consequences such as poor immunity, anemia, hair loss, defects in neuromuscular function[48].

Among micronutrient deficiencies, iron and zinc deficiencies were reported in about 17-45 % and 12-91 % of the individuals, respectively, in bariatric patients. The high prevalence of nutrient deficiencies after obesity surgery makes life-long nutritional monitoring and supplementation essential[47].

On the other hand, decreased inflammation after surgery was reported. This was associated with more efficient iron absorption and increased iron availability for erythropoiesis[49].

Nutritional deficiencies are common after malabsorptive procedures for bariatric surgery. They often need the prescription of oral/parenteral iron[50].

Obesity is commonly associated with poor sleep, excessive daytime sleepiness and depressive mood. Bariatric surgery has beneficial effects on sleep quality and excessive daytime sleepiness. These postoperative improvements can be related to a reduction in depressive symptoms[51].

Bariatric surgery is becoming widespread for adolescents with certain and special morbid obesity criteria. However, due to the moral issues such as definition of obesity and treatment end-points, problems with justice and trust, more evidence on outcomes is needed to balance benefits and risks[52].

Conclusion

Associations among trace elements, monoamine neurotransmitters, obesity and depression are quite important for the good understanding of the matter (Figure 2).

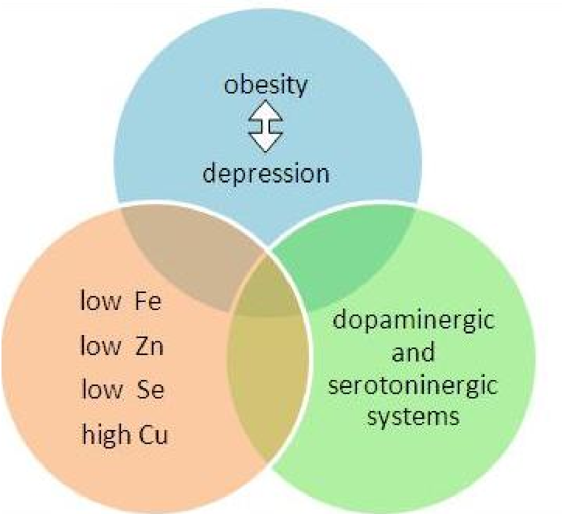

Figure 2. Associations among trace elements, monoaminergic systems, obesity and depression.

Weight gain increases the risk of life-threatening diseases. The relationship between obesity and hypoferremia is well-known. Protection of the developing brain from the negative effects of iron deficiency is important because of iron deficiency's association with poor mental development. Selenium supplementation significantly improves individuals' mood scores. Low selenium status is associated with depression and anemia, which may lead to poor mental development. Low selenium levels, adiposity, copper/zinc supplementation and reduced iron status are associated with obesity while zinc-α_2-glycoprotein serves as a lipid mobilizing factor. All display the significance of the close association between weight gain and the trace element status of the body.

The antidepressant-like activity of zinc involves interaction with the serotoninergic system. Reduced iron, zinc and selenium status, associations between copper and monoaminergic systems appear to lead to both depression and increased food consumption. Deficiency (iron, zinc, selenium) or overabundance (copper) of physiologically essential trace elements may lead to a range of diseases associated with obesity and depression.

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