OBES SURG
DOI 10.1007/s11695-007-9350-5

REVIEW

Nutritional Deficiencies in Morbidly Obese Patients: A New Form of Malnutrition?

Part B: Minerals

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Received: 23 September 2007 / Accepted: 1 November 2007

Abstract Even though in the Western world there is almost no limitation to a wide variety of food supply, nutritional deficiencies can be found in both normal-weight population and in the obese population. In this review, we examine the prevalence and manifestations of various mineral deficiencies in obese patients.

Keywords Mineral · Obesity · Deficiency
Metabolic syndrome

Introduction

Numerous factors influence our nutritional status. Consuming different amounts from a variety of foods does not necessarily mean that we meet our nutritional requirements. To evaluate these physiological requirements and translate them into dietary requirements, certain factors must be taken into account. The dietary-related factors include the chemical form of the nutrient, content of soil, geographic food origin, the nature of the dietary matrix, interactions between nutrients and other components, and food preparation and processing practices. The host-related factors include factors that influence intestinal absorption such as reductions in the secretion of hydrochloric acid, gastric acid, intrinsic factor, gastrointestinal surgery, and permeability of the intestinal mucosa; and systemic factors such as the patient's overall nutritional status, age, gender, body weight, ethnicity, genotype, and physiological state (such as pregnancy, lactation, and adolescences), and pathological state (such as infectious disease, status post-surgery, extensive burns, and other diseases). There are different suggested algorithms to evaluate the bioavailability of various nutrients, although their accuracy is limited [1]. As discussed in the previous review (part A), even though there is almost no limitation to a wide variety of food supply, nutritional deficiencies can be found in both normal-weight population and the obese population, mostly due to unbalanced dietary intake. It is interesting to note that the prevalence of nutrient deficiency is higher in overweight, obese, and morbidly obese compared to normal weight patients, suggesting that obese patients may consume an excess of dietary energy, but they may not meet their entire essential nutrient needs. Moreover, the absorption, distribution, metabolism, and/or excretion of these nutrients in overweight and obese individuals might be altered, as in the bioavailability of these nutrients. In this review, we examine the prevalence and manifestations of various mineral deficiencies in obese patients.

A literature search using PubMed, Ovid, and the Cochrane Databases (all until July 2007) was performed using the following terms in various combinations: obese, obesity, deficiency, diet, dietary, with all the essential minerals. Electronic links to related articles; references of selected articles were searched as well. Language restrictions were not applied.

(Part A: Vitamins was published in the previous issue of OBESITY SURGERY).

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Magnesium Deficiency

Magnesium is essential to all living cells. Maintaining normal concentration of extracellular magnesium and calcium is essential for regular neuromuscular activity. Only 1% of body magnesium is in the extracellular fluid, thus the serum levels of magnesium may not accurately reflect the total body magnesium stores [2].

Magnesium is absorbed mainly in the jejunum and ileum; this process is stimulated by 1,25-dihydroxyvitamin D [1,25(OH)2D] and can reach up to 70% of absorption in extreme cases of depletion. Magnesium is excreted in the urine, and renal reabsorption is the main method of regulation of the levels in the serum. Magnesium reabsorption is increased by parathyroid hormone (PTH) and inhibited by hypercalcemia or hypermagnasemia [2].

Hypomagnesemia can result from various mechanisms such as gastrointestinal loss, renal loss (primary or secondary to medications or endocrine disorders) and more. These reasons include malabsorption, Crohn's disease, protracted vomiting, diarrhea, gastrointestinal surgery, renal tubular disease, ethanol abuse, diuretics and other medications (such as cyclosporine, aminoglycosids), hyperaldosteronism, diabetes mellitus, post parathyroidectomy, vitamin D deficiency, and treatment of vitamin D deficiency [1, 2].

Most dietary magnesium comes from vegetables, particularly dark green and leafy vegetables (such as spinach). Other food sources of magnesium include: legumes, fish, fresh meat, soy products (soy flour and tofu), seeds, nuts, whole grains (unrefined grains), and fruits or vegetables (such as bananas, dried apricots, and avocados) [3]. Therefore, "junk food" is usually lacking this essential element. Tap water and/or mineral water can be a source of magnesium, but the amount varies according to the water source [4].

Signs of magnesium deficiency may include anorexia, nausea, vomiting, fatigue, irritability, insomnia, and weakness. As the deficiency worsens, numbness, tingling, muscle contractions and cramps, seizures, psychiatric symptoms, arrhythmia, coronary spasms, hallucinations, and delirium may ensue. Severe deficiency can result in hypocalcemia and/or refractory hypokalemia [5]. Magnesium deficiency has been shown to correlate with a number of chronic cardiovascular diseases, including hypertension, diabetes mellitus, and hyperlipidemia [6–8] all of which are often associated with obesity. It is speculated that dietary-induced magnesium deficiency increases the urinary concentration of thromboxane and enhances angiotensin-induced aldosterone synthesis. These effects are associated with a decrease in insulin action, suggesting that magnesium deficiency may be a common factor associated with insulin resistance and hypertension [8]. Therefore, magnesium deficiency may be a key factor in causing metabolic syndrome in obese patients [8–11].

Dietary menu with high fructose intake also appears to be an important causative factor in the metabolic syndrome [9]. Fructose is a monosaccharide found in many foods such as honey, fruits, some root vegetables, corn syrup, fruit juice extracts, and is often recommended for and consumed by patients with diabetes mellitus or hypoglycemia because it has a low glycemic index. There is some experimental evidence implicating that high fructose diet combined with low-magnesium diet is associated with a subclinical chronic inflammatory reaction, which might be an important causative factor in the development of metabolic syndrome. Accordingly, magnesium deficiency combined with a high-fructose diet induces insulin resistance, hypertension, dyslipidemia, endothelial activation, and prothrombotic changes in combination with the up-regulation of inflammatory markers and oxidative stress [9]. Thus, hypomagnesaemia may be associated with some micro- and macrovascular complications in diabetic patients, such as cardiovascular disease, retinopathy, and neuropathy [12].

The association between magnesium deficiency and insulin resistance was also found during childhood. Serum magnesium deficiency in obese children has been attributed to possible reduced dietary intake. Magnesium supplementation or increased intake of magnesium-rich foods was recommended as a potential tool for prevention of type 2 diabetes in obese children [13]. Low dietary intake of magnesium may not be the only factor causing hypomagnesemia; it is possible that excessive urinary magnesium loss associated with glycosuria in diabetic patients may contribute to hypomagnesemia even when the intake is adequate [14, 15].

Analyzes of micronutrient intake in obese and non-obese youth discovered that in the obese group, 27% had inadequate magnesium intake, whereas energy intake was 124% of estimated need, 32% of which came from fat. The investigators also found that the non-obese children had a similar prevalence of inadequate intake of micronutrients, and consumption of 107% of estimated need for energy; 31% of the energy came from fat [16]. Even in the non-obese population, the dietary intake of magnesium may be inadequate leading to subsequent deficiency.

Larger prospective studies are needed to substantiate the potential role of dietary magnesium supplementation as a possible public-health strategy in obese patients with regard to the risk of diabetes and metabolic syndrome.

Selenium

Selenium is required only in trace amounts; it is involved in anitoxidative reactions, and therefore it has a potential protective role against chronic diseases such as cancer and cardiovascular disease. It is also required for normal thyroid

functions and immunological reactions [17–20]. The content of selenium in food depends on the selenium content of the soil where plants are grown or animals are bred. Animals that eat grains or plants that were grown in selenium-rich soil have higher levels of selenium in their muscles. Selenium also can be found in seafood. In the US, meats and bread are common sources of dietary selenium. Some nuts also contain selenium, especially Brazilian nuts which are rich with this element [21].

Abnormally low levels and deficiency of selenium were found in up to 58% of morbidly obese patients before bariatric surgery. It is interesting to note that one year after the procedure, only 3% of patients had abnormal levels or deficiency of selenium [22]. Among premenopausal women, higher body mass index (BMI) was significantly associated with low selenium levels. Among men 19 to 64.9 years of age, high BMI was also associated with low selenium; however, this association was not found among men aged 65 years or older. The overall prevalence of low selenium levels in that study population was low [23].

A low selenium level is an independent risk factor for cardiovascular disease, but also has been associated with high homocysteine levels and increased rates of a variety of cancers [24–27]. Over-consumption of selenium should be avoided, since high blood levels of selenium (>100 μg/dl) can result in gastrointestinal symptoms, hair loss, fatigue, irritability, nerve damage, and more [27].

Iron Deficiency

Iron deficiency is the most common mineral deficiency [28]. A study that assessed whether overweight children and adolescents are at increased risk of iron deficiency included 321 children and adolescents. The patients were divided into groups by BMI, age and gender. Iron levels below 8 μmol/l (45 mcg/dl) were noted in 38.8% of the obese children and 12.1% of the overweight children, compared with 4.4% of the normal-weight group ($P<$ 0.001). There was a significant negative correlation of low iron levels with increasing BMI, but not with age or gender. Among the children with iron deficiency, 26.6% also had iron deficiency anemia. The obese group accounted for 58.3% of the children with iron deficiency anemia. The authors concluded that iron deficiency is common in overweight and obese children; a significantly greater proportion of obese than normal-weight children have iron deficiency anemia, and that obese children should be routinely screened and treated as indicated [30]. Moreover, an analysis of cross-sectional data on children 2 to 16 years of age from the National Health and Nutrition Examination Survey III (1988–1994) indicated that the prevalence of iron deficiency increased as BMI increased, and iron deficiency was particularly common among adolescents. It was also found that children who were at risk for overweight and children who were overweight had a doubled risk of being iron-deficient compared to children who were not overweight [31].

In morbidly obese adults before laparoscopic gastric bypass, deficiency and abnormal levels of iron were found in 14 and 16%, respectively; deficiency and abnormal ferritin levels were found in 6 and 9%, respectively [21]. Flancbaum et al. [32] also found significant preoperative deficiencies of iron, ferritin, and hemoglobin in adult patients before bariatric surgery. An alarming finding in his study was that anemia was statistically significantly more common in men (40.7%) than in women (19.1%), although the authors did not elaborate on the type of anemia. Patients younger than 25 years of age were more likely to be anemic than patients who were older than 60 years. This was in correlation with iron deficiency, which was more prevalent in the younger group. African-Americans had significantly lower preoperative hemoglobin. This group also had the lowest measured levels of vitamin D, iron, and thiamine; consequently, the authors related these findings to a possible dietary origin. Other studies also indicated that iron deficiency anemia is most prevalent in African-American women, but its prevalence in adult men was reported to be only 2% [29].

Chromium

Chromium (Cr), a heavy metal, is a popular weight-loss and muscle enhancement supplement since it has been postulated to have effects on body composition, including reducing fat mass and increasing lean body mass. Therefore it is found in many sports foods and drinks and a variety of weight loss products; however, its efficacy and long-term safety are uncertain [33, 34]. Some forms of chromium (which differ in their ionic quality and stability) have both cytotoxicity and genotoxicity potential and are considered as carcinogens [34, 35]. In selected cases, chromium supplementation can also be nephrotoxic and result in acute tubular necrosis. There is no data of the exact prevalence of chromium deficiency in the general population.

In mammals, chromium is an essential nutrient involved in the metabolism of glucose, carbohydrates, insulin, lipids, and protein, and is required only in trace amounts. It is found in variety of foods like egg yolk, Brewer's yeast, calf's liver, beef, cheese, whole wheat bread, and wheat germ. Refined sugar and carbohydrates contain little or no chromium.

In glucose metabolism, it serves as a cofactor with insulin to facilitate glucose uptake and energy release. When chromium is absent, the efficacy of insulin is decreased, resulting in impaired glucose tolerance. The exact mechanism

of its functions is not completely understood; it was postulated that chromium increases the binding of insulin to cells, the number of insulin receptor, and activates insulin receptor kinase, thus result in potentiation of insulin signaling [33–35]. Chromium was reported to improve glucose blood levels in patients with disturbed glucose metabolism including glucose intolerance, type 1, type 2, gestational, and steroid-induced diabetes [36, 37]. Moreover, additional supplemental chromium was accounted to reverse neuropathy and glucose intolerance in a patient who received total parenteral nutrition [38].

Chromium deficiency is considered relatively rare because this element is only needed in trace amounts, and is usually seen in patients who undergo hyperalimentation for long periods of time [38]. Because insulin resistance is a common denominator in a cluster of cardiovascular disease risk factors, inadequate dietary intake of chromium was assumed to be associated with increased risk of diabetes and cardiovascular diseases [36, 37]. Deficiency of this element is not easily diagnosed. Plasma concentrations do not accurately reflect the chromium stores in the body [38]. One study that evaluated the correlation between plasma levels of chromium and its content in blood cells in both non-diabetic blood donors and diabetics type 2 patients, reported that compared to non-diabetic blood donors, diabetic patients had higher chromium values in plasma, erythrocytes, and platelets, whereas these patients had significantly lower chromium contents in polymorphonuclear and mononuclear leukocytes. It was also reported that worse metabolic control as assessed by HbA1c, resulted in higher levels of chromium concentrations in plasma and lower values in mononuclear leukocytes. The authors assumed that the altered chromium levels in plasma and in mononuclear cells during worsening hyperglycemia could be the result of an intracellular/extracellular redistribution of chromium, and high plasma levels of chromium might explain the renal chromium losses in diabetic patients, whereas the low levels of chromium in lymphocytes could reflect a decreasing chromium body state [39].

Care should be taken when prescribing chromium supplementation [40, 41]. Chromium supplements are available as picolinate, nicotinate, or chloride. The former compound has superior absorption compared to the other complexes; however, there are various reports about its safety [40]. There is no consensus about the role of chromium supplementation with regards to weight loss, effects on body composition, and effects on blood plasma insulin and glucose concentrations [42–45]. Some scientific references suggested that supplementing with chromium, most effectively with chromium Picolinate [Cr(pic)3], enhanced insulin utilization [36]; other reports indicated that the supplement had no demonstrated effects on body composition and on blood plasma insulin and glucose concentrations [34, 40].

Further investigation is indicated to determine the role of chromium supplementation for weight loss and control of glucose metabolism. Moreover, its absence from refined carbohydrates and its role in the metabolism of sugar and insulin activity, calls for a reevaluation of the prevalence of chromium deficiency in morbidly obese patients. It might be that the discrepancy between the studies is a result of difficulty in measuring the exact chromium status in the body, and the confusing intracellular/extracellular redistribution of chromium as suggested by Rukgauer and Zeyfang [39].

Zinc Deficiency

Various reports indicate that standard dietary intake is frequently marginal or deficient in zinc (Zn) [46, 47]. Clinical studies indicate that zinc is needed for DNA synthesis, cell division, gene expression, and the activity of various enzymes in mammals, and therefore achievement of normal growth, sexual maturation and function, maintenance of a normal appetite, visual, taste and smell acuity, and normal psychocognitive function. Zinc is also important for immunological reactions, wound healing, and preservation of the integrity of epithelial surfaces. Deficiencies are often seen in patients with malabsorption disorders such as Crohn's disease and in patients who are on prolonged total parenteral nutrition [48, 49]. Urinary zinc excretion is markedly elevated after trauma or surgery, but the exact mechanism for its deficiency in these patients is poorly understood [50, 51].

Zinc is found in a wide variety of foods. Oysters contain more zinc per serving than any other food, and cooking the oysters does not significantly reduce it, but the majority of zinc in the Western diet is provided by red meat and poultry. Other rich food sources include fortified breakfast cereals, beans, nuts, certain seafood, whole grains, and dairy products [52]. The bioavailability of zinc from the diet depends on various factors [1, 48, 49]. Phytates, which are phosphorus compounds found primarily in cereal grains, legumes, and nuts, can bind with minerals such as zinc, iron, and calcium, and decrease their absorption [53, 54].

Signs of zinc deficiency may include growth retardation, hair loss, diarrhea, delayed sexual maturation and impotence, eye and skin lesions, and anorexia. Weight loss, delayed healing of wounds, taste abnormalities, mental lethargy, and chronic infections may also occur [48, 55].

Zinc has an important role in adipose tissue metabolism by regulating leptin secretion and by promoting free fatty acid release and glucose uptake. It also plays a key role in the synthesis and action of insulin, both physiologically and in diabetes mellitus, partly by stimulating insulin action and

insulin receptor tyrosine kinase activity [56–59]. Altered metabolism of zinc was reported in patients with hypertension [60, 61]. Zinc concentrations in the plasma and erythrocytes were reported to be lower and urinary zinc excretion and serum insulin levels were reported to be higher in obese patients. A balanced hypocaloric diet, which significantly reduced the body weight, BMI, body fat percentage, and amount of body fat with a slight lowering of blood pressure and plasma levels of triglyceride, resulted in improved plasma concentrations of zinc in obese patients [62]; similar findings were reported by Di Martino et al. [63], indicating the distorted zinc metabolism in obese patients which do not signify a short-term metabolic result [64–66]. A study that investigated whether the nutritional status of zinc was associated with hyperinsulinemia in obese children and adolescents, evaluated the nutritional status by measuring zinc levels in plasma, erythrocyte, and 24-h urine excretion, and by atomic absorption spectrophotometry. Insulin was measured by radioimmunoassay. The dietary analysis that was conducted indicated that dietary intake of zinc by both obese subjects and controls had marginal concentrations of zinc. Zinc concentrations in plasma and erythrocytes were significantly lower in the obese group, whereas urinary zinc excretion and serum insulin were significantly higher, although the insulinemia and the other parameters of the nutritional status of zinc were not significantly correlated [64]. Evaluation of zinc concentrations in both serum and hair in obese (n=135) and non-obese patients (n=57) established that serum and hair zinc contents in obese patients were markedly lower than in control subjects by 22 and 34%, respectively. Moreover, the zinc content was inversely related to the BMI [67]. In morbidly obese patients who were candidates for LRYGBP, preoperative abnormal zinc levels and deficiency, were found in 30 and 28%, respectively [21].

These findings cannot be ignored. Zinc deficiency or abnormal metabolism plays a role in the metabolic syndrome [68, 69]. Morbidly obese patients who underwent bariatric surgery are prescribed life-long vitamin and mineral supplementation to avoid zinc deficiency among other important nutrients. Nutrient deficiency in this population might be a result of both inappropriate dietary intake and the surgical procedure itself. Future trials are needed to evaluate the role of zinc supplementation in terms of severity and prevention of metabolic syndrome, incidence of diabetes mellitus, reduction of insulin resistance, quality of life, diabetic complications, cost, and more.

Summary

The Western diet, with an excess of refined products such as sugar, alcohol, and fats, is often lacking essential nutrients, resulting in obesity, atherosclerosis, disturbed immunity, infections, allergies, cancer, and other chronic diseases. Moreover, the bioavailability of these nutrients is often altered in the obese. The exact prevalence of these deficiencies in obese patients is yet unknown. Supplementation alone is not the ultimate solution for these deficiencies, and weight-reduction might promote resolution of some of these deficiencies. Weight-reduction approaches should be undertaken with extreme care since they can also be associated with reduced intake of nutrients. Further studies are required to determine the prevalence, mechanism, consequences, and prevention of these deficiencies in the morbidly obese population. The role of nurtition in the development of chronic disease and obesity is still evolving; a novel discipline in this field is nutrigenomics, which might be the answer for this enigma.

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