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REVIEW ARTICLE

Physiology

Overfed but undernourished: recognizing nutritional inadequacies/deficiencies in patients with overweight or obesity

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Abstract

Overweight and obesity are highly prevalent throughout the world and can adversely affect the nutritional status of individuals. Studies have shown that many people with obesity have inadequate intake of iron, calcium, magnesium, zinc, copper, folate and vitamins A and B_{12}, likely as a result of poor diet quality. Nutritional inadequacies or deficiencies may also occur due to altered pharmacokinetics in the individual with obesity and due to interactions in those with overweight or obesity with various pharmaceuticals. However, it has been demonstrated that the adult population in the United States as a whole is deficient in certain micronutrients as a result of the availability and overconsumption of high-calorie, low-nutrient processed foods. Poor nutrition may contribute to the development of certain chronic conditions, such as type 2 diabetes, which is already more prevalent in those with obesity. Clinicians need to be aware of these gaps, particularly in those individuals with obesity who are undergoing bariatric surgery or taking pharmaceutical products long term to facilitate weight loss. Patients with overweight or obesity likely struggle to achieve a balanced diet and may benefit from consultation with a dietitian. Along with providing recommendations for healthy eating and exercise, supplementation with specific micronutrients or multivitamins should be considered for individuals at the highest risk for or with established deficiencies. Further research is needed to understand the factors underlying nutritional inadequacies in individuals with overweight or obesity, as well as the outcomes of treatment strategies employed to address them.

Introduction

The prevalence of adults with overweight (body mass index [BMI] = 25.0–29.9 kg m^{-2}) or obesity (BMI ≥30 kg m^{-2}) is high not only in the United States (US), but also worldwide [1–3]. Among the leading causes of preventable death, obesity is related to as many as 400,000 deaths each year in the US [1]. According to the 2013–2014 National Health and Nutrition Examination Survey (NHANES), it was determined that approximately 78.3% of adults in the US aged 20 years and over had overweight or obesity, with 32.7% having overweight, 37.9% having obesity and 7.7% having extreme obesity (BMI ≥40 kg m^{-2}) [3].

Obesity has increasingly been recognized as a risk factor for several nutrient deficiencies, which may seem surprising given the likelihood of overconsumption of calories in these individuals [4]. However, many of these additional calories are not from nutritious sources [4], and according to surveys conducted in the US and Canada, many individuals do not meet the recommended levels of micronutrients through diet [5, 6]. Contributing to the increasing prevalence of obesity is the greater availability of inexpensive foods that are rich in calories and are nutrient deficient [2, 7, 8].

Moreover, higher body weight as a result of increased adipose tissue may result in lower serum levels of vitamin D [9]. In addition, the metabolic changes that occur in individuals with obesity may also increase the requirements for certain nutrients [10], and treatment for severe obesity involving surgical procedures can worsen these nutrient deficiencies, and in some cases, may cause new ones to develop [4].

Patients with overweight or obesity are at a higher risk for various chronic diseases that can be influenced by nutrition, including osteoarthritis, type 2 diabetes, cardiovascular diseases, psoriasis, respiratory problems and cancer [11, 12]. Increased chronic low-grade inflammation in patients with obesity has been posited as the mechanism

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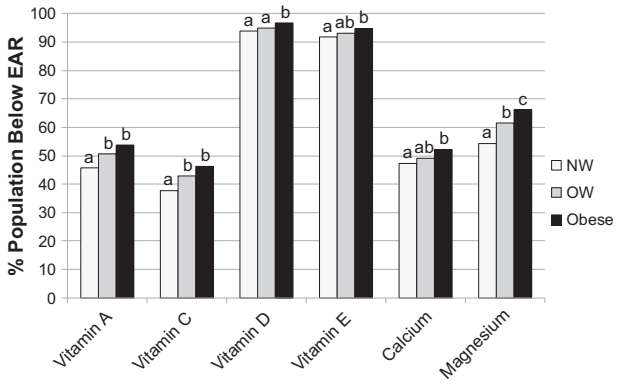

Fig. 1 Prevalence of vitamin and mineral intake below the Estimated Average Requirement by body weight status in adults ≥19 years of age. From Comparison of Prevalence of Inadequate Nutrient Intake Based on Body Weight Status of Adults in the United States: An Analysis of NHANES 2001–2008, Agarwal et al. Journal of the American College of Nutrition. 2015, Taylor and Francis Ltd. Reprinted by permission of Taylor and Francis Ltd (http://www.tandfonline.com) [19]. Based on data from National Health and Nutrition Examination Survey 2001–2008. [a,b,c]Bars with different letters are significantly different at $P < 0.05$. *EAR* estimated average requirement, NW normal weight, OW overweight

behind the increased risk [13, 14], and healthy dietary patterns have been shown to reduce markers of the chronic inflammatory response implicated in these conditions [15].

The purpose of this review is to increase awareness of the unique nutritional needs of patients with overweight or obesity, discuss the importance of addressing potential dietary gaps in this population and present strategies to improve overall nutritional status in individuals with overweight/obesity.

Nutritional status in individuals with overweight or obesity

Baseline data from studies of patients with morbid obesity prior to bariatric surgery have demonstrated the presence of micronutrient deficiencies in this population. In a study conducted in Chile of women with morbid obesity, 46% had vitamin D levels categorized as deficient (defined in this study as 25[OH]D <20 ng/mL), and blood levels of iron, calcium and vitamin B_{12} consistent with deficiency were measured in 13%, 13% and 11% of subjects, respectively [16]. In another study of women with morbid obesity in Spain, 10% were deficient in vitamin B_{12}, 25% in folic acid, 26% in vitamin D (defined as 25[OH]D <15 ng/mL), 68% in copper and 74% in zinc [17]. In a population of French women and men with BMI >35 kg m^{-2}, the most common inadequacy was in vitamin D, affecting 68% of subjects and with 25% having levels defined as deficient (25[OH]D <12 ng/mL); 35% were deficient in magnesium, 17% in iron and 17% in vitamin A [18]. Although these data were collected among patients seeking bariatric surgery, we expect that the findings would be representative of the general population with morbid obesity. Thus, it seems likely that micronutrient deficiencies are prevalent in individuals with morbid obesity. The specific causes or contributing factors underlying these findings remain to be proven.

Micronutrient deficiencies observed in individuals with obesity could be a function of a poor diet, with decreased intake of vitamins and minerals. An analysis of data from a nationally representative sample of normal-weight, overweight and obese adults from NHANES 2001–2008 [19] demonstrated that a considerable proportion of individuals across all weight categories had inadequate intake of multiple micronutrients, including vitamins A, C, D and E and the minerals calcium and magnesium. Compared with normal-weight subjects, obese individuals reported significantly lower levels of fruit intake, overall diet quality and micronutrient intake. Overweight and obese individuals had rates of micronutrient inadequacy that were comparable to or higher than the rates of those with normal weight (Fig. 1). These differences were small (absolute differences ranging from approximately 2–10%) but statistically significant and underscore the importance of evaluating potential gaps in micronutrient intake in this population with presumably greater macronutrient intake.

Besides inadequate dietary intake, deficiencies in micronutrients in individuals with obesity may also be a result of altered pharmacokinetics, including distribution, metabolism and elimination [20]. It has been demonstrated that the pharmacokinetics of some drugs, such as intravenous anaesthetics, benzodiazepines and aminoglycoside antibiotics, in patients with obesity are different from those of patients who are lean [10, 20, 21]. Most likely this is due to pathophysiological changes from increased adiposity in patients with obesity that affect pharmacokinetic parameters such as volume of distribution, protein binding, hepatic metabolism and renal clearance [10, 20, 21]. It could be hypothesised that the same pathophysiological changes that affect pharmacokinetics of drugs [21] (Table 1) affect micronutrient metabolism in similar ways. Obese subjects have increased blood volume, cardiac output, adiposity, lean mass and organ size, all of which can influence volume of distribution. The distribution of highly lipophilic compounds is more likely to be altered in obese patients; however, the exact degree to which these physiologic changes influence distribution can be highly variable and difficult to predict [21].

Data suggest that some micronutrients, such as vitamin D, may be sequestered in adipose tissue, which can result in

Table 1 Factors in individuals with obesity that can affect the pharmacokinetics of some drugs

Pharmacokinetic property	Altered physiology	Clinical observations
Absorption	↔,?	
Distribution		
Body composition	↑ Lean body mass ↑ Adipose tissue mass ↑ Organ size ↑ Blood volume ↑ Cardiac output	Lipid-soluble drugs tend to have ↑ volume of distribution
Protein binding	↔Albumin and total protein ↑ α_1-Acid glycoprotein ↑ Triglycerides ↑ Cholesterol ↑ Free fatty acids	↔Free fraction of acidic drugs ↑ Free fraction of basic drugs
Metabolism (hepatic)	↑ Splanchnic blood flow ↑ Number and size of parenchymal cells ↑ Parenchymal-cell degeneration ↑ Fatty infiltration ↑ Bile pigment retention ↑ Periportal fibrous tissue ↑ Periportal cellular infiltration	Studies have demonstrated ↓ clearance of high-extraction compounds
	↑ Focal necrosis ↔, ↓,? Phase 1 metabolism ↑ Phase 2 metabolism ↔Acetylation	Inconclusive studies on oxidation, reduction and hydrolysis Glucuronidated and sulphated drugs have ↑ clearance
Excretion (renal)	↑ Kidney size ↑ Glomerular filtration ↑ Tubular secretion	Drugs primarily filtered have ↑ renal clearance; compounds both filtered and secreted have demonstrated ↑ renal clearance values

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↔ No change, ? effect unknown, ↑ increased, ↓ decreased.

a decrease in their availability for metabolically active tissues [22–25]. It has also been hypothesised that simple volumetric dilution of vitamin D by the large fat mass in patients with obesity is responsible for apparent low blood 25(OH)D levels in this population [26].

Elevated levels of proteins and blood constituents involved in protein binding, such as triglycerides, cholesterol and free fatty acids, may influence the distribution of protein-bound micronutrients. Structural and functional changes in the liver and kidney in overweight and obese individuals can impair metabolism and clearance of exogenous substances. These changes are complex and may result in increases or decreases in elimination [21]. Further research is needed to determine whether micronutrient deficiencies in individuals with obesity are a result of changes in their metabolism or insufficient intake of these micronutrients, or both.

Another factor that can affect the metabolism of micronutrients and increase the risk of nutritional deficiencies is the use of bariatric surgery to facilitate weight loss in adults with extreme obesity [4, 27]. The type of bariatric surgery that is performed can have an influence on the incidence and significance of nutritional deficiencies of certain micronutrients and macronutrients, depending on which part of the alimentary canal is bypassed [4]. For example, iodine is absorbed in the stomach and small intestine [28], and folate, vitamin C and fat-soluble vitamins are absorbed in the ileum [27]. Copper is absorbed in both the stomach and duodenum, while vitamin B_{12} must bind to intrinsic factors in the stomach before being absorbed in the ileum [27]. Other micronutrients including iron, zinc, selenium, chromium, manganese, vitamins A, C, E and K, thiamine, riboflavin, folate, niacin, biotin, pyridoxine, pantothenate and calcium are absorbed in the duodenum and/or the jejunum [27]. Therefore, there is the potential for the absorption of certain micronutrients, such as those that are primarily absorbed in the stomach and the first part of the ileum, to be diminished in individuals undergoing gastric bypass and related surgeries [27].

While the causes of obesity may be due to various hormonal, genetic and metabolic processes, obesity is also a condition resulting from lifestyle factors including the excessive intake of food and/or insufficient physical activity

[11, 29–31]. The nutrient deficiencies associated with obesity may be partly due to overconsumption of foods that are high in calories but have low nutrient density [4]. This is most common in highly developed countries. For example, in children and adults living in the US, approximately 27–30% of the total daily consumption of calories comes from food that is low in nutrients, with added sugars and desserts providing nearly 18–24% of total calories [4, 32, 33]. In the general population, it has been demonstrated that an increase in the intake of low-nutrient-density foods is associated with a decrease in the consumption of nutrient-dense foods [33]. Specifically, diets in which more than 30% of energy intake comes from fats are correlated with lower intake of vitamins A and C and folate [4, 34]. In addition, consumption of sweetened beverages is inversely related to levels of calcium and vitamin D_3 due to lower intake of milk [4, 35]. Further causes of vitamin D_3 deficiency in individuals with obesity may involve decreased physical activity and, thereby, sun exposure, and increased storage of vitamin D_3 in adipose tissue, where it is unavailable for regulation of calcium and bone metabolism [4].

Consequences of poor micronutrient status

Because most micronutrients are present in all parts of the body and all body systems need all micronutrients, nutrient deficiencies can adversely affect the entire body, with more significant effects in some areas than in others [36]. It has been hypothesised that when there is an insufficient intake of micronutrients, there is a triage allocation of available vitamins and minerals in the body [37]. If the body does not receive enough necessary micronutrients, it will use whatever micronutrients are available to support the most important functions needed for short-term survival rather than those required for long-term health. For example, evidence suggests that when vitamin K is scarce it is directed toward its essential role in coagulation at the expense of its less critical role in bone metabolism [38]. Therefore, nutritional deficiencies may promote the development of chronic diseases [37].

As previously mentioned, individuals with overweight or obesity are at higher risk for other conditions/diseases that are also associated with poor nutrition, such as type 2 diabetes [8, 39, 40]. Individuals with obesity have a much greater risk of developing type 2 diabetes, with each unit of increase in BMI (approximately 2.7–3.6 kg) raising the risk of diabetes by 12.1% [41]. While the relationship between diabetes and obesity is multifaceted, lack of physical activity and excessive body fat mass contribute to the mechanisms for the development of diabetes, including increased insulin resistance and pancreatic β-cell dysfunction [42]. Excessive body fat, lack of physical activity and poor diet may account for as many as 87% of all new cases of type 2 diabetes [43]. Specific micronutrients are involved in glucose metabolic pathways, pancreatic β-cell function and the insulin-signalling cascade and, therefore, reductions in these vitamins and minerals (e.g., vitamin D and magnesium) in individuals with obesity may contribute to the development of diabetes [8, 44, 45].

The influence of micronutrient deficiencies on fat deposition has not been determined. Although the nature of the association is not well understood, the available evidence suggests that micronutrient deficiencies may contribute to the development of obesity [46] and obesity-related chronic diseases [47], suggesting that preventing or correcting nutritional inadequacies could be an economical means of preventing obesity and reducing the prevalence of chronic disease [46–48].

Emerging areas in obesity

Obesity has been associated with a decrease in focal grey matter volume of the brain, and deficits in cognitive performance have been demonstrated across almost all domains in these individuals [49–52]. In population-based studies, the length of time an individual had obesity across middle age was proportional to degree of cognitive impairment [52, 53]. Although the causal relationship between obesity and cognition has yet to be determined, obesity-induced inflammation and insulin resistance appear to have an effect on cognition in individuals with obesity [52, 54, 55]. In addition, some micronutrient deficiencies that are common in individuals with obesity, as well as those without (e.g., iron deficiency), may potentially diminish cognitive ability [56]. Studies have demonstrated that multivitamin supplementation can have some benefits in cognitive ability in apparently healthy older adults [57–59].

Stress is a factor that can be a barrier to weight loss, in that individuals find diets to be stressful and many people eat in order to cope with stressful situations [60, 61]. Results from animal studies [60] and clinical trials in humans [62–68] have demonstrated that supplementation with a combination of vitamins and minerals can decrease stress levels and improve mood. Whether or not an improvement of micronutrient status may help to reduce the stress associated with weight-loss diets remains to be elucidated.

A growing body of evidence suggests that the gut microbiota appear to be altered in obese individuals [69, 70]. Furthermore, a shift in the bacterial population of the microbiota has been observed following gastric bypass

[69], as well as with different weight-loss diets [71]. More recently, the impact of deficiencies in iron, folate, zinc and vitamin A have been shown to affect the microbiota of a defined human gut bacterial community in gnotobiotic mice [72]. Given the possible role of the gut microbiota in obesity and other metabolic conditions [73], the intersection of nutritional deficiencies in obese individuals and their impact on the microbiota is therefore of interest and a promising area of future research.

Evidence from long-term prospective cohort studies has demonstrated that inadequate sleep duration is associated with an increased risk of obesity, as well as various other chronic diseases [74]. Although small, difficult-to-detect chronic alterations are possible, the relationship between sleep and obesity does not appear to be driven by a substantial short-term impact on energy metabolism [75]. However, inadequate sleep has been shown to lead to poor dietary choices [76], and there is limited evidence of an association with lower dietary quality [77]. Moreover, a recent large community-based study in Korean men [78] demonstrated that the risk of obesity associated with inadequate sleep may be modified by micronutrient intake. Specifically, there was a higher risk of obesity observed among those individuals with poor sleep duration in combination with low dietary consumption of antioxidant vitamins (relative to those with higher intake), whereas those with optimal sleep did not have an increased risk of obesity, regardless of micronutrient intake. Finally, consistent with the emerging data mentioned above, there is some interesting preliminary evidence suggesting that the link between sleep loss and obesity could be mediated via subtle changes to gut microbiota that may promote increased energy uptake [79]. To what extent this plays a role in the development of obesity in the context of poor sleep requires further investigation.

Micronutrient gaps in individuals with overweight/obesity

Analyses of the prevalence rates of nutritional inadequacy in individuals with overweight or obesity have revealed several micronutrient gaps in this population [8].

Vitamins A and E

Low baseline serum levels of vitamin A among obese individuals prior to bariatric surgery have been demonstrated in up to 17% depending on the definition of inadequacy or deficiency [18, 44, 80–83]. In one such study, 14% of the population had vitamin A deficiency based on serum levels, while 24% showed clinical manifestations of deficiency (night blindness diagnosis via structured interview) [84]. Data from a nationally representative sample of adults in the US (NHANES III) showed lower levels of carotenoids among overweight and obese men and women relative to normal-weight subjects and lower vitamin E levels among obese/overweight women [85]. Analysis of dietary intake data of adults in the US from NHANES 2001–2008 [19] found significantly higher rates of inadequacy among overweight and obese individuals compared with normal-weight individuals for vitamin A intake and for obese individuals relative to those with normal body weight for vitamin E intake (Fig. 1). Specifically, the prevalence of inadequate intake among individuals with overweight or obesity was >50% for vitamin A and >90% for vitamin E. Use of supplementation significantly decreased the overall rates of inadequacy by 17–32% among obese individuals and by 20–39% among individuals with normal weight, indicating the potential value of supplementation with these vitamins in individuals not receiving adequate levels from their diets [19]. However, supplementation with retinol or beta-carotene should only be initiated after careful evaluation of individual requirement and family and lifestyle history. Higher intakes and elevated levels of retinol have been associated with adverse consequences (e.g., osteoporosis) [86]. Analyses have suggested that female versus male gender, region (USA versus Europe) and age at menopause are predictive of fractures associated with higher retinol intake [87]. Furthermore, a separate study conducted in home-dwelling older Norwegians found no increased risk of fractures associated with increased retinol intake, possibly due to a high intake of fish and cod liver oil in this population [88]. A determination of pre-supplementation vitamin A levels therefore may be warranted in developed countries with abundant sources in the normal diet (i.e., from meat and fish) [86]. Physiologic doses of beta-carotene, a vitamin A precursor that produces lower serum retinol levels [89], may provide a safer alternative than vitamin A, except for use of higher doses in smokers and asbestos workers [90]. Comparative studies on the relative safety of retinol and beta-carotene, however, are still required.

Vitamin B_1 (thiamine)

Low thiamine levels have been observed in 15–29% of individuals with obesity and in 17–79% of patients with diabetes [8, 91–95], with plasma concentrations being reduced 75% when compared with normal volunteers [93]. A number of studies have demonstrated beneficial effects of supplementation with thiamine on endothelial vascular function and oxidative stress in preclinical models, as well as in patients with type 2 diabetes [8, 96–99]. There are currently no data indicating that thiamine supplementation has any clinical benefit in patients with type 2 diabetes or obesity.

Vitamin B_{12}

Vitamin B_{12} deficiency, as a result of inadequate intake, malabsorption or lack of intrinsic factor, can result in haematological effects including megaloblastic anaemia, fatigue and weakness, gastrointestinal effects such as constipation, flatulence and loss of appetite and neurological effects including cognitive issues and numbness and tingling in the hands and feet [100]. Failure to address vitamin B_{12} deficiency may result in irreversible haematological and neuropsychiatric damage [101]. Supplementation with vitamin B_{12} has been shown to improve the rate of deficiency to roughly 4%; however, the use of multivitamins alone is not usually enough for preventing deficiency [4, 102, 103]. Vitamin B_{12} (350–600 µg/day orally) has been found to be effective in correcting this deficiency in most individuals, or a monthly injection given intramuscularly may be reserved for those who refuse or are unable to adhere to a daily oral supplement [4, 102, 104]. Inadequate levels of vitamin B_{12} have been reported in up to 11% of individuals with morbid obesity [16, 17, 105]. As a result, patients with obesity and clinical signs of vitamin B_{12} deficiency should receive supplementation.

Vitamin C

Vitamin C is a water-soluble antioxidant vitamin that is found in many fruits and vegetables [106]. It has been demonstrated that patients with diabetes have lower serum vitamin C levels than their healthy counterparts [107]. Analysis of the large National Institutes of Health—American Association of Retired Persons Diet and Health Study found a significantly lower rate of diabetes among those who took vitamin C supplements [108]. Vitamin C supplementation has also been associated with a significant improvement in insulin action, nonoxidative glucose metabolism and lower plasma insulin, LDL-cholesterol and apolipoprotein B concentrations in individuals with diabetes who take vitamin C supplements daily [109]. It has also been reported that almost 50% of individuals with obesity have inadequate levels of vitamin C (defined as serum vitamin C concentrations below the low end of the laboratory normal range [<4.6 mg/L]) [81] and that higher BMI is correlated with lower serum vitamin C levels [81, 85, 110]. In one study of patients undergoing elective abdominal surgery, preoperative rates of vitamin C deficiency (defined as serum vitamin C concentrations <0.3 mg/dL) ranged from 4% in individuals with BMIs in the normal range to 22% among individuals with class I obesity [110]. One patient in this study with vitamin C deficiency experienced postoperative bleeding requiring transfusion; however, no statistically significant association was found between the signs and symptoms of vitamin C deficiency and serum concentrations of vitamin C. Prospective studies demonstrating a clinical benefit of vitamin C supplementation in obese and/or diabetic patients are required.

Vitamin D

Vitamin D inadequacy is very common in individuals with obesity, with prevalence rates as high as 90% [8, 19, 111], and as described earlier, high rates of vitamin D deficiency have been reported in individuals with class II or III obesity (BMI ≥ 35 or ≥40 kg m^{-2}, respectively) [16–18]. In one study of obese prebariatric surgery patients, 57% were found to be vitamin D deficient (defined as 25[OH]D levels ≤ 20 ng/mL), 23% of whom had secondary hyperparathyroidism [105]. An inverse relationship between vitamin D levels and the incidence of type 2 diabetes has also been observed [112–117]. Some studies and meta-analyses show a potential benefit of supplementation with vitamin D in patients at risk for developing type 2 diabetes [8, 118, 119] and in patients with obesity and type 2 diabetes. In the Nurses' Health Study of 83,779 women, those who took vitamin D 800 IU/day were found to have a 23% lower risk of developing type 2 diabetes than those who took <200 IU/day [120]. A small study of short-term oral supplementation with 120,000 IU cholecalciferol administered every two weeks in males with obesity further demonstrated improved glucose tolerance and insulin sensitivity [121]. Taken together, these results suggest that vitamin D supplementation may prevent progression to diabetes and improve glucose sensitivity in the obese. Although it may seem rational to consider recommending vitamin D supplementation in patients with obesity [8] and perhaps particularly among individuals with obesity and prediabetes or type 2 diabetes, there are not yet any data to suggest that vitamin D ameliorates or reverses the condition.

Calcium

Most observational studies have reported an inverse relationship between the consumption of calcium and body fat, indicating that calcium has a positive effect on energy balance in individuals with overweight or obesity [122]. It has been hypothesised that a low-calcium diet may lead to hunger, poor compliance and, therefore, reduced weight loss in individuals who are trying to lose weight by decreasing their energy consumption [122, 123]. In one study, the impact of calcium plus vitamin D supplementation on the response to a diet-based weight-reduction program in females with overweight or obesity with very low calcium intake (≤600 mg/day) was tested

Table 2 Recommended dietary allowances or adequate intakes for vitamins and elements in adults according to the Food and Nutrition Board of the US National Academies Institute of Medicine 149

Micronutrient	RDA (plain type) or AI (italics) for adults/day
Vitamins	
Vitamin A	700–900 µg
Vitamin C	75–90 mg
Vitamin D	15–20 µg
Vitamin E	15 mg
Vitamin K	90–120 µg
Thiamine	1.1–1.2 mg
Riboflavin	1.1–1.3 mg
Niacin	14–16 mg
Vitamin B_6	1.3–1.7 mg
Folate	400 µg
Vitamin B_{12}	2.4 µg
Pantothenic acid	5 mg
Biotin	30 µg
Choline	425–550 mg
Elements	
Calcium	1000–1200 mg
Chromium	20–35 µg
Copper	900 µg
Fluoride	3–4 mg
Iodine	150 µg
Iron	8–18 mg
Magnesium	310–420 mg
Manganese	1.8–2.3 mg
Molybdenum	45 µg
Phosphorus	700 mg
Selenium	55 µg
Zinc	8–11 mg
Potassium	4.7 g
Sodium	1.2–1.5 g
Chloride	1.8–2.3 g

AI adequate intake, *RDA* recommended dietary allowance

[124]. Reductions in body weight and fat were substantially increased in those receiving supplementation compared with participants receiving placebo.

Magnesium

Obesity is a key risk factor for chronic diseases such as type 2 diabetes, atherosclerosis and cancer, and these conditions are also related to reduced magnesium levels [125, 126]. Studies in individuals with obesity have demonstrated that low magnesium levels are related to conditions that involve chronic inflammation [127–129]. Further studies are needed to determine the association of magnesium with obesity and comorbid conditions [125].

Iron

Iron deficiency (<8 µmol/L) has been documented to be 38.8% in children and adolescents with obesity and 12.1% and 4.4% in those with overweight and normal weight, respectively [130]. Iron deficiency and iron deficiency anaemia are general problems in the premenopausal, adult female population [131], but whether iron deficiency is aggravated in adult females with obesity remains to be seen. Another study has shown that iron deficiencies are more prevalent in younger patients (<25 years old) than in older patients (>60 years old) prior to receiving bariatric surgery [92]. Inadequate levels of iron may be the consequence of unbalanced nutrition, recurrent short-term restrictive diets or increased iron needs in individuals with obesity [130], as well as impaired absorption [132]. Therefore, iron levels in these individuals, and in particular, children and adolescents [130], should be monitored and treated to prevent the possible harmful effects of iron deficiency, such as anaemia.

Folic acid

An increased risk of inadequate intake of folate has been demonstrated in adolescents with waist circumference in or above the 80th percentile [133]. Studies conducted in Brazil and Spain have demonstrated folic acid deficiencies in up to 54.3% of adolescents and adults with obesity [17, 134]. In contrast, studies conducted in the US report very low prevalence rates of folic acid deficiency (0–6%), most likely due to folate-fortified foods [4, 105, 135].

Zinc

The incidence of reduced serum zinc in individuals with obesity has been observed in up to 28% of patients prior to bariatric surgery and in 36–51% of patients postsurgery [4, 82, 136].

Chromium

Chromium is an essential mineral that affects the action of insulin, and low levels in the body may lead to impaired glucose tolerance and the development of type 2 diabetes [137–140]. Studies have suggested that chromium supplements may help to increase lean muscle and stimulate fat loss, but these results have been conflicting [137, 141–144]. Data have indicated that chromium supplements may also decrease food consumption, hunger intensity and cravings for fat, although research on these effects is lacking [137, 145].

Table 3 Post-bariatric surgery vitamin supplementation recommendations

Supplement	Daily recommendations	
Mutlivitamin (contains folic acid)	AGB/VSG	One daily
	RYGB	One to two daily
	BPD-DS	Two daily
Calcium citrate with vitamin D_3	AGB	1200–1500 mg/day
	RYGB and BPD-DS	1800 mg/day
Vitamin D_3	RYGB	Consider 1000 IU/day
	BPD-DS	2000 IU/day
Vitamin B_{12}	RYGB	Crystalline 500 µg/day oral or 1000 µg/month IM
	BPD-DS	Monitor and start if needed
Elemental iron	RYGB and BPD-DS	65 mg elemental iron in menstruating females
Vitamin B_1	All procedures	Consider once daily in first six months
Vitamins A, K	BPD-DS	10,000 IU vitamin A and 300 µg vitamin K

Adapted from *Pediatric Clinics of North America*, volume 56, number 5, Xanthakos SA, Nutritional Deficiencies in Obesity and After Bariatric Surgery, pp. 1105–1121; Copyright 2009, with permission from Elsevier [4]

AGB adjustable gastric band, *BPD-DS* biliopancreatic diversion with duodenal switch, *IM* intramuscular, *RYGB* Roux-en-Y gastric bypass, *VSG* vertical sleeve gastrectomy

Biotin

Although data are lacking on the incidence of biotin deficiency in patients with obesity or diabetes, it has been demonstrated that patients with type 2 diabetes have lower biotin levels compared with healthy controls and that these low plasma levels are associated with hyperglycaemia [8, 146, 147].

Common-sense approaches to management of dietary gaps

The US Preventive Services Task Force recommends that clinicians counsel all patients on consumption of calories, fat, cholesterol, complex carbohydrates, fibre and sodium, as well as calcium and iron in women and adolescent girls [148]. The Food and Nutrition Board of the US National Academies Institute of Medicine has published the dietary reference intakes of 29 vitamins and minerals based on recommended dietary allowances or adequate intakes (Table 2) [149]. Physicians feel that, among many barriers, lack of time, teaching materials and sufficient training is the biggest obstacle preventing them from effectively counselling patients on nutrition [150, 151]. Individuals with overweight or obesity may already be struggling with eating a proper diet and may need to be referred to a dietitian or nutritionist for further counselling.

Role of dietary supplementation in the population with overweight/obesity

As detailed above, there are multiple potential micronutrient gaps in patients with overweight and obesity. Although more research is needed in most cases to understand the risks and benefits of supplementation with individual vitamins or minerals, for individuals with known deficiencies, such as those with documented iron-deficiency anaemia, supplementation is clearly indicated [152].

Individuals with overweight or obesity who are at higher risk for nutrient deficiencies include those undergoing bariatric surgery or taking pharmacological agents for long-term treatment of obesity, and these patients may need additional individual supplements [4, 153]. At a minimum, supplementation with a multivitamin is recommended following all bariatric surgical procedures, and additional supplementation has been recommended according to the type of bariatric surgery performed and risk for malabsorption (Table 3) [4]. Even patients undergoing purely restrictive procedures, such as laparoscopic adjustable gastric banding, which can cause micronutrient deficiencies due to the decrease in the amount of food that can be consumed, should receive supplementation with at least a multivitamin [153]. In addition, patients taking pharmacological agents long term for the treatment of obesity should be advised on dietary supplementation. For example, the use of orlistat has been shown to decrease the absorption of fat-soluble vitamins and, therefore, patients should take a daily multivitamin that contains vitamins A, D, E and K at least 2 h prior to its consumption [153].

For individuals with inadequate dietary consumption, a daily multivitamin can help ensure adequate intake of vitamins and essential minerals with minimal safety concerns [154]. NHANES data showed that the use of dietary supplements decreased the prevalence of inadequate intake of vitamins A, C and E and magnesium [155]. Similarly, many studies conducted in various populations have demonstrated improvement in micronutrient deficiencies through multivitamin and mineral (MVM) supplementation [156–159]. However, studies indicate that in populations with sufficient intake, dietary supplements may increase the risk of exceeding the tolerable upper intake level for some micronutrients [160–163] and thus may be more harmful than beneficial. Therefore, at present, dietary supplementation should be used routinely only in those with established inadequacies/deficiencies. More research is needed to clarify whether the micronutrient requirement is higher in

populations with overweight/obesity and to what extent any observed deficiencies are due to inadequate dietary intake, increased need based on size or both, and thus, if individuals with obesity may require tailor-made MVM supplementation to compensate for their specific deficiencies.

Preliminary findings, however, from two studies have promising clinical implications regarding the role of dietary supplementation for the population with overweight/obesity, suggesting that use of MVM supplements may have a beneficial effect on body weight, energy and appetite [164]. The Quebec Family Study compared body weight and composition, energy expenditure and Three-Factor Eating Questionnaires of users and nonusers of vitamins and dietary supplements. Compared with nonusers, male users of vitamins and dietary supplements had lower body weight ($P = 0.009$), fat mass ($P = 0.02$) and BMI ($P = 0.008$) and trended toward a greater resting energy expenditure ($P = 0.06$). Similar, though not significant, trends were seen in women [164]. Notably, however, individuals who use dietary supplements have been shown to have more healthy lifestyles in general than those who do not [165, 166], which may confound findings from observational studies and preclude any definitive conclusion that supplements had a direct effect on these outcomes. In a second study conducted by the same group, 45 adults with a BMI of 30–40 kg m^{-2} were randomized to receive either MVM or placebo in conjunction with an energy-restricted diet for 15 weeks. Although there was no difference between groups in terms of resting energy expenditure or anthropometric measures, there was a significant decrease in appetite in women randomized to MVM supplementation ($P < 0.05$) [164]. Although limited by the small sample size and the fact that the effect was found only in women, these findings in the context of a randomized, controlled trial are noteworthy and warrant further investigation in larger trials.

Conclusion

As the prevalence of obesity rises and the popularity of bariatric surgery increases, clinicians must be cognizant of potential pre-existing nutritional gaps in patients with overweight or obesity. These individuals are at risk for several micronutrient inadequacies/deficiencies, including vitamins A, C, D and E, as well as calcium and magnesium [19]. Patients with obesity should be counselled on the importance of preventing the development of diabetes and other complications through lifestyle changes and healthy food options [8]. In conjunction with dietary changes, MVM supplementation can serve an important role in preventing deficiencies in high-risk groups, including post-bariatric surgery patients and those taking certain medications, and in filling known gaps in those with inadequate intake/status. Additional studies are needed to better understand the unique causes of nutritional inadequacies in this population and outcomes of treatment strategies in individuals with overweight or obesity.

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Compliance with ethical standards

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