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Review Article

Nutritional deficiencies associated with anti-obesity pharmacotherapy

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ABSTRACT

Obesity is a chronic, multifactorial disease associated with substantial morbidity, mortality, and healthcare burden worldwide. The increasing prevalence of obesity has led to expanded use of anti-obesity pharmacotherapy as an adjunct to lifestyle modification for achieving sustained weight reduction and improving obesity-related comorbidities. Recent advances in pharmacological treatment, particularly with glucagon-like peptide-1 (GLP-1) receptor agonists and dual glucose-dependent insulinotropic polypeptide GLP-1 receptor agonists, have significantly improved weight-loss outcomes compared with earlier therapies. Despite these therapeutic benefits, growing evidence suggests that anti-obesity medications may influence nutritional status through mechanisms including reduced energy intake, appetite suppression, delayed gastric emptying, gastrointestinal adverse effects, and impaired nutrient absorption. These physiological changes may increase the risk of deficiencies involving both macronutrients and micronutrients, particularly during prolonged treatment or rapid weight loss. Orlistat has been consistently associated with reduced absorption of fat-soluble vitamins due to inhibition of intestinal fat absorption, whereas appetite-suppressing agents may contribute to inadequate intake of protein, iron, calcium, vitamin B12, folate, zinc, magnesium, and other essential nutrients by limiting overall food consumption. Individuals with obesity often present with pre-existing nutritional inadequacies, making them more susceptible to clinically significant deficiencies during pharmacological therapy. Preservation of lean body mass, maintenance of adequate protein intake, and ensuring sufficient dietary quality have become increasingly important considerations in modern obesity management. Nutritional assessment should therefore extend beyond body weight to include dietary evaluation, body composition, biochemical monitoring when indicated, and individualized nutrition support. Clinical management requires recognition of the distinct nutritional profiles associated with different classes of anti-obesity medications to facilitate appropriate dietary counseling, targeted supplementation, and regular follow-up. Integrating pharmacological therapy with comprehensive nutritional care may enhance treatment effectiveness while reducing the likelihood of adverse nutritional consequences. As the use of highly effective anti-obesity medications continues to expand, greater emphasis on nutritional monitoring and individualized patient management will be essential for maximizing long-term health outcomes and ensuring safe, sustainable weight management.

Keywords: Obesity, Anti-obesity pharmacotherapy, Micronutrient deficiencies, Macronutrient intake, Nutritional status

INTRODUCTION

Obesity is a chronic, multifactorial disease characterized by excessive adipose tissue accumulation that adversely affects health and increases the risk of type 2 diabetes mellitus, cardiovascular disease, metabolic dysfunction-associated steatotic liver disease, certain cancers, and premature mortality.[1] The global prevalence of obesity

has increased substantially over recent decades, making it one of the most significant public health challenges worldwide. Although lifestyle modification remains the cornerstone of obesity management, long-term weight loss maintenance through diet and physical activity alone is often difficult to achieve, leading to growing interest in pharmacological interventions as part of comprehensive obesity treatment strategies.[1,2]

The therapeutic landscape of obesity has evolved considerably with the introduction of newer anti-obesity medications (AOMs). Earlier pharmacotherapies such as orlistat primarily targeted nutrient absorption through inhibition of gastrointestinal lipases, thereby reducing dietary fat absorption.[3] More recently, GLP-1 receptor agonists (GLP-1 RAs), including liraglutide and semaglutide, as well as dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 receptor agonists such as tirzepatide, have demonstrated unprecedented efficacy in promoting weight loss through appetite suppression, delayed gastric emptying, and improved metabolic regulation.[1,2,4] These agents have transformed the management of obesity and expanded treatment options for individuals who do not achieve adequate weight reduction through lifestyle interventions alone.

Despite their effectiveness, anti-obesity medications may influence nutritional status through several mechanisms. Reduced energy intake resulting from appetite suppression can inadvertently decrease the consumption of essential macro- and micronutrients. Gastrointestinal adverse effects such as nausea, vomiting, diarrhea, and early satiety may further compromise dietary adequacy and nutrient intake.[4] In addition, certain medications directly interfere with nutrient absorption. Orlistat, for example, reduces intestinal fat absorption and has been associated with decreased absorption of fat-soluble vitamins, including vitamins A, D, E, and K, necessitating routine supplementation in many patients.[3]

Nutritional deficiencies are of particular concern because they may develop gradually and remain clinically unrecognized until significant physiological consequences emerge. Deficiencies in vitamins, minerals, protein, and other essential nutrients can negatively affect immune function, musculoskeletal health, hematological status, neurological function, and overall quality of life. Individuals with obesity may already exhibit pre-existing micronutrient inadequacies before treatment initiation, making them more vulnerable to further nutritional compromise during pharmacotherapy.[5] Consequently, assessment of nutritional status has become increasingly important as the use of highly effective weight-loss medications continues to expand. The growing popularity of GLP-1-based therapies has also generated interest in understanding their long-term nutritional implications. While these medications do not directly impair nutrient absorption to the same extent as orlistat, substantial reductions in food intake and rapid weight loss may alter dietary patterns and nutrient consumption.[4,5]

The increasing use of anti-obesity pharmacotherapy has highlighted the importance of evaluating nutritional consequences alongside weight-loss outcomes. While these medications effectively reduce body weight and improve metabolic health, their mechanisms of action may inadvertently affect nutrient intake and nutritional status. Orlistat, for example, reduces the absorption of dietary fat through inhibition of gastrointestinal lipases, which can subsequently impair the absorption of fat-soluble vitamins, including vitamins A, D, E, and K. Prolonged use without appropriate supplementation or monitoring may therefore increase the risk of clinically relevant micronutrient deficiencies.[5]

Newer incretin-based therapies, such as GLP-1 receptor agonists, present a different nutritional challenge. Rather than directly impairing nutrient absorption, these agents reduce appetite, increase satiety, and decrease overall food intake. Significant reductions in energy consumption may lead to inadequate intake of essential nutrients, particularly when dietary quality is poor. In addition, gastrointestinal adverse effects such as nausea, vomiting, and early satiety may further contribute to reduced nutrient consumption in some patients.[3] Rapid weight loss associated with these therapies may also increase the need for careful dietary planning to preserve lean body mass and ensure adequate protein intake.

MICRONUTRIENT DEFICIENCIES ASSOCIATED WITH ANTI-OBESITY PHARMACOTHERAPY

Micronutrient deficiencies represent an important yet often underrecognized consideration during anti-obesity pharmacotherapy. While the primary therapeutic goal of these medications is weight reduction and improvement of obesity-related comorbidities, alterations in nutrient intake, absorption, and metabolism may accompany treatment. The magnitude and nature of these nutritional effects vary according to the mechanism of action of the medication used, patient dietary habits, treatment duration, and the degree of weight loss achieved.[6,7]

Among currently available agents, orlistat has the clearest association with micronutrient depletion. By inhibiting gastric and pancreatic lipases, the drug reduces intestinal fat absorption by approximately 30%, thereby limiting the absorption of fat-soluble vitamins. Reduced bioavailability of vitamins A, D, E, and K has been reported in individuals receiving long-term therapy, particularly when dietary intake is inadequate or supplementation is not prescribed. Vitamin D deficiency deserves particular attention because obesity itself is frequently associated with low circulating vitamin D concentrations, creating a situation in which pharmacological treatment may further exacerbate an existing nutritional vulnerability.[7]

Nutritional concerns are not limited to medications that directly impair absorption. Appetite-suppressing therapies can substantially reduce total food intake, resulting in

lower consumption of vitamin- and mineral-rich foods. Clinical guidelines increasingly recognize the need to monitor nutritional status during pharmacological obesity treatment, especially in patients experiencing rapid or sustained weight loss.[7] Reduced dietary variety, early satiety, gastrointestinal discomfort, and food aversions may contribute to insufficient intake of micronutrients such as iron, folate, vitamin B12, zinc, magnesium, and calcium. These deficiencies may develop gradually and remain asymptomatic until physiological reserves become depleted.

The relationship between weight loss and micronutrient status is particularly relevant in individuals with pre-existing nutritional inadequacies. Obesity is frequently accompanied by suboptimal micronutrient profiles despite excessive energy intake, a phenomenon attributed to poor dietary quality, chronic inflammation, and altered nutrient metabolism. Consequently, significant reductions in food consumption during pharmacotherapy may increase the likelihood of clinically meaningful deficiencies if nutritional adequacy is not actively maintained.[1] Regular dietary assessment, biochemical monitoring when indicated, and individualized supplementation strategies are therefore increasingly incorporated into obesity management frameworks.

Growing reliance on highly effective anti-obesity medications has intensified interest in preserving nutritional health throughout treatment. Current evidence supports a more integrated approach in which weight reduction is evaluated alongside nutritional quality, micronutrient sufficiency, and long-term metabolic well-being, particularly in patients receiving prolonged pharmacological therapy or experiencing substantial reductions in caloric intake.[8]

MACRONUTRIENT INTAKE AND NUTRITIONAL STATUS DURING TREATMENT

Changes in macronutrient intake are frequently observed during anti-obesity pharmacotherapy and may have important implications for overall nutritional status. Most contemporary anti-obesity medications promote weight loss through appetite suppression, enhanced satiety, delayed gastric emptying, or reduced nutrient absorption, leading to a substantial decline in daily energy intake. While caloric restriction is essential for weight reduction, excessive reductions in food consumption may compromise the intake of protein, fats, and carbohydrates required to maintain physiological function and preserve lean body mass.[9]

Protein intake has received considerable attention in patients undergoing pharmacological weight management. Significant weight loss is often accompanied by reductions in both adipose tissue and fat-free mass. Inadequate protein consumption may accelerate the loss of skeletal muscle, potentially impairing physical function, metabolic health, and long-term weight maintenance. Reports involving GLP-1 receptor agonists have highlighted the importance of ensuring sufficient dietary protein during treatment, particularly among older adults and individuals with lower baseline muscle reserves. Preservation of muscle mass is increasingly recognized as a critical component of successful obesity management rather than focusing solely on reductions in body weight.[5]

Dietary fat intake may also be altered during treatment. Patients receiving orlistat frequently reduce fat consumption to minimize gastrointestinal adverse effects, including steatorrhea and fecal urgency. Although this behavioral adaptation may improve treatment tolerability, excessive restriction of dietary fat can influence energy balance, satiety, and the intake of essential fatty acids. Very low-fat diets may further limit the consumption of foods that provide fat-soluble vitamins and other bioactive compounds important for health maintenance.[10]

Carbohydrate intake often declines as overall food consumption decreases, although the extent of reduction varies according to individual dietary patterns. Reduced caloric intake can improve glycemic control and insulin sensitivity, particularly in individuals with obesity and type 2 diabetes mellitus. However, prolonged dietary inadequacy may contribute to fatigue, reduced exercise capacity, and diminished adherence to lifestyle interventions when nutritional planning is insufficient. The quality of carbohydrate sources remains relevant, as diets rich in whole grains, fruits, vegetables, and legumes provide dietary fiber and essential micronutrients that support metabolic health during weight-loss therapy.[11]

PHARMACOLOGICAL MECHANISMS CONTRIBUTING TO NUTRITIONAL DEFICIENCIES

The development of nutritional deficiencies during anti-obesity pharmacotherapy is closely linked to the distinct pharmacological actions of currently available medications. These agents influence nutrient status through multiple pathways, including impaired nutrient absorption, reduced dietary intake, altered gastrointestinal physiology, and changes in energy metabolism. The extent to which these mechanisms affect nutritional health depends on treatment duration, medication class, baseline nutritional status, and the magnitude of weight loss achieved during therapy.[12]

Orlistat provides the most direct example of a pharmacological mechanism capable of influencing nutrient availability. By inhibiting gastric and pancreatic lipases within the intestinal lumen, the medication prevents the hydrolysis and absorption of a substantial proportion of dietary fat. Since the absorption of vitamins A, D, E, and K depends on normal lipid digestion and micelle formation, long-term treatment may reduce the bioavailability of these fat-soluble micronutrients. Clinical recommendations therefore commonly include

routine multivitamin supplementation and periodic nutritional monitoring for patients receiving prolonged therapy.[13]

GLP-1 receptor agonists produce nutritional effects through a different pathway. These medications act on central and peripheral mechanisms regulating appetite and satiety, resulting in decreased hunger, earlier meal termination, and lower overall caloric intake. Delayed gastric emptying further contributes to prolonged fullness after meals. Although these actions support effective weight reduction, they may also limit the consumption of foods required to meet daily nutritional requirements. Persistent gastrointestinal symptoms such as nausea, vomiting, abdominal discomfort, and reduced appetite can intensify this effect, particularly during dose escalation phases of treatment.[14]

The physiological adaptations accompanying substantial weight loss may further influence nutritional status. Reduced energy intake often leads to lower absolute consumption of protein, vitamins, minerals, and essential fatty acids. Patients frequently modify food choices to avoid gastrointestinal symptoms or to accommodate diminished appetite, which may narrow dietary diversity and decrease nutrient density. Such dietary changes can become clinically relevant when treatment is maintained over extended periods or when weight loss occurs rapidly. Individuals with pre-existing micronutrient insufficiencies may be especially vulnerable because pharmacotherapy-related reductions in food intake can compound deficiencies already present before the treatment initiation.[15]

DRUG-SPECIFIC NUTRITIONAL RISKS AND CLINICAL CONSIDERATIONS

Nutritional risks associated with anti-obesity pharmacotherapy vary according to the mechanism of action of each medication, making drug-specific assessment an important component of patient management. Differences in nutrient absorption, appetite regulation, gastrointestinal tolerability, and patterns of food intake may influence both the type and severity of nutritional disturbances observed during treatment. Recognition of these variations allows clinicians to tailor monitoring strategies and dietary recommendations to individual therapeutic regimens.[16]

Orlistat remains the anti-obesity medication most consistently linked to nutrient malabsorption. Its inhibition of gastrointestinal lipases reduces the absorption of dietary fats and consequently affects the uptake of fat-soluble vitamins. Patients receiving long-term treatment may develop suboptimal levels of vitamins A, D, E, and K if supplementation is not provided. Reduced absorption of beta-carotene has also been reported. Clinical practice guidelines therefore recommend administering multivitamin supplements at a time separate from orlistat dosing and maintaining ongoing surveillance of nutritional status, particularly among individuals with restricted dietary patterns or pre-existing deficiencies.[17]

GLP-1 receptor agonists such as liraglutide and semaglutide present a different nutritional profile. These medications primarily influence appetite regulation through central and peripheral pathways that promote satiety and reduce food intake. Substantial decreases in caloric consumption may contribute to lower intakes of protein, vitamins, and minerals when food quality is not maintained. Gastrointestinal adverse effects, including nausea, vomiting, and early satiety, may further limit dietary adequacy. Patients experiencing persistent symptoms often modify food choices toward smaller and less varied meals, potentially reducing nutrient density over time. Clinical attention is therefore directed toward maintaining adequate protein intake and encouraging consumption of nutrient-rich foods during periods of reduced appetite.[18]

Combination therapies and emerging incretin-based agents capable of producing greater weight reduction may amplify nutritional concerns associated with prolonged decreases in energy intake. Individuals achieving large reductions in body weight may experience changes in body composition, including losses of lean mass when dietary protein intake is insufficient. Older adults, patients with chronic disease, and those with baseline nutritional inadequacies may require closer monitoring because physiological reserves are often lower in these populations. Nutritional screening, dietary counseling, anthropometric assessment, and selective laboratory evaluation may help identify deficiencies before clinically significant consequences develop.[19]

CONCLUSION

Anti-obesity pharmacotherapy has become an effective strategy for achieving clinically meaningful weight loss, but its impact on nutritional status warrants careful consideration throughout treatment. Drug-specific mechanisms may contribute to deficiencies in essential macro-and micronutrients, particularly during prolonged therapy or substantial weight reduction. Routine nutritional assessment, individualized dietary counseling, and appropriate supplementation can help minimize these risks while supporting treatment success. Integrating nutritional monitoring into obesity management is essential for optimizing both metabolic outcomes and long-term patient health.

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