Current and Future Medical Treatment of Obesity

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KEYWORDS

• Obesity • Pharmacotherapy • Weight management

KEY POINTS

- Obesity is a public health concern that continues to increase in prevalence in the United States.
- Obesity is a complex disease involving metabolic and neurohormonal processes.
- Several FDA approved drugs work on weight-regulating mechanisms to help with weight loss.

INTRODUCTION

Obesity is a global public health concern that has continued to spread. Epidemiologic data from 2014 reported the prevalence of obesity in the United States to be 35% among men and 40% among women.[1] Compared to 25 years ago when less than 15% of the nation was considered obese.[2] The obesity epidemic has placed an economic burden on the US health care system. The annual medical cost of obesity in the United States was estimated at $147 billion in 2008, with per capita medical expenses 42% higher per person with obesity compared with a person with normal weight.[3] In addition, obesity is associated with job absenteeism costing approximately $4.3 billion annually as well as lower productivity while at work, costing employers $506 per worker with obesity per year.[4,5]

In 2013, obesity was officially recognized as a disease state by the American Medical Association. For adults, the World Health Organization (WHO) defines normal weight as a body mass index (BMI, expressed in kilograms of body weight/height in meters squared) of 18.5 to 24.9 kg/m^2 and overweight as a BMI of 25 to 29.9 kg/m^2. Obesity is further classified into class I for BMI 30 to 34.9 kg/m^2, class II for BMI 35 to 39.9 kg/m^2, and class III for 40 kg/m^2 and above.[6]

Obesity results in many health complications. There are mechanical consequences of increased fat mass and body weight, such as osteoarthritis, obstructive sleep apnea, and urinary incontinence, as well as metabolic consequences due to the hormonal and inflammatory functions of adipose tissue, such as insulin resistance, type II diabetes, cancer, dyslipidemia, hepatosteatosis, and hypertension.[7–12] Tissue inflammation is an

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Table 1
WHO classification of Body Mass Index

BMI (kg of Body Weight/Height in Meters Squared)	WHO Classification
18.5–24.9	Normal weight
25.0–29.9	Overweight
30.0–34.9	Class 1 obesity
35.0–39.9	Class 2 obesity
40.0 and above	Class 3 obesity

important mechanism linking obesity to insulin resistance in metabolically active organs, such as liver, skeletal muscle, and adipose tissue.[13–15] Adipose tissue is an active endocrine organ that secretes a variety of hormones and proinflammatory cytokines, including leptin, interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-alpha), resistin, and adiponectin. The adipose tissue–derived hormone leptin exerts its inhibitory effects on food intake primarily by modulating the function of anorectic stimulating neurons in the arcuate nucleus of the hypothalamus.[16] Under conditions of diet-induced obesity, this body of neurons in the hypothalamus becomes resistant to leptin, and as a result, the signaling process for satiety appears to be blunted. Evidence of gliosis in the mediobasal hypothalamus of obese humans, assessed by MRI, suggests neuronal injury in an area crucial for body weight control.[17] Inflammatory markers IL-6 and TNF-alpha as well as resistin secreted by adipocytes promote insulin resistance linked to obesity.[18–21]

Because of counterregulatory neurohormonal mechanisms aimed at maintaining fat mass as a survival measure, weight regain is very common after diet-induced weight loss.[22] Antiobesity pharmacotherapy should be considered as an adjunct to diet and behavioral modification in order to facilitate weight loss or promote long-term weight maintenance. In addition to directly promoting weight loss, antiobesity pharmacotherapy can either directly or indirectly treat comorbid conditions associated with obesity, including prediabetes, type 2 diabetes mellitus (T2D), obstructive sleep apnea, hypertension, and dyslipidemia. Patients and physicians should recognize that expected weight loss from obesity pharmacotherapy is 5% to 10% of total body weight (TBW). For patients with severe obesity (class III), multiple medications or pharmacotherapy in addition to surgical intervention may be considered.

Adjuvant pharmacologic treatments should be considered for patients with a BMI greater than 30 or with a BMI greater than 27 who also have concomitant obesity-related diseases and for whom dietary modifications and physical activity has not been successful.[23] Obesity is a chronic disease requiring continuous management and ongoing interventional efforts, including long-term treatment. Several weight-loss agents have been approved by the US Food and Drug Administration (FDA) for weight management, including phentermine, orlistat, phentermine/topiramate ER, lorcaserin, buproprion/naltrexone, and liraglutide (**Table 1**).

PHENTERMINE

Phentermine was approved by the FDA in 1959 and has been the most commonly prescribed short-term (up to 12 weeks) medication for weight loss. Phentermine is primarily a noradrenergic and possibly dopaminergic sympathomimetic amine.[46] The standard adult dose is up to 37.5 mg daily before breakfast. However, dosages should be individualized to achieve adequate response with the lowest effective dose. A quarter tablet (9.375 mg) or a half tablet (18.75 mg) may be adequate for some patients. A 28-week, randomized, controlled trial compared phentermine 7.5 mg, phentermine 15 mg, topiramate ER 46 mg, topiramate ER 92 mg, with a combination of