PERSPECTIVE

Goals for the treatment of obesity using new pharmaceuticals and non-pharmacological agents

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ABSTRACT

Type 2 diabetes, the primary metabolic complication of obesity, has become a global epidemic, necessitating the development of fresh approaches to both treating and preventing the disease. While essential for treating obesity, a good diet and regular exercise are frequently insufficient. Pharmacotherapy can help with compliance maintenance, reducing obesity-related health concerns, and enhancing quality of life. In the last two decades, there has been a tremendous improvement in our understanding of the cerebral and peripheral mechanisms driving homeostatic and hedonic aspects of food intake. Obesity may result from an imbalance in one or more of these factors.

INTRODUCTION

The WHO reports that since 1975, the prevalence of obesity has nearly tripled worldwide. The prevalence of obesity in the United States is currently 42.4%, the first time the national rate has above the 40 percent threshold, confirming the existence of an obesity issue in the nation. Obesity prevalence averages 24% throughout European nations, and it is alarmingly rising in developing nations as well. especially given the possibility of developing metabolic issues like Type 2 Diabetes (T2D). The urgent need for a solution necessitates the creation of health care task forces, the adoption of organized cross-sector policies, and powerful and thorough medical interventions on obese patients. Obesity is typically thought to be caused by a long-term energy imbalance between too many calories taken and too few calories expended. Despite this, the primary approaches to treating obesity, which focus on increasing exercise and decreasing caloric intake, typically fail, pointing to a more complicated underlying etiology. In reality, a variety of additional factors, including age, sex, genetics, neuroendocrine parameters, gut microbiota, concurrent drugs, socio-cultural level, ignorance, homeostatic hunger, uncontrolled eating, and emotional eating, could influence the chronic positive energy balance in obesity. Effective treatment options for this complicated medical illness are urgently needed due to the worldwide rising rates of obesity and its life-threatening comorbidities and consequences, particularly T2D. Obesity management and treatment goals include not only weight loss but also lowering the risk of complications and enhancing health. It is believed that a little clinical improvement can be attained with a modest weight loss (i.e., 5 to 10% of the starting body weight), along with lifestyle changes (diet adjustments and a modest increase in physical activity). Other significant goals that should be taken into account in the management of obesity include maintaining body weight loss, preventing weight gain, improving body composition, preventing and managing comorbidities and complications, improving quality of life and wellbeing, and assessing psychological status. For the treatment of obesity, a change in lifestyle behaviors is often necessary yet insufficient. The most successful weight-loss method currently available is bariatric surgery. However, after surgery, 20% to 40% of people don't lose enough weight. For instance, persons with higher preoperative BMIs, older ages, male gender, and obesity-related comorbidities such T2D, arterial hypertension, and sleep

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apnea syndrome show insufficient weight reduction more commonly. Additionally, it was discovered that pre-surgery disordered eating habits, increased hedonic hunger, and psychopathological problems were poor indicators of post-surgery weight loss. A key treatment option in these circumstances is the use of pharmacotherapy to manage obesity. Pharmacotherapy can help to maintain compliance, reduce health risks associated with obesity, and enhance quality of life. According to the most recent recommendations, patients with a BMI of 30 or below and at least one obesity-related co-morbidity should take into account pharmaceutical treatment as part of a holistic plan for managing their disease. After the first three months of therapy, the effectiveness of medication should be evaluated. The U.S. Food and Medicine Administration (FDA) has set strict requirements for a drug to be licensed for the treatment of obesity since the mid-1990s. At one year, the new medication must cause a weight loss of >5% as compared to placebo, or >35% of patients must lose >5% of their body weight. Additionally, the FDA stipulates that the anti-obesity medication must enhance cardio-metabolic biomarkers including blood pressure, cholesterol levels, and glycaemic management. The following anti-obesity drugs have received U.S. FDA approval to date: orlistat, phentermine, naltrexone Sustained Release (SR)/bupropion SR, phentermine/topiramate Extended Release (ER), liraglutide, and semaglutide. Setmelanotide, a sixth approved medication, is only available to people who have been given a genetic test-verified diagnosis of one of three certain uncommon genetic illnesses. Due to serious side effects, the FDA suggested that the previously approved medicine for obesity, lorcaserin, be taken off the market in the early 2020s. The European Medicines Agency has also approved phentermine, orlistat, naltrexone SR/bupropion SR, and liraglutide among these medications (EMA). The licensed medications' capacity to cause weight loss is thought to be between 3% and 7% effective. All of the medications on the aforementioned list have been taken into account for long-term use based on their safety profiles. A collection of four medicationsâ €"diethylpropion, phendimetrazine, benzphetamine, and phentermineâ €"were simultaneously approved by the FDA and the EMA for the short-term (8 week to 12 week) treatment of obesity. Patients with an initial BMI of 30 k g/m^2 or greater who have not responded to a suitable weight-reduction regimen may utilize any of these medications. Due to potential long-term negative effects, particularly on the cardiovascular system, their usage has been temporarily prohibited. With the exception of orlistat, the majority of current medications for obesity work by altering certain neuro-endocrine systems that are involved in the intricate regulation of hunger/satiety balance. Several different pharmaceutical and non-pharmacological approaches have come under scrutiny and have shown promise in aiding body weight loss during the past few decades. The goal of the current review is to provide an overview of recent research that aims to identify new potential neuropharmacological targets for the treatment of obesity. This is because we now understand more about the central and peripheral mechanisms underlying homeostatic and non-homeostatic hunger.