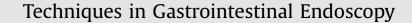
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Review of multimodal therapies for obesity treatment: Including dietary, counseling strategies, and pharmacologic interventions

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ABSTRACT

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1. Introduction

A multimodal approach to obesity management is supported by the significant failure rate of dietary, behavioral interventions, medical therapies, and the recognized recidivism after bariatric surgery [1-3]. This is similarly true for efforts to achieve maximum weight loss from minimally invasive weight loss procedures such as endoscopic gastroplasty, endoscopic balloon, and vagal blockade (18%-20%, 8%-15%, and 9.2% of loss of total body weight, respectively) [4,5]. Many patients who opt for minimally invasive bariatric methods would benefit from greater weight loss than the procedure can realistically provide. Bariatric surgery has been considered the gold standard treatment for severe obesity and the most effective option, but there are concerns about long-term efficacy with data demonstrating that more than 20% of patients experience weight regain with recurrence of comorbidities. In a longitudinal prospective study on 782 patients with obesity of both sexes, the mean

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There have been several recent advances in the field of obesity medicine in the areas of structured behavioral therapies, medically supervised diet programs, pharmacotherapy, and new interactive technologies. Patients with obesity now have several options for treatment beyond the standard lifestyle modifications of reducing calories and increasing exercise. Although bariatric surgery is the gold standard of treatment for patients with severe obesity, the problem of recidivism despite surgical intervention has lead obesity medicine specialists to develop multiple treatment modalities. The addition of tailored dietary intervention, targeted behavioral therapies, and the use of Food and Drug Administration approved antiobesity pharmacotherapy can allow patients to augment weight loss or to treat weight regain after bariatric surgery and endoscopic bariatric procedures. New technologies and webbased weight loss applications can allow patients to self-monitor in between office visits.

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increase in weight after Roux-en-Y gastric bypass was 8.8 kg within 60 months or 8.0% when compared with the lowest weight observed 18 months after surgery [1]. A cautionary tale may lie in the fact that laparoscopic gastric banding, once the most popular procedure, has experienced such a high rate of recidivism that the number of bands being inserted has declined drastically.

Our current understanding is that body weight and fat mass are subject to homeostatic control. In the disease of obesity, there is a disruption of this homeostasis owing to impaired neurohormonal signaling. There are 2 bodies of neurons in the arcuate nucleus of the hypothalamus that integrate information from peripheral signals coming from the fat cell, gut, and pancreas to regulate appetite and energy expenditure through thermogenesis. A body of neurons expresses the orexigenic peptides neuropeptide Y and agoutirelated peptide, which function to increase food intake and reduce energy expenditure. The other body of neurons express proopiomelanocortin (POMC), and cocaine- and amphetamine-regulated transcript, which are anorexigenic peptides that lead to a reduction in appetite and increase in energy expenditure by activation of downstream pathways [6]. Damage to POMC neurons and concomitant inflammation has been associated with diet-induced obesity and resistance to weight regulating hormones including leptin and insulin [7]. This physiologic disruption is an example of how the pathways regulating body weight are affected in the obese state.

According to the National Health and Nutrition Examination Survey published in 2012, one-third of US adults, and 1 in 6 US

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children and adolescents are obese [8]. Lifestyle interventions including a calorie deficit diet and physical activity remain the cornerstone of treatment for patients who are overweight and obese, and Roux-en-Y gastric bypass remains the gold standard to treat extreme obesity. However, neither lifestyle modification and medication nor bariatric surgery alone have been effective in providing lasting weight loss success. The rates of weight regain after bariatric surgery and diet-induced weight loss can be attributed to physiologic phenomena. Counter-regulatory neurohormonal mechanisms aimed at maintaining fat mass as a survival measure, as well as several environmental obstacles have been identified as promoting weight regain after diet-induced weight loss or even after bariatric procedures. Owing to the increased awareness of metabolic adaptation that occurs after weight loss, the concept of multimodal therapies aimed at helping patients lose weight and maintain loss of weight is of increasing interest.

Proper medical evaluation of the patient with obesity is necessary to initiate a stepwise multimodal approach. The patient evaluation can follow an algorithmic approach in the same way physicians evaluate other chronic diseases. The 2013 AHA/ACC/TOS guidelines propose assessing body mass index (BMI) to screen for overweight and obesity at each patient encounter [9]. Assessment should include height, weight, and calculation of BMI at each physician visit. If a patient is found to have a normal BMI (18.6 to <25), she or he should be advised to avoid weight gain, and potential risk factors for weight gain in the history should be clearly addressed. For example, medicines that have the potential to cause weight gain should be highlighted and possibly changed. If a patient meets criteria for overweight or obesity, the patient should be screened and treated for cardiovascular comorbidities including diabetes, hypertension, and hyperlipidemia. Intervention with antiobesity pharmacotherapy should be considered for patients with BMI > 30 or BMI > 27with comorbidity, and cases of BMI > 35 with medical complications or BMI > 40 should be offered bariatric surgical options. To maximize weight loss, all patients should have behavioral interventions and be introduced to technologies that can be incorporated into their routines that might facilitate long-term adherence.

2. Dietary approaches

In general, no dietary pattern of eating has proven superior in clinical trials. Trials suggest that the diet, which any given patient likes and finds easiest to comply with, will produce the greatest weight loss for that patient. In our opinion, lower carbohydrate diets appear to be associated with better compliance and increased metabolic rate in patients with prediabetes and diabetes [10]. More intensive approaches such as the use of liquid meal replacements may produce short-term weight loss, and in the case of weight regain, may be helpful at giving the patient a "kick-start" to induce greater weight loss.

2.1. Low-fat diets

Low-fat diets are a common strategy to help patients lose weight, and most dietary guidelines recommend a reduction in the daily intake of fat to 30% of energy intake or less. In a meta-analysis of trials comparing low-fat diets (typically < 25% of total calories from fat) with a control group consuming a regular diet (30%-40% of total calories), there was greater weight loss in the low-fat group compared with the moderate fat group (3 kg difference) [11].

2.2. Low-carbohydrate diets

Low- and very low carbohydrate diets are more effective than low-fat diets for short-term weight loss, but not for long-term weight loss. A meta-analysis of 5 trials showing superiority of low-carbohydrate diets for weight loss over low fat was not sustained at 12 months [12]. Low-carbohydrate diets likely have other benefits such as reduction in development of type 2 diabetes.

2.3. Meal replacements

A structured way to induce a calorie deficit is through liquid meal replacement. Meal replacements can be used in certain patients to achieve further weight loss. This approach can be used in the short term, or as a partial liquid diet in the long-term such as 1 or 2 meals replaced by low-calorie liquid (protein shake) and the remaining meals as energy balanced meals. A common use of low-calorie liquid is perioperatively around the time of bariatric surgery but can be done for longer periods if a patient can adhere [13]. A simple approach to induce weight loss can be a meal replacement program with calorie-controlled individually packaged foods. Frozen low-calorie meals containing < 400 kcal/package can be a convenient and nutritious way to restrict calories [14].

2.4. Mediterranean diet

For patients in whom cardiovascular health is a paramount concern, the Mediterranean diet can be suggested. There is no single definition of a Mediterranean diet, but these diets are high in fruits, vegetables, whole grains, beans, nuts, and seeds and use olive oil as an important source of monounsaturated fat; and allow moderate wine intake. There is low-to-moderate amounts of fish, poultry, and dairy products, with little red meat. The Mediterranean diet is associated with reductions in overall mortality, cardiovascular mortality, and cancer incidence [15].

A Mediterranean diet may reduce cardiovascular events. In a randomized trial of 7447 adults at high risk for cardiovascular disease, the 2 groups assigned to the Mediterranean diet supplemented either with extravirgin olive oil or mixed nuts had a lower rate of total cardiovascular events (stroke, myocardial infarction, and cardiovascular death) compared with a control group (counseled to eat a low-fat diet), hazard ratio of 0.7 (95% CI: 0.5-0.9) after 4.8 years. The absolute reduction in risk was approximately 3 cardiovascular events per 1000 person-years [16].

2.5. Intermittent fasting

Long-term energy restriction leads to metabolic changes that make continued weight loss difficulty [2]. Planned periods of negative energy balance during long-term weight loss efforts appear to mitigate metabolic adaptations to weight loss. This theory supports intermittent energy restriction (IER) as a way to stimulate weight loss or maintain a weight reduced state. There are several models of IER that have shown to be as effective for long-term weight control as a long-term balanced-deficit diet [17]. IER includes restricting caloric intake for some defined period of time, and eating ad libitum (ie, to satiety) during the nonenergy restricted period. The most common form of IER is "intermittent fasting," where caloric intake is severely restricted for short periods (often 2-4 d/wk). The periods of energy balance (ie, rest of the week) may or may not have restrictions. Meta-analyses on IER conclude that it is an alternative approach to chronic energy restriction for inducing weight loss but not superior, although some patients may demonstrate greater adherence. The data, on whether IER in fact mitigates the counterregulatory mechanisms, aimed at weight regain after diet-induced weight loss are equivocal [18].

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