Review: Several pharmacologic therapies promote modest weight loss

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Therapeutics

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Clinical impact ratings:★★★★★  Endocrinology ★★★★★  ★

Question
How effective and safe are pharmacologic therapies in the treatment of obesity?

Methods
Data sources: MEDLINE (to July 2003), the Cochrane Central Register of Controlled Trials, and existing systematic reviews.

Study selection and assessment: Randomized controlled trials that evaluated pharmaceutical agents for weight loss in patients with body mass index ≥ 27 kg/m² and reported ≥6-month weight outcomes. Study quality was assessed using the 5-point Jadad scale (5 = highest quality) and considered study design, method of random assignment, blinding, and withdrawal.

Outcomes: Weight loss and side effects.

Main results
The studies meeting inclusion criteria were 3 existing meta-analyses (39 RCTs) evaluating sibutramine, phentermine, and diethylpropion, and 47 RCTs that evaluated orlistat, bupropion, topiramate, and fluoxetine. All comparisons were with placebo, and most trials had a hypocaloric diet co-intervention. Meta-analyses were done using random effects. Most medications led to modest weight loss compared with placebo; side effects varied by drug (Table).

Commentary
Obesity is a chronic condition resulting from a myriad of factors causing an imbalance of energy intake and expenditure. Although lifestyle changes can result in weight loss for some, many obese patients need more efficacious interventions for weight reduction. The use of pharmacologic and surgical treatments has increased in response to the increasing prevalence of obesity.

Li and colleagues and a Cochrane review on this topic (1) agree that several available medications combined with dietary intervention result in average weight loss of about 3 to 5 kg in excess of placebo with relatively mild short-term side effects.

Although a 5% to 10% weight loss can result in reduced risk for chronic disease (2), Foster and colleagues showed that most patients achieving the degree of weight loss reported with pharmacotherapy by Li and colleagues would be "very disappointed" (3). A group underrepresented in pharmacologic trials, severely obese patients (BMI > 40 kg/m²), may perceive less palliation from a "modest" weight loss. Large loss to follow-up in trials and in clinical practice may, in part, reflect limitations of medical therapy and complicate the interpretation of trials.

With this in mind, clinicians should appreciate why some patients are enamored with surgical treatments for obesity. Maggs and colleagues noted that although current high-quality data are lacking, a large observational study from Sweden supports the efficacy and probable superiority of surgical treatments for severely obese patients. When considering the large, consistent differences in weight, major comorbid outcomes observed, and low risk for major complications in a large number of patients, they suggest it is more likely that the differences are attributable to surgical treatment and not due to unmeasured variables. Consistent findings from other investigators have been published (6). Still, RCTs are needed to establish causality and to detect small differences (particularly between surgical procedures) in outcomes important to patients, including quality of life and cost-effectiveness.

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