Does Sibutramine Keep the Weight Off?

Apfelboum M, Vague P, Ziegler O, et al. Long-term maintenance of weight loss after a very-low-calorie diet: a randomized blinded trial of the efficacy and tolerability of sibutramine. Am J Med 1999; 106:179-84.

Clinical question **Does sibutramine help maintain or improve weight loss following a very-low-calorie diet?**

Background The success of nonpharmacologic interventions (diet and exercise) to induce weight loss has been variable and generally disappointing. Very-low-calorie diets have been shown to effect substantial but transient weight loss, and the maintenance of weight loss remains a major challenge. This double-blind randomized controlled trial compared the use of sibutramine with placebo in maintaining or improving weight loss following a short-term very-low-calorie diet.

Population studied One hundred sixty patients were enrolled from 12 medical centers specializing in obesity in France. The subjects were adults with a body mass index of less than 30 kg/m^2 and an average weight of 229 lb (104 kg). Patients were excluded if they had obesity of endocrine origin, type 1 diabetes mellitus, insulin-requiring or poorly controlled type 2 diabetes mellitus, significant hypertension (diastolic pressure >100 mm Hg), or significant depression. Of the patients included in the randomized phase of this study, each lost an average of 7.5 kg on a 4-week very-low-calorie diet.

Study design and validity This was a 12-month double-blind randomized controlled trial. All eligible subjects were prescribed a 4-week very-low-calorie diet (220 to 800 kcal/day) to induce significant weight loss before randomization. Subjects who lost more than 6 kg entered the 12-month double-blind phase of the trial and were randomized to received 10 mg sibutramine (Meridia) or placebo once daily. At that point, the very-low-calorie diet was stopped, and the patients resumed meals with dietary counseling to reduce their caloric intake by 20% to 30% compared with their intake before the very-low-calorie diet.

Following the initial weight loss and after randomization to treatment groups (month 0), weight assessments were made at week 2, month 1, monthly until month 12, and 1 and 3 months after the trial was completed. Each patient was counseled by a dietitian at months 0, 3, 6, and 9. The study was designed to have more than 94% power. All study subjects were accounted for, and intention-to-treat analysis was used.

This trial was of good quality. The patients enrolled in the study were not well described, however, making it difficult to judge whether these patients are similar to those of family physicians. Behaviors, such as exercise, would be of particular interest. Attrition during the trial was high: 22% of the subjects withdrew during the very-low-calorie diet, and 32% of those randomized withdrew during the course of the trial.

Outcomes measured The primary outcome was the change in body weight measured from the initial weight loss through the 1-year treatment period. Other outcomes included change in body weight following cessation of the trial.

Results From the time of randomization (4 weeks after the start of the very-low-calorie diet) to the end point of the trial, the mean absolute weight change in the sibutramine group was a loss of an additional 5.2 kg (±7.5 kg), compared with a weight gain of 0.5 kg (±5.7 kg) in the placebo group ($P = .004$). Sibutramine-treated patients lost their weight in the first 6 months and maintained it (±0.5kg) during the rest of the trial.

At the end of the trial, patients in the sibutramine group had maintained a greater proportion of weight lost during their very-low-calorie diet than those in the placebo group.

After termination of the study medication, weight regain occurred in both groups, especially in the sibutramine-treated patients. By 3 months after treatment cessation, mean weight gain was 4.3 kg (±3.1 kg) in the sibutramine group compared with 2.3 kg (±2.9 kg) in the placebo group ($P = .009$).

Recommendations for clinical practice **Sibutramine was effective in maintaining and promoting further weight loss in patients who had successfully lost weight on a 4-week very-low-calorie diet. Therapy must be continuous; weight gain occurred rapidly when the drug was discontinued.**

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Correction

In the algorithm for adjusting warfarin doses according to international normalized ratio (INR) levels (J Fam Pract 1999; 48:251), the final INR entry on day 2 should read >2.5.