

The efficacy of orlistat vs. sibutramine in the treatment of obesity: A systematic literature review

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Abstract. Introduction: Since obesity is the second leading cause of preventable death in the United States, effective treatments are crucial in order to stop the progression of this epidemic. Currently, orlistat (Xenical) and sibutramine (Meridia, Reductil) are the only FDA approved obesity drugs for long-term weight loss in adults. The aim of this study is to compare the effectiveness of these two drugs in initial weight loss as well as long-term maintenance of that weight loss. **Methodology:** An evidence-based systematic literature review was conducted using the following databases: Medline, ECO, and Cochrane. Articles chosen for inclusion were from 1990 to present, level 1 or 2 evidence and from peer-reviewed journals. Participants were over 18 years old with a BMI greater than 27 kg/m². **Results:** There were 18 level 1 randomized controlled trials demonstrating the effectiveness of both medications to produce weight loss. Therefore, a Grade A recommendation can be made regarding the use of either orlistat or sibutramine in a primary care setting for 5-10% weight loss. Also, there were 10 level 1 randomized controlled trials demonstrating the management of the weight loss for up to 2 years, so a Grade A recommendation can be made regarding the use of either orlistat or sibutramine in the long-term management of weight loss. **Conclusion:** Both medications are effective for an obese patient who has failed on diet and exercise alone, so selection of which medication to prescribe is primarily determined on which medication the patient is most able to tolerate.

1. Introduction

Obesity is standardly defined according to body mass index (BMI). This measurement divides the weight of the patient in kilograms by the square of the patient's height in meters. A patient having a BMI greater than 30 kg/m² is considered obese, and the risk of morbidity and mortality increases. Annually, there are over 300,000 obesity related deaths with an estimated \$117 billion of United States healthcare dollars spent in an effort to treat this condition.[1] The prevalence of chronic diseases such as hypertension, Type 2 diabetes mellitus, and high cholesterol also increases with obesity, so effective treatments are crucial in order to stop the progression of this epidemic and its comorbidities. Since 64% of the U.S. population is classified as either overweight or obese, primary care providers are most likely to encounter as well as provide treatment for this condition.

In obese patients, conservative measures such as diet and exercise are limited in their ability to produce and sustain weight loss, so the next step in the treatment of obesity is pharmacotherapy. Pharmacotherapy, in accordance with a low calorie diet and exercise, has been shown to induce more weight loss as well as maintain more of the lost weight for up to four years when compared to diet and exercise alone. Currently, orlistat (Xenical) and sibutramine (Meridia, Reductil) are the only FDA approved drugs for long-term management of obesity in adults, and these medications typically reduce body weight by 5-10% in the average patient.[2]

Orlistat, approved by the FDA in 1999, is an inhibitor of pancreatic and gastric lipases, enzymes which are involved in the conversion of dietary fat into an absorbable form for the body. When these are blocked, absorption of fat is reduced by approximately 30%. The recommended dose of orlistat is 120 mg three times a day to be taken with each main meal.[3] Sibutramine, approved by the FDA in 1997, is an appetite suppressant. It is an inhibitor of the reuptake of serotonin and norepinephrine, and it generates weight reduction by boosting the feeling of fullness after a meal in addition to enhancing the metabolic rate. The recommended dose of sibutramine is 10 mg daily initially. It may be increased to 15 mg daily after 4 weeks if there is inadequate weight reduction.[4]

Studies have shown these medications are efficacious in producing and sustaining long-term weight loss when used with a low-fat diet and exercise. A key question is which anti-obesity medication is more effective. Therefore, the aim of this study is to compare the effectiveness of these two drugs in reduction and long-term maintenance of weight.

2. Results, Discussion, and Significance

To assess the efficacy of orlistat and sibutramine, an evidence-based systematic literature review was conducted using search engines PubMed, First Search, and Cambridge Scientific Abstracts to search the following databases Medline, ECO, and Cochrane. Articles chosen for review met the following inclusion criteria. They were from 1990 to present because that was when initial studies were conducted testing the optimal dose as well as efficacy. Articles were from peer-reviewed journals, and the primary outcome measures of the studies were clinically significant weight loss of 5-10% from baseline weight and/or weight maintenance after the weight loss. The patients included in these articles were over 18 years old with a BMI greater than 30 kg/m² or 27 kg/m² if hypertension, Type 2 diabetes, and/or hyperlipidemia were present. Articles were included if they studied orlistat and/or sibutramine in combination with a low calorie diet and were level 1 or 2 evidence. Level 1 evidence included high quality randomized clinical trials, systematic reviews with homogeneity of randomized controlled trials, and high quality meta-analyses. Level 2 evidence included nonrandomized clinical trials, lower quality randomized controlled trials, and cohort studies.

Orlistat produced significantly more weight loss in the trials where subjects without comorbidities like hypertension, Type 2 diabetes, and hyperlipidemia were recruited. Since orlistat has little systemic absorption it is safer to use in regards to drug interactions and other contraindications. However, the side effects of orlistat, like oily stools, fecal incontinence, and diarrhea make it harder for patients to tolerate. Clinicians, as well as their patients, should consider those before prescribing this medication.

Sibutramine produced clinically significant weight loss as well, but it was associated with increases in blood pressure and heart rate in many of the trials included in this systematic review. However, these increases were not clinically significant, and patients with borderline hypertension and/or increased heart rate can be monitored more closely while taking this medication. Sibutramine was also associated with more tolerable side effects. Last, in both head to head trials comparing the amount of weight loss produced between patients taking orlistat or sibutramine, sibutramine treated patients lost slightly more weight.

3. Conclusions

Obesity should be regarded as an important medical condition requiring treatment. In conjunction with a reduced calorie diet and exercise, pharmacotherapy is a vital addition in the treatment. However, orlistat's gastrointestinal side effects make it less tolerable when compared to sibutramine's side effects. Also, when initiating sibutramine in a patient with hypertension, as well as borderline hypertension, the patient's blood pressure and heart rate should be monitored more closely due to the potential slight increase in blood pressure and heart rate it may cause. Both medications are safe and effective and should be considered in conjunction with diet and exercise by any clinician treating obesity.

After thorough analysis of 26 randomized controlled trials demonstrating the ability of orlistat and sibutramine to produce and sustain clinically significant weight loss, a Grade A recommendation can be made regarding the use of orlistat or sibutramine in a primary care setting for 5-10% weight loss as well as long-term management of that weight loss.

- [1] Friedman N, Fanning EL. Overweight and Obesity: An Overview of Prevalence, Clinical Impact, and Economic Impact. *Disease Management* 7, no Supplement 1 (2004): S-6.
- [2] Feigenbaum A, Pasternak S, Zusk E, Sarid M, Vinker S. Influence of intense multidisciplinary follow-up and orlistat on weight reduction in a primary care setting. *BMC Fam Pract.* Jan 29 2005;6(1):5.
- [3] Curran MP, Scott LJ. Orlistat: A Review of its Use in the Management of Patients with Obesity. *Drugs* 64, no 24 (2004): 2845-2864.
- [4] Nisoli E, Carruba MO. An assessment of the safety and efficacy of sibutramine, an anti-obesity drug with a novel mechanism of action. *Obesity Reviews* 1, no 2 (2000): 127-139.