Brief Report – Weight loss in patients taking a combination of phentermine and lorcaserin

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Abstract

The medical treatment of obesity continues to be a challenge even with the approval of new medications for long-term therapy. It has become apparent that a combination of medications with different mechanisms may give superior results compared to the use of individual medications alone. This is the first report describing the combined use of phentermine and lorcaserin for weight management. The results appear superior to reported results of the medications used individually.

Here we report weight loss results of twenty-two patients followed in a private practice setting for twelve weeks. The mean weight loss of this group was 11.83% from baseline (28.0 pounds). A decrease in mean blood pressure was noted. Lean body mass was measured and appeared to be conserved. No significant side effects were reported by the patients. Variables affecting our results might include follow-up visit frequency, personal interaction with the physician at each visit and the emphasis on a low-glycemic diet.

The results of this small short-term observational study warrant further investigation. given the observed efficacy, a large-scale randomized, double blinded, and placebo-controlled trial to demonstrate both safety and efficacy is needed.

Introduction

The era of modern medical therapy for the treatment of obesity was ushered in with the 1992 publication of the "Long-term Weight Control: The NHLBI Multimodal Intervention Study" by Michael Weintraub, MD .Using a combination phentermine and fenfluramine during one 34 week segment, a 15.9% (32 pound) weight loss was noted in the treatment group.

The combination of medications was unique in several respects. Phentermine via adrenergic pathways, and fenfluramine through serotonergic pathways result in appetite supression by different mechanisms. When used in combination, patients reported not only a supression of appetite, but a marked decrease in food cravings. Unfortunately, reports of valvular heart disease and primary pulmonary hypertension led to the voluntary withdrawal of fenfluramine and its d-enantiomer dexfenfluramine from the US market in 1997.

Lorcaserin was approved by the FDA in June 2012 for the long-term treatment of obesity. Lorcaserin is a selective $5HT_{2C}$ receptor agonist unlike fenfluramine and dexfenfluramine which had affintity for the cardiac $5HT_{2B}$ receptor. In the 3 year multimodal, placebo controlled (BLOOM) study, the use of Lorcaserin 10 mg bid in conjunction with diet and exercise counseling produced a mean weight loss of 4.4 Kg (9.7 lbs) in one 12 week period of active treatment.

As demonstrated by Weintraub with phentermine and fenfluramine ,we reasoned that the additive or synergistic weight loss effect of the two medications lorcaserin and phentermine should produce a greater weight loss than the medications used individually.

Methods

During a 23-week period, 30 patients in a private obesity medicine practice were begun on a 12 week treatment regimen that included the combination of phentermine and lorcaserin.

All underwent initial evaluation including a detailed medical history and physical exam. Fasting bloodwork included a CBC, CMP, Lipid Profile, HgbA1c, fasting insulin, TSH w reflex fT4, and 25-OH Vitamin D level. All had an initial electrocardiogram, body composition by bioelectrical impedance (Model BCS-2, Valhalla Scientific) and completed a sleep apnea questionnaire. 12 subjects had hypertension, 12 dyslipidemia, 6 impaired fasting glucose, and 1 type 2 diabetes. Written informed consent was obtained.

A low glycemic eating plan was prescribed.[3] Participants were encouraged to eat at least 3 meals per day until satiated. They were asked to commit to 30 minutes of moderate exercise daily to minimize loss of lean body mass and consume at least 64 ounces of water per day. Lorcaserin 10 mg and phentermine HCL 37.5 mg were prescribed to be taken together orally each morning before 10 am. Participants were encouraged to weigh daily and requested to return for follow up visits every two weeks.

Initial evaluations and follow up visits were all performed by RH. Follow up visits included a questionnaire reviewing any possible side effects, a brief physical exam including vital signs, a body composition analysis, and behavior counseling. Adherence to exercise and diet guidelines was assessed.

Results

- 22 of the initial 30 patients completed 12 weeks treatment
  - 4 participants dropped out of treatment entirely
  - 4 participants changed to a very low calorie diet using no medication for appetite suppression
  - There were 19 females and 3 males
  - The mean duration of treatment was 11.9 weeks
  - The mean weight loss was 28.0 pounds
  - The mean starting weight was 237 pounds
  - The mean starting body fat percentage was 39.2%
  - The only side effects noted were minor:
    - 3 episodes of sleep disturbances resolved by taking medication earlier in the day
    - 2 episodes of constipation resolved with fiber supplementation

	Baseline	At 12 Weeks Treatments
Mean body weight (pounds)	237.0	209.0
Mean weight loss from baseline (pounds)		28.0
Mean weight loss from baseline (%)		11.83
Mean body fat (%)	39.2	36.0
Mean muscle mass (%)	15.9	17.5
Mean heart rate (beats per minute)	77.3	81.2
Mean systolic BP (MM Hg)	133.3	128.0
Mean diastolic BP (mm Hg)	82.7	80.9

Discussion

This observational study is the first reported series describing the use of phentermine and lorcaserin together for weight reduction.

The results obtained in this private practice setting with close follow up are worth noting. No significant side effects were seen. Loss of lean muscle mass was not observed. Weight loss using this combination of medications was approximately 1% per week over 12 weeks and greater than described with either lorcaserin or phentermine alone. A decrease in both systolic and diastolic blood pressure was seen.

Longer, double blinded, and placebo-controlled trials are needed. Although premarketing studies of lorcaserin alone revealed no valvular changes on echocardiagram, close observation using this drug combination is warranted.

References

1. Weintraub M, Sundaresan PR, Madan M, Schuster B, Balder A, Lasagna L, Cox C. Long-term weight control: The National Heart, Lung, and Blood Institute funded Multimodal Intervention Study. *Clin Pharmacol Ther* 1992;51(5):581-646.
2. Smith SR, Weissman NJ, Anderson CM, Sanchez M *et al*, and the Behavioral Modification and Lorcaserin for Overweight and Obesity Management (BLOOM) Study Group. Multicenter, Placebo-Controlled Trial of Lorcaserin for Weight Management. *N Engl J Med* 2010; 363:245-256.
3. Agaston, A. (2008). *The South Beach Diet Supercharged*. New York, N.Y.: St. Martin's Press.
4. Ballor DL, Poehlman ET. Exercise-training enhances fat-free mass preservation during diet-induced weight loss: a meta-analytical finding. Int J Obes Relat Metab Disord 1994 18:35–40.
5. Heymsfield SB, Thomas D, Nguyen AM, Peng JZ, Martin C, Shen W, Strauss B, Bosy-Westphal A, Muller MJ. Voluntary weight loss: systematic review of early phase body composition changes. *Obes Rev.* 2011;12(5):e348-61.