Nutrition, Metabolism & Cardiovascular Diseases (2008) **18**, 207–210

ELSEVIER

Nutrition, Metabolism & Cardiovascular Diseases

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Effects of sibutramine and orlistat on mood in obese and overweight subjects: A randomised study

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Received 29 June 2006; received in revised form 15 September 2006; accepted 5 October 2006

KEYWORDS
Weight loss;
Sibutramine;
Orlistat;
Mood;
Depression

Abstract *Background and aim:* Intentional weight loss results in improvement in mood. Very few data exist regarding the effects of sibutramine on the mood of obese and overweight patients in general clinical samples. Moreover, no study has evaluated the effects of orlistat treatment on mood. The purpose of our study was to assess the effects of sibutramine and orlistat on mood in obese and overweight subjects.
Methods and results: Sixty obese and overweight women were divided into three groups. The first group ($n = 20$) received a low-calorie diet and sibutramine 10 mg; the second group ($n = 20$) received a low-calorie diet and orlistat 120 mg three times a day, and the third group received only the low-calorie diet.
Conclusion: A psychiatric assessment was performed with the Hamilton Depression Rating Scale (HAMD) before and after 3 months of treatment. In all the groups a statistically significant decrease in HAMD scores was observed. However, the decrease in the sibutramine group was greater compared to that observed in the two other groups ($P < 0.01$). These results suggest that sibutramine treatment may improve mood more than diet alone or orlistat therapy in a general clinical sample of obese patients.

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doi:10.1016/j.numecd.2006.10.003

Introduction

Obese patients very often have increased depression scores [1,2]. Several studies have shown an improvement of these scores after weight loss [3]. Two studies on sibutramine treatment, a drug that was first studied as an antidepressant agent and now used for weight management, reported a reduction in depression scores in obese binge eaters [4,5]. Only one study examined the effects of sibutramine on depression in a general clinical sample of obese patients [6], which showed a significant improvement. However, this study was not placebo controlled or even diet controlled. Therefore it cannot be ruled out that the beneficial effect of sibutramine on depression scores was only due to weight loss. Additionally, to the best of our knowledge no study has evaluated the effects of orlistat treatment on mood. Therefore we undertook the present study in order to assess the effects of the two currently available anti-obesity drugs on mood in obese and overweight otherwise healthy subjects.

Methods

We initially screened 75 subjects, who were referred to the obesity outpatient clinic of the University Hospital of Ioannina for weight loss. Sixty obese overweight women with a mean age of 45 ± 8.3 years and with a body mass index [BMI] > 28 kg/m^2 were included in the study. All the patients gave informed consent before participation in the study. The Scientific Committee of the University Hospital of Ioannina approved the study.

Exclusion criteria included hepatic dysfunction (levels of transaminases $\geq$ to the upper limit of normal), renal insufficiency (serum creatinine $>$1.6 mg/dl), proteinuria, diabetes mellitus, thyroid-stimulating hormone (TSH) levels >5 μU/ml, consumption of drugs that may influence the metabolism of lipoproteins, psychiatric disease according to the DSM IV criteria and any other chronic condition precluding successful completion of the study. The DSM IV is a widely accepted description of psychiatric diseases along with clinical criteria for each one of them. Moreover, subjects taking drugs that could affect their psychiatric status were also excluded. All participants reported no significant change in their body weight for at least 3 months prior to entry into the study. Furthermore, none of the subjects were taking any medication at the beginning of the study.

A low calorie diet was prescribed for every patient (1200—1600 kcal). The subjects were randomly divided into three treatment groups. We used a table of random numbers in which numbers 1—25 were assigned to diet intervention only; numbers 26—50 were assigned to orlistat treatment and numbers 51—75 were assigned to sibutramine treatment. In addition the sibutramine group ($n = 20$) received sibutramine 10 mg and the second group ($n = 20$) received orlistat 120 mg three times a day. The third group ($n = 20$) were given only the low calorie diet, promoting a 500—1000 kcal reduction in daily energy.

The primary hypothesis of our study was to examine the effects of sibutramine, orlistat or dietary intervention on the mood of overweight and obese subjects and to investigate possible differences of these interventions on their psychological status.

The psychiatric assessment was performed by an experienced physician with the Hamilton Depression Rating Scale (HAMD), which is a useful tool for the assessment of depression before and after 3 months of treatment.

The statistical analysis was performed with the Student's *t*-test (paired and unpaired accordingly) and analysis of covariance (ANCOVA), adjusted for baseline values, was used for comparisons between treatment groups. Correlations were assessed with the Spearman correlation coefficient. A P value less than 0.05 was considered statistically significant.

Results

The three groups did not differ significantly regarding age, weight, body mass index and depression scores at baseline. The changes in body mass index (BMI) as well as in depression scores (HAMD) are shown in Table 1. Patients who received sibutramine and orlistat lost more weight compared to those who received only dietary treatment (ANCOVA adjusted for baseline values). In all the groups a statistically significant decrease of HAMD scores was observed (from 11.4 to 9.8 in the diet group, from 11 to 9.2 in the orlistat group and from 12 to 7.2 in the sibutramine group). However, the decrease in the sibutramine group was greater compared to that observed in the two other groups ($P < 0.01$). In the whole study population, as well as in every separate group there was no statistically significant correlation between the degree of weight loss and the changes of HAMD scores (Fig. 1). Only two patients in the orlistat group exhibited gastrointestinal side effects, which occurred early during treatment, were mild and resolved spontaneously. In the sibutramine group two patients exhibited mild