Comparative effects of sibutramine and orlistat on weight loss, glucose metabolism and leptin levels in non-diabetic obese patients: A prospective study

Sir,

Obesity is a serious public health problem, associated with an increased risk of cardiovascular mortality and all-cause mortality. The aim of the present study was to evaluate the effect of sibutramine and orlistat on weight loss, Insulin Resistance (IR), leptin High-Sensitivity C-Reactive Protein (hsCRP) in non-diabetic obese patients.

This was a 12-week prospective non-randomized open-label study. Patients were assigned to either sibutramine or orlistat. Lipidemic profile, fasting plasma glucose, HbA1c and IR indexes, leptin, and hsCRP were measured before and after 4 and 12 weeks. The study was terminated early due to sibutramine's recent withdrawal from the market.

In all, 31 patients met the eligibility criteria and were assigned to either sibutramine (18 patients, 16 female/2 male; age 43.2±14.9 years) or orlistat (13 patients, 12 female/1 male, aged 48.3±16.0 years) treatment. All of them completed the four-week visit, but only 21 patients completed the 12-week visit [10 of the sibutramine (8 female/2 male) and 11 of the orlistat (10 female/1 male) group] mainly due to sibutramine withdrawal from the market (n=5). Mild adverse events developed mainly in the sibutramine group and one patient dropped out due to development of hypertension.

At four weeks of treatment, body weight and Body Mass Index (BMI) were significantly reduced in both groups [-5% or -4.8±0.8 kg (P=0.001) and -10% or -4.2±2.1 kg/m^2 (P<0.001), respectively, for sibutramine and -3% or -2.9±0.5 kg, (P=0.001) and -3% or -1.7±0.2 kg/m^2, (P=0.003), respectively, for orlistat]. Change in weight was greater in the sibutramine group as compared with the orlistat group (P=0.018). Regarding those who completed the 12 weeks of treatment, both drugs led to further weight reduction [from 106±18 kg at baseline to 95±14 kg at 12 weeks with sibutramine (P<0.001) and from 93±12 kg to 87±11 kg with orlistat (P< 0.001)], although without significant differences between the two drugs. Orlistat led to a significant reduction in diastolic Blood Pressure (BP) (-8.6 ± 3.0 mm Hg or 9%, P=0.011) at four weeks, whereas sibutramine was associated with a non-significant increase in both systolic and diastolic BP and pulse rate.

Orlistat led to significant reduction in Total Cholesterol (TC), Low-Density Lipoprotein-Cholesterol (LDL-C), triglycerides and non–High-Density Lipoprotein-Cholesterol (HDL-C) after 4 weeks of treatment (11%, 13%, 13%, and 11%, respectively), whereas sibutramine decreased TC and HDL-C (7% and 11%, respectively). However, these differences were not significant in between-group comparisons. In those who completed 12 weeks of treatment, the differences remained significant only for orlistat in terms of total cholesterol reduction (P=0.024), mainly due to a trend towards LDL-C reduction (P=0.084). However, all changes in serum lipid levels did not remain statistically significant after adjustment for weight loss.

Both agents led to significant reduction in leptin levels, which were dependent on deltas in weight. Regarding fasting plasma glucose metabolism and hsCRP, no significant differences within or between groups were observed.

Our study, despite its early termination, demonstrated that both drugs were effective in weight reduction at 4 and 12 weeks of treatment. Sibutramine resulted in a greater weight loss at 4 weeks and orlistat to a significant decrease in diastolic BP. Conflicting data exist regarding the weight-lowering efficacy of these drugs.[1,2] In terms of BP, sibutramine may be associated with an increase or no effect at all.[3] A meta-analysis has reported that 1-year treatment with orlistat is associated with a mild decrease in BP and pulse rate.[4] In our study, orlistat exerted a trend towards more favourable effects on lipid levels. Regarding lipid metabolism, conflicting data exist for sibutramine.[4] In a meta-analysis of 15 studies, orlistat led to a significant reduction in TC levels, independent of weight loss.[5]

The impact of both drugs on glucose metabolism seems to be beneficial in most studies, associated with weight loss.[3] However, we failed to show any effect of both drugs on glucose metabolism or IR, perhaps due to the small number of patients. Both drugs led to comparable reductions in leptin levels, although dependently on weight loss, as has been shown previously.[3]

In conclusion, sibutramine and orlistat were effective in weight reduction, with orlistat having a more favourable effect on lipid profile. Their effect on glucose metabolism was similarly neutral.

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