Addition of a low dose of rimonabant to orlistat therapy decreases weight gain and reduces adiposity in dietary obese rats.

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Source

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Abstract

1. The aim of the present study was to determine whether the addition of a subeffective dose of rimonabant (1 mg/kg) to orlistat would be beneficial in the treatment of diet-induced obesity in rats compared with orlistatmonotherapy. 2. Male rats were divided into five groups: (i) rats fed a low-fat diet for 4 months; (ii) rats fed a high-fat diet (HFD) for 4 months and treated daily with vehicle (0.2% Tween-80 solution); (iii) orlistat (10 mg/kg per day)-treated HFD-fed rats; (iv) rimonabant (1 mg/kg per day)-treated HFD-fed rats; and (v) HFD-fed rats treated with a combination of orlistat plus rimonabant. Fasting blood glucose, serum insulin, leptin and adiponectin levels were measured. Liver and adiposity indices were calculated and liver and adipose tissues were processed for histological examination. 3. Over the 4 months of the study, vehicle-treated HFD-fed rats exhibited increased cumulative food intake, bodyweight and liver and adiposity indices. Moreover, vehicle-treated HFD-fed rats exhibited a deterioration in liver function and an abnormal lipid profile. Insulin resistance and serum leptin were increased in this group, whereas serum adiponectin levels were decreased. Orlistatmonotherapy or combination therapy with orlistat plus rimonabant improved all these parameters. 4. The addition of the low subeffective dose of rimonabant to orlistat therapy ameliorated HFD-induced obesity to a much greater extent than orlistatmonotherapy. This combination showed better weight control and metabolic profile compared with orlistat alone. Therefore, the results of the present study encourage reassessment of the use of a low dose of rimonabant to potentiate the effect of orlistat in the clinical management of obesity if proper clinical safety data are available.