

Orlistat with diet was effective and safe for weight loss and coronary risk reduction in obesity

Lindgärde F, on behalf of the Orlistat Swedish Multimorbidity Study Group. *The effect of orlistat on body weight and coronary heart disease risk profile in obese patients: the Swedish Multimorbidity Study.* *J Intern Med* 2000 Sep;248:245–54.

QUESTION: What is the effectiveness of orlistat for weight loss and coronary artery disease risk factor reduction in people who are obese and have ≥ 1 coronary risk factor?

Design

Randomised (unclear allocation concealment*), blinded (patients, outcome assessors)*, placebo controlled trial with 1 year follow up.

Setting

33 primary care centres in Sweden.

Patients

376 patients between 18 and 75 years of age (mean age 53 y, 64% women) who had a body mass index between 28 and 38 kg/m². Patients had to have ≥ 1 of the following: fasting serum glucose concentration ≥ 6.7 mmol/l or type-2 diabetes mellitus treated with sulfonylurea or metformin (not insulin); cholesterol concentration ≥ 6.5 mmol/l or low density lipoprotein (LDL) cholesterol concentration ≥ 4.2 mmol/l on ≥ 2 occasions, or lipid lowering medication; or diastolic blood pressure concentration ≥ 90 mm Hg on ≥ 2 occasions or on hypertension treatment. Exclusion criteria were lactation, pregnancy, or not using adequate contraception; recent myocardial infarction; gastrointestinal surgery for weight reduction; gastrointestinal disorders; pancreatic disease; history of postsurgical adhesions; excessive alcohol intake; substance abuse; or use of systemic steroids or weight or lipid altering drugs.

Intervention

After a 2 week run-in period, patients were allocated to orlistat, 120 mg (n = 190), or placebo (n = 186) 3 times daily to be taken with main meals. All were encouraged to follow a mildly hypocaloric diet. After 6 months, an additional 1.254 mj/day reduction was made to the diet. All patients received dietary counselling and self help materials and were encouraged to walk every day.

Main outcome measures

Weight loss, waist and hip circumferences, blood pressure, serum lipid concentrations, fasting glucose concentrations, haemoglobin (Hb) A_{1c} concentrations, and adverse events.

Main results

Analysis was by intention to treat. Mean weight loss was greater with orlistat than with placebo (5.9% v 4.6% of initial body weight, $p < 0.05$). Orlistat led to greater mean reductions than placebo in total serum cholesterol concentrations (0.24 v 0.09 mmol/l, $p < 0.05$), LDL cholesterol concentrations (0.25 v 0.07 mmol/l, $p < 0.05$), fasting glucose concentrations (0.55 v 0.09 mmol/l, $p < 0.01$),

and HbA_{1c} levels (0.25% v 0.05%, $p < 0.05$). Groups did not differ for reductions in waist and hip circumference, blood pressure, or drug related adverse effects.

Conclusion

Treatment with orlistat combined with a mildly hypocaloric diet was safe and more effective than diet alone for weight loss and coronary heart disease risk factor reduction in people who are obese and have high coronary risk.

*See glossary.

COMMENTARY

Weight loss is associated with multiple benefits but is difficult to achieve and even more difficult to maintain¹. The effects of orlistat, an intestinal lipase inhibitor, were evaluated by Lindgärde *et al* in this well designed, 1 year, multicentre trial of weight loss and cardiovascular risk reduction. The beneficial effects of orlistat were evident but not impressive. Orlistat treatment was safe and was associated with greater weight loss and risk factor reduction than placebo; however, the difference in mean weight loss between orlistat and placebo groups was small (1.3%, or 1.3 kg, $p < 0.05$). Although orlistat achieved a greater rate of reaching a $\geq 5\%$ weight loss than placebo (54% v 41%, $p < 0.001$), the likelihood of a $\geq 10\%$ weight loss was not different between groups (19% v 15% for orlistat v placebo).

The amount of weight loss with orlistat was slightly less than that observed in previous studies,² but this finding probably reflects the trial's primary care approach. Changes in global cardiovascular risk estimates were not reported, and clinical cardiovascular end points were not examined in this study or previous orlistat trials.

Although the average weight loss with orlistat tends to be modest, weight loss of 5% to 10% of body weight appears to produce significant health benefits.¹ The reduction in fat absorption caused by orlistat² may further improve the lipid profile independent of weight loss. As better cost effectiveness data for orlistat and other weight loss and cardiovascular treatments become available, orlistat's role in the clinical management of obesity will be more clearly defined.

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1 Davidson MH, Hauptman J, DiGirolamo M, *et al*. Weight control and risk factor reduction in obese subjects treated for 2 years with orlistat: a randomised controlled trial. *JAMA* 1999;281:235–42.

2 Executive summary of the clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. *Arch Intern Med* 1998;158:1855–67.

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