BACKGROUND: Orlistat reduces energy uptake by the impairment of fat digestion and some evidence indicates it also lowers plasma cholesterol. AIM: To examine total, low-density lipoprotein- and high-density lipoprotein cholesterol during a weight reducing regimen, and assess the effect of orlistat in lowering cholesterol levels independent of its weight reducing efficacy. METHODS: A total of 448 patients with elevated cholesterol according to cardiovascular risk factors entered a 2 week single-blind run-in period on a hypocaloric diet. Of 384 patients were subsequently assigned double-blind treatment with orlistat (3 x 120 mg/day) or placebo for 6 months in conjunction with the hypocaloric diet. RESULTS: Weight loss in the orlistat group was 7.4 kg vs. 4.9 kg with placebo. Total and low-density lipoprotein cholesterol decreased by 25-30 mg/dL vs. 10-15 mg/dL with placebo. Reduction of cholesterol with orlistat was significantly greater than anticipated from weight loss alone. In patients with cardiovascular risk factors entering the study with lower cholesterol values orlistat was also superior to placebo. On the contrary, reduction of cholesterol concentrations never exceeded 20%. CONCLUSION: Orlistat has a cholesterol lowering efficacy independent of its weight reducing effect. Because of the limited therapeutic effectiveness, patients at high cardiovascular risk should receive rather early additional cholesterol lowering medication during
weight loss programmes.