Institutionen för medicin, Huddinge

VERY LOW ENERGY DIETS IN THE TREATMENT OF OBESITY
Studies of Obstructive Sleep Apnoea, Side-Effects, and Treatment Discontinuation

AKADEMISK AVHANDLING
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ABSTRACT

Background The prevalence of obesity has increased dramatically during the last decades worldwide. Obesity is associated with increased risk of morbidity and mortality, leading to an increased suffering for the individual patient and an increased burden on the health care system. Currently, the most effective treatment is bariatric surgery. Since bariatric surgery cannot be provided to all obese patients, other non-surgical obesity treatment methods are needed.

Aim The overall objective of this thesis was to evaluate effects and side-effects of very low energy diets (VLEDs), as well as to characterise treatment discontinuation. Specific objectives were to evaluate weight loss as treatment option for patients with obstructive sleep apnoea (OSA; Study I&II); to assess the risk of gallstones requiring hospital care, and cholecystectomy, in a commercial weight loss programme using VLED or low energy diet (LED; Study III); and to characterise discontinuation patterns in obesity treatment programmes by analysing data from anti-obesity drug trials (Study IV).

Methods The study on OSA and weight loss (Study I&II) consisted of a randomised controlled trial (RCT) followed by an observational follow-up for a total duration of one year. Included were obese men (n=63, BMI 30-40, aged 30-65 years) with moderate to severe OSA (apnoea-hypopnoea index (AHI) ≥15) treated with CPAP. The intervention consisted of a hospital-based weight loss programme, using VLED (554 kcal/day) to promote weight loss for nine weeks. After the RCT was finished the controls also received VLED. The VLED, in both groups, was followed by a 43-week weight loss maintenance phase. Study III was a one-year matched cohort study of consecutively enrolled adults in a commercial weight loss programme in Sweden between 2006 and 2009 (n=6,640; mean age 46y; 83% women; mean BMI 33). The intervention included a three-month weight loss phase, consisting of either VLED (500 kcal/day) or LED (1,200-1,500 kcal/day), followed by a nine-month weight loss maintenance phase. Gallstones requiring hospital care and cholecystectomies during the one-year programme were collected from the National Patient Register. Study IV was a systematic review and meta-analysis including published placebo-controlled anti-obesity trials of orlistat, sibutramine and rimonabant (n=13,457).

Results Study I&II: After the nine-week RCT the intervention group’s mean body weight was 20 kg lower than that of the control group, and its mean AHI was 23 events/h lower. In total 70% (44/63) completed the one-year pooled observational follow-up. The AHI changes after nine weeks of VLED (-58%) were largely maintained at one-year (-47%) following the initial weight loss of 18 kg, and 12 kg at one year. Study III: The absolute risks of gallstones requiring hospital care and cholecystectomy were found to be low, but three times higher in the VLED than the LED programme (hazard ratio 3.4 and 3.1, respectively; both P<0.001). While the risks were greater in the VLED compared to LED group, the benefits in terms of one-year weight loss was also greater (11 vs 8 kg; P<0.001), and the proportion remaining in the programme (82% vs 78%; P<0.001). Study IV: The overall combined one-year dropout rates were high in both the drug (30-39%) and placebo arms (37%) of placebo-controlled anti-obesity drug trials, but marginally lower in the drug arms (pooled risk ratio 0.9; P=0.001).

Conclusion VLED-induced weight loss resulted in a significant reduction of moderate to severe OSA, with the majority of the initial improvement maintained at one year. Albeit low, the risks of gallstones and cholecystectomy were greater with VLED than LED treatment, as was weight loss. Treatment discontinuation was lower both in the hospital-based weight loss programme and in the commercial weight loss programme, as compared to pooled data from the placebo arms in anti-obesity drug trials.