Long-term effects of weight-reducing interventions in hypertensive patients: systematic review and meta-analysis

CRD summary
The authors concluded that weight loss diet or orlistat reduced weight and blood-pressure (BP) in patients with essential hypertension. Although sibutramine reduced weight, it did not reduce BP. This was generally a well-conducted and clearly presented review and the authors’ conclusions are likely to be reliable.

Authors’ objectives
To evaluate the long-term effects of dietary, pharmacological and invasive weight-reducing interventions on patient-relevant outcomes and blood-pressure (BP) in patients with essential hypertension.

Searching
MEDLINE, EMBASE, the Cochrane Library (including the Cochrane CENTRAL Register), BIOSIS Previews and CINAHL were searched in June 2006. Searches of MEDLINE, EMBASE and the Cochrane CENTRAL Register were updated to March 2007. The search terms were not reported. In addition, reference lists of relevant articles and overviews were screened, study registries and internet sites of the European Agency for the Evaluation of Medicinal Products and the Food and Drug Administration were searched, and manufacturers of relevant drugs were contacted. Studies reported in English, German, Dutch, French, Italian, Portuguese and Spanish were eligible.

Study selection
Randomised controlled trials (RCTs) that compared the long-term (at least 24 weeks) effects of dietary, pharmacological or invasive weight-reducing interventions with placebo or usual care in adults aged 18 years or older with essential hypertension were eligible for inclusion. Studies had to assess mortality, cardiovascular outcomes, adverse events or BP. Studies were excluded if they involved pregnant women or if they evaluated combinations of non-pharmacological interventions, unless the results were reported separately for each intervention. Any cointerventions had to be used in both treatment groups.

The primary review outcomes were total mortality, cardiovascular morbidity and adverse events. The secondary outcomes were the duration and extent of BP and weight reduction.

The included studies compared dietary advice interventions (with and without advice about salt, alcohol and physical activity) with usual care, or compared drugs (orlistat 120 mg three times daily or sibutramine 10 or 20 mg daily) with placebo for periods ranging from 6 to 48 months. The duration of follow-up for dietary interventions ranged from 6 to 36 months. The participants ranged in age from a mean of 45 to 66 years for dietary studies and from 46 to 55 years for drug studies. None of the included studies evaluated surgical interventions.

Two reviewers independently selected the studies and resolved any differences through discussion or consultation with a third reviewer.

Assessment of study quality
Two reviewers independently assessed validity using the following criteria: adequacy of randomisation, allocation concealment, blinding, baseline comparability of the treatment groups, follow-up and handling of withdrawals in the analysis, statistical methods and consistency of reporting. Studies were then graded for quality, according to the extent of the methodological flaws detected, as A (none), B (slight) or C (major).

Data extraction
Two reviewers independently extracted the data onto a standardised form. Where possible, for each study, the change in BP and weight were reported with standard deviations for each treatment group.
Methods of synthesis
The studies were grouped by intervention and outcome. Studies reporting adequate data were pooled and weighted mean differences (WMDs), with 95% confidence intervals (CIs), calculated using a random-effects model. Statistical heterogeneity was assessed using the $I^2$ statistic. Other studies were combined in a narrative.

The authors stated that there were too few studies to undertake the planned subgroup analyses or to use funnel plots to assess publication bias.

Results of the review
Fifteen RCTs (n=5,374) were included. Of these, seven compared dietary interventions with usual care (n=1,632), four compared orlistat with placebo (n=3,132) and four compared sibutramine with placebo (n=610).

Dietary interventions.
Two studies were graded B for quality and five were graded C. Flaws included inadequate randomisation and allocation concealment, and a lack of blinding.

The only RCT that assessed a measure that included cardiovascular outcomes reported that the dietary intervention was associated with a statistically significant reduction in the combined outcome (reinstating antihypertensive treatment and severe cardiovascular complications) compared with usual care (hazard ratio 0.70, 95% CI: 0.57, 0.87). Dietary interventions were associated with a statistically significant reduction in systolic BP (WMD -6.26 mmHg, 95% CI: -9.82, -2.70; $I^2$=0%; 2 studies), diastolic BP (WMD -3.41 mmHg, 95% CI: -5.55, -1.27; $I^2$=36%; 3 studies) and weight (WMD -4.14 kg, 95% CI: -4.98, -3.30; $I^2$=36%; 4 studies) compared with usual care. None of the studies reported any information about adverse events.

Pharmacological interventions.
Three of the 4 studies of orlistat were graded B for quality; the other was graded C. All 4 studies of sibutramine were graded C.

Orlistat was associated with a statistically significant reduction in systolic BP (WMD -2.46 mmHg, 95% CI: -4.01, -0.90; $I^2$=37%; 4 studies), diastolic BP (WMD -1.92 mmHg, 95% CI: -2.99, -0.85; $I^2$=47%; 4 studies) and weight (WMD -3.74 kg, 95% CI: -4.70, -2.78; $I^2$=68%; 4 studies) compared with placebo. The most commonly reported adverse events with orlistat were gastrointestinal problems.

All 4 studies of sibutramine reported adverse effects on BP with sibutramine. A meta-analysis of the only 2 studies reporting adequate data showed that sibutramine was associated with a statistically significant increase in systolic BP compared with placebo (WMD 3.16 mmHg, 95% CI: 1.40, 4.92; $I^2$=0%). Sibutramine was associated with a statistically significant reduction in weight (WMD -3.72 kg, 95% CI: -4.85, -2.59; $I^2$=3%; 4 studies).

Authors’ conclusions
None of the studies assessed patient-relevant outcomes. Treatment with a weight loss diet or orlistat reduced weight and BP in patients with essential hypertension. Although sibutramine reduced weight, it did not reduce BP.

CRD commentary
The review question was stated clearly. Several relevant sources were searched and attempts were made to minimise publication and language bias. Appropriate methods were used to minimise reviewer error and bias during the review process. Only RCTs were included, and validity was assessed and the results reported. Little information other than age was provided about the participants in the included studies, which makes it difficult to assess how generalisable the results of the review are. Appropriate methods were used for the meta-analyses and heterogeneity was assessed. Unexplained heterogeneity was found for some outcomes (such as weight in orlistat studies) implying differences in results between studies. This was generally a well-conducted and clearly presented review and the authors’ conclusions are likely to be reliable. However, the clinical significance of the findings is uncertain.

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