Effect of sibutramine on weight management and metabolic control in type 2 diabetes: a meta-analysis of clinical studies


CRD summary
This review assessed the effects of sibutramine on weight and glycaemic control in obese patients with type 2 diabetes mellitus. The authors concluded that sibutramine may help to improve glycaemic control because it reduces weight. Inadequate reporting of the quality assessment, characteristics of the included studies, drop-outs and some review methods makes interpretation of the evidence difficult.

Authors' objectives
To assess the effects of sibutramine on weight and glycaemic control in obese people with type 2 diabetes mellitus.

Searching
The Cochrane Library, MEDLINE and EMBASE were searched for studies lasting up to October 2004; the search terms were reported. The reference lists of all relevant studies were checked. The manufacturers of sibutramine (Abbott Laboratories) were contacted for unpublished data. Only articles published in full in English were included; studies reported only as abstracts were excluded.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs, including blind, parallel or crossover RCTs, were eligible for inclusion.

Specific interventions included in the review
Studies of sibutramine that lasted at least 3 months were eligible for inclusion. All of the included studies recommended a lower calorie diet in addition to treatment. The included studies compared sibutramine (5 to 20 mg) with placebo or hypocaloric diet alone for between 3 and 12 months. Cointerventions included sulphonylureas, metformin, insulin and glibenclamide.

Participants included in the review
Studies of obese and overweight patients with type 2 diabetes were eligible for inclusion.

Outcomes assessed in the review
Inclusion criteria for the outcomes were not specified. The review assessed body weight, waist circumference, fasting blood glucose, serum insulin, glycated haemoglobin (HbA1c), fasting serum triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), systolic and diastolic blood-pressure (BP), and heart rate.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The studies were assessed using the Verhagen Delphi criteria (the source was referenced but no further details were given). The authors did not state who performed the validity assessment.

Data extraction
One reviewer extracted the data and a second reviewer checked the extraction. For each study, an effect size (ES)
(standardised mean difference) was calculated.

**Methods of synthesis**

**How were the studies combined?**
The studies were combined using meta-analysis. Pooled ESs with 95% confidence intervals (CIs) were calculated using standardised mean differences between treatments for each outcome. Publication bias was not assessed.

**How were differences between studies investigated?**
Statistical heterogeneity was assessed using the chi-squared statistic.

**Results of the review**

Eight RCTs (n=1,093) were included.

Sibutramine significantly reduced weight compared with placebo: decrease of 5.5 kg versus increase of 0.9 kg with placebo; the ES was -0.87 (95% CI: -1.00, -0.74, P=0.0000). Statistically significant heterogeneity was found (P=0.0026).

Sibutramine significantly reduced waist circumference compared with placebo: decrease of 5.32 cm versus increase of 1.13 cm; the ES was -0.67 (95% CI: -0.83, -0.51, P=0.0000). Statistically significant heterogeneity was found (P=0.001).

There was a small but statistically significant decrease in blood glucose with sibutramine; the ES was -0.17 (95% CI: -0.32, -0.03, P=0.0187). No statistically significant heterogeneity was found (P=0.9).

Sibutramine significantly decreased HbA1c compared with placebo; the ES was -0.28% (95% CI: -0.42, -0.13, P=0.0002). There was borderline statistically significant heterogeneity (P=0.0104).

Sibutramine significantly reduced plasma triglycerides (ES -0.24, 95% CI: -0.39, -0.09, P=0.0024) and increased HDL (ES 0.20, 95% CI: 0.05, 0.35, P=0.0087) compared with placebo. No statistically significant heterogeneity was found (P>0.1). There was no significant difference between treatments for total cholesterol or LDL cholesterol (the results were reported).

None of the studies assessed systolic BP. Compared with the control, sibutramine was associated with a small but statistically significant increase in diastolic BP (ES 0.22, 95% CI: 0.07, 0.38, P=0.0050) and heart rate (ES 0.53, 95% CI: 0.39, 0.67, P=0.000). No significant statistical heterogeneity was found (P>0.49).

**Authors' conclusions**

Sibutramine may help improve glycaemic control because it reduces weight. This reinforces recommendations that weight management may be a priority for obese patients with type 2 diabetes.

**CRD commentary**
The review question was clear in terms of the study design, intervention and participants. Several relevant sources were searched and attempts were made to locate unpublished studies, thus limiting the possibility of publication bias. However, the restriction to studies reported in English might have resulted in language bias. The methods used to select studies and assess validity were not described, so it is not known whether any efforts were made to reduce reviewer errors and bias. Only RCTs were included; the validity of the included studies was assessed systematically although the results were not reported.

There was minimal information on the included studies and no information on drop-outs. In addition, the effect of drop-outs on the results was not considered. Meta-analyses were performed but it was not stated whether fixed-effect or random-effects models were used. Although most of the studies in the meta-analyses showed a similar direction of treatment effect, the size of the effect varied across studies. Where significant statistical heterogeneity was found, there
was no examination or discussion of potential causes. Since the trials included in the meta-analysis varied considerably, both by dosage and the length of treatment, further exploration of how study characteristics were related to the observed results would have been useful. It was somewhat difficult to assess the clinical significance of results reported as ESs rather than natural units.

It is difficult to interpret the evidence given the inadequate, or lack of, reporting of the quality assessment, characteristics of the included studies and drop-outs, and methodological aspects of the review.

**Implications of the review for practice and research**

**Practice:** The authors stated that strict glycaemic control should be combined with proven treatments for dyslipidaemia and hypertension that reduce cardiovascular events.

**Research:** The authors did not state any implications for further research.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.