Long-term randomized clinical trials of pharmacological treatment of obesity: systematic review

Castaneda-Gonzalez L, Camberos-Solis R, Bacardi-Gascon M, Jimenez-Cruz A

CRD summary
The review concluded that pharmacological interventions achieved modest weight loss and resulted in a high incidence of adverse events. Unexplained baseline differences between studies and the fact that the relative influence of other components within the intervention package could not be determined mean that some caution is warranted in judging the reliability of the authors' conclusions.

Authors' objectives
To assess the effectiveness of pharmacological interventions on long-term weight loss.

Searching
PubMed and SCIELO were searched from 1999 to December 2008 for articles published in English and Spanish. Some search terms were reported.

Study selection
Randomised controlled trials that evaluated the efficacy of treatments with orlistat, sibutramine and rimonabant, that followed participants for at least 24 months and that measured weight loss were eligible for inclusion.

Participants with hypertension (sibutramine studies) and neuro-psychiatric diseases (rimonabant studies) were excluded. Most studies included clinically obese white women (without cardiac, renal, liver and gastrointestinal illnesses or neuro-psychological diseases) aged at least 17 years. Drug regimens varied. All studies except one offered nutritional counselling, encouraged physical activity or prescribed restricted diets. Most studies initiated a four-week lead-in period with hypocaloric diet or placebo before randomisation.

It appeared that two reviewers selected the studies.

Assessment of study quality
Two reviewers independently assessed the quality of the included studies on randomisation, double-blinding and withdrawal/dropout using the Jadad scale. The score for each quality component could range from zero to a maximum of 5. Disagreements or inconsistencies were resolved by consensus; a third reviewer made the final decision on unresolved disagreements.

Data extraction
The difference between pre- and post-treatment weights was extracted. Where possible, p-values were presented.

It appeared that two reviewers extracted data.

Methods of synthesis
Studies were summarised in a narrative synthesis grouped according to intervention.

Results of the review
Eleven RCTs (n=11,710, range 61 to 3,305 participants) met the inclusion criteria. Seven studies assessed orlistat and two studies each assessed sibutramine and rimonabant. One study scored 5, three studies scored 4, five studies scored 3 and one study scored 2 on the Jadad scale (score for one study not reported). Eight studies were double blind. Nine studies were analysed by intention to treat (ITT). Baseline differences were reported to be significant. Withdrawal/dropout rate ranged from 10% to 66% for to four years of follow-up.
Percentage weight loss achieved at the end of two years with orlistat ranged from 5% to 12%. Mean weight loss was 8kg (seven studies), a difference of 3.7kg when compared to placebo.

Sibutramine achieved weight loss of 4% to 10% and mean weight loss of 7.4kg (two studies), a difference of 5.5kg when compared with placebo.

Rimonabant achieved 7% weight loss and mean weight loss of 7.3kg, a difference of 4.4 kg when compared with placebo.

Overall, 26% of participants who used orlistat reported adverse events (mostly gastrointestinal events), which led to many participants suspending treatment. The main adverse events with sibutramine and rimonabant were incidence of treatment-associated infections and other generalised symptoms. Specific adverse events and rate of occurrence were reported in the main paper.

Cost information
The treatment costs of each intervention were estimated from market prices in Mexico in 2008. The price of each drug was calculated from the number of pills taken during the study period.

The total costs for two years of treatment were calculated as: orlistat given as 120mg three times a day would cost US dollars $4,500; sibutramine administered as 20mg/day would cost $5,300; and rimonabant 20mg/day would cost $4,100. Based on minimum wage in Mexico, these costs translated to the equivalent of 850 to 1,100 working days income. When evaluations and counselling by a physician, nutritionist, psychologist, physical activity trainer, laboratory and X-ray examination were added to the cost of drug, this translated into $750 for rimonabant, $1,000 for sibutramine and $1,200 for orlistat for each kilogramme of weight lost.

Authors’ conclusions
Pharmacological treatment for obesity led to modest weight loss and a high incidence of adverse events.

CRD commentary
This review addressed a well-defined question in terms of interventions, outcomes and study design. Relevant databases were searched, but there was no apparent search of secondary data sources or for unpublished data. Therefore, not all relevant data might have been included in this review. The restriction of the search to English and Spanish meant there was potential for language bias. Two reviewers independently assessed the quality of included studies to minimise errors and bias; although not explicitly stated, it appeared that the same number of reviewers selected studies and extracted data. Characteristics of individual studies were presented and an appropriate tool was used for assessing their quality. There were no apparent attempts to explore potential sources of heterogeneity.

The possibility of language bias, unexplained baseline differences between studies and the fact that the relative influence of other components within the intervention package could not be determined mean that some caution is warranted in judging the reliability of the authors’ conclusions.

Implications of the review for practice and research
Practice: The authors stated that pharmacological treatment for obesity was not justified, given that weight loss was modest and incidence of adverse events as well as costs were high. They suggested that it might appropriate to prescribe in specific cases where short-term weight reduction was mandatory due to medical reasons. For sibutramine treatment, constant medical evaluation was recommended due to effects on blood pressure and cardiac frequency.

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

Funding
The study was funded partly by CONACYT.
Bibliographic details

Original Paper URL
http://colombiamedica.univalle.edu.co/index.php/comedica/article/view/681

Indexing Status
Subject indexing assigned by CRD

MeSH
Anti-Obesity Agents; Appetite Depressants; Body Weight; Cyclobutanes; Humans; Lactones; Obesity; Randomized Controlled Trials as Topic; Weight Loss

AccessionNumber
12010004441

Date bibliographic record published
15/09/2010

Date abstract record published
19/01/2011

Record Status
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.