Acetato de megestrol: una revision sistematica de su utilidad clinica para la ganancia de peso en los enfermos con neoplasia y caquexia [Megestrol acetate: a systematic review usefulness about the weight gain in neoplastic patients with cachexia]
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Authors' objectives
To review the effectiveness of megestrol acetate for weight gain in patients with cancer-associated cachexia.

Searching
MEDLINE and the Cochrane Library were searched up to 2000. In addition, the references of retrieved articles were examined and the Spanish manufacturers of megestrol acetate were contacted to locate any unpublished trials. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
The review was restricted to randomised placebo-controlled trials (RCTs).

Specific interventions included in the review
The included trials had to compare megestrol acetate with placebo. The doses ranged from 40 to 480 mg/day. The duration of follow-up ranged from 8 to 80 weeks.

Participants included in the review
Specific inclusion criteria were not given, but the trials appeared to be concerned with cancer patients with cachexia.

Outcomes assessed in the review
The outcome assessed was weight gain, expressed as the difference in weight at the start of treatment compared with that at the end. Trials that expressed weight gain only as a percentage were excluded unless the authors provided suitable information for the calculation of weight gain.

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

Assessment of study quality
The validity of the included trials was assessed according to published methodological guidelines, including an assessment of randomisation and blinding. Two reviewers assessed the validity of the included trials and, where discrepancies existed, the decision of another reviewer was accepted as final.

Data extraction
The mean weight increase or decrease and variance were determined for the treatment and placebo groups for each of the studies. The actual process of extracting the data was not entirely clear.

Methods of synthesis
How were the studies combined?
The mean weight increases or decreases in the treatment and placebo groups for each trial were pooled in a meta-analysis, weighted by the inverse of the trial variance. A random-effects model was used.
How were differences between studies investigated?
Issues of clinical heterogeneity and differences in the conduct of the trials were briefly discussed in the report. Statistical heterogeneity was investigated, although the method was unclear. A random-effects model was used to allow for heterogeneity.

Results of the review
Eight RCTs with a total of 719 patients were included in the review.

The methodological quality of the included trials was poor: they scored between 0 and 3 out of 5 on the quality checklist used.

Patients treated with placebo had an average weight loss of 1.090 kg (95% confidence interval, CI: -1.620, -0.561), whereas those treated with megestrol acetate gained an average of 0.423 kg (95% CI: 0.078, 0.769). At a dose of 240 mg or less, patients taking megestrol acetate had an average weight gain of 0.448 kg (95% CI: 0.021, 0.874). No statistically-significant effect was observed when using higher doses; the weight gain was 0.358 kg (95% CI: -0.135, 0.851).

Cost information
The authors reported that 30 days’ treatment with megestrol acetate at 800 mg/day cost 334.17 euros.

Authors’ conclusions
Megestrol acetate at doses equal to or lower than 240 mg/day led to a slight weight gain in patients with cancer-associated cachexia. However, the majority of the included studies were of low methodological quality, pointing to the need for further well-designed studies in this area.

CRD commentary
The review had clear inclusion criteria for the study design, intervention and outcome. The criteria for the participants were less clear. The authors used a range of methods to locate published and unpublished trials and no language restrictions were applied. The validity of the included trials was assessed, but the meta-analysis did not include an assessment of the impact of quality on the pooled results. It is questionable whether the trials should have been combined in a meta-analysis given the differences in populations, doses of drug and duration of follow-up. Furthermore, the trials did not appear to have been pooled correctly. The mean weight gains for the treatment and placebo groups were pooled separately. A more appropriate method would be to pool the between-group weighted mean difference for each trial. In view of these comments and the omission of trials with weight gain expressed as a percentage, it is necessary to be cautious when interpreting the results. The authors highlighted the need for appropriately powered well-designed studies to clarify this clinical issue.

Implications of the review for practice and research
Practice: The authors questioned the need for high doses of megestrol acetate given their finding of no significant gain in weight with doses above 240 mg/day.

Research: The authors stated that there was a need for further well-designed studies on this topic.

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