Effects of megestrol acetate in patients with cancer anorexia-cachexia syndrome: a systematic review and meta-analysis
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CRD summary
This review assessed the effect of megestrol acetate in patients with cancer anorexia-cachexia syndrome (ACS) and concluded that compared to placebo, megestrol acetate reduced the symptoms of ACS, but did not affect survival and may not affect quality of life. The authors' conclusions appear over-optimistic given the limited evidence available and should be interpreted with caution.

Authors' objectives
To review the effect of megestrol acetate in patients with cancer anorexia-cachexia syndrome (ACS).

Searching
The review searched MEDLINE and EMBASE for studies published between 2002 and 2007, and Cochrane Central Register of Controlled Trials (CENTRAL). Search terms were specified. No language restrictions were applied.

Study selection
Eligible studies had to: use a randomised design; enrol patients diagnosed with non-hormone sensitive advanced stage cancer and ACS; assess the effects of megestrol acetate in terms of survival rate, weight change, performance status (Karnofsky scale, Eastern Cooperative Oncology Group scale) or selected quality of life parameters (such as appetite, nausea, pain, fatigue, depression, wellbeing, mood); compare megestrol acetate with either placebo, other drugs used in practice or clinical studies with ACS (included glucocorticosteroids, cisapride, dronabinol, eicosapentaenoic acid, fluoxymesterone) or with different doses of megestrol acetate.

Type of cancer varied and included lung, head and neck cancer. Some cancers were hormone insensitive. The authors stated that follow-up ranged from one week to two years. Median or mean follow-up periods ranged from two to 24 weeks. Doses of megestrol acetate ranged from 160mg/day to 1,600mg/day. Most studies were placebo-controlled. One study used dietary counselling as the control treatment; other (concomitant or alternative) treatments included cisapride, dronabinol, eicosapentanoic acid, prednisolone, dexamethasone and fluoxymesterone.

It appeared that two reviewers independently selected studies for inclusion.

Assessment of study quality
Two reviewers independently assessed studies in terms of randomisation, use of intention-to-treat analysis and completeness of follow-up.

Data extraction
Two reviewers independently extracted a wide range of relevant outcomes, with 95% confidence intervals (CIs).

Methods of synthesis
A wide range of relevant outcomes were pooled using DerSimonian and Laird random-effects models in order to produce pooled estimates with 95% CIs. Statistical heterogeneity was calculated using the Q test.

Results of the review
Thirty studies were included in the review (total sample size not stated). Quality was assessed, but not disaggregated at the item or study level. The review reported that most studies were placebo controlled and blinded, but the randomisation process was not adequately described. Many studies did not use intention-to-treat analyses.

Based on nine studies judged to be of high quality and not statistically heterogeneous, the review identified a
statistically significant difference that favoured megestrol acetate over placebo in the likelihood of any weight gain around three months after the start of the trial (relative risk 1.71, 95% CI 1.24 to 2.36, $I^2=42.6\%$).

The authors identified a statistically significant difference that favoured megestrol acetate over placebo in appetite (relative risk 3.00, 95% CI 1.86 to 4.84, $I^2=62.9\%$; seven studies with significant heterogeneity but judged overall as high quality).

Some statistically significant results were reported for outcomes that compared only particular doses of megestrol acetate to placebo or that compared two doses of megestrol acetate. Favourable outcomes were suggested in terms of reduced physical status worsening and absolute weight gain, but these differences were not statistically significant.

Authors' conclusions
The authors concluded that compared to placebo, megestrol acetate reduced symptoms of anorexia-cachexia syndrome, but this did not affect survival and whether it had any beneficial effects on overall quality of life had not been confirmed.

CRD commentary
This review addressed a clear review question using appropriate and clear study selection criteria. The search appeared adequate. Many primary study details were reported. The quality assessment appeared appropriate, although results were not reported at the primary study level and this made it difficult to evaluate the reliability of individual studies. It appeared that most stages of the review were conducted in duplicate, which reduced the risk of reviewer error and bias. The threshold used to identify whether studies were statistically heterogeneous was not reported and test results were only reported obliquely, which reduced review transparency. It appeared that results of the Q test for assessing statistical heterogeneity were only reported indirectly (within the "consistency" column of a table of findings). A wide range of outcomes were reported in a consistent though somewhat opaque format, and appeared to show results consistent with the conclusion.

The authors' conclusions appear over-optimistic given the limited evidence available and should be interpreted with caution.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that, because of the low quality of the included studies, a new randomised controlled trial was needed for valid assessment of the effects of megestrol acetate.

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