

High-dose progestins for the treatment of cancer anorexia-cachexia syndrome: a systematic review of randomised clinical trials

Maltoni M, Nanni O, Scarpi E, Rossi D, Serra P, Amadori D. *Ann Oncol* 2001;12:289-300

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Received during: Journal Club on the Tertiary Palliative Care Unit

Abstract:

Background: The aim of the present study was to summarise evidence from scientific studies on cancer anorexia-cachexia syndrome in order to assess and highlight the efficacy of high-dose progestins (megestrol acetate and medroxyprogesterone acetate) compared with placebo in patients with hormone-independent tumors.

Material and methods: A systematic review of published randomised clinical trials was carried out by an extensive electronic and hand search through databases, relevant journals and books, congress proceedings, reference lists, without any language or year of publication restriction. The research was conducted by two independent operators who collected the data in a form specifically designed for this review. Among the several possible outcomes, appetite and body weight were chosen.

Results: Fifteen randomised clinical trials (more than 2000 patients) were retrieved for the review. There was a statistically significant advantage for the high-dose progestins as regards improved appetite: pooled odds ratio (OR) = 4.23, 95% confidence interval (CI): 2.53-7.04. Although the effect of high-dose progestins on body weight was less impressive, statistical significance was also reached for this outcome: pooled OR = 2.66, 95% CI: 1.80-3.92. Treatment morbidity was low, due to the brief period of the treatment in most of the studies.

Conclusion: The effects of high-dose progestins on appetite and body weight were clearly demonstrated. However, further studies are undoubtedly warranted to investigate other aspects of progestin activity, especially as regards dosage, duration and timing with best therapeutic index.

Comments:

Strengths/uniqueness: This work represents the first systematic review of studies evaluating the effect of progestins in the treatment of cancer anorexia-cachexia syndrome. A focused clinical question was addressed. Study inclusion criteria were appropriate. The search for relevant studies was extensive. Study characteristics and outcomes were methodically described. Statistical heterogeneity amongst studies was tested for.

Weakness: Individual studies were not systematically appraised for validity. Although two independent researchers were involved, inter-observer agreement was not reported. The analysis of outcomes as dichotomous data (weight gain/increased appetite @ yes/no) excluded a significant number of studies that did not report results in this manner; also, this type of analysis does not convey the magnitude and clinical significance of the effects of progestin treatment. The studies themselves were heterogeneous in many respects (e.g. drug dosage, duration of treatment), although outcomes were consistent.

Relevance to Palliative Care: This systematic review supports the use of progestins for the treatment of appetite and weight loss in advanced cancer patients. As the authors point out in their discussion, unresolved issues include optimal dose, duration of treatment, and timing of initiation. However, even with refinements in treatment, the impact of progestins is likely to remain limited, given the complex pathophysiology of the anorexia-cachexia syndrome. Investigations of therapies and combinations of therapies with specific pathophysiological targets are ongoing.