Dronabinol versus megestrol acetate versus combination therapy for cancer-associated anorexia: a North Central Cancer Treatment Group Study.


Prepared by: Dr. Sharon Watanabe

Received during: Journal Club on the Tertiary Palliative Care Unit

Abstract:

Purpose: To determine whether dronabinol administered alone or with megestrol acetate was more, less, or equal in efficacy to single-agent megestrol acetate for palliating cancer-associated anorexia.

Patients and Methods: Four hundred sixty-nine assessable advanced cancer patients were randomized to (1) oral megestrol acetate 800 mg/d liquid suspension plus placebo, (2) oral dronabinol 2.5 mg twice a day plus placebo, or (3) both agents. Eligible patients acknowledged that loss of appetite or weight was a problem and reported the loss of 5 pounds or more during 2 months and/or a daily intake of less than 20 calories/kg of body weight.

Results: Groups were comparable at baseline in age, sex, tumor type, weight loss, and performance status. A greater percentage of megestrol acetate-treated patients reported appetite improvement and weight gain compared with dronabinol-treated patients: 75% versus 49% (P = .0001) for appetite and 11% versus 3% (P = .02) for ≥10% baseline weight gain. Combination treatment resulted in no significant differences in appetite or weight compared with megestrol acetate alone. The Functional Assessment of Anorexia/Cachexia Therapy questionnaire, which emphasizes anorexia-related questions, demonstrated an improvement in quality of life (QOL) among megestrol acetate-treated and combination-treated patients. The single-item Uniscale, a global QOL instrument, found comparable scores. Toxicity was also comparable, with the exception of an increased incidence of impotence among men who received megestrol acetate.

Conclusion: In the doses and schedules we studied, megestrol acetate provided superior anorexia palliation among advanced cancer patients compared with dronabinol alone. Combination therapy did not appear to confer additional benefits.

Comments:

Strengths/uniqueness: This is the first study to directly compare megestrol acetate with dronabinol for the treatment of cancer-associated anorexia. It exhibits the major features of a well-designed study: randomization, double-blinding, intention-to-treat analysis, adequate follow-up, and balanced treatment group characteristics.

Weaknesses: The dose of dronabinol may have been too low; this possibility is corroborated by the lack of adverse effects in patients who took this drug. The study did not exclude patients with prostate cancer, who could have benefited from megestrol acetate via tumour response, rather than an appetite stimulant effect.
**Relevance to Palliative Care:** Given the current debate over the role of cannabinoids for treatment of medical conditions, this study is a particularly useful addition to literature. Progestins remain the therapy of choice for anorexia in cancer patients who have an expected survival of months. However, these agents do not reverse the cachectic process, and many patients who take them do not experience symptomatic benefit. Therefore, novel approaches that target the complex pathophysiology of this syndrome are needed.