FPIN's Clinical Inquiries

Megestrol for Palliative Care in Patients with Cancer

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Clinical Question

Does the benefit of megestrol (Megace) outweigh the risks in patients with cancer?

Evidence-Based Answer

Megestrol may be considered as a component of palliative care nutritional support in patients with cancer. (Strength of Recommendation [SOR]: C, based on expert opinion.) Megestrol improves appetite in patients with anorexia-cachexia syndrome but does not improve quality of life. (SOR: B, based on a meta-analysis of heterogeneous randomized controlled trials [RCTs].) Megestrol is associated with an increased risk of venous thromboembolic events (VTE) when given during chemotherapy. (SOR: C, based on a cohort study with historical control.) It may increase the risk of symptomatic adrenal suppression. (SOR: C, based on a case report.)

Evidence Summary

A 2018 systematic review examined the effectiveness of megestrol for treatment of anorexia-cachexia syndrome in patients with multiple causes of cachexia, including cancer.[1] All trials compared megestrol, 160 to 320 mg per day, with placebo for 14 to 126 days. Primary outcomes included improved appetite, as measured by weight gain, and quality of life, as measured by multiple validated tools. Researchers converted outcomes to a standardized mean difference (SMD), where a magnitude of 0.2 was considered small, 0.6 moderate, 1.2 large, and 2.0 very large. Four RCTs included patients with only cancer (n = 250, primarily adults). Megestrol therapy resulted in more weight gain than placebo (mean gain: 5.25 lb [2.38 kg]; 95% CI, 2.20 to 8.16 lb [1.0 to 3.7 kg]), but it did not improve quality of life (two trials, n = 99; SMD = –3.9; 95% CI, –14 to 6.3). Megestrol was similar to placebo in terms of adverse outcome rates (two trials, n = 101; relative risk [RR] = 0.9; 95% CI, 0.39 to 2.08) and mortality (two trials, n = 90; RR = 1.01; 95% CI, 0.42 to 2.45). The included trials had high heterogeneity (I^2 = 68%), but randomization protocols and allocation concealment were unclear.

A retrospective cohort study evaluated the risk of VTE in patients with metastatic cancer who were receiving megestrol therapy.[2] The study included 97 patients (median age: 62 years; range: 33 to 84) who received megestrol at a median dosage of 160 mg per day (range: 160 to 480 mg) for a median of seven months (range: four to 19) while receiving chemotherapy. Researchers identified 11 cases of VTE (11.3%) during therapy: four occurred in patients with metastatic pancreatic cancer, and five occurred in patients receiving platinum-based chemotherapy. The rate of VTE

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in this cohort was higher than rates reported in the literature; the authors postulated that concomitant use of megestrol during chemotherapy may be the source of the increased risk. This study had several limitations, including small sample size, use of historical controls, and inclusion of patients receiving different chemotherapy regimens.

A case report highlighted three men with cancer who developed hypogonadism, adrenocortical suppression, and symptomatic adrenal insufficiency while receiving megestrol.[3] The patients (20, 63, and 71 years of age) reported fatigue, dyspnea, or feeling "low," and all developed decreased serum testosterone, cortisol, and adrenocorticotropic hormone levels. The patients also had an inadequate response to an adrenocorticotropin stimulation test, which is consistent with adrenal insufficiency. The patients reported significant improvement in their symptoms after discontinuation of megestrol and supplementation with androgens and corticosteroids.

Recommendations from Others

A 2014 guideline from the French Speaking Society of Clinical Nutrition and Metabolism recommends dietary counseling, sip feeds, enteral nutrition, and immune function–modifying nutritional substrates for cancer-related weight loss.[4] For palliative care in patients with cancer, the guideline states that megestrol, medroxyprogesterone (Provera), and corticosteroids increase appetite and weight and may be used if there are no contraindications (consensus opinion).

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