

Anorexia

Systematic Review / Meta-analysis Table

Review Author	Study Information	Conclusions and Implications
<p>Systematic Review of Megestrol Acetate (MA) in the Treatment of Anorexia-Cachexia Syndrome (ACS)</p>		
<p>PEP Weight of Evidence Category: Recommended for Practice</p>		
<p>Lopez, A, Figuls,M., Cuchi, G., Berenstein, E., Pasies, B., Alegre, M., et al. (2004).</p>	<p>Search Strategy: Data Bases: Cochrane Collaboration, Cochrane Controlled Trials Register, Medline, EMBASE, hand search of reference lists Key Words: randomized controlled clinical trial, double or single-blind, megestrol acetate and variants, terminally ill, terminal care, wasting syndrome No language restriction Data extracted by two reviewers using JADAD scale to assess quality with use of 3rd reviewer if needed</p> <p>Study Aims: Assess efficacy and safety of MA in improving appetite, weight gain, and health-related quality of life in patients with advanced cancer, AIDS, or other underlying pathologies, and anorexia-cachexia syndrome. Other aims were to evaluate efficacy of different doses and safety of MA.</p> <p>Trials Evaluated: Of 296 studies identified, 26 published between 1980 and 2002 met inclusion criteria. Of the 26, 19 compared MA to placebo, six compared MA to other drugs, and six studied the effectiveness of different dose levels. The quality of the studies was rated on the JADAD scale: 10 were high quality, seven were medium, and nine were low.</p> <p>Sample: 3887 patients with clinical diagnosis of anorexia/cachexia or symptoms indicative of anorexia/cachexia (loss of appetite, decrease in muscle mass, etc.) with diagnosis of cancer or AIDS. 3368 (86%) had cancer, 427 (11%) had AIDS, 81 (2%) had other diagnoses. Of the patients with cancer, 40% had lung cancer, 23% had GI cancer, 7% had head and neck cancer, 2% had pancreatic cancer, 2% had gynecologic cancer, 26% had other cancers Mean age of MA group: 57 years with 31% women. Mean age of placebo group: 59 years with 32% women. No difference in sociodemographic characteristics between groups. Doses of MA ranged from 160-1600 mg/day. Most frequently used dose = 480 mg. Ten of the 26 studies used 800 mg/day.</p> <p>Outcomes: Meta analysis of studies assessing appetite had homogeneous results showing</p>	<p>Significant improvements in appetite and weight gain in patients with cancer treated with MA compared with placebo</p> <p>Confirms results of earlier systematic reviews in demonstrating the advantages of MA over placebo in terms of weight gain and improved appetite</p> <p>This review did not define the optimal dose of MA.</p> <p>Given the adverse events profile, MA is a safe treatment option.</p>

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	<p>statistically significant improvement with MA over placebo, RR=2.33, (95% CI 1.52-3.59) For weight gain, results were homogeneous and in favor of MA but not statistically significant, RR=1.88, (95% CI 1.43-2.47) For quality of life, there was significant heterogeneity because of the variety of instruments used. When the results using only the Karnofsky Performance Scale were analyzed, heterogeneity was not observed, and the results were positive in favor of MA, RR=1.64, (95% CI 1.06-2.55).</p> <p>Subgroup analysis in patients with cancer showed positive results in favor of MA over placebo on appetite, RR=2.33, (95% CI 1.52-3.59), weight gain, RR=2.16 (95% CI 1.45-3.21) and quality of life, RR=1.81 (95% CI 1.13-2.89).</p> <p>In comparing MA to other drugs, MA showed benefit in terms of weight gain. No difference between MA and other drugs in terms of quality of life. For appetite, MA was superior to dronabinol but showed no advantage to other drugs studied.</p> <p>In comparing efficacy of different doses of MA, the only statistically significant result was observed in patients with cancer in whom higher doses were associated with greater weight gain, RR=1.65 (95% CI 1.00-2.73).</p> <p>There were no statistically significant differences between treatment and placebo groups in terms of adverse events except edema, which was greater in MA group RR=1.67, (95% CI 1.22-2.28).</p>	
<p>High- dose Progestins for the Treatment of Cancer Anorexia-Cachexia Syndrome: A Systematic Review of Randomized Clinical Trials</p>		
<p>PEP Weight of Evidence Category: Recommended for Practice</p>		
<p>Maltoni, M., Nanni, O., Scarpi, E., Rossi, D., Serra, P., & Amadori, D. (2001).</p>	<p>Search Strategy: MEDLINE, CANCERLIT, EMBASE, CINAHL, hand searching reference lists.</p> <p>Study Aim: To review the prospective randomized clinical trials (RCTs) that evaluate the use of progestins in CACS compared with placebo in patients with hormone-independent tumors.</p> <p>Trials evaluated: Of the 38 studies identified, 15 RCTs, published between July 1990 and June 1999, met inclusion criteria. The studies selected used various drug dosages, duration of treatment, eligibility criteria, type of population, study</p>	<p>There was a significant advantage for the use of high-dose progestins regarding improved appetite and body weight gain and support the safety and feasibility of treatment with oral progestins.</p> <p>Most of the studies were short in duration, lasting from one to 12 weeks. Important issues, such as dosage, duration of treatment, best time to start treatment, and eventual impact on the overall improved quality of life have yet to be defined.</p>

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	<p>design, methods of assessment, methods of reporting results and outcomes.</p> <p>Sample: 2,102 patients compiled of six studies of 557 patients that received neither chemotherapy nor radiation and nine studies of 1,545 patients that received some form of concomitant therapy.</p> <p>Outcome: among the several outcomes analyzed, effect on body weight was assessed in all studies and only two studies did not evaluate the effect on appetite. The most frequent method of assessing appetite was the visual analogue scale.</p>	
<p>A Systematic Review of the Evidence on Symptom Management of Cancer-Related Anorexia and Cachexia</p>		
<p>PEP Weight of Evidence Category: Recommended for Practice</p>		
<p>Brown, J.K. (2002).</p>	<p>Search Strategy: A literature search was conducted using the Cochrane Library, MEDLINE, CANCERLIT, CINAHL, dissertation abstracts, EBM reviews- Best Evidence, EMBASE and CRISP</p> <p>Study Aim: to review the studies regarding cancer-related anorexia and cachexia symptom management and make recommendations for future directions</p> <p>Studies evaluated: All studies focused on increasing food intake. Studies evaluated included:</p> <ol style="list-style-type: none"> 1. Three overviews of the problem from 1998-2000 2. Seven nonpharmacologic randomized clinical trials (RCTs) that examined the effects of nutritional counseling and/or commercial oral liquid supplements. Sample sizes ranged from 26 -180 patients. Clinical trials were included if the major focus was increasing food intake, decreasing energy usage, or minimizing weight loss. 3. Four topical research reviews- pharmacologic and exercise 4. One meta analysis on oncology nursing symptom-management interventions. 28 RCTs testing cancer symptom management interventions were identified from published and unpublished studies from 1981-1990. Only one study focused on anorexia and cachexia. 	<p>Conclusions: All nonpharmacologic RCTs reported improved caloric intake resulting from nutritional counseling and oral liquid supplements.</p> <p>Implications: Patients with cancer should be screened at diagnosis and reevaluated at regular intervals for current and potential nutritional problems. If nutritional screening identifies a patient at risk, a comprehensive nutritional assessment should be completed. A valid screening tool is needed.</p> <p>The meta-analysis concluded that insufficient evidence existed at the time to recommend any of the nursing interventions.</p> <p>Weight, appetite, and well-being were improved with progestational agents, and megestrol acetate had the most supporting evidence.</p>



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Systematic Review of Treatment of Cancer-Associated Anorexia and Weight Loss		
PEP Weight of Evidence Category: Recommended for Practice		
<p>Yavuzsen, T., Davis, M.P., Walsh, D., LeGrand, S., & Lagman, R. (2005).</p>	<p><u>Selection criteria:</u> studies involving adult patients > 18 years of age, non-hematologic malignancy, anorexia or symptoms of anorexia (such as lack of appetite), weight loss, poor performance status, and decreased quality of life</p> <p>The review involved only prospective RCTs (double- and single-blind or unblinded and Phase III trials).</p> <p>Quality of studies assessed using validated scale published by Jadad et al (1996).</p> <p><u>Sample size</u> = 55 studies meeting eligibility criteria</p> <p><u>Findings</u> Twenty-nine studies reviewed the safety and efficacy of progestins (23 examine megestrol acetate [MA], and six investigated medroxyprogesterone acetate [MPA]). Results favored progestins over placebo and found side effects were tolerable. Ten studies assessed the influence of MA on QOL; these demonstrated that the effect of MA on QOL was minimal.</p> <p>Six studies investigated the use of corticosteroids in 647 patients. Some improvements in appetite were found; however, dosage and type of steroid varied such that optimal dose and duration of therapy could not be determined.</p> <p>Two studies investigated prokinetics for anorexia in a total of 55 patients. No improvement in caloric intake or appetite was noted.</p> <p>Five studies investigated the use of hydrazine sulfate in 796 patients. Multicenter RCTs in patients with lung and colon cancers did not demonstrate any benefit when compared to placebo.</p> <p>Two studies investigated the use of cyproheptadine in 344 patients; these investigations had conflicting outcomes.</p> <p>One study investigated the use of pentoxifylline in 70 patients and found no benefit.</p>	<p>Multiple RCTs investigating the safety and efficacy of pharmacologic agents to stimulate appetite have been conducted.</p> <p>Only two therapeutic interventions for cancer-related anorexia are available for which there is enough evidence to support their use in patients with cancer: corticosteroids and progestins.</p> <p>Other studies had mixed outcomes, positive results in only a single randomized trial, or were not placebo-controlled.</p> <p>There is strong evidence supporting the use of progestins in patients with cancers. The most commonly reported drugs were MA and MPA. There was increased weight with both progestins. There was also evidence of a dose-response, but higher doses did not confer any additional benefit with regard to appetite.</p> <p>Metaclopramide is effective for nausea and early satiety but has not been shown to directly stimulate appetite.</p> <p>There is not sufficient evidence from RCTs to justify the use of dronabinol, EPA, EPO, ghrelin, interferon, melatonin, nandrolone, NSAIDs, or pentoxifylline in cancer-related anorexia.</p> <p>Cyproheptadine is a weak appetite stimulant, but side effects are limiting.</p> <p>The optimal dose, time to start, and duration of treatment for many appetite stimulants still is unknown. A more systematic approach to research methodology is needed. In addition, uniform outcome measures to</p>

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	<p>Melatonin was investigated in two studies involving 186 patients; these did not demonstrate any improvement in appetite or intake.</p> <p>Erythropoietin (EPO) was investigated in two studies involving 417 patients. In one investigation, EPO was administered in combination with a Cox-2 inhibitor +/- a specialized nutritional program. The intent-to-treat analysis was negative. No differences in food intake were noted.</p> <p>Three studies investigated the use of EPA in 689 patients; these reported conflicting results.</p> <p>Androgenic steroids were studied in two studies involving 512 patients; no significant benefit was demonstrated.</p> <p>Ghrelin was investigated in one RCT involving seven patients; differences between groups were noted, but long-term safety data on the agent are not available.</p> <p>Interferon was investigated in one study involving 57 patients; no differences were found.</p> <p>NSAIDs were investigated in two trials involving 417 subjects. These investigations failed to demonstrate a benefit in the NSAID arm.</p> <p>Cannabinoids were studied in one RCT involving 469 patients. Cannabinoids did not confer an additional benefit.</p> <p>Thalidomide has not been investigated in prospective RCTs.</p>	<p>better assess the value of various appetite stimulants are needed; these should include subjective ratings of appetite and associated symptoms, such as early satiety, and objective measures, such as food consumed, weight gain, and loss.</p>
<p>Megesterol Acetate for the Treatment of Anorexia-cachexia Syndrome (review)</p>		
<p>PEP Weight of Evidence Category: Recommended for Practice</p>		
<p>Berenstein, E.G., & Ortiz, Z. (2005).</p>	<p>The objectives of this investigation were to evaluate the safety, efficacy, and safety of megestrol acetate in palliating anorexia-cachexia syndrome in patients with cancer and AIDS and other underlying pathologies.</p> <p>Eligibility criteria: studies assessing the use of MA compared to placebo or other drug treatments in RCTs with patients diagnosed with anorexia-cachexia related to cancer, AIDS, or other underlying pathology. RCTs could be double-blind, single-blind, or unblinded; crossover studies were included if they reported the results of the first phase of the study</p>	<p>MA improves appetite and weight gain in patients with cancer. No overall conclusion can be drawn about QOL due to study heterogeneity.</p> <p>MA cannot be recommended for use in patients with AIDS or anorexia-cachexia related to other pathologies.</p> <p>A more systematic approach to the measurement of QOL in the trials was suggested.</p>

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	<p>Methods: data extraction was conducted by two independent authors, and methodological quality was evaluated. Studies where more than 50% of patients were lost to follow up were excluded from the analysis; methodological quality assessed using the Oxford scale (Jadad, 1996); scores for methodological quality were generally high.</p> <p>Sample: 30 trials that included a total of 4,123 patients met eligibility criteria; the mean age of patients was 58 years in treatment groups versus 57 years in the controls; the proportion of males to females in the treatment groups was 1,140/502 versus 1,733/731 in the controls; doses of megestrol administered ranged from 100 mg to 1600 mg per day.</p> <p>Outcomes: appetite increase, weight gain, mid-arm circumference, QOL</p> <p>Findings: Twenty-one trials compared MA at different doses with placebo; four compared different doses of MA versus other drugs; two compared MA with other drugs and placebo; and three compared different doses of MA.</p> <p>Results for MA versus placebo In patients with cancer, a statistically significant improvement in appetite was observed in the patients treated with MA. Weight gain also was observed in this group</p> <p>Results for MA versus other drugs MA did not show benefits in terms of appetite improvement in comparison to other drugs. Significant differences in QOL were not reported.</p> <p>Results for different dose levels of MA Using 400-800mg as a cutoff and comparing high to low doses, significant differences in appetite outcomes could not be appreciated.</p>	<p>Clinical effects of MA appear not to be dose-related</p> <p>The mechanism by which MA increases is unknown.</p> <p>The adverse event profile of MA includes edema as the only significant difference between placebo and MA.</p>