



## TODAY'S QUESTION:

### What is better for appetite stimulation: megace or dronabinol?

#### Background:

Anorexia is a common symptom in patients with palliative care needs. It may be especially prevalent in elderly patients. In a European series of 3030 palliative care patients with a variety of illnesses, moderate or severe anorexia was present in 26%. In a second report of 2382 inpatient palliative care consultations, adults 65 to 84 were significantly more likely to report anorexia than were younger adults (odds ratio 1.57, 95% CI 1.23-2.00).

Two of the most familiar pharmacological treatments for anorexia are megestrol acetate (Megace®) and dronabinol (Marinol®). Megestrol acetate is a progesterone derivative with predominantly progestational and anti-gonadotropic effects. Among patients with cancer-related anorexia and cachexia, megestrol acetate has beneficial effects on appetite and overall weight; however, it has no effect on overall quality of life or lean body mass. It also carries a significant risk for thromboembolic events. Dronabinol is synthetic THC and is FDA approved for anorexia associated with weight loss in patients with HIV/AIDS.

#### Importance:

It is important for palliative care providers to understand the differences between megestrol acetate and dronabinol when considering for patients with anorexia. Some of the important differences between these agents are: safety concerns, tolerability profiles, efficacy, price, and administration simplicity.

#### The Literature:

Let's first look at the Cochrane reviews:

- [Cochrane Database Syst Rev. 2013 Mar 28;\(3\):CD004310.](#)  
**Megestrol acetate for treatment of anorexia-cachexia syndrome.**
  - **Objective:** To evaluate the efficacy, effectiveness and safety of megestrol acetate (MA) in palliating anorexia-cachexia syndrome in patients with cancer, AIDS and other underlying pathologies
  - **Results:** 35 trials were included in the update with 3963 patients for effectiveness and 3180 for safety
    - Sixteen trials compared MA at different doses with placebo, seven trials compared different doses of MA with other drug treatments and 10 trials compared different doses of MA
    - There was a lack of benefit in the same patients when MA was compared to other drugs
    - There was insufficient information to define the optimal dose of MA, but higher doses were more related to weight improvement than lower doses. Edema, thromboembolic phenomena and deaths were more frequent in the patients treated with MA.
  - **Conclusion:** "This review shows that MA improves appetite and is associated with slight weight gain in cancer, AIDS and in patients with other underlying pathology. Despite the fact that these patients are receiving palliative care they should be informed of the risks involved in taking MA."
  - **Discussion:** So the authors here inferred that the risks of MA may not outweigh the benefits... The biggest risk being the thromboembolic phenomena
- [Cochrane Database Syst Rev. 2013 Apr 30;\(4\):CD005175.](#)  
**The medical use of cannabis for reducing morbidity and mortality in patients with HIV/AIDS.**
  - **Objective:** To assess whether cannabis (in its natural or artificially produced form), either smoked or ingested, decreases the morbidity or mortality of patients infected with HIV
  - **Results:** A total of seven relevant studies were included in the review, reported in eight publications.
    - Data from only one relatively small study (n=139, of which only 88 were evaluable), conducted in the period before access to highly-active antiretroviral therapy (HAART), showed that patients administered dronabinol were twice as likely to gain 2kg or more in body weight (RR 2.09), but the confidence interval for this measure (95% CI 0.72 - 6.06) included unity. The mean weight gain in the dronabinol group was only 0.1kg, compared with a loss of 0.4kg in the placebo group
  - **Conclusion:** "Whether the available evidence is sufficient to justify a wide-ranging revisiting of medicines regulatory practice remains unclear."
  - **Discussion:** Although this Cochrane looked at a lot more than weight, it might be helpful to see the results of this outcome

Alright – so to compare?

- [J Clin Oncol. 2002 Jan 15;20\(2\):567-73.](#)  
**Dronabinol versus megestrol acetate versus combination therapy for cancer-associated anorexia: a North Central Cancer Treatment Group study.**
  - **Objective:** 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.
  - **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
  - **Results:** 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 > or = 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,

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which emphasizes anorexia-related questions, demonstrated an improvement in quality of life (QOL) among megestrol acetate-treated and combination-treated patients.

- **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 benefit.”
- **Discussion:** Wow – ok so I guess when it comes to efficacy, megestrol wins?

### So... What does this all mean Jenn?:

- Yes it is true – when compared head to head, megace actually appears to have a bigger improvement in weight and also weight gain
- So you are asking, why don't we use it more then? Well - it is because of the other medication specific considerations. Overall, when considering the STEPS (safety, tolerability, efficacy, price and safety) of these products, here is how they compare:

Parameter	Megestrol	Dronabinol	Winner?
Safety:	There biggest risk is thromboembolic events: rate is approx. 32% (depending on the study)	Little risk expect for psychomimetic effects	Although you could argue with me – I would say dronabinol on this one
Tolerability:	Usually tolerable	Some psychomimetic effects that are usually tolerable	Again you could argue – but I would say dronabinol
Efficacy:	Has been shown to improve appetite and weight	Also has been shown to have improvements in appetite and weight	As above, technically megestrol
Price:	40 mg/mL (240 mL): \$143.95 So: \$1.20/day	5 mg (60): \$735.85 So: ~\$25/day	This time; megestrol
Simplicity:	Dosed QID. Max dose: 800mg/day	Dosed BID. Max dose: 20 mg/day	Well dronabinol I guess

**Look forward to other PCP Phast Phacts on appetite stimulants.**

### CLINICAL PEARL:

**Although megestrol acetate has a greater effect on anorexia when compared to dronabinol, it has a less desirable adverse drug reaction profile. Therefore consider to weight the risks and benefits of these agents. Dronabinol may be a more advantageous agent to initiate first.**