



**UPMC PALLIATIVE AND
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Palliative Care Pharmacy PHAST PHACT

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TODAY'S TOPIC:

Appetite Stimulants What should I be considering?

Background:

Anorexia and cachexia are common symptoms that can be seen in palliative care patients and can severely impact their quality of life. A study of 3,030 palliative care patients in Europe in 2009 found that 26% of patients experienced moderate-severe anorexia; cachexia incidence varies widely but is estimated to affect anywhere from 15-80% of patients with advanced illness.

There are many pharmacologic options used for anorexia/cachexia including: antidepressants (such as mirtazapine), anticonvulsants, corticosteroids, cannabinoids, progesterones, and anabolic steroids. The FDA-approved agents for appetite stimulation include megestrol acetate, dronabinol, and oxandrolone. The efficacy and safety of each agent varies and there is a lack of comparative clinical evidence between agents, making choice of the most appropriate agent unclear.

Importance:

Palliative care providers should be aware of the evidence behind different agents used as appetite stimulants and their respective adverse effects. Understanding the differences in the agents can help guide selection of the most beneficial product for individual patients.

The Literature:

Literature for megestrol acetate and dronabinol were discussed in a previous Phast Phact (attached) so let's look at some data for the other agents:

- [Am J Hosp Palliat Care. 2010 Mar;27\(2\):106-10.](#)

Phase II trial of mirtazapine for cancer-related cachexia and anorexia.

- **Objective:** To investigate effects of mirtazapine on weight, appetite, and quality of life of non-depressed patients with cancer related cachexia and anorexia
- **Methods:** 8-week, open-label, single-center study conducted in Canada with 17 patients treated with mirtazapine 15mg QHS x3 days then 30mg daily

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- **Results:**
 - Efficacy – 24% of patients had weight gain of ≥ 1 kg (range 1-3.6 kg) at 4 weeks
 - Only 5 patients completed the full 8-weeks of the study; 3 patients continued to put on weight at week 8, 1 patient showed improvement in quality of life
 - Mirtazapine was well tolerated with low withdrawal due to side effects
- **Conclusions:** Mirtazapine may have potential for treatment of cancer-related cachexia/anorexia
- **Discussion:** It is known that mirtazapine can induce weight gain and appetite when used as an antidepressant. This study showed that perhaps it can be used for those effects even in non-depressed patients but is limited by its small sample size

- [J Palliat Med. 2014 Apr;17\(4\):482-5.](#)

Use of corticosteroids for anorexia in palliative medicine: a systematic review.

- **Objective:** To identify evidence for use of corticosteroids and safest effective dose and duration for use in patients with anorexia in palliative care
- **Methods:** Review of 8 trials with 1356 total patients treated with a range of corticosteroids
- **Results:**
 - All studies showed some improvement of appetite with corticosteroid use
 - Not enough information to define optimal treatment dose and duration
 - Side effects were common and were more prevalent as trial duration increased
- **Conclusions:** Corticosteroids show benefit for patients with malignant disease but there is no evidence for use in anorexia in patients with nonmalignant disease
- **Discussion:** Corticosteroids may potentially be useful but intolerable side effects significantly limit their use, plus there is limited evidence to provide guidance on a specific agent or dose

- [J Cachexia Sarcopenia Muscle. 2018 Feb 5. \[Epub ahead of print\]](#)

Systematic review and meta-analysis of cannabinoids in palliative medicine.

- **Objective:** To evaluate the efficacy, tolerability, and safety of cannabinoids as an adjunct in palliative care patients
- **Methods:** Systematic review and meta-analysis
- **Results:** Of the 108 screened studies, nine studies (all with moderate bias) with a total of 1561 participants were included. 6 studies used dronabinol, 3 used combination of THC & CBD, and 1 used herbal cannabis
 - Studies in cancer patients showed a small benefit in increase of appetite and studies in HIV patients showed that cannabinoids were superior to placebo for both appetite and weight gain – all low-quality evidence
 - Comparison of herbal cannabis and synthetic cannabinoids (dronabinol) showed no difference in weight gain, tolerability, or safety in HIV patients
 - Adverse effects and drop-out rates were similar between cannabinoids and placebo
- **Conclusions:** Low quality of evidence does not allow for recommendations for cannabinoids for cancer or HIV-related anorexia and cachexia

- *Discussion:* Limited benefit shown for cannabinoids based on this review... will medical marijuana perhaps provide more benefit? Maybe this also makes sense why some patients say dronabinol doesn't work, while marijuana does?

So... What does this all mean Jenn Michelle?

- In a previous PCP Phast Phact, dronabinol won over megestrol acetate. Although megestrol acetate has a greater effect on anorexia, it has a less desirable adverse drug reaction profile, therefore risks may outweigh benefits
- As seen here, other medications commonly utilized are mirtazapine, steroids, and now cannabinoids – which all have marginal benefit
- When considering what agent should be first line, consider the following parameters:

Parameter	Megestrol	Dronabinol	Other CBDs	Mirtazapine	GCS
Safety	Most serious AE is thromboembolic events (NNH 11-55)	Limited AEs except for CNS effects	CNS effects are common	Most common AEs somnolence, dry mouth	Hyperglycemia, GI bleeding, HTN, psychological effects, etc.
Tolerability	Usually tolerable	Usually tolerable	Tolerable?	Usually well tolerated	Less tolerable
Efficacy	Shown to improve appetite, slight weight gain, & potentially QoL vs placebo (NNT 4-12); shown to be superior to dronabinol	Small benefit in appetite and potentially weight gain (NNT 10-72); shown to be inferior to megestrol	Anecdotal reports of stimulated appetite Questionable benefit? May depend on strain/ concentration of THC/CBD	Benefit most evident when used also as an antidepressant; small studies show some benefit in non-depressed individuals vs placebo	Improvement in appetite seen in most trials vs placebo (variable significance); limited evidence of ideal agent/dose
Price (inpatient)	800 mg /day = \$5.20/day	5-20 mg/day = \$6.80-24.96/day	N/A	7.5-15 mg/day = \$0.09/day	D: \$0.82/day P: \$0.24/day M: \$3.44/day
Simplicity	QID dosing	BID dosing	Ideal dosing unknown	Once daily dosing	Once daily to QID dosing

Key: CBDs: cannabinoids; GCS: glucocorticosteroids; AE: adverse effect; NNT: number-needed-to-treat; NNH: number-needed-to-harm; D: dexamethasone; P: prednisone; M: methylprednisone

- Megestrol acetate and corticosteroids appear to have the most benefit on weight gain and appetite but both are significantly limited by adverse effects
- Dronabinol (another cannabinoids) and mirtazapine seem to have a more favorable adverse effect profile but neither currently have great evidence for use in anorexia/cachexia

- There is no clear cut “best” agent for appetite stimulation – consider patient specific factors including safety, tolerability, efficacy, price, and safety!
 - Patients with cancer – may be best to avoid megestrol due to increase in risk of thrombotic events in already at-risk population (see NNH data above)
 - Patients with concomitant depression or trouble sleeping may benefit from a trial of mirtazapine
 - Least expensive: corticosteroids and mirtazapine → Most expensive: dronabinol

Geriatric Considerations:

- Although little evidence exists to support, mirtazapine is usually tolerable for most adults – it is still a Beers list medication
- Older adults are at higher risk of steroid-induced adverse effects – especially the psychiatric effects
- There is little information regarding the correlation between age and marijuana. It may be inferred the age will increase the risk of cannabinoid-induced ADRs, but this has not been confirmed
- Megesterol is a Beers list medication – used with caution in older adults

Stay tuned for future PCP Phast Phact on appetite stimulants!

CLINICAL PEARL:

Megestrol acetate or corticosteroids may be more efficacious than dronabinol and mirtazapine, however their adverse effects may limit their use. More information is needed regarding the role of cannabinoids. Always consider patient specific factors when choosing an appetite stimulant.