UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

# THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

## TODAY'S TOPIC:

### New Literature: Mirtazapine for cancer-associated anorexia and cachexia

**Background:**

Cachexia is common among patients with advanced cancer. The pathophysiology of cancer cachexia is multifactorial. To date, there is no known intervention that can reverse the progress of cancer cachexia. Few available pharmacologic options include: cannabinoids, megestrol acetate, steroids, stimulants, antipsychotics. Mirtazapine is a noradrenergic and specific serotonergic antidepressant that is also prescribed to improve appetite.

**Importance:**

Mirtazapine is commonly used in our seriously ill patients to "improve appetite" given its association with weight gain and proposed appetite stimulation when compared to other antidepressants. A new RCT was published aiming to assess the efficacy and tolerability of mirtazapine in patients with incurable solid tumors and cancer-related anorexia and cachexia. Palliative care clinicians should be aware of this new literature and its implications for clinical practice.

**The Literature:**

J Pain Symptom Manage. 2021 May 26;S0885-3924(21)00369-9.

**Mirtazapine in cancer-associated anorexia and cachexia: A double-blind placebo-controlled randomized trial.**

Objective: To determine the efficacy and tolerability of mirtazapine in patients with incurable solid tumors with cancer-related anorexia and cachexia

Methods: Double-blind, parallel-group, placebo-controlled randomized trial

- N= 100 (per-protocol analysis) ; N=113 (intention to treat analysis) incurable cancer patients with cancer-associated anorexia and cachexia
- Mirtazapine 15mg PO QHS for 28 days (having option to continue for another 28 days), placebo given for same duration

Outcomes:

- Primary: Change in appetite (0-10 scale)
- Secondary: Change in quality of life, fatigue, depressive symptoms, body weight, lean body mass, handgrip strength, inflammatory markers, adverse events, survival

Results:

- Efficacy:
  - Appetite score increased significantly from day 0 to day 28 in mirtazapine arm by 2 points as well in the placebo arm by 1.5 points on a 0-10 scale. No significant difference in change from baseline to day 28 between treatment arms.
- Safety:
  - No significant difference between arms in change of all other outcome measures, except for HADS-depression score which was higher in the placebo arm at day 28 (higher score indicates worse depression)
  - Adverse effects encountered more often in the mirtazapine arm including sleepiness, hand tremors, visual hallucinations, and abnormal dreams

Discussion:

- Positive anti-depressant effects and increased somnolence in mirtazapine group can continue to support mirtazapine's use for depression and insomnia
- Some patients did not tolerate mirtazapine and discontinued it because of undesirable adverse effects of somnolence/hallucinations

Conclusion: Mirtazapine 15mg is no better than placebo in improving the appetite of incurable solid tumor patients with cancer-associated anorexia and cachexia

**Maria's thoughts:**

- Progression of depression was less with mirtazapine (Great! Considering it is an antidepressant!)
- Is a 2-point change on a 0-10 scale is clinically meaningful? Possibly…
- This trial makes me wonder if small improvement in appetite is really related to a "placebo effect" when mirtazapine is administered…

**Bottom Line**:

- Treating depression (or one of the possible underlying causes of poor appetite) could improve poor appetite
- Mirtazapine did not make a significant difference when compared to placebo for improving appetite in patients with advanced cancer
- Are we surprised at these results? Maybe not… this gives us more evidence to decrease polypharmacy and prescribing cascade

**CLINICAL PEARL: Mirtazapine may not be better than placebo in improving appetite associated with cancer-related cachexia. If no improvement after adequate trial (~1 month), would discontinue.**