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 EVIDENCE: Olanzapine (Zyprexa®) for Chemo-related Anorexia

Background:

Olanzapine is an atypical (2nd generation) antipsychotic that has shown off-label efficacy for the treatment of nausea, especially in the oncology population and is recommended in the ASCO guidelines for the treatment of chemotherapy-related nausea. It has a unique receptor affinity profile; it is an antagonist for dopamine, serotonin, muscarinic, alpha, and histamine receptors which plays into the roles for use as well as its side effect profile. It can be sedating and anticholinergic, although has less risk for extrapyramidal symptoms and QTc prolongation than other antipsychotics. Evidence within the psychiatry literature shows that it has ability to increase appetite and promote weight gain, typically considered unfavorable side effects. Doses utilized for psychiatric conditions are commonly higher than what is utilized for nausea, although it may be possible that we can see improved appetite and weight gain at smaller doses. Limited data in the seriously ill/palliative care population exists.

Importance:

Patients with advanced malignancy undergoing chemotherapy commonly experience anorexia. Palliative care clinicians should be aware of the evidence for olanzapine when used for appetite and weight gain.

The Literature:

J Clin Oncol. 2023 Mar 28;JCO2201997.

Randomized double-blind placebo-controlled study of olanzapine for chemotherapy-related anorexia in patients with locally advanced or metastatic gastric, hepatopancreaticobiliary, and lung cancer

Objective: Assess efficacy of olanzapine in stimulating appetite and improving weight gain in patients receiving chemotherapy

Methods: Randomized, double-blind, parallel-group, placebo-controlled trial

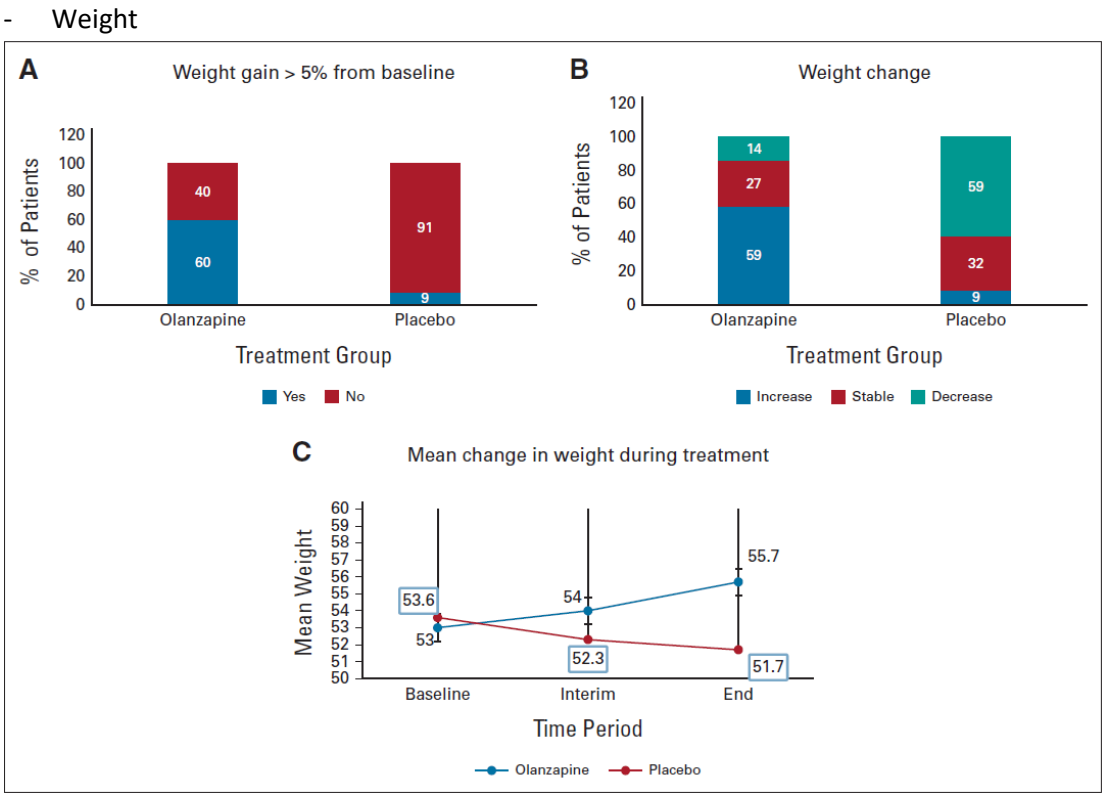
- Anorexia defined as any subjective loss of appetite within 6 months of diagnosis, and if persisted during chemotherapy, considered chemotherapy-related anorexia
- Randomized to receive olanzapine 2.5mg PO daily for 12 weeks versus placebo
- Evaluation occurred at baseline, during each visit for chemotherapy and at end of 12 weeks

Outcomes:

- Weight, height, BMI, mid-arm circumference, triceps skin-fold thickness
- Subjective global assessment tool (SGA) used to document nutritional status
- FAACT ACS (Functional Assessment of Chronic Illness Therapy) and VAS used for symptoms associated with anorexia

Results: n = 124, median age = 55 years, 66% male, 84% with Stage IV disease, treated with chemotherapy with palliative intent

- Weight



- Appetite
  - Improvement in appetite using VAS from baseline to week 12 was significantly higher in olanzapine group (43% v 13%)
  - FAACT ACS score of > 37 seen in 22% of olanzapine group versus 4% of placebo group
- Nutrition:
  - Improvement in nutrition scores (SGA) among 43% and 9% in olanzapine and placebo group, respectively
- Less chemotherapy toxicity in olanzapine group
- Adherence to trial medication – 90% and 93% respectively in olanzapine and placebo groups
- No difference between side effects in either group: hyperglycemia, cardiac abnormalities, headache, drowsiness, constipation, or transaminitis

Conclusion: "Low-dose, daily olanzapine is a simple, inexpensive, well-tolerated intervention that significantly improves appetite and weight gain in newly diagnosed patients on chemotherapy."

Bottom Line:

- This is a 12-week study, that showed improvement in appetite and weight gain in an oncology population with advanced disease receiving chemotherapy. We do not have data for use longer than 12 weeks
- Studies examining olanzapine for chemotherapy-related nausea are typically, short-term and have not shown these improvements
- Weight gain is potentially an objective way to measure changes in appetite although other confounders may be present leading to this particular outcome
- Based on this study, continued use of low dose olanzapine seems relatively safe
- Evidence for other pharmacologic options in the oncology population (progestins, steroids) have limited data to support their use, especially in terms of weight gain. Side effects of these agents (reduced immunotherapy efficacy, increased clot risk) make them less than ideal options for oncology patients
- We already use olanzapine frequently for nausea in oncology; a low dose (2.5mg) seems to be safe and effective (based on a singular study) to use in this population when trying to target symptoms of anorexia

CLINICAL PEARL: Low dose (2.5mg) daily olanzapine may be a safe and effective pharmacologic option to improve anorexia in the oncology population