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:

Requested topic: Bupropion (Wellbutrin®) for Cancer-Related Fatigue

Background:

Bupropion is an antidepressant that weakly inhibits neuronal uptake of norepinephrine (NE) and dopamine (DA). This mechanism potentially mimics psychostimulant action. It is FDA-approved for depression and smoking cessation. It has also been used off-label to treat fatigue associated with other conditions such as depression and MS. The specific underlying pathophysiology of cancer-related fatigue (CRF) is unknown and other symptoms could contribute to ongoing fatigue, making it difficult to palliate. The 2020 NCCN guideline for cancer-related fatigue recommend treating underlying causes, trying nonpharmacologic therapy, and using psychostimulant, methylphenidate, when other causes of fatigue have been excluded. NCCN does not currently recommend use of antidepressants, including bupropion for cancer-related fatigue, given limited evidence.

Importance:

Fatigue is a common symptom that burdens patients with cancer and adversely affects a person's quality of life. Although not currently a recommendation by NCCN, we often utilize medications off-label to help palliate symptoms when other modalities have failed. Palliative care clinicians should be aware of the literature for bupropion use for CRF, given its potential psychostimulant properties.

The Literature:

BMC Cancer. 2020 Feb 27;20(1):158.

Efficacy and safety of bupropion in cancer-related fatigue, a randomized double blind Placebo controlled clinical trial

Objective: To evaluate the efficacy of bupropion in CRF

Methods: Randomized, double-blind, placebo-controlled trial (n=30); bupropion 75mg/day x3 days then increased to 75mg BID for the rest of the study versus placebo x 6 weeks. Assessments were completed at baseline, end of weeks two and six.

Outcomes:

- Fatigue measured by Brief Fatigue Inventory (BFI) and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) where lower scores indicate worse fatigue
- Hospital Anxiety and Depression Scale (HADS) and performance status measured by Karnofsky and ECOG

Results:

- Efficacy:
  - No difference between placebo and bupropion at baseline or at the end of the second week for BFI or FACIT questionnaires
  - For BFI, difference between placebo and bupropion groups at end of week 6 exists, favoring bupropion
  - FACIT scores improved over the 6-week time period in the bupropion group more so than placebo
  - Significant difference seen at the end of the six weeks in bupropion group on ECOG score and Karnofsky score
- Safety
  - Well-tolerated; n=2 lack of appetite and insomnia

Conclusion: Six weeks of bupropion was effective in management of CRF and improves the performance status of cancer patients

Asian Pac J Cancer Prev. 2018 Jun 25;19(6):1547-1551.

Potential role of bupropion sustained release for cancer-related fatigue: a double-blind, placebo-controlled study

Objective: To determine efficacy of bupropion sustained release (SR) as a treatment for fatigue in patients with cancer

Methods: Randomized, double-blind, placebo-controlled trial (n=40); bupropion SR 150mg daily versus placebo x 4 weeks. Assessments completed at baseline and at end of week 4.

Outcomes:

- Improvement in fatigue (measured by FACIT-F questionnaires)
- Quality of life (QLQ-C 30 questionnaire) and depression (Hamilton depression rating scale)

Results:

- Efficacy:
  - Fatigue significantly improved in patients taking bupropion SR than for patients receiving placebo (P=0.000)
  - Improvement in functional, symptoms, and global quality of life domain (P<0.001)
- Safety: Most common side effects were GI-related, otherwise bupropion was well-tolerated

Conclusion: Four weeks of bupropion SR 150mg PO daily improved fatigue in cancer patients

Maria's thoughts & Bottom Line:

- Both trials were placebo controlled, makes me wonder how bupropion would stack up compared to other agents with more immediate benefit (ie. methylphenidate)
- Bupropion can cause tachycardia, N/V, headache, insomnia, anxiety, irritability, or lower seizure threshold. These side effects were not witnessed in the above trials
- Consider patient's prognosis and time to benefit (TTB) of bupropion.
- These studies suggest TTB of at least 4 weeks. Of note, in the *Asian Pac J Cancer Prev* study, included patients had life expectancy of > 6 months. If your patient has months to live, bupropion trial for CRF might be worthwhile, although it would be reasonable to counsel patients on expectation of timeline of therapeutic benefit. Patience is a virtue!

CLINICAL PEARL: May consider bupropion for CRF when life expectancy outweighs expected time to benefit of medication (at least 4 weeks)