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:

As Needed Methylphenidate for Cancer-Related Fatigue

Background:

Treating underlying causes of cancer-related fatigue is our first treatment strategy, although this is usually difficult and ineffective alone given the fatigue is a physiological result of the progression of the cancer in our patient population. We then turn to nonpharmacologic and pharmacologic therapy to treat the fatigue directly. Psychostimulants, such as methylphenidate, have been used. Methylphenidate is FDA-approved for ADHD and narcolepsy. Previous RCTs and meta-analyses have been done but results are mixed. These studies have examined methylphenidate routine use. Given its quick onset of action (~20-60 minutes) and short duration of action (immediate release: ~3-5 hours), utilizing on an as needed basis may be favorable to reduce adverse effects of continued use of psychostimulant.

Importance:

Cancer-related fatigue is common in our palliative care population. It is important for palliative care clinicians to be aware of the evidence for stimulants for our patient population.

The Literature:

J Pain Symptom Manage. 2020 Nov;60(5):992-1002.

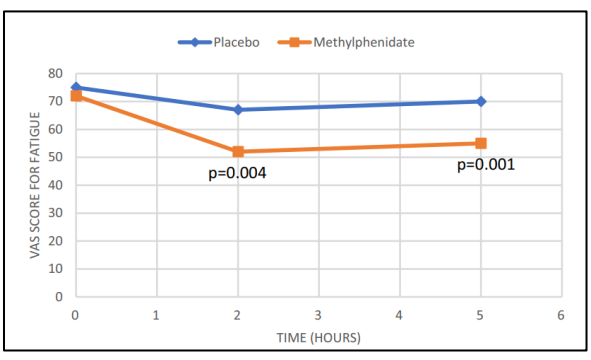
Methylphenidate as Needed for Fatigue in Patients with Advanced Cancer. A Prospective, Double-Blind, and Placebo-Controlled Study

Methods:

- Prospective, double blind RCT (data collected from 1999-2003); patient acted as their own control
- 1 week study period: Random assortment of placebo or methylphenidate 10mg tabs TID PRN (max 3 doses per day) with last dose being no later than 5pm
- No restrictions on concomitant steroid or opioid use
- Assessments in the form of questionnaires: VAS (100 point- higher point value worse fatigue): tiredness, function scales, QOL scale, symptom scale, and Multidimensional Fatigue Inventory (MFI-20) prior to dose, 2 hours after dose and 5 hours after dose

Results:

- N=28 patients, mean age = 69 years



- Efficacy
  - Methylphenidate was more effective in reducing tiredness (VAS score) at both 2 and 5 hours after dose administered compared to placebo
  - Methylphenidate was more effective at reducing drowsiness and improving activity at 2 hours after the dose, this effect was not sustained for 5 hours
- Safety
  - No difference in other ESAS (concentration, etc) scores

Discussion

- Clinically important difference on a 100 point scale is at least 5 points; in this study differences in were ≥ 10 for drowsiness and tiredness

Conclusion

- Methylphenidate 10mg was more effective than placebo in improving CRF

J Clin Oncol. 2006 May 1;24(13):2073-8.

Patient-controlled methylphenidate for cancer fatigue: a double-blind, randomized, placebo-controlled trial

Methods:

- Prospective, double-blind RCT
- 1 week study period: Random assignment of methylphenidate 5mg or a placebo every 2 hours PRN (max of 4 doses per day), then day 8 patients were offered open-label methylphenidate 5mg every 2 hours as needed for fatigue
- Functional Assessment for Chronic Illness Therapy-Fatigue (FACIT-F), 13 item fatigue subscore (0-52 scale, higher value less fatigue) administered on day 8 (primary), 15 for those who continued the study ; ESAS (0-10) rating for symptoms including fatigue recorded on days 8 and 15

Results:

- Efficacy
  - N=112 (52 in methylphenidate group, and 53 in placebo group), median age = 56
  - No significant difference in FACIT-F or ESAS scores between methylphenidate and placebo groups at day 8
  - Mean daily number of capsules of methylphenidate between days 1 and 8 were: 2.3
- Safety
  - Common adverse effects restlessness, tachycardia, insomnia, and anorexia were present in both groups
  - More patients in the methylphenidate group experienced vertigo

Conclusion:

- Methylphenidate is not superior to a placebo for the management of CRF

Bottom Line:

- Differences in the outcome measurements exist: post-administration response versus overall response. This could account for the difference in findings of these two RCTs…
- A higher dose may have a more noticeable effect (ie. 10mg in the first study and 5mg in the second study).
- I still recommend using the lowest effective dose, so neither study would really influence my starting dose… would still start low (2.5mg may be appropriate in some situations)
- As needed administration is likely is safer than scheduled use, given such short half life and quick onset of action of methylphenidate, and may provide less overall side effect burden
- Both are short-term studies like most studies in patients with advanced cancer, which may not matter as long-term outcomes likely don't apply to this patient population…
- This may suggest that methylphenidate produces immediate noticeable improvement in fatigue for patients but this improvement is not sustained/noticed over a period of time

CLINICAL PEARL: Methylphenidate on an as needed basis may be helpful in reducing CRF. Recommend using lowest effective dose to decrease psychostimulant-related side effects.