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:

Dexamethasone for Cancer-related fatigue

Background:
After attempting to treating underlying causes of cancer-related, we turn to nonpharmacologic and pharmacologic therapy to treat the fatigue directly. Different classes of medications have been used to improve fatigue, including steroids. Dexamethasone is a favorable choice as it is a long-acting glucocorticoid that could be dosed once daily for this indication. Physiologic activity is mediated by the glucocorticoid receptor, which is expressed in almost every tissue of the body. This likely accounts for the vast array of off-label clinical uses of steroids in the palliative care population, including for fatigue. It has been hypothesized that dexamethasone's peripheral effects on proinflammatory cytokines aids in its mechanism for improving fatigue.

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 steroid use in our patient population.

The Literature:
J Clin Oncol. 2013 Sep 1;31(24):3076-82.

Reduction of cancer-related fatigue with dexamethasone: a double-blind, randomized, placebo-controlled trial in patients with advanced cancer

Methods:
- Randomized, double-blind, parallel controlled trial, duration = 14 days
- Dexamethasone 4mg or placebo orally twice daily

Outcomes:
- Change in FACIT-F (QOL instrument) fatigue subscale score from baseline to day 15, FAACT (symptom specific subscale with focus on anorexia/cachexia) subscale baseline, day 8 and day 15, ESAS individual symptoms, psychological distress

Results:
- N= 84; 41 (placebo), 43 (dexamethasone)
- Efficacy
  - Improvement in FACIT-F fatigue subscale in dexamethasone group versus placebo group at 15 days (mean difference = 5.9 points) and 8 days (mean difference = 4.95 points)
  - Improvement in with dexamethasone compared to placebo: FACIT-F total quality of life score at day 15, FACIT physical well-being score at days 8 and 15, ESAS physical distress score at days 8 and 15, FAACT score at day 15, and ESAS pain score at day 8
- Safety
  - No significant difference in frequency of adverse effect between groups

Discussion
- Short study duration supports quick benefit of de
- Short study period; unable to assess long-term outcomes or side effects of daily steroid use
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Conclusion
- Dexamethasone was more effective than placebo in reducing fatigue in patients with advanced cancer

Clin Drug Investig. 2017 Apr;37(4):387-392.

Predictors of the usefulness of corticosteroids for cancer-related fatigue in end-of-life Patients

Methods:
- Retrospective cohort study of patients who received betamethasone (most widely used corticosteroid for treatment of CRF in Japan)
- Regression analysis to determine factors related to CRF in EOL patients and logistic regression analysis for purpose of identifying potential predictive factors for usefulness of corticosteroids in treatment of CRF in terminal cancer patients

Results:
- N=87
- Significant predictors of effect of betamethasone efficacy were: days from the start date of betamethasone administration to the date of death, initial daily dose of betamethasone, age, and administration of fentanyl
  - Cut-off values for improvement in CRF: initial dose ≥ 4mg (about the same equivalent dose for dexamethasone), ≥ 16 days from start date to date of death (ie. prognosis of ≥2.5 weeks), age ≥60

Conclusion:
- Potential predictors of usefulness of corticosteroids for CRF is starting dose, prognosis of ≥2.5 weeks, and older age

Bottom Line:
- The major limitation in the RCT by Yennurajalingam et al is the short duration of the study (14 days). If dexamethasone is effective, it is likely that it will be continued longer than a 2-week duration. We do not know the efficacy or safety implications extending past the 14-day trial period…
- Although no significant difference is found between dexamethasone and placebo treatment groups, there is a trend towards higher (≥ grade 3) AEs in the dexamethasone group, which makes me question what the longer term safety implications are when used for CRF
- Hyperglycemia was not an adverse effect monitored in this study… although this may not be as important in end-of-life scenarios, this could provide us more insight into long-term consequences to steroid use
- Given long duration of action of dexamethasone, I would be curious in knowing if there is a legacy effect… Does the improvement in fatigue persist even after discontinuation? …this would help us narrow down an appropriate duration of treatment…
- Patients starting with at least dexamethasone 4mg PO daily, with life expectancy > 14 days, and of older age (>60 years) may benefit from a trial of dexamethasone. Would consider this along with other patient-specific factors to determine if patient is appropriate for a steroid trial for CRF
- Another limitation is co-administration of immunotherapy which limits the utilization of steroids in our oncology population unless immunotherapy is no longer being pursued

CLINICAL PEARL: Short-term dexamethasone may be helpful in reducing CRF. Appropriate duration guidance requires more evidence.