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TODAY'S DEBATE:

Antipsychotics and Delirium: To prescribe or not to prescribe?

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Background:

Delirium is a common symptom experienced by palliative care patients, especially near the end of life. Currently, there are no FDA-approved medications indicated for the prevention or treatment of delirium. Guidelines recommend antipsychotics for the treatment of delirium when it is associated with behavioral disturbances and other nonpharmacological options have proven unsuccessful. Antipsychotics carry a black box warning for increased mortality in elderly patients with dementia-related psychosis and may cause other adverse effects, such as extrapyramidal symptoms and anticholinergic effects.

Importance:

Delirium can be a distressing symptom for palliative care patients and has been associated with cognitive decline and increased risk of death. Appropriate management of these symptoms is necessary to promote comfort and minimize suffering.

The Literature:

Have you seen the newest study on this topic?:

- JAMA Intern Med. 2017 Jan 1;177(1):34-42.
  Efficacy of Oral Risperidone, Haloperidol, or Placebo for Symptoms of Delirium Among Patients in Palliative Care: A Randomized Clinical Trial.
  - Double-blind, randomized, controlled trial
  - Population: individuals diagnosed with delirium per DSM IV; Memorial Delirium Assessment Scale (MDAS) score of ≥7; and score of ≥1 on Nursing Delirium Screening Scale (NuDESC) for items 2, 3, and 4 which correspond with inappropriate behavior, inappropriate communication, or illusions/hallucinations, respectively
  - Intervention: placebo (n=84), haloperidol (n=81), or risperidone (n=82) every 12 hours and titrated to effect
    - All participants received nonpharmacological therapy for delirium
    - Midazolam available every 2 hours as needed for safety or distress
  - Primary Outcome: average of the last 2 delirium symptom scores on day 3 using NuDESC scoring of items 2, 3, and 4
  - Results: Two hundred forty-seven participants (mean [SD] age, 74.9 [9.8] years; 85 women [34.4%]; 218 with cancer [88.3%]) were included in intention-to-treat analysis
    - Baseline delirium symptom scores were similar for all three groups
    - Most participants received total daily antipsychotic doses of <4 mg and <2 mg for those ≤65yo and >65 yo, respectively
    - Compared to placebo, delirium symptom scores were 0.48 units higher with risperidone (p=0.02) and 0.24 units higher with haloperidol (p=0.001) after 72 hours. Using a mixed-model analysis, daily delirium symptom scores were on average 0.24 units higher with risperidone (p<0.001) and 0.21 units higher with haloperidol (p=0.002)
    - Survival was better with placebo compared to haloperidol (HR 1.73; 95% CI1.2-2.5) but not risperidone (HR 1.29; 95% CI 0.91-1.84)
    - Midazolam use was significantly lower in placebo group compared to risperidone or haloperidol groups (p<0.05)
  - Conclusions: Using antipsychotics for the treatment of delirium resulted in higher delirium symptom scores compared to supportive strategies alone.
  - *Discussion:* This is a tricky trial and it is highest debated. Here are some notes to consider
    - CAM may be a more reliable way to identify delirium compared to NuDESC (sensitivity 13-98% vs 96%, specificity 77-100% vs 69%)
    - Midazolam may have contributed to poorer delirium symptom scores, since the group receiving antipsychotics also received more midazolam
    - These individuals may have received inadequate antipsychotic doses, since total daily doses of up to 20 mg haloperidol and 6 mg risperidone are used in clinical practice
    - Most individuals achieve steady state in 2-6 days with haloperidol and 4 days with risperidone. Patients may not have experienced the maximum benefit from these agents after only 3 days

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

But we never check just one study…

- J Am Geriatr Soc. 2016;64(4):705-714.
  Antipsychotic Medications for Prevention and Treatment of Delirium in Hospitalized Adults: A Systematic Review and Meta-Analysis.
  - Objectives: Determine whether antipsychotics reduce incidence of postoperative delirium or improve outcomes when treating delirium in adults admitted to medical or surgical inpatient units
  - Results: Included 7 trials evaluating prevention of postoperative delirium and 12 trials evaluating treatment of delirium
    - No significant association between antipsychotic use and the following:
      - Incidence of delirium in the postoperative setting
      - Duration of delirium
      - Severity of delirium
      - Hospital length of stay
      - ICU length of stay
      - 30-day mortality after hospitalization
  - Conclusion: "…antipsychotic pharmacotherapy does not improve outcomes when used for prevention or treatment of delirium in hospitalized adults."
  - *Discussion*: The studies included were heterogeneous in design due to a lack of available studies regarding this topic. Additionally, symptomatic relief was not an outcome for any of the included studies, which is commonly the treatment goal for palliative care patients.

So… What does this all mean ~~Jenn~~ Gina?:

- Recent literature suggests that antipsychotics may be ineffective at treating or preventing delirium and may even worsen delirium symptoms compared to nonpharmacological methods alone.
- Consider the benefits and risks of medications, such as benzodiazepines, which have the potential to contribute to delirium.
- Nonpharmacological methods, such as presence of family, use of vision or hearing aids, and reorientation, remain first-line treatment of delirium.
- Antipsychotics, should be reserved for treating delirium that is associated with hyperactive or aggressive behavior that causes the patient to suffer or threatens a patient's safety.
- Particular antipsychotic selection is often based on side effect profile and cost – as per previous PCP Phast Phacts, always consider haloperidol (with a target dose of 2mg)

Look forward to other PCP Phast Phacts on delirium - or take a look at last year's "Demystifying Delirium" mini-series.

CLINICAL PEARL:

Antipsychotics should be used cautiously in patients with delirium but remain a potential treatment option when nonpharmacological agents have failed.