Clinical Pearls in Psychiatry:
Antipsychotics in Acute Care

Joshua Caballero, PharmD, BCPP, FCCP
Professor, Chair
Clinical and Administrative Sciences
Larkin University, College of Pharmacy

Objectives

• Discuss recent literature related to the treatment of the following:
  • Agitation/delirium in non-critically ill patients
  • Antipsychotics and CV adverse effects/QT changes
  • De-prescribing strategies and algorithms for antipsychotics

Objectives

• Describe opportunities for pharmacists in the administration of long acting antipsychotic medications
• Apply practice strategies to monitor antipsychotic use for patients in the acute care setting

Agitation vs. Delirium

Agitation
• Psychomotor disturbance characterized by a marked increase in both motor and psychological activities, often accompanied by a loss of control of action and a disorganization of thought

Delirium
• Acute decline in attention and cognition
• Subtypes include:
  • Hypoactive
  • Hyperactive*
  • Mixed
* Agitation is a component of hyperactive delirium

Disclosures

• At this time, I do not have any relevant financial/non-financial relationships with any proprietary interests

Delirium

• Approximately 50% of older adults during hospital admission or stay may experience delirium
• Hospital delirium persisted at discharge in approximately 45% of cases
• Associated with higher morbidity and mortality
• Healthcare costs: over $160 billion annually
Delirium: Risk Factors\(^3-6\)

- Predisposing factors
  - Dementia
  - > 65 years of age
  - Sensory/functional impairment
  - Comorbidities
    - Depression
    - Renal/hepatic impairment

- Precipitating factors
  - Immobilizations
  - Medications
  - Dehydration
  - Pain
  - Sleep deprivation
  - Urinary retention/constipation
  - Acute illness

Delirium: Medications that Increase Risk\(^3,7-9\)

- Anticholinergics
- Anticonvulsants
- Antipsychotics
- Benzodiazepines
- Corticosteroids
- Histamine-2 (H\(_2\)) blockers
- Non-benzodiazepine hypnotics
- Opioids
- Sedative-hypnotics
- Also consider alcohol and/or drug withdrawals

Delirium: Anticholinergic Risk Scale\(^10,11\)

<table>
<thead>
<tr>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbidopa-levodopa</td>
<td>Cetirizine</td>
<td>Tolterodine</td>
</tr>
<tr>
<td>Selegiline</td>
<td>Cyclobenzaprine</td>
<td>Amantadine</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>Loperamide</td>
<td>Loratadine</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>Clonazpine</td>
<td>Tizanidine</td>
</tr>
<tr>
<td>Trazodone</td>
<td>Desipramine</td>
<td>Diphenhydramine</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Baclofen</td>
<td>Chlorpheniramine</td>
</tr>
</tbody>
</table>

Delirium: Prevention and Management

- Rule out underlying cause(s)
- Medications
- Infection
- Electrolyte imbalance
- Manage symptoms
  - Non-pharmacologic options
  - Pharmacologic options

Delirium: Non-Pharmacologic Options\(^5,12\)

- Multi-component protocols
  - Goal: decrease risk factors (e.g., medication, environment)
  - Requires interdisciplinary approach
- Targeted risk factors
  - Immobility
  - Sensory impairment (e.g., visual/hearing impairment)
  - Dehydration
  - Cognitive impairment
  - Sleep deprivation

Delirium: Non-Pharmacologic Options\(^13-17\)

- Studies using non-pharmacologic/multicomponent options show decreases in:
  - Incidence
  - Duration of delirium
  - Length of hospital stay
  - Accidental falls
  - Mortality

Note: minimal effects on decreasing severity or recurrences
Delirium: Pharmacologic Options

- Currently, there are no FDA approved medications to treat delirium

Delirium: Efficacy of Antipsychotics

Guidelines Examples on Treatment of Delirium

- American Psychiatric Association: Low dose haloperidol as first-line agent in symptomatic management of delirium episodes
- National Institute for Health and Clinical Excellence: Consider short term haloperidol or olanzapine for distressed person with delirium who is posing a risk to themselves or others
- American Geriatric Society: May use antipsychotics at the lowest effective dose for the shortest possible duration for severely agitated patients who are threatening harm to self and/or others

Antipsychotic Medication for Prevention and Treatment of Delirium in Hospitalized Adults: A Systematic Review and Meta-Analysis

- Objective: Evaluate effectiveness of antipsychotics in preventing and treating delirium (post-operative patients)
- Design: Systematic review and meta-analysis
- Inclusion: 19 studies (12 treatment + 7 prevention)
- Medications: First (haloperidol) and second generation (risperidone, olanzapine, quetiapine) antipsychotics
- Outcomes: Delirium: incidence, severity, and duration
- Length of stay: hospital and intensive care unit

Conclusions (on post operative patients)

- No improvement in incidence, severity, or duration
- No improvement in length of stay
- Hospital and intensive care unit

Note: Some good news with no association with mortality up to 30 days

Delirium: Antipsychotic Adverse Effect Profile

- Anticholinergic: sedation, orthostasis, dizziness, falls, urinary incontinence
- Extrapyramidal symptoms
- Cardiovascular side effects: QTc prolongation (possible cutoff of > 450-500 msecs)
- Ventricular arrhythmias
- Venous thromboembolism
- ... and increased mortality
Delirium: Antipsychotic Contraindications

"WARNING: Increased Mortality in Elderly Patients With Dementia-Related Psychosis"

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials (modal duration* of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infections (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. [DRUG BRAND NAME (drug generic name)] is not approved for the treatment of patients with dementia-related psychosis."

Delirium: Antipsychotic Final Recommendation

- Second generation antipsychotics should be reserved as a last treatment option when
  - non-pharmacologic interventions have failed
  - Symptoms cause the patient to be a threat to themselves or others
  - Accompanying severe aggressive behavior

Delirium: Discontinuation of Antipsychotics

- A study on approximately 500 patients showed 30% of patients were discharged on an initiated antipsychotic
  - Of those, fewer than 13% of discharge summaries had instructions on antipsychotic discontinuation

- Role for a residency project or APPE students to develop protocol?
**Delirium: Discontinuation of Antipsychotics**

- PRN antipsychotics in long-term care facilities
- 14 day limitation and cannot be extended
- New order may be written if the prescriber:
  - DIRECTLY examines and assesses the patient
  - Documents clinical rationale for the new order including:
    - Benefit of the medication and
    - Have symptoms improved as a result of the PRN medication
  - Can be used as PRN in emergent situation

---

**Long Acting Injectable (LAI) Antipsychotics**

- **Haloperidol decanoate** (Haldol Decanoate)
- **Aripiprazole lauroxil** (Aristada)
- **Aripiprazole monohydrate** (Abilify Maintena)
- **Olanzapine pamoate** (Zyprexa Relprevv)
- **Paliperidone palmitate-monthly** (Invega Sustenna)
- **Paliperidone palmitate-3 months** (Invega Trinza)
- **Risperidone microsphere** (Risperdal Consta)

---

**Florida Statute 465.1893: Administration of antipsychotic medication by injection**

(1) (a) A pharmacist, at the direction of a physician licensed under chapter 458 or chapter 459, may administer a long-acting antipsychotic medication approved by the United States Food and Drug Administration by injection to a patient if the pharmacist:

1. Is authorized by and acting within the framework of an established protocol with the prescribing physician and
2. Practices at a facility that accommodates privacy for non-deltoid injections and conforms with state rules and regulations regarding the appropriate and safe disposal of medication

---

**LAI Antipsychotics: FLORIDA LAI Administration Workgroup**

- Official protocol development for the state under construction
- Will include educational component
- Eight hours of training + active learning (administering injection)
- Protocol development
  - Alberto Augsten, PharmD, MS, BCPP, DABAT
  - Soheyla Mahdavian, PharmD, BCGP, TTS
  - Cynthia R. Hal, PharmD, JD, MS
  - Jacquelyn Canning, PharmD, BCPP

---
LAI Antipsychotics: LAT Clinic

- Goals for 2018
  - Medication efficacy and side effect monitoring
  - Glasgow Antipsychotic Side-effect Scale (GASS)
  - 22 items asking about side effects over past 7 days
  - Examples include: feeling sleepy, restless legs, dizziness, drooling, blurry vision, thirsty, swollen nipples, enjoying sex, getting an erection, frequent urination, weight gain
  - Scores less than 12 mild, 13-26 moderate, over 26 severe
  - Data presented in abstract form conclude less side effects per GASS when using LAI antipsychotics (exception aripiprazole)

- Care coordination
  - Patients will have a consent for release of information authorizing for direct care coordination between LAT clinic staff and the patient's primary psychiatric prescriber
  - Interaction with patient financial representative
  - Visit summary forms faxed to physician
LAI Antipsychotics: LAT Clinic

- Goals for 2018
  - Follow-up Calls
    - Clinic patients will receive an outreach call within 7-10 days of visit to address any patient questions or concerns prior to next scheduled appointment

Conclusions

- Long acting injectable antipsychotics
  - Pharmacist may be able to administer with proper vetting process
  - When using, oral cross titration is needed for aripiprazole and risperidone microspheres
  - Monitoring parameters include personal/family history, weight, waist circumference, blood pressure, glucose, and lipids

References

References