#FSHP2018

Clinical Pearls in Psychiatry:

Antipsychotics in Acute Care

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Break Through Branch Out

Disclosures

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

Break Through #FSHP2018 Branch Out

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

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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

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Agitation vs. Delirium[1-2]

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

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Delirium[2-5]

- 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

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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]

Low	Medium		High	
Carbidopa-levodopa	Cetirizine	Tolterodine	Amitriptyline	Promethazine
Selegiline	Cyclobenzaprine	Amantadine	Benztropine	Oxybutynin
Metoclopramide	Loperamide	Loratadine	Meclizine	Imipramine
Ranitidine	Olanzapine		Tizanidine	Hydroxyzine
Trazodone	Desipramine		Diphenhydramine	
Quetiapine	Baclofen		Chlorpheniramine	

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 (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[18-20]

Guidelines Examples on Treatment of Delirium	
American Psychiatric Association- APA (1999)	Low dose haloperidol as first-line agent in symptomatic management of delirium episodes
National Institute for Health and Clinical Excellence-NICE (2010)	Consider short term haloperidol or olanzapine for distressed person with delirium who is posing a risk to themselves or others
American Geriatric Society-AGS (2015)	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

Delirium: Efficacy of Antipsychotics[21]

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

Delirium: Efficacy of Antipsychotics[21]

- 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: Efficacy of Antipsychotic[21-24]

- Data on other populations with delirium
  - Some benefits
    - Decrease severity
    - Decrease duration

Delirium: Antipsychotic Adverse Effect Profile[21-25]

- Anticholinergic: sedation, orthostasis, dizziness, falls, urinary incontinence
- Extrapyramidal symptoms
- Cardiovascular side effects
  - QTc prolongation *(possible cutoff of > 450-500 msecs)*
  - Ventricular arrythmias
  - 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 FDA Public Health Advisory[26-28]

- Second generation antipsychotics associated with increased mortality (due to cardiovascular events and infections) in elderly patients with dementia (2005)
- First and second generation antipsychotics associated with increased mortality in elderly patients treated for dementia-related psychosis (2008)
- Studies in elderly patients show higher rates for cerebrovascular side effects and mortality

Delirium: Antipsychotic Final Recommendation[5,6,19]

- 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: Antipsychotic Final Recommendation[6,19,29,30]

- 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
- Second generation antipsychotics may be preferred
  - Risperidone, olanzapine, quetiapine, aripiprazole
  - Start low and go slow

Delirium: Antipsychotic Final Recommendation [5,6,19,30]

- Discuss with family/caregivers risk vs. benefits and document
- Obtain electrocardiogram (ECG) when initiation and **periodic** ECG monitoring
  - Aripiprazole may be preferred, if concerned
- Evaluate need for continuing antipsychotic

Delirium: Discontinuation of Antipsychotics[31]

- 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[32]

Centers for Medicare and Medicaid Services (CMS)

- 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 **and**
    - 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 Antipsychotics (Brand)

- 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)

Long Acting Injectable (LAI) Antipsychotics[33]

	Administration	Oral Cross-titration	Dose Adjustments
Haloperidol decanoate	monthly	Not required	• Adjust dose if elderly, debilitated
Aripiprazole lauroxil	monthly	First 21days	• If > 2 weeks, watch strong CYP3A/CYP2D6 inhibitors and CYP3A4 inducer; CYP2D6 poor metabolizers
Aripiprazole monohydrate	monthly	First 14 days	• If > 2 weeks, watch strong CYP3A/CYP2D6 inhibitors and CYP3A4 inducer; CYP2D6 poor metabolizers
Olanzapine pamoate	monthly	Not required	• None noted (based on efficacy/side effects)
Paliperidone palmitate-M	monthly	Not required	• Adjust if CrCl 50-80 ml/min; avoid if CrCl < 50 ml/min
Paliperidone palmitate-3M	3 months	Not required	• Adjust if CrCl 50-80 ml/min; avoid if CrCl < 50 ml/min; • Avoid concomitant therapy with a strong CYP3A4 or P-glycoprotein inducer
Risperidone microsphere	2 weeks	3 weeks	• Renal/hepatic impairment may need lower dose

Long Acting Injectable (LAI) Antipsychotics[33]

	Oral Supplement for Missed LAI Doses?	Special considerations
Haloperidol decanoate	None specified	• Watch extrapyramidal symptoms
Aripiprazole lauroxil	None if ≤ 6 weeks*	----
Aripiprazole monohydrate	None if ≤ 6 weeks*	----
Olanzapine pamoate	None specified	• Post-Injection Delirium/Sedation Syndrome (administer in a registered healthcare facility) • Must be observed for at least 3 hours after injection • Available only through restricted distribution program (REMS) and requires prescriber, healthcare facility, patient, and pharmacy enrollment
Paliperidone palmitate-monthly or 3 months	None specified	• Must follow initial dosing schedule for monthly only
Risperidone microsphere	Provide oral (not specified)	----

* If greater than 6 weeks refer to package insert

Florida Statute465.1893: 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
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 and medical waste
3. Has completed the course required under subsection

(2).(b) A separate prescription from a physician is required for each injection administered by a pharmacist under this subsection

(2)(a) A pharmacist seeking to administer a long acting antipsychotic medication by injection must complete an 8-hour continuing education course offered by:

1. A statewide professional association of physicians in this state accredited to provide educational activities designated for the American Medical Association Physician's Recognition Award (AMA PRA) Category

1 Credit or the American Osteopathic Association (AOA) Category 1-A continuing medical education (CME) credit; and

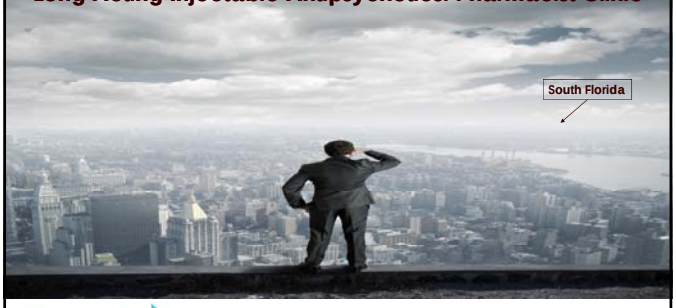
2. A statewide association of pharmacists

(b) The course may be offered in a distance learning format and must be included in the 30 hours of continuing professional pharmaceutical education required under s. 465.009(1)

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. Hall, PharmD, JD, MS
  - Jacquelyn Canning, PharmD, BCPP

Long Acting Injectable Antipsychotics: Pharmacist Clinic



LAI Antipsychotics: Pharmacist Clinic[34]

- Memorial Regional Hospital Long Acting Therapy (LAT) Clinic
  - Alberto Augsten, PharmD, MS, BCPP, DABAT
  - Daniel Bober, DO
  - Simone Cousins, PharmD
  - Maria Vento, PharmD, BCPP
  - Bertha Rojas, PharmD
  - Samantha Themas, PharmD
  - Rafael Guzman, LCSW
  - Claudia Vicencio, PhD, LCSW, LMFT

LAI Antipsychotics: LAT Clinic[34]

- Started in May 2015
  - Preliminary outcomes
    - Almost 200 unduplicated patients have received a LAI antipsychotic
    - Approximately 40 patients are seen monthly
    - LAT readmission rates in 2017 were approximately 7% vs. 25% for the national average
    - Routine audits to make improvements

LAI Antipsychotics: LAT Clinic

- Goals for 2018
  - Metabolic monitoring: American Diabetes Association (ADA) Guidelines

	Baseline	1 month	2 months	3 months	Quarterly	Annually
Personal/Family History						X
Weight (BMI)	X	X	X	X	X	X
Waist circumference	X				X	X
Blood pressure	X		X			X
Fasting plasma glucose	X		X			X
Fasting lipid profile	X		X			(every 5 years)

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)

LAI Antipsychotics: LAT Clinic

- Goals for 2018
  - 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

LAI Antipsychotics: LAT Clinic

- Goals for 2018
  - Missed Appointment Follow-up Calls
    - Clinic staff will complete an outreach call to the patient and to the patients primary prescriber within 48 hours of a missed scheduled appointment
  - Action plan includes:
    - LAT Clinic staff will review previous day's scheduled next working day
    - Any patient missing a scheduled appointment will receive a missed appointment follow up call with an opportunity to reschedule
    - If patient will discontinue LAT clinic services, documented in Epic with reason for discontinuing
    - Education provided to new residents assisting in staffing LAT clinic

LAI Antipsychotics: LAT Clinic

- Goals for 2018
  - LAT Manager will complete Patient Record Reviews quarterly to ensure completion of notes, billing, medication administration record, vitals and completion of full visit metrics

Conclusions

- Delirium
  - Rule out underlying causes for delirium before treating
  - If treating, attempt non-pharmacologic options first
- Antipsychotic use in delirium
  - If using antipsychotics, use lowest dose possible and monitor for efficacy and side effects
  - Must weigh risk/benefits
  - Orders for "as needed" have a 14 day limit in long term care facilities

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

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