Common Drug-drug and Drug-disease interactions in Hospice

Objectives
- Identify common interactions found in hospice patients
- Point out clinical presentations of these interactions
- Understand when to discontinue meds vs when to continue
  - Identify the risks vs benefits of continuing
  - Know drug of choice

Background information on hospice
- Terminal dx
  - Pertinent meds needed for care and to Palliate symptoms
- Comorbidities
  - Palliative
  - Non-Palliative
  - Recommend D/C to avoid multiple interactions

Common interactions in hospice

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Serotonin Syndrome
- Occurs due to overstimulation of serotonin receptors
  - Central
  - Peripheral
- Under diagnosed due to symptoms being non-specific
- Can occur due to different mechanisms
  - Increase serotonin production
  - Decrease serotonin reuptake
  - Stimulation of receptors

Serotonin Syndrome contd.
- Occurs within few hours to 24 hours of:
  - Increase in the serotonergic agent
  - Overdose
  - Addition of Serotonergic agent
- Causative agents
  - Antidepressants - Citalopram, Prozac, Duloxetine, Effexor, Amoxapine
  - Pain meds - Buprenorphine, Fentanyl IV
  - MAO-I - L-tryptophan, Phenelzine, Selegiline, Trypticpsinine
    - (largest culprit, allow for 2 week washout)
  - Supplements - St. John’s wort, ginseng, nutmeg
  - Antihistamines - H1 blockers, promazine, zolpidem

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### Serotonin Syndrome Clinical Presentation

<table>
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<tr>
<th>Mental Status</th>
<th>Agitation, Confusion, Delirium, Hallucinations</th>
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<tr>
<td>Neuromuscular</td>
<td>Hyperreflexia, Increased muscle tone, Rhabdomyolysis, Rigidity, Shivering</td>
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<td>Autonomic</td>
<td>Diarrhea, Mydriasis, Fever, Flushing, Increased bowel sounds, Increased respiratory rate</td>
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### Serotonin Syndrome - Management

- **Mild Symptoms**
  - Resolve within 24 to 72 hours
  - Diarrhea, sweating, shivering
  - Drug discontinuation. Benzodiazepine (reduce tonicity) and supportive care

- **Moderate to Severe**
  - Rapid increase in temperature and muscle rigidity
  - Medical emergency
  - Antipyretics not recommended
  - D/C causative agents
  - May need sedation or intubation

### QT Prolongation

- Life threatening arrhythmia associated with prolongation of QT interval
  - Can lead to Torsades de pointes
- Risk factors
  - Advanced age
  - Female Sex
  - Acute MI
  - Heart failure with reduced ejection fraction
  - Hypokalemia/Hypomagnesemia
  - Drug-drug interactions
  - Inadequate dose adjustment in patients with renal/hepatic failure
  - Genetic predisposition

### QT Prolongation - Prevention/Management

- ECG Monitoring (not commonly done in hospice)
  - Unless compelling reasons to continue
- Monitor serum Potassium, Magnesium and Calcium
- High risk meds
  - Paroxysmal atrial fibrillation
- Adjust drug dose in patients with kidney disease
- Avoid QT-prolonging drugs in patients with Heart failure and LVEF < 20%
- Avoid QT drugs in patients with a history of drug induced torsades de pointes

### QT Prolongation

- Somatic symptoms
  - Abnormal heart rhythms
  - Bradycardia
  - Syncope
  - Light-headedness
  - Seizures
  - Sudden death
- Causative drugs (commonly found in hospice patients)
  - Antihypertensives (Clonidine, Lisinopril)
  - Antipsychotics (Haloperidol, Risperidone)
  - Antiarrhythmics (Amiodarone, Sotalol)
  - Antimicrobials (Fluoroquinolones, Macrolides, Bactrim)
  - Antidepressants (Amitriptyline, Sertraline, Fluoxetine)

### Drug Induced Hyperkalemia

- Hyperkalemia results from:
  - Increased intake of Potassium
  - Reduced excretion of Potassium
- Life threatening
  - Levels > 7.0 mmol/L
- Causes
  - Acute/chronic renal failure
  - Drug-drug interactions
  - Rhabdomyolysis
  - Hypokalemia
Drug induced hyperkalemia contd.

- Symptoms of Hyperkalemia
  - Muscle weakness
  - Intergas and heart failure (palpitations)
  - Feeling too tired
  - Tingling sensation
  - Fainting
  - Muscle pain

- Meds that cause Hyperkalemia
  - Spironolactone and ACE inhibitor combination
  - See in patients with HF and renal impairment
  - Careful monitoring
  - Blood pressure meds (ARBs, Beta blockers)
  - NSAIDs in renal failure/diabetes
  - Trimethoprim
  - Supplements

Management of Hyperkalemia

- Mild symptoms
  - Muscle weakness, tiredness, tingling sensation, nausea
  - Identify and eliminate source of Potassium intake
  - Drugs
  - Diet
  - Administer Kayexalate
  - Don’t require ICU/hospital stay

- Moderate to Severe
  - Signs of heart attack
  - Call 911
  - ECG monitoring
  - Not common practice in hospice

Multi opioid use

- Opioids are used for the management of severe chronic pain
- Breakthrough pain and intermittent pain
  - Use short acting opioids
    - Eg. Roxanol, Oxycodone
- Continuous pain
  - Long-acting and sustained release opioids
  - Fentanyl, MS Contin
  - Used in combination with non-opioids
  - Permits use of lower doses of opioids

Multi Opioid use

- Prescribing errors with opioids in palliative care
  - Failure to prescribe Around-the-clock opioids for constant pain
    - Use of multiple short acting opioids
  - Long acting opioids preferred to create more stable serum levels
  - Using incorrect dosing intervals leading to fluctuating serum levels
  - Use of multi opioids and formulations
  - Leads to accumulation and toxicity
  - Use with caution in patients with impaired ventilation, bronchial asthma and liver failure

Side effects of multi opioid use

- Sedation
- Confusion
- Respiratory depression
- Pruritus (itching)
- Nausea and vomiting
- Constipation

Management of opioid side effects

- Monitor respiration status during first 24 hours of treatment in opioid naive patients
  - Step opioid use and respiratory depression resolves and start at 75% of previous dosage
  - Admit patient if patient is minimally responsive or unresponsive
  - Use Symmetry and oxygen as needed
  - Titrate drug doses slowly
  - Consider changing dosing regimen to obtain constant blood levels
  - Add nonopioid or adjuvant analgesic
  - Consider switching to another opioid
  - Assume constipation will develop and treat for it
  - Consider use of antihistamines for pruritus
Antipsychotics in Parkinson’s

- Psychosis is found to be very common in patients with Parkinson’s.
  - Usually seen in later stages (>5.5 years).
- Exposure to PD meds over years leads to psychosis:
  - L-dopa, dopamine agonist, MAO, anticholinergics
- Treatment with certain antipsychotics can worsen disease:
  - Leads to drug-induced extrapyramidal symptoms (EPS)

Clinical presentation of EPS

- Dyskinesias and dystonic reactions
- Tardive dyskinesia
- Parkinsonism
- Akinesia
- Akathisia
- Neuroleptic malignant syndrome.

First Generation Antipsychotics in Parkinson’s

- Worsen Parkinson’s symptoms, therefore should be avoided:
  - Induce significant movement disorders such as bradykinesia, tremor, and rigidity
  - Anticholinergic side effects:
    - Constipation, urinary retention, dry mouth
  - Sedation
  - Orthostatic hypotension
- Drugs in this class include:
  - Haloperidol, Chlorpromazine

Second Generation Antipsychotics

- Less risk of worsening extrapyramidal symptoms.
- Safety profiles differ amongst members in this class:
  - Majority have cardiometabolic effects which include:
    - Weight gain, dyslipidemia, hypertension, increased insulin resistance
    - Avoid Clozapine and Olanzapine in patients with diabetes, obesity, or dyslipidemia
    - Avoid Clozapine and Quetiapine in patients with heart failure and QTc prolongation
- Drugs in this class include:
  - Seroquel, Risperidone, Clozapine, Olanzapine

Antipsychotics of choice

- Quetiapine
  - Low dose
  - Major cardiometabolic effects
  - First choice
- Olanzapine and Risperidone
  - Low dose
  - Atypical antipsychotics
  - Still have a risk of aggravating PD.

Treatment contd.

- Avoid Clozapine and Quetiapine in patients with Heart failure and QTc prolongation
Management of EPS symptoms

- Taper off offending antipsychotic and D/C
  - Monitor patient closely for improvement in symptoms/exacerbation of psychotic symptoms
  - May require adding using Benzo, Dopamine agonists, or anti-histaminic
- Switch to atypical antipsychotic/use lowest effective dose
  - Seroquel, Risperidone, Olanzapine

NSAIDs in CHF

- NSAIDs stand for Non-steroidal anti-inflammatory drugs
- Seroquel, Meloxicam, Celecoxib
- Clinical guideline discourages use in CHF patients
  - American heart association
  - Patients with high risk of cardiovascular disease
  - COX-2 vs COX-1
- Cause fluid retention or reduced cardiac function
  - US boxed warning
  - Increased risk of cardiovascular thrombotic events
  - Risk seen at higher doses

NSAIDs in CHF

- Interaction with loop diuretics
  - Most CHF patients on loop diuretics
  - Patients have reduced renal function
- NSAIDs cause Na and H2O retention
  - Negates effects of loop diuretics
- Clinical presentation
  - New onset HTN
  - Worsening fluid retention
- Weight checks
- Use with caution in patients with hx of edema
  - Hyperkalemic state
- Monitor for dyspepsia
- Renal injury
- GI bleeds

NSAIDs in CHF – Management of Sx

- D/C NSAIDS
  - Evaluate the risks vs benefits
- If NSAIDs are desired
  - Non-selective NSAIDS are preferred
    - Ibuprofen and Naproxen (avoid using high doses for a long period of time)
    - Have more GI side effects therefore use with PPI
  - Consider Acetaminophen or other weak opiates

Bleeding risk in hospice patients

- Hospice providers decide when or when not to continue anticoagulant therapy
  - Weigh risks vs benefits of continuing
  - Prophylaxis vs treatment?
- Anticoagulants used for patients who are symptomatic
  - Relief of chest pain
  - Dyspnea
  - Painful swelling of lower extremities
Factors that increase risk of bleeding

- Hospice patients most often in a debilitated state
- Increased risk of falls
- Multiorgan failure
- Reduction in renal or hepatic function
- Reduced metabolism/elimination of drugs
- Production of bleeding factors
- Reduced production of clotting factors
- Multiple co-morbidities
- History of GI bleed, low hematocrit, or on other meds that increase bleeding

Clinical presentation

- Blood in urine
- Dark stools
- Nose bleeds
- Vomiting or coughing up blood
- Bleeding gums
- Purple/blue bruise on body

Medications include

- Anticoagulants - Warfarin, Lovenox
- Antiplatelets - Plavix, Aspirin
- NSAIDS
- Antidepressants (SNRI and SSRI)
- Supplements e.g. Ginseng, Garlic, Gingko, Fish oil

Management

- Patient education
- Report falls
- Decision to stop meds usually made by attending physician