On-Demand Clinical News

Parkinson's Disease: Considerations for Hospice Patients

By: Joelle Potts, PharmD, BCGP

Parkinson's disease (PD) was first described in 1817 as a "shaky palsy" by English physician Dr. James Parkinson, but it wasn't until the 1960s that it was realized that PD is associated with a decrease in dopamine activity in the brain due to a breakdown of the substantia nigra pars compacta. This decrease in dopamine activity leads to greater inhibition of the thalamus, which in turn leads to reduced activation of the motor cortex. It is thought that clinical improvement in PD is associated more with restoring activity at the D_2 dopamine receptor, rather than the D_1 dopamine receptor.

Medications used to treat the motor symptoms of PD [medications in italics are considered preferred/Tier 1 or 2]:

- Carbidopa/levodopa – (*Sinemet®, Sinemet CR®,* Parcopa®, Rytary®, Duopa Enteral Suspension®; also: carbidopa (Lodosyn®), *carbidopa/levodopa/entacapone (Stalevo®))*
- Anticholinergics – *benztropine (Cogentin®),* trihexyphenidyl (Artane®)
- MAO-B inhibitors – *selegiline (Eldepryl®, Zelapar®),* rasagiline (Azilect®), safinamide (Xadago®)
- Dopamine agonists – *bromocriptine (Parlodel®), pramipexole (Mirapex®), ropinirole (Requip®),* rotigotine (Neupro®), apomorphine (Apokyn®)
- COMT inhibitors – *entacapone (Comtan®),* tolcapone (Tasmar®)
- Miscellaneous – *amantadine (Symmetrel®,* Gocovri®)

MAO-B inhibitor drug interactions and contraindications

MAO-B inhibitors should typically be avoided, or are specifically contraindicated (per labelling), with opioids that are commonly used at end of life. The use of MAO-B inhibitors is typically contraindicated with meperidine, tramadol, methadone, and morphine, while the use of MAO-B inhibitors with hydromorphone, oxycodone, and hydrocodone are not labelled as contraindicated, but should generally be avoided if possible.

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Management of Community-Acquired Pneumonia in the Adult Hospice Patient

By: Shaun Gutstein, PharmD

Community-acquired pneumonia (CAP) is an infection of the lower respiratory tract (trachea, bronchi and lungs), in which inoculation occurs outside of healthcare facilities, resulting in inflammation and accumulation of pus in the airways. Microorganisms, such as bacteria and viruses, inoculate the lower respiratory tract by three routes: inhalation, via bloodstream from an extra pulmonary site, or aspiration. A weakened immune system or other impaired defense mechanisms allow the pathogen to overwhelm the host and cause an infection. Pneumonia is the seventh leading cause of death in the United States and almost 1 million cases of CAP occur annually in adults of at least 65 years old. As a result, pneumonia is common and oftentimes the terminal event for many hospice patients. Improving antimicrobial stewardship and the care of terminally ill patients with infections requires interdisciplinary collaboration.

Etiology and Clinical Presentation

As an infectious disease, CAP is most commonly caused by *Streptococcus pneumoniae* (a gram-positive bacteria); *Mycoplasma* and *Chlamydophila* species (atypical bacteria); *Haemophilus influenza* (a gram-negative bacteria), as well as respiratory viruses, such as Influenza (Flu). However, pathogens vary by geography, epidemiologic setting, and presence of comorbidities/conditions (e.g. COPD or aspiration). Although a variety of pathogens may cause pneumonia, considering these factors may provide clinical insight to guide antimicrobial selection.

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The gold standard for pneumonia diagnosis is the chest x-ray (which may not always be possible in hospice), and this can be paired with identification of pertinent signs and symptoms.

Signs and Symptoms:

- Abrupt onset of fever, chills, difficult or labored breathing, and productive cough
- Colored or blood-stained sputum
- Chest pain, especially with coughing or breathing
- Rapid breathing or increased heart rate
- Diminished breath sounds over affected area
- Inspiratory crackles during lung expansion

CAP severity calculators are utilized as an aid to determine the most appropriate environment of care (outpatient, hospital and/or intensive care unit), empiric antibiotic selection (oral, parenteral, spectrum of activity), and mortality risk. In hospice, clinicians may utilize severity scores to assess the impact oral antibiotics may have on overall treatment outcomes when more aggressive treatment does not align with the goals of care.

- CURB-65 score: ≥ 2 may warrant intensive services
  - Confusion, Uremia, Respiratory rate, low Blood pressure, age ≥ 65 years or greater
- Pneumonia Severity Index (PSI): Risk classes IV-V may warrant intensive services
  - Algorithm-based mortality risk calculator; point values for clinical /laboratory parameters

Treatment *[medications in italics are considered preferred/Tier 1 or 2]*:

Antimicrobials are a mainstay of treatment with a goal of eradicating the infecting organism and resolution of clinical disease. Empirical therapy, or utilization of broad-spectrum antibiotics, is based on prediction of the most likely pathogen(s). Pharmacokinetics/pharmacodynamics, compliance, safety, cost, and special treatment considerations (e.g. aspiration or *Pseudomonas* species) also influence antibiotic selection. Appropriate antibiotic selection increases rate of successful treatment, and decreases risk of antibiotic resistance, adverse effects, and cost.

- Low-risk for drug-resistant *Streptococcus pneumoniae* (DRSP):
  - Previously healthy and no use of antimicrobials within the previous 3 months
    - Selection: A macrolide (*azithromycin or clarithromycin) or doxycycline*
- High-risk for drug-resistant *Streptococcus pneumoniae* (DRSP):
  - Antimicrobials within the previous 3 months and/or:
  - Chronic heart, lung, liver, or renal disease, diabetes mellitus, alcoholism, malignancy, or immunodeficiency
    - Selection: A respiratory fluoroquinolone* (*levofloxacin,* moxifloxacin, or gemifloxacin) OR: a β-lactam (*amoxicillin or amoxicillin-clavulanate)* plus a *macrolide*
      - *Doxycycline* is an alternative to a macrolide
      - *Cefuroxime* (2nd-Gen. cephalosporin), cefpodoxime (3rd-Gen.), and cefdinir (3rd-Gen.) are alternative β-lactam antibiotics for penicillin-allergic patients**

Treatment with antibiotics should be for at least 5 days. The patient should be afebrile for 48–72h, and should have no more than 1 CAP-associated sign of clinical instability before discontinuation (i.e. most/all of the following are within normal limits: heart rate, respiratory rate, systolic blood pressure, and arterial oxygen saturation).

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These cautions and contraindications are due either to the risk of developing serotonin syndrome or the increased risk of opioid toxicities such as respiratory depression. SSRI, SNRI, and tricyclic antidepressants are usually not specifically contraindicated but should typically be avoided with MAO-B inhibitors if possible – although in clinical practice they are often used concurrently with MAO-B inhibitors at therapeutic anti-PD doses. Note, however, that SNRIs and tricyclics are specifically contraindicated for use with safinamide, which is a relatively new MAO-B inhibitor. Cyclobenzaprine, dextromethorphan, and St. John's Wort are also typically contraindicated for use with MAO-B inhibitors. Sympathomimetics (e.g. pseudoephedrine, phenylephrine) should typically be used with caution with MAO-B inhibitors, although they are specifically contraindicated for use with safinamide.

It is also typically recommended to allow for a 14-day washout period between use of MAO-B Inhibitors with these interacting medications. For example, if a patient is taking an MAO-B inhibitor and you wish to start methadone, it is recommended to stop the MAO-B inhibitor 14 days before starting methadone to allow the MAO-B-inhibiting effects of the anti-PD medication to clear from the patient's system.

Gradually taper PD medications:
Typically, the doses of anti-PD medications should gradually be tapered before discontinuation whenever possible, unless the patient is already taking the lowest/starting dose. Abrupt discontinuation or too rapid of a taper can cause malignant syndrome, which can present as high fever, altered level of consciousness, a significant increase in muscle tone, and autonomic disturbances (e.g. sweating, hypersalivation, and tachycardia).

Psychotic symptoms:
Behaviors, hallucinations, and delusions can occur in 25-30% of patients with advanced PD. Evaluate for drug-induced psychosis (e.g. due to anti-PD meds such as amantadine, anticholinergics, COMT inhibitors, and/or dopamine agonists), and taper off these medications if possible and as appropriate. Also, evaluate for other causes (e.g. UTI or respiratory infections). Finally, consider decreasing the dose of levodopa if severe psychosis persists. Note that decreasing or discontinuing anti-PD medications could worsen PD symptoms.

If it is necessary to add an antipsychotic, note that haloperidol is specifically contraindicated in PD, and most other antipsychotics (e.g. risperidone, chlorpromazine, olanzapine) are not recommended. These antipsychotics are strong D_2 receptor antagonists, and therefore can worsen movement disorders and have significant drug-drug interactions with anti-PD medications. Quetiapine and clozapine are typically considered safe and low-risk in PD patients, as they have low affinity for the D_2 receptor. Quetiapine is considered the antipsychotic-of-choice in hospice patients with PD, and the use of clozapine is likely very limited in the hospice population due to the requirements for frequent lab monitoring and potential for serious adverse effects.

Pimavanserin (Nuplazid®) is a relatively new antipsychotic that is specifically indicated for the treatment of hallucinations and delusions associated with PD psychosis; it does not have dopaminergic affinity and does not worsen motor function. It works via serotonin mechanisms. However, it is considered a non-preferred medication to initiate in a hospice patient, as it is currently very high-cost and appears to have a significant delay in onset of benefit. One trial compared pimavanserin to placebo and evaluated patients at 15 days, 29 days, and 43 days after initiation; this trial found no significant difference in efficacy between pimavanserin and placebo at 15 days, with a significant difference (pimavanserin superior to placebo) found at days 29 and 43. In contrast, quetiapine has demonstrated an onset of beneficial effect within one week for acute schizophrenia exacerbation, across a broad spectrum of symptoms.

Nausea/Vomiting:
Anti-emetic medications that are strong D_2-receptor antagonists should generally be avoided in patients with PD, including haloperidol, chlorpromazine, prochlorperazine, and metoclopramide. Promethazine has less D_2 affinity than these other anti-emetics, so it is typically considered safer for use in hospice patients with PD. Other generally safer options to treat nausea/vomiting in Parkinson's patients include ondansetron, meclizine, diphenhydramine, scopolamine, lorazepam, and dexamethasone.

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Prevention

- Vaccination (pneumococcal, annual influenza, and others according to CDC recommended schedule)
- Avoid contact when sick
- Frequent hand washing with optimal technique
- Cleaning frequently-touched surfaces
- Coughing or sneezing into a tissue or into your elbow or sleeve; masks to cover mouth of sick patients
- Avoidance of unnecessary gastric acid suppressing agents (PPIs, H2-antagonists)
- Elevate the head of the bed to 30°- 45°

To guide optimal empiric therapy for CAP, ProCare clinical pharmacists are available 24/7 for recommendations.

*Note that ciprofloxacin is not considered a respiratory fluoroquinolone, as there are generally high resistance rates with *Streptococcus pneumoniae.*

**The incidence of allergic reactions among penicillin-allergic patients varies with the chemical side chain similarity as opposed to the presence of a β-lactam ring. Avoid if previous history of severe reaction (i.e. anaphylaxis, Stevens-Johnson Syndrome)

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Gratitude can transform common days into thanksgiving, turn routine jobs into joy, and change ordinary opportunities into blessings.

~William Arthur Ward

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Presenter: Paige Erdeljac, PharmD, BCAPC
Tuesday, November 7, 2017 at 3:00pm ET; Wednesday, November 8, 2017 at 12:00pm ET

December: Physician-Assisted Suicide
Presenter: Michaela Simpson, PharmD, CGP
Tuesday, December 12, 2017 at 3:00pm ET; Wednesday, December 13, 2017 at 12:00pm ET

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