Clinical Resource Guide:
Psychosis in Parkinson's Disease

INTRODUCTION

In advanced stages of Parkinson's disease, as many as 40% of patients may experience paranoid delusions and hallucinations. There are several potential contributing causes including underlying dementia, adverse effects of medications, and comorbid systemic conditions such as infections. Dopaminergic agents which are used to treat motor symptoms such as rigidity, tremor, bradykinesia, and postural instability may increase the risk of developing psychosis. Additionally, other signaling pathways have been linked to the pathophysiology of this type of psychosis including serotonin and acetylcholine neurotransmitter systems. Parkinson's disease psychosis is associated with considerable caregiver stress and burnout. This resource is designed to equip hospice teams with strategies and practical insights to effectively manage psychosis in advanced Parkinson's disease.

Pharmacist Corner Objectives

1.) Learn to recognize the signs of psychosis in Parkinsons disease
2.) Explore the potential causes of PD psychosis
3.) Develop a stepwise treatment approach which focuses on maximizing comfort

IDENTIFY SYMPTOMS

Symptoms of PD psychosis include visual hallucinations, delusions, panic attacks, paranoia, and auditory hallucinations. A formal diagnosis requires at least one psychotic symptom, a primary diagnosis of PD, symptoms that are recurrent or continuous for at least one month and occur after PD onset, and no other identified causes of psychosis.

EVALUATE TRIGGERS

The first step in managing psychosis in PD is to identify and treat possible underlying causes such as:

- Infections such as UTI, pneumonia
- Metabolic abnormalities
- Medications
  - Anxiolytics, antidepressants, antipsychotics, anticholinergics, antiemetics
  - Commonly used agents in hospice include metoclopramide, prochlorperazine, promethazine, risperidone, olanzapine, chlorpromazine, valproic acid, haloperidol, and oxybutynin
  - These agents should be evaluated for dose reduction, discontinuation, or interchange to more appropriate options

REDUCE OR STOP PARKINSON'S MEDICATIONS

If symptoms persist, a dose reduction of anti-Parkinson's medications may be attempted to balance treatment of motor symptoms against the likelihood of worsening psychotic symptoms. Careful monitoring should guide the deprescribing process to ensure optimal symptom management and improved quality of life. The suggested order of discontinuation is as follows:

1.) Anticholinergic agents
2.) Amantadine
3.) Dopamine agonists
4.) MAO-B inhibitors (selegiline)
5.) COMT inhibitors (entacapone)
6.) Levodopa (last resort)

REFRACTORY SYMPTOM MANAGEMENT

For patients who continue to experience refractory symptoms of psychosis despite recommended medication adjustments, consider initiating or optimizing antipsychotic therapy with agents that have the lowest antidopaminergic properties (Table 1). Quetiapine tends to be the agent of choice in hospice due to its relatively low cost per dose compared to agents such as pimavanserin (Nuplazid®). When starting quetiapine, initiate at a dose of 12.5mg at HS. It may be titrated according to response and tolerability to BID-TID. Clozapine use in end-of-life care may be limited due to its requirement for hematologic monitoring.

Table 1.

Parkinsonism Risk of Antipsychotics	
Low (preferred)	aripiprazole, clozapine, pimavanserin, quetiapine, ziprasidone
Moderate	chlorpromazine, perphenazine, lurasidone, olanzapine, paliperidone, risperidone
High (non-preferred)	fluphenazine, haloperidol

PHARMACOLOGICAL MANAGEMENT: CLINICAL PEARLS

1. For the management of nausea at end of life in patients with Parkinson's disease and psychosis, consider agents with little to no dopaminergic activity such as ondansetron and corticosteroids.

2. Limit the use of bladder antispasmodics, antidepressants, benzodiazepines, and muscle relaxants and consider deprescribing as they have been associated with psychosis.

3. Rapid discontinuation of multiple PD medications should be avoided to prevent withdrawal syndromes which manifest as pain, nausea/vomiting, drug cravings, anxiety, muscle rigidity, or neuroleptic malignant syndrome. Take a stepwise approach and deprescribe in order of greatest psychosis induction potential.

4. Consider developing PD-specific comfort kits to ensure appropriate agents are used.

SUMMARY

The etiology of PD psychosis is complex and involves several external and internal factors. Hospice teams aim to provide care that supports comfort and may be tasked with balancing the dopaminergic treatment of physical motor symptoms with emotional stability. It may make sense to discontinue agents which were once helpful to manage the complications of Parkinson's disease as they may eventually contribute to an increased risk of psychosis and reduced quality of life in end-stage disease.

REFERENCES

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