Inpatient Parkinson's Care: Challenges and Special Considerations

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WHY DO WE CARE?

The hospital is often a haven for people in need of care. However, for people with Parkinson's disease (PD), hospitalizations can turn into a nightmare. In one study, 33% of people with PD experienced one or more complications, 25% received incorrect anti-Parkinson's medications and 21% experienced deterioration of motor symptoms.[1]

People with PD are admitted to the hospital more frequently than those without PD[2], with as high as 34% hospitalization rate per year and a longer average length of stay compared to non-PD patients.[3,4] Only 15% of hospitalizations are directly related to PD complications while the rest are for indirect disease-related morbidities such as pneumonia, fractures from falls, etc, and non-PD related causes including surgeries.[5–7] In addition, people with PD have significant comorbidities, and comorbid illnesses are related to an increased risk of hospitalization.[8,9]

Although PD progression is not abrupt, PD symptoms can be more severe temporarily when patients are ill. Infections, metabolic changes, exposure to anesthesia, changes in medication regimen or new medication changes are some common factors that may worsen PD symptoms during hospitalization. More importantly, the inherent complexity of PD pathophysiology creates challenges in management. Therefore, understanding PD pathophysiology and recognizing care gaps enable optimization of inpatient care among this vulnerable population.

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WHAT CAN GO WRONG?

Complications may arise from multiple aspects of care. Broadly, these include medication administration, diet status and progression, management of agitation and psychosis, mobilization strategies, and perioperative considerations.

Levodopa administration is time critical.

Accuracy of medication administration times in the hospital is extremely vital in preventing deterioration. Levodopa, the most efficacious medication for PD for over 50 years now[10], has a short half-life and requires multiple times a day dosing.[11] With longer dosing intervals, problems related to wearing off arise. These include mobility problems, falls, worsening of tremor, dystonia, dysphagia, freezing of gait and other nonmotor symptoms, including shortness of breath and anxiety. On the other hand, dosing too early may cause dyskinesias, which predisposes patients to falls, inability to participate in therapy, psychosis, orthostasis and syncope.[12,13] For these reasons, management of PD medication regimen is a crucial aspect of inpatient care.

The multifactorial nature of deviations is well recognized. The staff's unawareness of time critical nature of PD medication administration, unavailability of medications, high patient-to-nurse ratio, and nothing per orem (NPO) status are some factors

that prevent accurate administration of medications. Inaccuracies in medication administration occur at alarming rates; up to half with missing doses[14] and administrations occurring 30 minutes later from order times in 51% of doses and one hour later than order times in 30% of doses.[15]

Furthermore, people with PD have individualized outpatient regimens with varying doses, formulations and time intervals that are tailored to their symptoms throughout the day. One significant source of error is orders written as "qd," "bid," and "tid," to suit hospital schedules, which are inappropriate for time-dependent dopaminergic PD medications and are often deviant from the patient's home regimen.[12] We examined deviation rates between hospital administration times and the patient's home regimen[16] and found that 47% had an average hospital dose timing interval that differed from outpatient timing interval by greater than 30 minutes. Admissions where at least one day included a 30-minute or greater deviation in the dosing interval had a longer length of stay (median 4.6 days vs 2.0 days). Delays in administration of inpatient orders and when compared to outpatient regimens have demonstrated poor outcomes, emphasizing the need for strict adherence to patients' individualized outpatient medication regimens.

PD medication regimens are varied and complex.

Levodopa formulations are varied and complex with different pharmacokinetic and pharmacodynamic properties by formulation.[11,17] For example, carbidopa/levodopa immediate release (IR) when combined with entacapone has the same half-life but takes longer to absorb and has a 30% higher levodopa equivalent daily dose. Of note, entacapone should be administered concomitantly with levodopa for its effect of increased and more sustained plasma levodopa concentrations. Another formulation, carbidopa-levodopa controlled release (CR) has a bioavailability of 70% of IR with a maximum serum concentration of 30%, thereby requiring individual doses to be as high as three times IR doses to achieve the same plasma levels.[17] Aside from variations in levodopa, patients are on a wide variety of PD medications including dopamine receptor agonists, catechol-O-methyltransferase (COMT) inhibitors, adenosine 2A receptor antagonists, anticholinergics and other medications used to treat non-motor symptoms including those for psychosis, orthostatic hypotension, etc. Each medication has a different levodopa equivalent daily dose[18,19], which makes conversion from one to the other error prone, especially for clinicians relatively inexperienced with PD care.

Certain medications are contraindicated due to PD pathophysiology.

Another common issue is that contraindicated medications are often given when patients decompensate, which further worsens motor function, resulting in immobility and falls. An acutely agitated patient may be given haloperidol, or a nauseated patient may be given metoclopramide. Due to the fundamental PD pathophysiology involving loss of dopaminergic cells, it is important to take note of medications that affect dopaminergic states. Relatively commonly encountered medications with dopamine receptor blocking properties include antipsychotic drug classes (haloperidol, fluphenazine, chlorpromazine, risperidone, olanzapine, ziprazisone, aripiprazole, etc.) and antiemetic drug classes (metoclopramide, promethazine, prochlorperazine, etc).

Administration of contraindicated medications in PD patients experiencing delirium has been associated with increased lengths of stay compared to individuals without PD.[20] These further worsen mobility, cognition and swallowing [4,12,21] resulting in extended hospital stays and increased fatalities.[16,22,23] Medication selection is critical when managing behavioral issues to avoid worsening motor function and medical complications.

Patients with PD are at an increased risk of mental status changes in-hospital.

People with PD have as high as a five-fold risk of experiencing delirium or psychosis in the hospital.[24] Manifestations are variable, including confusion, hallucinations, agitation and hypomania[25], and underlying etiologies are multifactorial. Patients are being managed for acute and active conditions such as metabolic derangements, infections, or surgical procedures, which predisposes them to mental status changes secondary to systemic illnesses or exposure to new medications including certain classes of

antibiotics and anesthetic agents. Among patients undergoing surgical procedures, as high as 60% of patients with PD experienced acute postoperative confusion lasting an average of 2.5 days with the relative risk between 2.8% to 8.1%.[26]

The hospital is also an unfamiliar environment with continuous monitoring that often disrupts patients' circadian rhythm. These create challenges for patients with PD who thrive on familiarity and routine. Lastly, patients may have baseline cognitive impairment prior to hospitalization. This lowers the threshold for mental status changes in an unfamiliar environment when compounded by active metabolic derangements, infectious/inflammatory processes and/or exposure to new medications.

Patients with PD are at an increased risk for falls.

Hospitalized patients are at an increased risk for falls.[27] This risk is even higher in patients with PD due to several factors aside from their baseline motor impairment or gait instability. Orthostatic hypotension is experienced by up to 40% of patients with PD[28] which increases the risk for falls, morbidity and mortality.[29] This can be aggravated by dehydration or discontinuation of medications for orthostatic hypotension when supine hypertension is encountered by relatively inexperienced clinicians. Nocturnal urinary frequency is also common. The need to void during times of the day when lighting may be poor or when assistance is unavailable predisposes them to falls. Staffing constraints were found to be associated with increased risk of falls.[30] Another important aspect to consider is polypharmacy or the use of new medications including sedatives or antihistamines.[31] The use of antidopaminergic medications has been shown to increase falls with an odds ratio of 5.0[32], which in turn reduces patients' ability to participate in rehabilitation, and thereby increasing the length of stay.[33]

Prolonged NPO status results in complications.

Given that carbidopa/levodopa is dosed several times per day due to its short half-life, problems arise when patients are placed on NPO for a longer period than necessary. A study on perioperative medication withholding found that levodopa median withholding time was 12.35 hours[34], equivalent to 2-4 doses missed depending on patient profile. Another reason a patient may be placed on NPO includes nausea, often without proper dysphagia screening or consultation with a speech language pathologist (SLP). As emphasized, missed doses predispose patients to mobility problems, falls, worsening of tremor, dystonia, dysphagia, freezing of gait and other non-motor symptoms, including shortness of breath and anxiety. Due to consequences with missed doses, circumstances that preclude patients from receiving their medications call for special considerations, which are discussed below.

Certain factors increase their risk for infections.

Patients with PD often experience sialorrhea and may have silent aspiration which increases risk of respiratory infections,[35] emphasizing the need for proactive interventions in this population. Despite pervasive swallowing problems in PD[36], swallow evaluations were performed in only 25% of cases and only 1/8 of patients had swallowing evaluations performed prior to an aspiration event.[37] Increased risk of aspiration can be further aggravated by being placed on prolonged NPO or with prolonged duration of intubation. Considering their baseline swallowing problems, screening and monitoring of swallowing problems should be the standard of care in this population.

Perioperative management of PD presents unique scenarios.

A considerable proportion of people with PD are admitted for emergent or elective surgeries. Perioperative states often predispose this vulnerable population to critical care gaps, which often result in post-procedural deterioration and complications.[38] Patients with sialorrhea and dystonic neck posturing may present challenges in airway management. Dysautonomia and neurogenic orthostatic hypotension is experienced by up to 40% of patients[28] with possible arterial hypertension when supine,[39,40] giving rise to fluctuations in blood pressure control intraoperatively. Patients are also predisposed to medication interactions, particularly those with QT prolongation effects in the setting of concomitant general anesthesia

(antiemetics such as ondansetron, antipsychotics such as quetiapine, antidepressants such as citalopram). In cases of postoperative nausea and agitation, a patient is commonly either placed on NPO or given medications with antidopaminergic properties, which further worsen motor function. Mobilization post-surgery is also critical to prevent further deterioration of motor function. Lastly, surgical devices such as deep brain stimulation (DBS) leads and implantable pulse generators (IPG) warrant preoperative preparations.

HOW DO WE OPTIMIZE INPATIENT CARE?

Given what we know about the fragility of people with PD when hospitalized, identifying controllable risk factors and minimizing the impact for this population is paramount. An ideal strategy utilizes a three-pronged approach involving education, technology and proactive intervention utilizing specialists as part of a multifaceted approach.

Medication administration

As individuals with PD are admitted for a myriad of reasons other than PD-related issues, they receive care from units other than those specialized in neurologic care. Therefore, there is a need to educate all providers on complexity of PD medications, emphasizing the need for timeliness of administration and avoidance of substitutions and contraindicated medications. Nursing education and other measures including pharmacist review of medications and improved stocking of medications have reduced length of hospital stay and improved medication administration.[13,41,42]

Technology can also enable facilitation of medication administration and avoidance of contraindicated medications. The use of medication order constraints which forces custom hour/minute time orders, drug-disease interactions and missed dose timing alerts, are reminders for all healthcare providers and may be particularly helpful for those relatively inexperienced in PD inpatient care. A full list of medications to be avoided or used in caution among patients with PD can be found in the American Parkinson Disease Association page.[43] Electronic medical record alerts and in-service didactic training sessions for nurses and physicians have indeed been shown to significantly reduce prescribing of contraindicated medications.[42] Along these lines, the clinical pharmacist's role is extremely vital, especially among institutions without the electronic medical record system. Another strategy is to utilize active interventions to improve PD care. Similar to stroke care, it has been suggested that involving PD specialists or advanced practice nurses can improve a patient's hospitalization experience.[44,45] A specialized PD unit where the nursing staff is specifically trained in the care of PD has been shown to result in reduced medication delays, shorter length of stay and fewer episodes of acute delirium.[46] In hospitals where a specialized PD unit may not be feasible, active intervention via PD consultation services is an option. This involves having a physician or nurse trained in PD care as a resource for concerns surrounding special circumstances other staff may be unfamiliar with. In relation to medication availability, it is a common practice for hospital pharmacies to practice judicious selection of specific medications to be stocked. At a minimum, IR carbidopa/levodopa should be stocked with efforts to ensure a supply of at least 24 hours when a patient is admitted. When other levodopa formulations are unavailable, consider using medications from the patient's personal supply, until such a time when the specific formulation is available. As a last resort, levodopa equivalent doses can be calculated with the guidance of a therapeutic exchange protocol. [18,47] The goal, however, is to avoid substitutions unless absolutely necessary, and to maintain all patients on their outpatient regimen as closely as possible (within 15 minutes of outpatient schedule, 100% of the time) unless there is convincing evidence that a recent change in the regimen has created a change in symptoms that have led to hospitalization.

Diet status and progression, speech and swallow

Unnecessary NPO status should be avoided. If NPO status is to be initiated related to swallowing problems that were identified, it is prudent to refer to an SLP for swallowing evaluation prior to placing a patient on NPO. For procedures other than major gastrointestinal surgeries, NPO status should be classified as NPO except for PD medications. Strict NPO including medications status should be reserved only for major gastrointestinal surgeries. If strict NPO status is necessary, alternative routes

of administration such as nasogastric tube if without contraindications or alternative formulations should be considered when appropriate for the patient. Options depending on availability include disintegrating via sublingual, inhaled levodopa, intestinal gel infusion through pump, rotigotine transdermal patch, or apomorphine sublingual, subcutaneous injection.

To minimize the risk for aspiration, a standard protocol for screening should be established to assess dysphagia risk. This should also include patients without known swallowing problems prior to admission as silent aspiration and sialorrhea may increase aspiration risks in this population.[35] Screening for dysphagia is to be done within 24 hours ideally, with measures taken to minimize the risk of aspiration pneumonia. Ideally, bedside nurses should be trained to complete bedside swallow screening for all patients with PD and to notify the team of abnormal results, which should prompt referral to SLP for further management. Measures to minimize the risk of aspiration should be in place. These include ensuring that patients are sitting upright in a chair instead of bed when eating or if confined to bed, ensuring that the head of bed is as upright as possible. Patients identified to be at high risk for aspiration based on SLP evaluation warrant closer supervision. Lastly, patients experiencing varying degrees of dysphagia should be placed on the appropriate regimen that prioritizes closest adherence to their home regimen. This entails consulting neurology when considering holding PD medications due to a concern for dysphagia.

Management of mental status changes

Mental status changes (agitation, delirum, psychosis, confusion, hallucinations) are often multifactorial in nature. As PD patients thrive on familiarity and routine, they need to be frequently reoriented to the hospital setting and time of the day. When there is no urgent need for monitoring, minimize nighttime sleep interruptions to allow the patient to rest as best as possible. Maintain a home regimen that worked well prior to admission and correct underlying problems such as metabolic disturbances. Carefully review medications to remove offending factors such as medications that could precipitate delirium. This may entail multidisciplinary management with services involved (eg, infectious disease discussion as certain antimicrobials may lower the threshold to develop mental status changes). When medications are necessary, consider using clozapine, quetiapine or pimavanserin based on best current evidence.[48] Classifications of mental status changes in PD are variable[25] and a consensus on management for acute agitation among patients with PD admitted in-hospital is yet to be established.

Mobilization strategies

Immobilization not only results in poor motor function, but also increases risk for deep venous thrombosis which was present among 5% of PD patients on outpatient workup.[49] Patients should not be confined to bed. Consider reinstating mobilization orders as tolerated and postoperatively when stable with fall precaution. Monitor mobilization of patients with gait problems, use toileting strategies for patients with incontinence, and adjust medications that may predispose patients to falls. Ensure adequate staffing and train allied care professionals (physical and occupational therapists) to allow timely and safe mobilization.

Management of orthostatic hypotension should be optimized as it can be a barrier to effective rehabilitation sessions. When orthostatic hypotension is present, pay careful attention to increases in dopaminergic medications. Consult with a neurologist when considering adjustments in dopaminergic medications. Avoid aggressive management of hypertension in a patient with neurogenic orthostatic hypotension. Hydrate adequately, use medications (midodrine, fludrocortisone, etc.) when appropriate, allow liberal salt in the diet, and elevate the head of bed.

Perioperative considerations

A multidisciplinary approach is warranted to avoid complications that may arise at multiple levels perioperatively. The admitting team, nurses and pharmacy should coordinate to ensure timely administration of medications. Surgeries should be scheduled earlier during the day if the patient is to be placed NPO overnight to minimize disruptions in PD medication regimen. Nuances of NPO and necessary planning before, during and after surgery should be developed through team training and standard perioperative care. Continue to take

anti-PD medications with sips of water. Providers should be aware of dopamine agonist withdrawal syndrome manifesting as psychiatric and autonomic manifestations, which may sometimes be mistaken for symptoms of wearing off or mental status changes in hospital.[50]

Intraoperatively, the medical team should be aware of possible challenges that may arise in airway management, especially among patients with dystonic neck posturing and sialorrhea. A careful review of the patient's non-motor symptoms is critical to determine any history of dysautonomia as this may give rise to fluctuations in blood pressure control intraoperatively. Fluid volume status and pain should be controlled adequately to prevent blood pressure fluctuations. For patients with PD, paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) are generally safe. Carefully review medications as PD patients may be on medications which may be associated with QT prolongation in the setting of concomitant general anesthesia.

For patients with a DBS device, the IPG should be switched off prior to the procedure and switched back on after the procedure. Electromagnetic interference with the IPG by electrical appliances used during surgery and resuscitation (eg, diathermy, electrocautery, external cardiac defibrillator) can alter stimulation and possibly result in IPG failure.[51–53]

Postoperatively, ensure resumption of PD medications when appropriate (ie, all surgeries other than major gastrointestinal surgery, etc). For patients who are nauseated, consider disintegrating levodopa formulation. Certain institutions utilize a standard postoperative order set intended for the general patient population. Take note of and exclude antidopaminergic medications for nausea and agitation. If an antiemetic is to be given, prefer ondansetron and domperidone instead of metoclopramide, promethazine and prochlorperazine. Finally, ensure early involvement of SLP/occupational therapy to prevent aspiration and physical therapy to prevent deconditioning.

SUMMARY/TAKE HOME POINTS

Individuals with PD are vulnerable during hospitalizations due to the underlying complexities of PD pathophysiology.

A detailed understanding of factors driving the risk for deterioration among hospitalized people with PD is necessary to guide development of targeted care delivery.

Management should involve ensuring accurate medication administration, avoidance of prolonged NPO, fall precaution, appropriate medications for mental status changes, early referral to allied care services, optimization of perioperative care, and timely management of acute changes of PD symptoms impacted by hospitalization.

An integrated care approach involving the patient, caregiver, primary physician, nurse, pharmacist, outpatient neurologist and anesthesiologist is vital in optimizing inpatient care.

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