Perioperative Management of Patients with Parkinson’s Disease

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ABSTRACT

Parkinson’s disease is the second most common neurodegenerative disease worldwide, leading to a wide range of disability and medical complications. Managing patients with Parkinson’s disease in the perioperative hospital setting can be particularly challenging. Suboptimal management can lead to medical complications, prolonged hospital stays, and delayed recovery. This review aims to address the most important issues related to caring for patients with Parkinson’s disease perioperatively who are undergoing emergent or planned general surgery. It also intends to help hospitalists, internists, and other health care providers mitigate potential in-hospital morbidity and prevent prolonged recovery. Challenges in managing patients with Parkinson’s disease in the perioperative hospital setting include disruption of medication schedules, “nothing by mouth” status, reduced mobility, and medication interactions and their side effects. Patients with Parkinson’s disease are more prone to immobility and developing dysphagia, respiratory dysfunction, urinary retention, and psychiatric symptoms. These issues lead to higher rates of pneumonia, urinary tract infections, deconditioning, and falls compared with patients without Parkinson’s disease, as well as prolonged hospital stays and a greater need for post-hospitalization rehabilitation. Steps can be taken to decrease these complications, including minimizing nothing by mouth status duration, using alternative routes of drugs administration when unable to give medications orally, avoiding drug interactions and medications that can worsen parkinsonism, assessing swallowing ability frequently, encouraging incentive spirometry, performing bladder scans, avoiding Foley catheters, and providing aggressive physical therapy. Knowing and anticipating these potential complications allow hospital physicians to mitigate nosocomial morbidity and shorten recovery times and hospital stays.

KEYWORDS: Movement disorders; Parkinson’s disease; Perioperative complications; Perioperative management

Parkinsonism classically refers to a clinical syndrome characterized by tremor at rest, bradykinesia, rigidity, postural instability, shuffling gait, flexed posturing, masked facies, and micrographia. Parkinson’s disease is the most common form of parkinsonism and the second most common neurodegenerative disease, with an annual health care cost of $2000 to $20,000 per patient. Approximately 1% of the population aged more than 60 years has Parkinson’s disease, with a male predominance. The cause of Parkinson’s disease classically is attributed to depletion of dopamine-containing neurons in the substantia nigra, although other neuronal circuitries have been shown to be involved. This process is associated with intracytoplasmic inclusions containing alpha-synuclein called “Lewy bodies.” Although pathology confirms the diagnosis, Parkinson’s disease is diagnosed clinically. Parkinson’s disease is characterized classically by a rest tremor, “cogwheel” rigidity, bradykinesia, asymmetric onset of symptoms, and a positive response to levodopa. Additional features include dysautonomia, sleep disturbances, depression, and dementia.

Parkinson’s disease management consists of pharmacologic treatment, surgery, and physical and speech therapy. The mainstay of pharmacologic therapy is levodopa; however, other dopaminergic medications can be used as monotherapy or in conjunction with levodopa. These include dopamine agonists, amantadine, anticholinergics, monoamine

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oxidase-B inhibitors, and catechol-O-methyl transferase inhibitors.\textsuperscript{8,9} Most of these medications are for symptomatic treatment only; however, there is some evidence to suggest that monoamine oxidase-B inhibitors have disease-modifying effects in addition to symptomatic relief, although this is controversial.\textsuperscript{10,11} Deep brain stimulation is another option for certain patients, which requires neurosurgical insertion of electrodes that stimulate targets within the basal ganglia (typically the subthalamic nucleus or the globus pallidus pars interna).\textsuperscript{2} Presumed to modulate neural signaling, deep brain stimulation has been shown to modify Parkinson’s disease motor symptoms and decrease the need for medications in most cases.\textsuperscript{2,12,13}

Patients with Parkinson’s disease are hospitalized for multiple reasons, including elective and emergent surgeries, procedures related to deep brain stimulation, and medical, neurologic, and psychiatric issues. Whether the need for hospitalization and surgery is related to Parkinson’s disease or not, these patients are at an increased risk for nosocomial morbidity. Dysphagia develops in 50% to 80% of patients with Parkinson’s disease at some point during the disease course, leading to increased risk of aspiration and malnutrition.\textsuperscript{14,15} As a result, aspiration pneumonia is a leading cause of death in patients with Parkinson’s disease.\textsuperscript{14} In addition, patients with Parkinson’s disease have decreased respiratory function, likely secondary to bradykinesia and insufficient respiratory muscle movement, putting them at greater risk for developing pneumonia.\textsuperscript{16,17} Patients with Parkinson’s disease also are at an increased risk for falls and urinary tract infections.\textsuperscript{18-20} One study by Mueller et al\textsuperscript{19} retrospectively compared 51 patients with Parkinson’s disease with 51 controls treated in the hospital by surgical teams using matched-pair analysis over 13 years.\textsuperscript{19} They found that postoperative falls were more common (\(P < .03\)), postoperative stays were longer (\(P < .03\)), overall duration of treatment was significantly longer (\(P < .02\)), and discharge to home occurred less often secondary to a need for ambulatory rehabilitation (\(P < .03\)) in patients with Parkinson’s disease compared with controls.\textsuperscript{19}

Another retrospective cohort study by Pepper and Goldstein\textsuperscript{20} found that in patients undergoing major abdominal surgery there was a higher incidence of aspiration pneumonia, bacterial infections, and urinary tract infections in 234 patients with Parkinson’s disease compared with 40,979 patients without Parkinson’s disease.

When hospitalized, patients with Parkinson’s disease are at risk of developing deep vein thromboses as any hospitalized patient may be. However, as immobility worsens with exacerbation of parkinsonism, this risk may increase further, thus emphasizing the importance of maximizing symptomatic treatment of parkinsonism throughout the hospital stay, as well as using standard deep vein thrombosis prophylaxis measures.

In addition to infectious and mobility issues, patients with Parkinson’s disease require special consideration when undergoing anesthesia. Many drugs used during anesthesia interact with Parkinson’s disease medications or may worsen parkinsonian symptoms on their own,\textsuperscript{21} which is discussed further in this review.

One of the most common issues for hospitalized patients with Parkinson’s disease is the appropriate administration of oral medications. The inability to administer anti-parkinsonian medications properly, most of which are taken orally, may lead to worsening in motor symptoms and delayed recovery. Thus, optimal Parkinson’s disease management and anticipation of issues related to Parkinson’s disease (Table 1) will allow the physician providing perioperative care to avert morbidity associated with hospitalization when possible and hasten the overall recovery of patients with Parkinson’s disease. With this said, patients with early stages of Parkinson’s disease may have only minor parkinsonian symptoms. These patients typically do not require different perioperative care than patients without Parkinson’s disease, except that they may be taking monoamine oxidase-B inhibitors, which should be stopped 1 to 2 weeks before the procedure, as discussed next.

### Clinical Significance

- Patients with Parkinson’s disease are prone to developing immobility, dysphagia, respiratory dysfunction, urinary retention, and psychiatric symptoms.
- Challenges in managing these patients perioperatively include disruption of medication schedules, inability to take medications by mouth, reduced mobility, and medication interactions and side effects.
- These challenges lead to increased complications and prolonged hospitalizations.
- Anticipating potential complications allows physicians to mitigate nosocomial morbidity and shorten recovery times and hospital stays.

### Preoperative Management

Certain perioperative complications in patients with Parkinson’s disease can be avoided by planning in advance. Most important, continuing a patient’s home medication regimen will help avert exacerbation of Parkinson’s disease symptoms or symptoms of overdosing. Parkinson’s disease medications are given on a strict schedule that is unique to each patient; for example, dosing at 8:00 AM, 12:00 PM, and 4 PM is not the same as “3 times per day.” Maintaining patients’ established regimens may be complicated by an unavoidable nothing by mouth status; thus, planning ahead to minimize medication interruptions will be helpful. For example, scheduling a procedure for early morning will limit how many medication doses the patient must miss.

If missing multiple doses of oral anti-parkinsonism medication is unavoidable, dopaminergic agents such as
| **Table 1** General Recommendations |  |
| **Issue** | **Complication** | **Considerations for Prevention and Management** |
| Difficulty maintaining Parkinson’s disease medication schedule | Exacerbation of Parkinson’s disease, increased rigidity → increased fall risk, and decreased mobilization and associated complications | Attempt to follow patients’ home regimens as closely as possible with regard to time of administration and dosing. If a patient must be strictly NPO, consider alternative medications (apomorphine subcutaneously or rotigotine transdermally) and reassess ability to take oral medications often. |
| Parkinsonism hyperpyrexia syndrome | Parkinsonism hyperpyrexia syndrome |  |
| Dysphagia, sialorrhea, dysmotility | Aspiration, pneumonia, Constipation | With sedation, risk may increase and patients with Parkinson’s disease may need intubation more readily than patients without these symptoms. Incentive spirometry Aspiration precautions: suctioning Botulinum toxin type B for sialorrhea Glycopyrrolate or ipratropium spray for sialorrhea Aggressive bowel regimen |
| Deep brain stimulator | Damaging leads during cauterization Controversial contraindication of MRI | Plan ahead. Consult movement disorder neurologist. Minimize electrocautery use. If MRI is indicated, contact manufacturer and radiology department to determine safety. Limited MRI sequences of the brain using 1.5 tesla coil typically are safe. |
| General anesthesia | Certain medications might exacerbate Parkinson’s disease symptoms or interact with Parkinson’s disease medications. | Discontinue MAO-B inhibitors 1-2 weeks before surgery. Avoid halothane in patients taking levodopa because it increases cardiac sensitivity to catecholamines. Propofol has anti-parkinsonian effects, but may aggravate dyskinesias. Opioids (especially fentanyl) may worsen rigidity. |
| Postoperative nausea | Certain anti-emetics can worsen/cause extrapyramidal symptoms. | Use domperidone, ondansetron, or trimethobenzamide. |
| Postoperative pain | Immobility Interactions between analgesic and anti-Parkinson’s disease medications | Discontinue MAO-B inhibitor 1-2 wks before surgery. If MAO-B inhibitor is not discontinued, opioids should be used with caution (meperidine is contraindicated). Encourage physical therapy early on. |
| Fluctuations in blood pressure | Orthostatic hypotension Hypertension | Adequate hydration Blood pressure monitoring Discontinue MAO-B inhibitor 1-2 weeks before surgery. |
| Cognitive impairment | Agitation and hallucinations Falls | Avoid typical and most atypical antipsychotics, except for quetiapine and clozapine, which will not worsen Parkinson’s disease symptoms. Benzodiazepines should be used with caution. Safety precautions |
| Urinary retention | Urinary tract infection | Frequent bladder scans to assess for retention Early removal of Foley catheter High suspicion for infections, assess and treat if needed |
| Rigidity/immobility | Contractures Pressure ulcers General deconditioning | Consider foot and hand braces/support, physical therapy Frequent repositioning Adequate pharmacologic anti-parkinsonian treatment |

**Abbreviations:** MAO-B monoamine oxidase-B; MRI = magnetic resonance imaging; NPO = non per os.
apomorphine subcutaneously or rotigotine transdermally should be considered.22 Apomorphine is a potent dopamine agonist that is usually effective as a rescue medication in treating patients with advanced Parkinson’s disease taking high doses of levodopa.22 However, side effects of nausea and emesis may be significant, and pretreatment with antiemetics is required.22,23 Hypotension is another important side effect, although this is usually transient and abates with subsequent doses.23 Less common adverse reactions, although worth noting, are injection site nodules and ulcerations, somnolence, and, rarely, sleep attacks.23 We recommend starting with 2 mg of apomorphine, and if tolerated, increasing the dose gradually by 1 mg as needed.23 Another option is transdermal rotigotine. Although this may not be as potent as apomorphine and possibly insufficient for patients taking high doses of levodopa, it is usually well tolerated. Common side effects are mild to moderate nausea, somnolence, and application site reactions.22,24 Dose equivalence ratios between levodopa and rotigotine are estimated to be between 20 and 30 to 1.22,25 Adequate gastrointestinal absorption of oral medications is another issue worth noting, because patients with Parkinson’s disease are prone to gastrointestinal slowing. With the additional risk of postoperative ileus in patients with Parkinson’s disease after a procedure, enteric administration of medication may provide suboptimal treatment temporarily.19 An aggressive bowel regimen may be helpful in promoting gastrointestinal motility. Both apomorphine and rotigotine may be useful in the interim; however, they may be less tolerated or less effective than a patient’s established regimen. Thus, returning to a patient’s home medication schedule as soon as possible should be the goal. Note that carbidopa/levodopa comes in an orally disintegrating form that does not require water to swallow and an immediate release form that can be chewed, dissolved in carbonated water, or administered via nasogastric or percutaneous gastrostomy tube if needed. The controlled release form should not be chewed or crushed.

An abrupt cessation or decrease of dopaminergic drugs (especially levodopa) can be life-threatening, leading to parkinsonism hyperpyrexia syndrome. This presents similarly to neuroleptic malignant syndrome, with altered mental status, rigidity, tremors, fevers, and autonomic dysfunction. Overall incidence is 4%, with mortality reported as 4% in treated patients and 20% in untreated patients.26 Although rare, parkinsonism hyperpyrexia syndrome is a grave complication.

If a patient is taking a monoamine oxidase-B inhibitor, such as rasagline or selegiline, it is recommended to discontinue it 1 to 2 weeks before surgery. These medications interact with opioids and may contribute to labile blood pressures and increase the risk of serotonin syndrome.10,11,21 Unlike the dopaminergic medications, it is safe to stop these medications; thus, it is advised to do so to avoid unnecessary perioperative complications. However, if surgery is emergent, it may be impossible to stop these medications in advance. In these situations, it is still recommended to discontinue monoamine oxidase-B inhibitors when able, avoid medications that interact with them both intraoperatively and postoperatively, and watch for signs and symptoms of dangerous interactions, including serotonin syndrome, as discussed in the “Postoperative Management” section.

**INTRAOPERATIVE MANAGEMENT**

Particular considerations should be made with regard to anesthesia medications. Halothane should be avoided in those taking levodopa because it can increase cardiac sensitivity to catecholamines.21 Propofol is commonly used in patients with Parkinson’s disease and can have antiparkinsonian effects; however, it may aggravate dyskinesias (a common side effect of levodopa) to the point of interfering with the procedure.21,22 When treating intraoperative and perioperative pain, opioids, particularly fentanyl, may worsen rigidity and thus should be avoided.21 Sialorrhea secondary to impaired swallowing can be problematic in patients with Parkinson’s disease and may worsen during sedation and anesthesia. Both glycopyrrolate by mouth and ipratropium spray have been found to be effective for short-term treatment of sialorrhea in patients with Parkinson’s disease.7 Botulinum toxin injection in the parotid glands is another method used to alleviate excessive sialorrhea.2 It takes several days before the toxin produces an effect and may take several rounds of injections before the optimal dose is achieved to produce the desired effect. Thus, this is likely not a good option for botulinum toxin-naïve patients who do not require prolonged hospital stays. However, for those patients already receiving treatment, it may be useful to schedule injections before admission.

Symptoms of dysphagia and excessive sialorrhea are important to note when evaluating the need for intubation in patients with Parkinson’s disease, because it puts them at an increased risk for aspiration.15 Intubation may be needed more readily than in patients without Parkinson’s disease.

Some patients with Parkinson’s disease have deep brain stimulators, which may need to be turned off during certain tests and procedures. It is recommended to consult a movement disorder specialist with deep brain stimulation knowledge before a procedure for more specific recommendations. In general, electrocautery may damage stimulator leads and should be used with caution.27 If cautery must be performed, bipolar cautery is preferred and the stimulator should be turned off.27 The safety of magnetic resonance imaging for patients with deep brain stimulators currently remains unclear.28 The risks associated with magnetic resonance imaging in these patients include heating along the leads, movement of the device, induced stimulation or turning the device on or off, and distorting the magnetic resonance images.29 Deep brain stimulator manufacturers indicate that only brain magnetic resonance imaging is safe in patients with stimulators (with the device turned off), and body imaging (including spine) is contraindicated.30 However, some data suggest that brain and body magnetic resonance imaging may be safe.28,31 Ultimately, there are
insufficient data to fully assess the risks of magnetic resonance imaging for patients with deep brain stimulators; thus, if a patient with a stimulator needs magnetic resonance imaging, it is recommended to discuss with the device manufacturer and radiologist beforehand.

POSTOPERATIVE MANAGEMENT

In the acute postoperative period, it is common for patients to have anesthesia-reemergence shivering; this is benign and not related to Parkinson’s disease. Postoperative delirium, confusion, and hallucinations are more common in patients with Parkinson’s disease compared with general geriatric patients. Unfortunately, most antipsychotics will worsen parkinsonism and must be avoided (see “Psychiatric Issues” section).

When treating postoperative pain, opioids should be minimized or avoided. Opioids with serotonin reuptake inhibitory activity especially should be avoided in those taking monoamine oxidase-B inhibitors. Meperidine in particular is contraindicated in these patients, although tramadol, methadone, dextromethorphan, and propoxyphene also have weak serotonin reuptake inhibitory activity. Morphin, codeine, oxycodone, and buprenorphine do not have serotonin reuptake inhibitory activity. This interaction can cause agitation, rigidity, diaphoresis, hyperpyrexia, and even serotonin syndrome and death. In addition, monoamine oxidase-B inhibitors inhibit the metabolism of opioids in the liver, putting patients at risk for overdose. It is recommended that monoamine oxidase-B inhibitors be stopped 1 to 2 weeks before the procedure if possible to avoid these complications.

With regard to anti-emetic agents, domperidone or ondansetron are preferred. Metoclopramide, prochlorperazine, and promethazine should be avoided because of their dopamine antagonistic actions and associated extrapyramidal side effects.

Swallowing and respiratory status are important issues for patients with Parkinson’s disease. As previously discussed, dysphagia and a reduced cough are common features of advanced Parkinson’s disease, putting these patients at an increased risk for aspiration pneumonia. It also is common for them to experience bronchospasm. Incentive spirometry and aspiration precautions are essential. Risk of aspiration must be balanced against restarting a patient’s oral anti-parkinsonian medications as soon as possible to facilitate recovery. One meta-analysis found that levodopa therapy may improve respiratory function in patients with Parkinson’s disease, suggesting that restarting oral anti-parkinsonian medication may help decrease the risk of pneumonia. Repeated assessment of a patient’s ability to take solids and liquids orally may be necessary to determine the earliest time to reintitate oral intake safely.

Patients with Parkinson’s disease are at risk for developing autonomic disturbances as part of their underlying pathology and as a side effect of Parkinson’s disease medications. Orthostatic hypotension is common and can be exacerbated by dehydration. Maintaining adequate hydration in these patients is important, which may be difficult if patients have advanced disease and difficulty feeding themselves.

Tremor may be a predominate manifestation of Parkinson’s disease. Despite being bothersome to the patient and interfering with his or her ability to perform activities, tremor is usually not dangerous. However, it may interfere with the healing process after certain procedures. For example, if a patient has undergone an orthopedic surgery that requires postoperative immobility to allow the affected area to heal properly, pronounced tremors may interfere with this recovery process. In these situations, it may be necessary to use physical restraints or sedation until the tremors can be brought under control or immobility is no longer needed.

Physical therapy is another key component in the recovery of patients with Parkinson’s disease. Ordering this early and continuing throughout the hospital stay will improve mobility and facilitate overall recovery, helping to prevent deep vein thrombosis, pulmonary embolism, constipation, contractures, pressure ulcers, and pneumonia.

PSYCHIATRIC ISSUES

Psychiatric disturbances are common in advanced Parkinson’s disease, as well as other parkinsonian syndromes (e.g., Parkinson’s disease dementia and diffuse Lewy body dementia). These may include agitation, hallucinations, paranoia, delusions, and delirium. A rapid worsening of Parkinson’s disease symptoms with alterations in mental status is due most commonly to a toxic-metabolic cause, so infectious and metabolic derangements should be investigated first. If found, the underlying cause should be treated before making any adjustments to Parkinson’s disease medications. If psychiatric medications are needed, typical and most atypical antipsychotics (e.g., haloperidol, risperidone, olanzapine, aripiprazole, and ziprasidone) should be avoided because they will worsen Parkinson’s disease symptoms. Only clozapine, and possibly quetiapine, will not worsen Parkinson’s disease and are the preferred antipsychotic medications for patients with Parkinson’s disease. Benzodiazepines may be helpful; however, it is recommended to use them with caution and at low doses, because patients with advanced Parkinson’s disease seem to be more sensitive to benzodiazepines and may develop confusion, sedation, and paradoxical agitation.

CONCLUSIONS

Patients with Parkinson’s disease are admitted to the hospital for many different reasons, including surgery of various types. Perioperative management of these patients poses unique challenges for the hospitalist, internist, and other health care providers. A common and important issue is maintaining adequate pharmacologic treatment for a patient’s parkinsonism. Adherence to home regimens of
dopaminergic medications and minimizing missed doses and nothing by mouth status will help prevent exacerbations of Parkinson’s disease and further motor complications. If necessary, using subcutaneous or transdermal dopamine agonists can be useful to treat motor symptoms of Parkinson’s disease when a patient is unable to take oral medications. Avoiding medications that can worsen Parkinson’s disease or interact with Parkinson’s disease medications also will prevent adverse events. Aggressive physical therapy, respiratory therapy, and prophylactic measures to prevent deep vein thrombosis and ileus will help facilitate postoperative recovery. In addition, psychiatric sequelae of hospitalization in patients with Parkinson’s disease should be treated with medications that do not worsen Parkinson’s disease. Patients with deep brain stimulators also need particular consideration perioperatively, and in these cases a neurologic consultation with a movement disorder specialist especially is advised. Anticipation and knowledge of these issues (Table 1) can help minimize complications and avoid prolonged hospital stays.

References