

Nurse AdviseERR®

Educating the Healthcare Community About Safe Medication Practices

Delayed administration and contraindicated drugs place patients with Parkinson's disease at risk

One-third of all patients with Parkinson's disease visit an emergency department or hospital each year, making it a surprisingly common occurrence.¹ The disease affects about 1 million people and is currently the fourteenth leading cause of death in the US. Hospitalization can be risky for patients with Parkinson's disease when viewed from the perspective of pharmacological management.

Patients with Parkinson's disease require strict adherence to an individualized, timed medication regimen of antiparkinsonian agents. Dosing intervals are specific to each individual patient because of the complexity of the disease. It is not unusual for patients being treated with carbidopa/levodopa to require a dose every 1 to 2 hours. When medications are not administered on time, according to the patient's unique schedule, patients may experience an immediate increase in symptoms.^{2,3} Delaying medications by more than 1 hour, for example, can cause patients with Parkinson's disease to experience worsening tremors, increased rigidity, loss of balance, confusion, agitation, and difficulty communicating.² Studies show that three out of four hospitalized patients with Parkinson's disease do **not** receive their medications on time, or have had doses entirely omitted.⁴ According to the National Parkinson Foundation, 70% of neurologists report that their patients do **not** get the medications they need when hospitalized.²

Undergoing surgical procedures can be particularly risky for patients with Parkinson's disease. Antiparkinsonian agents have been inappropriately withheld because patients were NPO for surgery, and surgical patients have been given a contraindicated anesthetic agent, or a centrally acting antidopaminergic drug such as haloperidol, metoclopramide, or prochlorperazine, postoperatively. One in three patients with Parkinson's disease has been prescribed contraindicated drugs during hospitalization. Serious complications, mostly neuropsychiatric, have occurred in more than half of these patients.^{4,5}

Two case examples

The first case reported to ISMP involved a woman with Parkinson's disease who was admitted to a hospital with a urinary tract infection. Upon admission, the patient's medications were recorded during medication reconciliation. The patient told the nurse that she needed her medications right away. But she had been uncertain about the dose of a few medications, and it took several hours to collect further information about these doses.

Once ordered, the medications were scheduled using the hospital's standard administration times. However, for patients with Parkinson's disease, it is safest to administer antiparkinsonian drugs according to the scheduled times the patient takes the medications at home.^{2,4} In this case, the patient received all of her antiparkinsonian medications several hours late. While awaiting the medications, the patient found it hard to talk and communicate with hospital staff and her family. Her tremors intensified and she had difficulty maintaining her balance. She became so confused and

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⚡ Possible dosing dilemma for infants.

In September 2014, the US Food and Drug Administration (FDA) clarified an earlier warning (www.ismp.org/sc?id=427) about using **REVATIO** (sildenafil) for treatment of pulmonary arterial hypertension (PAH) in children. FDA recognized there may be situations in which the benefit-risk profile of the drug may be acceptable in certain children. Now, Pfizer has introduced a commercial oral liquid formulation of Revatio 10 mg/mL (once reconstituted). This is a welcome addition for pediatric patients who suffer from PAH because, previously, a suspension had to be compounded from tablets.

The recommended oral dose of Revatio is 5 mg or 20 mg three times a day, administered 4–6 hours apart. However, some patients may need doses other than 5 mg or 20 mg. For example, *Pediatric and Neonatal Lexi-Drugs* provides dosing information for neonatal and infant patients with PAH based on a mg/kg/dose that may not equate exactly to 5 mg or 20 mg. Unfortunately, the product comes with a 2 mL oral syringe with only 0.5 mL (5 mg) and 2 mL (20 mg) dose markings. Thus, pharmacies will need to provide 1 mL oral syringes to correctly administer doses that don't conform to the provided oral syringe scale. Pharmacists must be aware of the current packaging shortcoming and determine a process for when doses for a child are not exactly 5 mg or 20 mg. Since the product labeling includes only the 5 mg and 20 mg dose, it is unlikely Pfizer will change the dosing device.

⚡ Look-alike prefilled syringes. If you

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agitated from not receiving her medications that her physician ordered haloperidol 5 mg intramuscularly. The physician was not aware that haloperidol can worsen the symptoms of Parkinson's disease,^{6,7} and the pharmacist and nurse did not detect the prescribing error. The adverse symptoms worsened after receiving haloperidol, thus lengthening the patient's hospitalization.

Later, when this patient required hospitalization for an elective surgery, the family selected a facility associated with the patient's neurologist. The family assumed the staff would be more knowledgeable about the disease, but they ran into similar problems. The patient did not receive her medications on time and experienced the same symptoms as during the previous hospital admission. Once again, this extended her hospital stay unnecessarily.

In another case, reported to the National Parkinson Foundation, a hospitalized patient with Parkinson's disease had surgery for a herniated disc.² During the admission process, the patient's wife alerted the staff about the need to administer her husband's antiparkinsonian drugs exactly according to his schedule at home. She found staff were unaware of the need for timely drug administration and, thus, repeated the warning with each shift change. However, when the patient's wife was not by her husband's side, he did not get his medications on time. He was also prescribed and administered a contraindicated drug. The patient suffered significant hallucinations and was unable to communicate until his medications were readjusted to his schedule at home.

Other medication safety concerns

Even with correct medication administration timing based on the patient's home schedule, dosing errors have been reported with carbidopa/levodopa. The drug is available in many different strengths and forms, from an orally disintegrating tablet to extended- and immediate-release formulations. Levodopa, which converts to dopamine in the brain, can cause episodes of acute psychosis and dyskinesia when given in large doses, which can unnecessarily extend hospitalization. Also, patients may take different strengths of carbidopa/levodopa each time throughout the day, increasing the risk for errors. Documenting a complex schedule, even if well understood, may be difficult and even more challenging in some electronic health records.

Dysphagia is another manifestation of Parkinson's disease and can affect the patient's ability to swallow medications. The symptoms include frequent coughing while drinking and taking medications and a gurgling voice.⁸

When patients with Parkinson's disease are hospitalized and experience problems with incorrect timing of drug administration, or receive drugs that exacerbate disease symptoms, their stay may be prolonged. Also, the loss of disease control at the hands of those who should be experts undermines the patient's faith in their healthcare team. Healthcare providers should consider the following recommendations to improve the medication management of hospitalized patients with Parkinson's disease.

Expedited reconciliation. Establish an expedited medication reconciliation process upon admission for all patients with Parkinson's disease. Set the goal of obtaining an accurate list of medications within 2 hours of admission, whenever possible, that includes the exact doses and timing of medications that the patient took as an out-patient. Consider an automatic pharmacy consultation when patients with Parkinson's disease are admitted to assist with timely medication reconciliation. Some patients with Parkinson's disease have memory impairment, so family members who have close contact with the patient may need to be contacted. The reconciliation process may also require calling the patient's neurologist.

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iSecure syringes in patient care units, be aware of the risk of mix-ups. The most predominant feature of the iSecure device is the bold purple and lime green color combination of the syringe that makes the different products look alike at first glance (**Figure 1**). The names of the medications appear on the barrel of the prefilled syringe, and the manufacturer, Hospira, provides color differences on some of the product labels. However, ISMP has received reports of mix-ups between these syringes. The latest mix-up involved administering IV ondansetron instead of midazolam to a patient in the surgical suite.

If you use more than one type or dose of medication available in iSecure syringes in any patient care area, take



Figure 1. iSecure syringes by Hospira have been mixed up.

steps to reduce the risk of mix-ups. Examples include providing discrete and separate storage areas for syringes when possible, applying auxiliary labels, using barcode scanning at the bedside, or purchasing one of two look-alike syringes from another company that provides prefilled syringes. While reading labels is paramount, syringes that look similar are prone to *confirmation bias*—where we see what we want to see and don't see any disconfirming evidence—and *inattention blindness*—where our brain makes do with a flickering glimpse and fills in the gaps with what we think we should be seeing.

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Build a unique schedule. Establish a method and process to create and communicate the patient's individualized medication schedule in order to control symptoms throughout the day. This requires clear communication between the patient care unit and the pharmacy so patient-specific schedules are not overridden with standard dosing schedules.

Avoid nonformulary delays. To the extent possible, ensure that your formulary provides common Parkinson's disease medications and doses so that drug administration is not delayed while the pharmacy obtains nonformulary medications.

Know the symptoms. Upon admission, obtain information regarding the patient's current symptoms, ability to carry out daily activities, and mental status as a baseline to observe for increasing symptoms potentially due to the effects of drug therapy.

Avoid contraindicated drugs. Some medications alter the brain's dopamine receptors causing symptoms, while others chemically interact with antiparkinsonian medications causing side effects. These contraindicated medications (e.g., dopamine blockers; older antipsychotics and antidepressants; certain antiemetics, pain medications, and anesthesia agents) should be avoided.⁹ If the patient is taking selegiline or rasagiline, other medications must also be avoided, for example, meperidine, tramadol, methadone, mirtazapine, St. John's Wort, cyclobenzaprine, dextromethorphan, pseudoephedrine, phenylephrine, and ephedrine. There are alternative choices within these categories of medications that are safer to use for patients with Parkinson's disease.

Build alerts. Develop strategies to alert prescribers and pharmacists to drug-drug and drug-disease interactions. For example, develop a pop-up warning to alert prescribers and pharmacists when a contraindicated drug is ordered for a patient who is already receiving carbidopa/levodopa and/or selegiline or rasagiline.

Neurology consultation. When patients with Parkinson's disease are hospitalized, consider consulting the patient's neurologist or other specialist to evaluate antiparkinsonian medications to ensure safety. At a minimum, let the patient's neurologist know the patient has been hospitalized. (Only 25% of neurologists are confident they would be contacted if their patients were admitted to the hospital.²) If the neurologist is not consulted, require a clinical pharmacist or expert in Parkinson's disease to review the patient's medications on the first day of admission. If possible, generate a computer alert, triggered by the patient's diagnosis or prescribed drugs, to let the knowledgeable clinician know that a patient has been admitted, thus enabling their involvement early in the course of the admission.⁴

Manage NPO status. If there is any plan to keep a patient with Parkinson's disease NPO that would interfere with the patient's unique schedule of medication administration, a neurologist or neurology team should oversee the medication regimen change to avoid complications.

Do not abruptly discontinue medications. Never abruptly discontinue antiparkinsonian medications. Serious reactions such as neuroleptic malignant-like syndrome can occur when antiparkinsonian medications are discontinued or the dose of levodopa has been reduced abruptly.¹⁰ This can result in a high fever, sweating, unstable blood pressure, stupor, muscular rigidity, and autonomic dysfunctions, which can be life-threatening.

Promote swallowing. When taking medications, patients should be asked to sit upright with their hips flexed at 90 degrees, and to remain sitting if possible for 45 minutes. They should also be encouraged to swallow twice after taking pills or drink-

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DOXOrubicin liposomal mix-up. At an outpatient infusion center, a patient coming in for an IV dose of conventional DOXOrubicin HCl 50 mg was given DOXOrubicin HCl liposome injection (DOXIL or generic equivalent) by mistake. The pharmacy prepared the dose, and a nurse administered it via IV push. Whereas conventional DOXOrubicin can be administered slow IV push via a running IV line, the liposomal product should not be administered undiluted or by IV push due to the risk of infusion reactions. The patient in this report did experience an infusion reaction with flushing, vomiting, and hypotension. The infusion was stopped, and the patient received methylPREDNISolone and prochlorperazine.

Since 1996, we have been warning practitioners about accidental administration of the liposomal form of DOXOrubicin instead of the conventional form of DOXOrubicin. These drugs should never be substituted for one another on a "mg for mg" basis. The Doxil product is marked, "Liposomal Formulation—Do Not Substitute for DOXOrubicin HCl," in a red color band on the front label panel. Below that, the label states, "For Intravenous Infusion Only." Still, mix-ups occur, resulting in severe side effects and even death.

All staff handling and administering chemotherapy need to be aware of the consequences of confusing DOXOrubicin liposome injection with conventional DOXOrubicin, and vice versa. Include the potential for mix-ups in continuing educational programs for pharmacy and nursing staff. These products should always be stored in separate areas, away from one another. Encourage staff to refer to all liposomal products by their brand names. At least two healthcare professionals should conduct an independent double check of the patient, drug, dose, and route/mode (slow IV push or IV infusion) of administration before dispensing and administering any DOXOrubicin product.

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ing liquid.⁸ Do not crush or allow the patient to chew extended- or controlled-release medications (e.g., **SINEMET CR**).

Optimal surgery time. When possible, schedule surgery as early in the day as possible (8 a.m. to 9 a.m. is optimal) for patients with Parkinson's disease to promote best symptom management.¹¹ Antiparkinsonian medications should be administered as close as possible to the patient's medication schedule pre- and postoperatively, and restarted immediately after surgery.

Focused education. Educate staff regarding the importance of timing with antiparkinsonian medications—that they must be on time, every time. Focusing education in particular areas such as the emergency department, orthopedic units, and key medical units, may be the most effective strategy given that many units will have a low census of patients with Parkinson's disease.⁴ Identify when patient symptoms are not controlled/managed and consult the neurologist. Also remind staff to be alert to the risk of falls.

Patient education. Obtain a free copy of an **Aware in Care** kit provided by the National Parkinson Foundation for patients and caregivers with an aim to ensure every patient with Parkinson's disease receives the best care possible during hospitalization. The kit includes a plan for hospitalization; a medical identification bracelet; a Medical Alert Card that states, "I have Parkinson's disease....I am not intoxicated," along with space for listing current medications and emergency contacts; medication forms; disease fact sheets; and more. Teach patients how to obtain their own **Aware in Care** kit by calling 800-473-4636 or visiting: www.awareincare.org.

Report adverse reactions. All adverse drug events or reactions that happen to patients with Parkinson's disease should be reported to the primary neurologist who is taking care of the patient, because a dose adjustment, change to a different medication, or gradual discontinuation of a medication may be necessary.¹²

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Join us on **June 24** for our **2015 Update on The Joint Commission Medication-Related Standards**. Learn the most troublesome Medication Management Standards and National Patient Safety Goals along with successful approaches taken by healthcare organizations to accomplish the intent of these Standards. A second presenter will provide personal insight into the Standards, based on a recent Joint Commission survey at a large, nonprofit, teaching hospital. The speaker will share opportunities at both the pharmacy and health-system level.

For more details and to register, visit: www.ismp.org/sc?id=349.

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