ISMP Medication Error Report Analysis

Delayed Administration and Contraindicated Drugs Place Hospitalized Parkinson's Disease Patients at Risk

Doxorubicin Liposomal Mix-up

Avoid Mix-ups Between Hydroxyprogesterone and Medroxyprogesterone

Michael R. Cohen, RPh, MS, ScD, and Judy L. Smetzer, RN, BSN†*

These medication errors have occurred in health care facilities at least once. They will happen again—perhaps where you work. Through education and alertness of personnel and procedural safeguards, they can be avoided. You should consider publishing accounts of errors in your newsletters and/or presenting them at your inservice training programs.

Your assistance is required to continue this feature. The reports described here were received through the Institute for Safe Medication Practices (ISMP) Medication Errors Reporting Program. Any reports published by ISMP will be anonymous. Comments are also invited; the writers' names will be published if desired. ISMP may be contacted at the address shown below.

Errors, close calls, or hazardous conditions may be reported directly to ISMP through the ISMP Web site (www.ismp.org), by calling 800-FAIL-SAFE, or via e-mail at ismpinfo@ismp.org. ISMP guarantees the confidentiality and security of the information received and respects reporters' wishes as to the level of detail included in publications.

DELAYED ADMINISTRATION AND CONTRAINDICATED DRUGS PLACE HOSPITALIZED PARKINSON'S DISEASE PATIENTS 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 United States. 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 a patient's unique schedule, the patient 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 3 out of 4 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

*President, Institute for Safe Medication Practices, 200 Lakeside Drive, Suite 200, Horsham, PA 19044; phone: 215-947-7797; fax: 215-914-1492; e-mail: mcohen@ismp.org; Web site: www.ismp.org. †Vice President, Institute for Safe Medication Practices, Horsham, Pennsylvania.

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 3 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}

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. She was uncertain about the doses 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. 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 agitated 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 patient's adverse symptoms worsened after receiving haloperidol, thus lengthening her hospitalization.

Later, when this patient required hospitalization for an elective surgery, the family selected a facility that was associated with the patient's neurologist. The family assumed that the staff would be more knowledgeable about the disease, but they ran into similar problems with medication administration. 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, this one 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 that staff were unaware of the need for timely drug administration, so she repeated the warning with each shift change. However, when she was not her husband's side, he did not get his medications on time. He was also prescribed and administered a contraindicated drug. He 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 timing of medication administration 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; this 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 may be difficult and even more challenging in some electronic health records.

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

When hospitalized patients with Parkinson's disease 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 by the actions of those who should be experts undermines the patient's faith in their health care team. Health care 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 that includes the exact doses and timing of medications that the patients took as outpatients, whenever possible. 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 patients may need to be contacted. It may also be necessary to contact the patients' neurologist.

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 that 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 from which 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, whereas others chemically interact with antiparkinsonian medications causing side effects. Avoid these contraindicated medications (eg, dopamine blockers; older antipsychotics and antidepressants; certain antiemetics, pain medications, and anesthesia agents).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 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 their neurologist or other specialist to evaluate antiparkinsonian medications to ensure safety. At a minimum, let the neurologists know that their patients have 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 and if 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° and to remain sitting if possible for 45 minutes. They should also be encouraged to swallow twice after taking pills or drinking liquid.⁸ Do not crush or allow the patients to chew extended- or controlled-release medications (eg, *Sinemet CR*).

Optimal surgery time. When possible, schedule surgery early in the day (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 — medications must be on time, every time. Focus education in particular areas such as the emergency department, orthopedic units, and key medical units; these 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. Remind staff to be alert to the risk of falls.

Patient education. In preparation for Parkinson's Awareness Month in April, obtain a 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 is free and 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; and disease fact sheets. Inform patients that they can obtain the Aware in Care kit by calling 800-473-4636 or visiting www.awareincare.org.

Report adverse reactions. Report all adverse drug events or reactions in patients with Parkinson's disease to the primary neurologist who is taking care of them; a dose adjustment, change to a different medication, or gradual discontinuation of a medication may be necessary.¹²

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DOXORUBICIN LIPOSOMAL MIX-UP

At an outpatient infusion center, a patient coming in for an intravenous (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 doxorubicin HCl can be administered 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 experienced an infusion reaction with flushing, vomiting, and hypotension. The infusion was stopped, and the patient received methylprednisolone and prochlorperazine.

Since 1996 when the liposomal form of the drug was first marketed, ISMP has warned practitioners about accidental administration of this form of doxorubicin instead of the conventional form, doxorubicin HCl. 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.

These drugs should never be substituted for one another on an “mg for mg” basis. All staff handling chemotherapy need to be aware of the consequences of confusing doxorubicin liposome injection with conventional doxorubicin and vice versa. In the pharmacy, these products should be stored in areas separate from one another. The potential for mix-ups should be included in continuing educational programs. Special quality control checks need to be in place, including independent checks by at least 2 health care professionals and a system of documenting all drugs, diluents, lot numbers, and expiration dates for each patient. Encourage staff to refer to all liposomal products by their brand names.

AVOID MIX-UPS BETWEEN HYDROXYPROGESTERONE AND MEDROXYPROGESTERONE

A medication error was recently reported to ISMP that involved confusion between hydroxyprogesterone caproate injection (*Makena*) and medroxyprogesterone acetate injectable suspension (*Depo-Provera*).

Makena is used to prevent preterm labor and is often given as an intramuscular (IM) injection of 250 mg. *Depo-Provera* is a contraceptive with a dose

of 150 mg given IM. It should never be given to pregnant women. A 400 mg/mL preparation of *Depo-Provera* is also available for use as adjunctive therapy and palliative treatment of inoperable, recurrent, and metastatic renal or endometrial carcinoma. Given that both medications are commonly used in obstetrics and gynecology patients, there is a strong possibility that these medications will be confused with one another due to their look- and sound-alike names and similar dosages and routes of administration.

One way to prevent errors between these products would be to use the brand name *Makena*, the only US Food and Drug Administration (FDA)–approved hydroxyprogesterone product, when prescribing the drug. Although medroxyprogesterone is available generically, it might be ordered by the brand name, too, with the pharmacist substituting a generic product as appropriate.

In the hospital where this error happened, the staff have adjusted their computerized prescriber order entry screens to reflect the indication for each drug to guide prescribers to the appropriate agent depending on patient circumstances. It’s important to be sure that relevant hospital staff are aware of this potential mix-up. ■