Sound-alike—Look-alike drugs and the risk for error

Actos and Actonel. Lamictal and Lamisil. Zyprexa and Zyrtec. All of these pairs of drugs have been involved in medication errors due to name similarity, which led to some degree of harm to the patient. According to the United States Pharmacopeia (USP), more than 3100 pairs of drugs marketed in the United States have brand or generic names that are close enough that confusion between the agents has resulted in a medication error. Although the majority of these errors were intercepted before the medication reached the patient or had no adverse consequences, a small percentage did cause harm, with some resulting in fatalities.

Errors due to sound-alike/look-alike name confusion usually occur in the dispensing phase of the medication process (64%) involving pharmacy technicians or pharmacists; however, about 20% of the errors have been attributed to nurses and 7% to physicians. Additional factors, such as poor handwriting or poor oral communication, can add to the confusion and potential for error.

To address this issue, the Joint Commission has included confusing drug names in its National Patient Safety Goals with recommendations to minimize the risk of error. Healthcare organizations must have a list of at least 10 drug combinations (based on recommendations from the Joint Commission) that have a risk for confusion and potential error. The University of Illinois Hospital (UIH) list of sound-alike/look-alike drugs is given in the Table.

Specific strategies for preventing errors are also recommended by the Joint Commission and include modified computer entry screens to differentiate drug names (eg, use of color, boldface, and/or “tall man” letters), well-defined storage areas for the different products, maximum dose warnings on computer entry, and staff education on the differences and risks of similar sounding products.

In addition to recommendations by the Joint Commission, the Food and Drug Administration (FDA) launched the Safe Use Initiative in 2009 as a means to reduce preventable medication errors. Part of this initiative included the formation of a specific division of the FDA to reduce process errors, including errors related to similar drug names or packaging. One of the most recent actions by the FDA was to request a change in the brand name of dexlansoprazole, a recently approved proton pump inhibitor, to Dexilant. The original name, Kapidex, was similar to Casodex (bicalutamide) and Kadian (morphine sulfate); several dispensing errors had been reported due
to name confusion shortly after the product was marketed. The FDA has also revised the guidance documents for industry on proprietary names to ensure better compliance to regulations.

Actions have also been taken by the USP to reduce the risk of name confusion and medication errors. The USP’s Healthcare Quality and Safety Group was created to provide healthcare practitioners tools and resources to improve patients’ safety in regards to medication use. One tool developed by this group is the Drug Error Finder, an online program that allows practitioners to search for drugs involved in medication errors due to name similarity. Information in the program includes the level of error—that is, potential for error, intercepted error, error with no harm, error with harm, or error with death. The program is based on reported medication errors from 2003 through 2006 and is available at http://www.usp.org/hqi/similarProducts/drugErrorFinderTool.html.

Another organization that has worked to reduce the risk of medication errors due to name confusion is the Institute for Safe Medication Practices (ISMP). The ISMP is a nonprofit organization that provides education to both healthcare practitioners and patients on the safe use of medications. Various medication safety tools and resources available from the ISMP (http://www.ismp.org) include a high-alert medication list, an error-prone abbreviations list, a listing of products with drug name suffixes, as well as an updated list of sound-alike/look-alike drugs.

Summary

Errors due to sound-alike/look-alike drug names are of major concern to all healthcare providers, industry, and regulatory agencies and have the potential to result in serious harm to a patient. Therefore, all efforts should be made to minimize this risk. Several organizations, including the Joint Commission, USP, ISMP, and the FDA have taken actions to implement additional safeguards to prevent these errors. Healthcare providers can also prevent errors due to name confusion by being aware of the problem and taking the following steps:

- Maintain awareness of sound-alike/look-alike drug names with frequently updated lists.
- Specify dosage form, strength, directions, and use when prescribing.
- Use both brand and generic names when prescribing drugs pairs that are similar in name.
- Encourage patients to be aware of the potential for name confusion and be familiar with the names and appearance of their medications.
- Consider the potential for name confusion when adding new drugs to the formulary.

**Clostridium difficile clinical practice guidelines: summary of treatment recommendations**

The Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA) have recently published guidelines for the diagnosis and treatment of Clostridium difficile infections (CDIs). The guidelines consist of 4 major content areas: collecting and reporting of surveillance data, diagnostic testing, infection control measures including prevention, and treatment. The purpose of this summary is to review the guidelines’ recommendations for appropriate prevention and treatment of CDIs. For further information, the reader is referred to the IDSA website, where copies of the full guidelines may be downloaded: http://www.idsociety.org/content.aspx?id=4430#cd.

_Clostridium difficile_, a gram-positive spore-forming anaerobe, is the most common cause of hospital-acquired diarrhea. Infections with _C difficile_ can result in severe disease such as pseudomembranous colitis, but some patients are asymptomatic carriers and others have only mild or moderate diarrhea. The current guidelines define a CDI as: the presence of diarrhea (3 or more unformed stools in 24 or fewer consecutive hours) with either a stool test positive for toxigenic _C difficile_ (or its toxins) or findings of pseudomembranous colitis with colonoscopy.

**Prevention**

One important element for the prevention of CDIs is the use of appropriate infection control measures such as hand washing and contact precautions to limit the spread from person to person. However, it is also important to minimize an individual patient’s risk for developing a CDI. Proper antimicrobial use is vital in helping to minimize the occurrence of CDIs, as prior exposure to antibiotics is a major risk factor. An increase in the number of antimicrobials, the number of doses, or duration of therapy can increase the risk of infection. The role of probiotics in preventing CDIs has recently prompted a great deal of discussion; however, the guidelines do not recommend their use for primary prevention at this time based on limited clinical efficacy data and the possibility for bacteremia or fungemia resulting from their use.

**Treatment**

The guidelines identify a number of key points for the treatment of CDIs. One of the primary recommendations is to discontinue the offending antimicrobial agent to reduce the risk of CDI recurrence. Vancomycin and metronidazole are the antimicrobials recommended for treatment. The choice of agent is based on the severity of the infection and whether it is a first episode or recurrence. The following Table summarizes the antimicrobial therapy recommendations.
Although the systemic absorption of oral vancomycin is low, patients with renal failure may achieve high serum levels with 2 grams per day for an extended duration. In these cases, serum trough monitoring is recommended. Metronidazole is not recommended for use beyond the first recurrence due to cumulative neurotoxicity. The use of intravenous immunoglobulins (150 to 400 mg/kg) has been reported in patients with severe, complicated cases or in those with recurrence. In addition, fecal transplants are being used for some patients with recurrent infections. In these cases, stool (administered either via nasogastric tube or enema) from a healthy donor is given to the patient. Other antibiotics such as nitazoxanide can also be considered.

Other key treatment measures include recommendations to:
- Initiate empiric therapy as soon as possible in patients with suspected severe or complicated CDI
- Make a patient-specific decision to initiate, continue, or discontinue therapy in patients with negative stool toxin assays
- Avoid antiperistaltic agents when possible
- Consider colectomy for patients who are severely ill

**Conclusion/role of the pharmacist**
These guidelines are a reminder that although antimicrobial agents are a beneficial and necessary part of the care of many hospitalized patients; their use is not without risk. It is important for pharmacists to remain vigilant of the antimicrobial use within their institution and serve as advocates for appropriate use. When treating patients with CDIs, pharmacists should recommend appropriate therapy with metronidazole, vancomycin, or the combination in select cases.
generally considered to be safer and less nephrotoxic than iodinated contrast media. For iodinated contrast media, the reported frequency of adverse reactions ranges between 5% and 12% for high osmolality agents and between 1% and 3% for low osmolality agents. For gadolinium-based agents, the frequency of adverse reactions is lower, ranging between 0.07% and 2.4%.

However, new concerns have emerged recently regarding the safety of gadolinium-based agents since a report in 2000 described 14 patients with chronic kidney insufficiency who developed a scleroderma-like disease (nephrogenic systemic fibrosis or NSF) following exposure to a gadolinium-based agent. Most gadolinium-based agents have an elimination half-life of between 1 and 2 hours, and in patients with normal renal function these agents are eliminated completely without any complications. However, in patients with renal insufficiency the half-life is extended and hence the exposure to these agents is prolonged, increasing the risk of toxicity.

**Literature Review**

The increasing usage of gadolinium-based agents in combination with imaging as a diagnostic tool, the approval of new agents, and the association between these agents and adverse reactions has led some researchers to investigate the safety of these drugs. Although long-term adverse events must be considered, the risk of acute adverse events is also an important issue, since prompt treatment in the radiology department may be required. The frequency of acute adverse reactions varies between each gadolinium-based agent, but overall range from 0.017% to 18.4%.

Abujudeh and colleagues conducted a retrospective study to assess the frequency, manifestations, and severity of acute adverse reactions following the administration of gadopentetate dimeglumide or gadobenate dimeglumide. Data from the safety reporting system of the institution, covering a 15-month period, were reviewed, and any adverse reactions associated with either of the gadolinium-based agents were recorded. A reaction was considered acute if it occurred before the patient left the radiology department. A gadolinium-based agent was administered intravenously in 32,659 instances during the study period; 27,956 for gadopentetate dimeglumine and 4,703 for gadobenate dimeglumine. According to this study, a total of 51 acute adverse reactions (0.16%) were reported. Gadopentetate dimeglumide caused 38 (0.14%) adverse reactions—36 were mild and 2 were moderate. Gadobenate dimeglumide was associated with 13 (0.28%) adverse reactions—7 were mild, 4 were moderate, and 2 were severe. The most common mild reactions were hives, rash, nausea, vomiting, cough, flushing, dizziness, numbness, double vision, and back pain. Moderate reactions observed included swelling, bronchospasm, wheezing, dyspnea, and diffuse erythema. Acute respiratory distress with seizures and cardiopulmonary arrest were among the severe reactions seen in the gadobenate dimeglumide group. Information on any potential risk factors that may have been present in the patients experiencing an acute adverse reaction was not provided.

Although this study only included gadopentetate dimeglumide and gadobenate dimeglumide, the results are consistent with those reported by Dillman and colleagues in an investigation on the frequency of acute allergic-like reactions in 13,344 pediatric patients (age <19 years) and 65,009 adults after the intravenous administration of gadolinium-based agents. In this study most of the procedures were done using the same 2 gadolinium-based agents investigated by Abujudeh, plus gadodiamide (which was used in only a small percentage of the procedures performed). Similar to the study by Abujudeh, an acute reaction was one occurring before the patient left the radiology department. A total of 54 patients (0.07%) experienced an acute allergic-like reaction following administration of a gadolinium-based agent—6 were pediatric patients (0.04%) and 48 were adults (0.07%). Although the incidence of acute adverse reactions was low, the authors noted that 26 of the patients who experienced a reaction had an identifiable risk factor—prior allergic-like reaction to a gadolinium-based agent (6 patients), prior allergic-like reaction to an iodinated contrast agent (3 patients), and prior allergic reactions to other drugs (20 patients).

A third and the largest trial was a retrospective review by Hunt and colleagues designed to determine the frequency and characteristics of adverse effects of low-osmolality iodinated agents and gadolinium-based agents. The authors reviewed all cases of acute adverse reactions to a contrast agent, either iodinated or gadolinium-based, during a 5-year period. In this study, an acute adverse reaction was one occurring during or within 30 minutes of administration of the contrast agent. During the study period, a total of 456,930 doses of a contrast agent were given—298,491 were low-osmolality iodinated agents and 158,439 were gadolinium-based agents. A total of 522 (0.114%) adverse reactions were identified; 458 (0.153%) were associated with the iodinated agents and 64 (0.04%) followed the use of a gadolinium-based agent. Among patients who experienced an adverse reaction to an iodinated agent, 34 had a self-reported history of iodine allergy. Three patients who reacted to a gadolinium-based agent reported a history of a reaction to a contrast agent (2 to iodinated agents and 1 to a gadolinium-based agent).

**Summary**

According to the results presented and other studies published in the literature, it is prudent to conclude that the administration of gadolinium-based agents is safe and that the rates of acute adverse reactions are very low. Most adverse effects experienced were mild and were managed in the radiology department. In these 3 large studies, the adverse reactions reported were consistent and mild reactions such as urticaria (hives), rash, nausea, and vomiting. However, precautions must be taken, and the need for premedication with antihistamines or
corticosteroids should be evaluated prior to the exposure of any patient to a gadolinium-based agent. A complete medical history (including respiratory disorders such as asthma), an allergy history, and history of previous reactions to gadolinium-based or iodinated-based contrast agents must also be obtained prior to any procedure.

Regardless of which procedure is being performed or which contrast media are being used, it is necessary to keep in mind that these agents are prescription drugs and should be handled as such. Like any other pharmaceuticals, these compounds are not devoid of risks or adverse reactions.

**P&T Committee Formulary Action**

**Additions**
- Bortezomib: Restricted to Hematology/Oncology
- Mycophenolic acid: Restricted to Transplant
- Pneumococcal conjugate vaccine 13

**Deletions**
- Phenylephrine 1% nasal drop
- Pneumococcal conjugate vaccine 7

Authors:
Courtney Krueger, PharmD, BCPS
Julio Rebelledo, PharmD candidate
Joan Stachnik, PharmD, BCPS

Editor:
Joan Stachnik, PharmD, BCPS