ISMP Medication Error Report Analysis

Prescribing Errors with Levetiracetam Oral Solution

Communicate Insulin Dose and Concentration on Separate Lines

Risperidone and Ropinirole Mix-ups

IV Line Disinfection Caps Can Become Foreign Bodies

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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.

PRESCRIBING ERRORS WITH LEVETIRACETAM ORAL SOLUTION

A 3-month-old baby girl was evaluated in an emergency department (ED) for a cough, congestion, difficulty breathing, and lethargy. A medication history was obtained from the baby's parents to begin the reconciliation process. According to the parents, the baby was receiving 8 mL of *Keppra* (levetiracetam) (800 mg of a 100 mg/mL solution) every 12 hours to treat a seizure disorder that had developed after birth. The clinician taking the medication history did not recognize the dose as being excessive for the baby.

It was determined that the baby required admission to treat her respiratory infection. Based on the medication history provided by the parents, the pediatric resident prescribed *Keppra* in the same dose, 800 mg, with instructions to administer each dose every 12 hours. Although the resident knew the baby's age and weight, he failed to recognize that the *Keppra* dose was excessive, and there was no dose alert issued by the computerized prescriber order entry system to warn him.

The hospital pharmacist reviewed the order and noted the dose was excessive based on the baby's age and weight. After verifying the dosing recommendations in

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a pediatric drug reference, the pharmacist contacted the pediatric resident about the excessive dose. The resident asked the baby's parents to bring the bottle of *Keppra* into the hospital for verification. The baby's mother told the pediatric resident that the prescription bottle did not have a pharmacy label on it, so she did not bring it into the hospital. The pharmacy label had been placed on the outer carton, which she had discarded after removing the bottle of medicine from the carton. The hospital pharmacist then called the community pharmacy to clarify the details of the dispensed medication. It was confirmed with the community pharmacy that a bottle of liquid *Keppra* 100 mg/mL had been dispensed with directions to "give 8 mL by mouth every 12 hours." Suspecting that the baby had been receiving an overdose of the drug at home, the hospital pharmacist then continued to investigate how the error had happened.

The hospital pharmacist determined that the baby had been admitted to the hospital about 3 weeks earlier. During that hospitalization, the baby had been receiving *Keppra* 80 mg every 12 hours, a 20 mg/kg/dose for the 4 kg baby. The hospital pharmacy had dispensed the commercially available product (100 mg/mL) in pharmacy-prepared oral syringes containing 0.8 mL (80 mg) of the drug. So during hospitalization, the baby had received the proper dose. However, upon discharge, the physician had electronically prescribed "8 mL" of *Keppra* twice daily, without listing the intended total dose or concentration. The reason for prescribing the drug by mL only and in the incorrect volume (8 mL instead of 0.8 mL) is unknown—perhaps it was simply a mental slip and lapse. Another possibility is that the prescriber actually ordered ".8" mL of the drug, which, without a leading zero, could have been misread as "8" mL. The hospital pharmacy did not have access to the electronic prescription at discharge for verification, and the unit nurses did not notice the error in the discharge summary, which listed all prescribed medications. The community pharmacy used the only commercially available strength of 100 mg/mL to fill the prescription, for which the prescribed 8 mL was equivalent to 800 mg.

When the community pharmacist received the prescription, he failed to recognize the significant dosing error. He did not verify the actual dose with the discharging physician, despite the volume-only dose of 8 mL, likely because the oral solution was commercially available in a single 100 mg/mL strength, which might have been included on the electronic

prescription. It is not known if the retail pharmacist recognized that the prescription was for a 4 kg baby. (The baby's previous prescription for *Keppra* 80 mg twice daily had been filled at a different pharmacy shortly after her birth.) A dose alert did not appear when the order was verified in the retail pharmacy system, likely because the child's weight or age was not in the pharmacy computer. Thus, the drug was dispensed as 800 mg twice daily, resulting in the baby receiving a 10-fold overdose at home for about 3 weeks prior to presentation in the ED.

Fortunately, the baby did not seem to have any significant clinical adverse effects upon evaluation of the overdose. The child's initial *Keppra* serum level was supratherapeutic at 63.4 mcg/mL. (According to *Lexi-Comp & Diagnostic Procedures*, toxic levels have not been well established, but most patients display an optimal response to levels between 5 and 45 mcg/mL.) *Keppra* was held upon hospital admission. A repeat level several days later yielded a value of 7.8 mcg/mL. The baby was eventually discharged after her respiratory infection was resolved. This time, the baby's physician prescribed *Keppra* 100 mg (1 mL) by mouth twice daily upon discharge for maintenance of seizure control. The baby was seen in a follow-up visit several weeks later and was doing well clinically.

A number of errors reported to ISMP have been caused by practitioners prescribing an oral solution by volume rather than in metric units by weight. For example, the September 2015 column ["Life-threatening Errors with Flecainide Suspension in Children," *Hosp Pharm.* 2015;50(8):657-661] described a series of errors that occurred with flecainide oral suspension—the dose was prescribed in volume, but the dispensed concentration was different than what the prescribers thought would be used. One error involved a 9-month-old infant whose parents were told to increase the dose of flecainide to 4 mL, assuming the concentration was 5 mg/mL as in the original prescription. But the parents refilled the prescription at another pharmacy, receiving the drug in a 20 mg/mL concentration. The infant received 80 mg/4 mL, a 4-fold overdose, resulting in wide complex tachycardia and QRS prolongation.

As a result of this levetiracetam error, the hospital has put safeguards in place that will help prevent future medication errors of this type in the pediatric population. These safeguards and other strategies recommended by ISMP are provided below for consideration and implementation in other hospitals to avoid similar errors.

Order doses by weight in metric units. Express single-entity medication doses in metric weight (eg, mg, mEq, mcg, units) not the volume alone (eg, mL), even if an oral solution is available in a single strength. Exceptions are some combination oral liquid products in a single strength that can be safely expressed in volume alone or powders that are not dosed by weight. Including a metric weight dose improves safety because the volume could differ depending on the concentration of the medication.

Include patient's weight in kg (g) on discharge prescriptions. To improve dosing accuracy of weight-based medications in populations at high risk for dosing errors (eg, patients weighing 50 kg or less), include the weight in kg (g) on discharge prescriptions. If there is no designated field for this information in the electronic prescribing application, include it in the notes/additional information field until vendors provide a designated field for weight. (Community pharmacists may miss information in nondesignated, nonrequired fields with an electronic prescription; thus, vendors should evaluate the need to include this field for both prescribers and dispensing pharmacists to best safeguard pediatric patients and even adult patients given the influx of newer, weight-based medications.) Including the patient's weight on prescriptions allows an ambulatory care pharmacist to confirm the ordered dose on the prescription for weight-based medications.

Include the patient's age/date of birth on prescriptions. For appropriate dosing and patient identification, include the patient's age/birthdate on outpatient prescriptions.

Include weight-based and calculated doses. For pediatric medication orders and outpatient prescriptions, include the mg/kg or other dose expression (eg, mcg/kg) used to calculate the dose, along with the total dose (eg, 20 mg/kg/dose, 80 mg).

Convert an inpatient order to an outpatient prescription. Require the ordering prescriber to perform the discharge medication reconciliation so that all inpatient and preadmission home medications and doses are reviewed and, if appropriate, converted to outpatient prescriptions. Changes, discontinuations, or the addition of medications upon discharge should be clearly noted in the discharge summary given to the patient.

Verify discharge orders. Require nurses to verify the medications prior to discharge by comparing them with the patient's inpatient medication administration record (MAR) and home medication list.

For high-risk patients, such as pediatric patients, also require pharmacists to review all medications listed on discharge summaries, preferably before discharge but at least within 24 hours of discharge. Like nurses, hospital pharmacists have access to inpatient medication doses to check whether there are mismatches with the discharge prescriptions. Report any unexplained discrepancies to the discharging physicians. Be sure to initially and periodically monitor and measure your success with implementing this intervention.

Involve pharmacists in reconciliation. Increase pharmacy involvement in medication reconciliation upon patient admission to the ED and/or hospital. According to the Agency for Healthcare Research and Quality, the most effective medication reconciliation process involves pharmacists' interventions to clarify doses. Pharmacists, because of their knowledge and skills, are qualified to lead the interdisciplinary effort to maintain an effective medication reconciliation process. Pharmacist involvement is most needed during the initial capture or review of the medications that the patient has been taking at home.

Provide dosing alerts. Enable or build alerts to warn both prescribers and pharmacists about unsafe doses, including weight-based doses, that could cause patient harm. For the dose warning system to work, the order entry systems should not allow entry of an order without the patient's age/birthdate and weight populating the requisite, interactive fields. Test the alert system periodically, and ensure that the dose alerts are enabled and cannot be bypassed easily without documentation.

Educate patients. Prior to discharge, review each prescribed medication and how to measure each dose with the patient/parents/caregivers. Require the parents/caregivers to demonstrate proper dose measurement of all liquid medications for pediatric patients. (This might have alerted the nurse to the discharge prescribing error or alerted the parents that an 8 mL dose was a possible mistake.) Remind parents that the measurement device provided at the community pharmacy may be different than that used in the hospital, and they should ask the pharmacist if they have any questions about dose measurement. Also remind patients and parents to keep the outer carton of prescription medications if it contains the pharmacy label so they can refer back to the instructions for use. Pharmacists need to do their best to label the container that holds the drug, not just the carton.

COMMUNICATE INSULIN DOSE AND CONCENTRATION ON SEPARATE LINES

In a draft version of the *ISMP Guidelines for the Safe Electronic Communication of Medication Information* (www.ismp.org/sc?id=1685), we included a recommendation to avoid entries on a medication administration record (MAR) where the name of the drug and available dosage strength are on the first line and the patient-specific dose is on the next line. This applies to oral solids as well as liquids and injectables. This includes insulin for which electronic orders on the MAR often list the name of the insulin product followed immediately by its concentration.

The recommendation should also apply to outpatient prescription labels. Recently an ambulance was called for a 76-year-old man who was sweating and confused after receiving an insulin dose. Emergency service personnel initially treated the patient with IV dextrose 50% while transporting him to an ED where he was admitted to the hospital. When speaking to the man's son, the ED staff learned that he had given his father 100 units of *Novolog* (insulin aspart) that day. The son brought the insulin vial and package to the hospital. The pharmacy label read "insulin aspart 100 units/mL." The son mistook this as the dose, which was actually much lower.

Such confusion has happened many times in the past. In "Selected medication safety risks to manage in 2016 that might otherwise fall off the radar screen—Part I," [*Hosp Pharm.* 2016; 51(5):353-357], we wrote about a physician who accidentally ordered 100 units of *Lantus* (insulin glargine) instead of 6 units every evening. The physician reviewed the list of home medications that displayed the concentration right next to the drug name on the first line and the patient's dose on the second line: "Insulin glargine (*Lantus*) 100 units/mL," followed on the next line with "6 units subcutaneous daily every evening." With all the new insulin concentrations, this situation could become even more dangerous depending on how U-200, U-300, and U-500 concentrations are understood by patients and caregivers.

Physicians and nurses typically anticipate seeing the drug name and patient's dose side by side, while pharmacists may be accustomed to first viewing the available concentration to determine how best to dispense the patient-specific dose. Our recommendation is to list the drug name, patient-specific dose, route, and frequency on the first line of the MAR and patient medication lists, and the available concentration and any directions on how to prepare the dose below it. Information technology vendors and drug

information vendors are asked to consider this recommendation, which was also made by attendees at ISMP's November 2015 safety summit, Optimizing Safe Subcutaneous Insulin Delivery Across the Continuum of Care.

RISPERIDONE AND ROPINIROLE MIX-UPS

Risperidone 0.25 mg orally every evening was prescribed for a patient who suffered from oppositional defiant disorder. In error, the pharmacy dispensed ropinirole 0.25 mg. The patient's grandmother called the doctor to say the medication was not working and was making the patient worse, with nonstop wild behavior and uncontrollable laughing. Risperidone was increased to 0.5 mg; this time the pharmacy dispensed the correct drug. Later, in a therapy session, the grandmother brought in the medication bottle, which was labeled ropinirole. All medications were prescribed electronically, and medication records and reconciliation indicate that risperidone 0.25 mg was the drug prescribed and electronically transmitted. It was later confirmed that the pharmacy had dispensed the wrong medication.

Risperidone (*Risperdal*) is an antipsychotic agent, whereas ropinirole (*Requip*) is a dopamine agonist used in Parkinson's disease and restless legs syndrome. There's a long history of mix-ups between these drugs. In a similar case, a patient experienced nausea and a sedative effect after taking what was thought to be 6 mg (2 x 3 mg tablets) of risperidone but was actually ropinirole 3 mg tablets. The US Food and Drug Administration (FDA) warned the public about confusion with this name pair in 2011 after reviewing over 200 errors sent to ISMP and the FDA Adverse Event Reporting System (<http://www.fda.gov/Drugs/DrugSafety/ucm258805.htm>). Some patients required hospitalization. FDA asked manufacturers to use tall-man lettering on container labels and carton packaging (risperidONE, rOPINIrole) to help distinguish between the 2 products, and this may be helping. Electronic prescribing is likely also playing a role. The number of error reports sent to FDA and ISMP has decreased markedly since 2011.

Other causes of confusion with this similar drug name pair include illegible, handwritten prescriptions, which we see less of with computerization of order systems. Also, similar strengths, dosage forms, and dosing intervals; proximity of storage; appearance of product names together in computer listings; and look-alike container labels if the same company manufactures both products.

By addressing these known causes of confusion, you can minimize the risk of an error. When prescribing either drug, the purpose should be included. In pharmacies, the products should not be stored near each other, and tall-man letters should be used for storage, computer listings, and labels (except for patients).

IV LINE DISINFECTION CAPS CAN BECOME FOREIGN BODIES

Hospitals commonly utilize colorful alcohol-impregnated disinfection caps applied to intravenous (IV) catheter hubs and needleless injection ports to help prevent catheter-associated bloodstream infections (see **Figure 1**). These can often be found packaged in sleeves that hang from IV poles along with IV solutions. Unfortunately, in some cases, used ones may be left on a table near the patient.

A recent report cautioned about use of these caps around hospitalized pediatric patients, and it should serve to remind clinical staff of the potential for the caps to be ingested by children.¹ In one case, a child who was seen chewing on a cap was also experiencing drooling, vomiting, and refusing to eat meals. Esophagoscopy revealed a cap lodged in the lumen

of the child's esophagus. In another child, a cap that had just been removed from a port for drug administration accidentally popped into the child's mouth after sudden movement of the child's arm caused the health professional to mishandle the cap. The cap was swallowed and later found lodged in the esophagus. In both cases there was no long-term morbidity, but it is possible for a cap to lead to airway obstruction.

The authors of these publications call for disinfection caps to be used with caution and discretion in the pediatric population. They also suggest limiting the use of caps on peripheral lines, noting that, although studies support use on central and peripherally inserted central lines, a 2014 study showed no infection reduction with caps on peripheral lines.²

REFERENCES

1. Tawfik KO, et al. The catheter hub disinfection cap as esophageal foreign body. *Laryngoscope*. 2015;125:2820-2822.
2. DeVries M, et al. Reducing bloodstream infection risk in central and peripheral intravenous lines: Initial data on passive intravenous connector disinfection. *J Assoc Vasc Access*. 2014;19:87-93. ■

Figure 1. Green injection port cap sometimes left loose near patient, posing danger to child who puts it in the mouth.