Prescribing Errors with levETIRAcetam Oral Solution

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PROBLEM

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 too 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 excessive dose based on the baby's age and weight. After verifying the dosing recommendations in 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 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 if the decimal point was missed. 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-Lab & 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, in our April 23, 2015 newsletter, we published a series of errors that had 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 (www.ismp.org/sc?id=1710). 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.

SAFE PRACTICE RECOMMENDATIONS:

As a result of this 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 (e.g., mg, mEq, mcg, units), not the volume alone (e.g., mL), even if an oral solution is available in a single strength. (Exceptions are with 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 (e.g., 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 your 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 non-designated, non-required 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 (e.g., mcg/kg) used to calculate the dose, along with the total dose (e.g., 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 see if 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 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. The order entry systems should not allow entry of an order without the patient's age/birthdate and weight populating the requisite, interactive fields to allow the dose warning system to work. Test the alert system periodically, and ensure that the dose alerts are enabled and not 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 patient/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 to ask the pharmacist if any questions arise 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 the carton alone. Pc

PRACTICE TIP!

Avoid complaints to the College - Be diligent in counselling patients before releasing new medication to them and make use of effective communication techniques (such as paying attention to patients' non verbal cues to ensure they understand)
http://www.ocpinfo.com/library/practice-related/download/CloseUpOnComplaintsWinter2016.pdf