

A Fatal Zinc Overdose in a Neonate

Confusion of Micrograms With Milligrams

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PROBLEM: An infant received a lethal dose of zinc stemming from an error that occurred during the order-entry process and compounding of a total parenteral nutrition (TPN) solution. Although the Institute for Safe Medication Practices (ISMP) was not privy to a full root-cause analysis, details about this unfortunate event are presented in hopes that the lessons learned can be applied in hospitals across the nation to prevent similar mishaps.¹⁻³

TPN therapy was prescribed for a preterm infant born at 26 weeks of gestation. On the day of the birth, the physician's TPN order included directions to add zinc in a concentration of 330 mcg/100 mL. Because the automated compounder used for TPN required entry of zinc in a mcg/kg dose, the pharmacist converted the mcg/mL dose to a mcg/kg dose. She performed this calculation correctly but accidentally entered the zinc dose in the pharmacy computer in *mg*, not *mcg*. This resulted in a final concentration of 330 mg/100 mL—a 1,000-fold overdose.

Another pharmacist checked the work and product labels that were printed for preparation of the TPN, but she did not notice the error involving the erroneous change from mcg to mg. A pharmacy technician prepared the TPN using a 500-mL bag. The technician had to replenish the compounder syringe that contained zinc 11 times while preparing the solution, which required dozens of vials of zinc sulfate. Several TPN additives had to be added manually, which the technician prepared and brought to a third pharmacist to check before adding them to the solution. The final TPN bag was then dispensed to the neonatal intensive care unit (NICU).

Around 3 a.m., a nurse hung the bag of TPN. Around 6 a.m., the technician who prepared the TPN discussed the previous evening's work with the oncoming lead technician, noting the unusual preparation of the TPN that required numerous replenishments of the zinc syringe. The latter technician checked the order, discovered the error, and alerted a pharmacist, who immediately called the unit to stop the infusion. The pharmacist quickly called Poison Control and searched the Internet for treatment guidelines.

The infant received edetate calcium disodium (calcium disodium versenate, or calcium EDTA), which had been compounded by an external pharmacy. The chelation therapy was unsuccessful, and the infant died. The coroner listed cardiac failure caused by zinc intoxication as the cause of death.

Several mistakes resulted in the fatality:

1. **The method used to prescribe the zinc additive differed from the method required to enter the order into the automated compounder software program.** This factor contributed to an order-entry error. The automated compounder required entry of the zinc additive in *mcg/kg*. A preprinted order form was used to prescribe neonatal TPN. The usual TPN ingredients listed on the order form prompted the physician to prescribe doses by patient weight (e.g., mEq/kg, mg/kg). However, zinc was not listed on the form, and the physician wrote a free-text order for zinc, 330 mcg/100 mL. The pharmacist had to convert the dose to *mcg/kg*, after which she mistakenly chose *mg* instead of *mcg* from a pull-down list when entering the dose of zinc (the units of measure were next to each other on the pull-down list).

2. **Dosing alerts did not occur when the TPN order was entered into the pharmacy computer or when directions for preparation were scanned**

into the automated compounder. The pharmacy computer order entry system and the automated compounder used to mix the TPN did not alert the pharmacist that a 1,000-fold overdose had been entered into the systems for the zinc additive.

3. **The TPN order was processed in the evening, when staffing was limited despite the hospital's policy that TPN orders must be received and TPN solutions must be prepared before 5 p.m.** On the day of the error, the physician prescribed TPN at 4:30 p.m., but the order was not scanned and transmitted to the pharmacy until after 5 p.m. The pharmacist entered the order after 7 p.m., and the TPN solution was compounded later in the evening, when fewer pharmacy staff members were available to process complex orders. Staffing was further reduced that evening because of the absence of a technician who usually compounded products.

4. **Limited education and experience, along with ineffective competency validation in compounding products, particularly for infants, contributed to the technician's failure to notice the TPN order entry error.** The technician who prepared the TPN did not have sufficient experience to appreciate the significance of the large volume of zinc required by the automated compounder to prepare the TPN. Her prior training had consisted of a week of shadowing another technician. During that period, she compounded fewer than 20 products using the automated compounder. In that time, she had never replenished a syringe on the compounder. She thought it was unusual to replenish the zinc syringe 11 times during the course of making the TPN but did not mention this to a pharmacist. She also did not question the need to use a 500-mL bag to make the TPN (normally, a 250-mL bag is used for neonatal TPN).

Although staff members had raised concerns about the technician's level of



training, on the day of the error, the technician was asked to compound some products because the usual compounding technician was not available.

5. The inexperienced technician reported replenishing the zinc syringe 11 times while compounding the TPN to the lead technician the next morning but had not mentioned her concern to the on-duty pharmacist the previous evening. She reported feeling intimidated talking to the pharmacist about a condition she considered unusual, uncertain about whether it signaled an actual error. She believed that the pharmacist who entered the order was correct and that she should not question the pharmacist.

6. Ineffective or nonexistent systems for independent double-checks allowed the error to bypass at least six staff members without notice. At several points during dispensing and administration, pharmacists or nurses checked the TPN orders and labels but did not recognize the error. The first check failed, primarily as a result of human error, when the pharmacist who compared the work and product labels with the original order did not notice that the zinc dose was expressed in milligrams, not micrograms.

The next faulty check involved verifying only the additives that had been added manually to the TPN. Hospital policy required pharmacists only to check the vials and syringes of the additives against the label; they were not required to compare the TPN product label with the original order. To verify the additives, the pharmacist looked at the identifying information on the top of the label, then skipped down to the bottom of the label to identify the additives to be added manually. As a result, he failed to read the middle of the label, which noted that 481.8 mL of zinc had been added to a bag that contained 560 mL.

In the NICU, one nurse read the “numbers” associated with the dose for each ingredient from the TPN label but not the units of measure (e.g., mg/kg, mg/dL) to another nurse, who was reading the original order. Although the numbers (including 330 for the zinc additive) matched, again the accidental entry of *mg* instead of *mcg* was not noticed. Many clues that indicated an error were overlooked during verification, including the

fact that the TPN bag was unusually large.

SAFE PRACTICE RECOMMENDATIONS: Some strategies to prevent errors follow:

1. Prescribing methods should be standardized. The method of ordering TPN solutions should be standardized for neonates, pediatric patients, and adults so that each prescribed ingredient matches the dosing templates used for entering the orders into the computer system and automated compounder. Preprinted forms or standard order sets should be used to list typical ingredients and to prompt the correct dosing method. On the rare occasions when calculations are necessary, two clinicians should be available to check the dose independently and to compare their answers for verification.

2. Prescribing and transmitting TPN orders should take place during the day. Policies that require prescribers to order TPN during the day shift should be established and enforced to maximize safety. The pharmacy staff should know which patients are receiving TPN and should check whether orders have been received by the established deadline.

3. Manual-only additions of low-volume ingredients should be allowed. For TPN ingredients that typically require very small volumes, the staff should prepare, check, and inject those ingredients manually. A trace element such as zinc should not be allowed to be loaded onto a compounder for automated preparation.

4. Automated warnings must be built and heeded. Automated dose-limit warnings should be installed, tested, and maximized in the pharmacy computer system and automated compounders, particularly for high-alert medications such as TPN and its ingredients. All alerts encountered during order entry could be printed so that the person checking it can also view and respond to the alerts. The importance of reading and reacting to the alerts should be reinforced with all staff.

5. Suspicion of an error should be raised. The following “red flags” should be continually emphasized to trigger a full review of the patient’s medications and treatment plan to ensure that an error has not occurred:

- needing to use more than a few dosage containers (tablets, capsules, vials, or ampules) to prepare or administer a single dose of any drug
- unexpected differences in the appearance of a drug or solution
- other unusual circumstances regarding a drug or solution
- unexpected patient response to a medication

Technicians who compound products should be required to stop the process if they find that they need to add an electrolyte or mineral in large doses or in large volumes in order to complete a single preparation. A full review of the work label and order by a pharmacist should be required before the technician proceeds. Nurses who work in pediatric units and NICUs should question products that are dispensed in larger quantities than typically supplied for children or neonates. A culture that encourages all staff, despite their level of experience or education, to speak up about unusual conditions should be fostered.

6. Effective redundancies should be performed. Independent double-checks should be conducted during TPN-related dispensing and administration processes. At least three verification processes should occur in the pharmacy:

- after initial order entry of TPN
- before additives are injected manually into the TPN
- after TPN is compounded

For each verification, a pharmacist should compare the actual prescriber’s order with the printed labels and the printed labels should be compared with the additives and final product. For verifying the manual additives, the vials and syringes that contain the additives should be inspected.

The final verification of the compounded TPN should include a comprehensive review of the TPN order, the product label, and the work label. Quality-control checks and verification of replacement solutions on the compounder, either manually or via bar coding, should be conducted, and an independent double-check of any calculations should be made. Before administering TPN, two nurses should also independently com-

continued on page 409

MEDICATION ERRORS

continued from page 394

pare the label on the solution with the physician's order.

7. Education should be offered, and competency should be validated.

A formal training process should be established for pharmacy staff members who enter TPN orders into the pharmacy computer, compound the solutions, or check the products after preparation. Selected staff members should be designated and trained to act as preceptors to provide one-on-one supervision until trainees are comfortable providing the service and have demonstrated the skills and knowledge necessary to function independently. Training should focus on dosage and dose concentration, not just the volume of additives, during solution preparation.

If compounding services are provided for neonatal and pediatric patients, age-specific training that emphasizes weight-based dosing should be included and the competency of all staff who serve these groups should be validated. Learning modules and competency-validation tools should be developed to expose trainees to a broad spectrum of responsibilities that they might not encounter during their on-the-job orientation.

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REFERENCES

1. Wells A. Error that led to baby's death slipped through many hands. *Las Vegas Review J* August 5, 2007. Available at: www.lvrj.com/news/8921512.html. Accessed June 2, 2011.
2. Wells A. Answers bring more tears. *Las Vegas Review J*, July 26, 2007. Available at: www.lvrj.com/news/8723912.html. Accessed June 2, 2011.
3. Nevada State Board of Pharmacy Order of August 9, 2007. Available at: <http://bop.nv.gov/Minutes/2007/2007-07-25-Minutes-BOP.pdf>. Accessed June 2, 2011.

The reports described in this column were received through the ISMP Medication Errors Reporting Program (MERP). Errors, close calls, or hazardous conditions may be reported on the ISMP Web site (www.ismp.org) or communicated directly to ISMP by calling 1-800-FAIL-SAFE or via e-mail at ismpinfo@ismp.org. ■