August 24, 2023 | Volume 28 ■ Issue 17

ISMP
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Acute Care
ISMP Medication Safety Alert!®
Educating the Healthcare Community About Safe Medication Practices

Obstetrical patient receives ampule of digoxin instead of BUPivacaine for spinal anesthesia

Problem: A pregnant patient with no significant past medical history was undergoing a scheduled cesarean delivery in an operating room (OR) and was to receive spinal anesthesia. An anesthetist typed in "bupivacaine" at an automated dispensing cabinet (ADC), and a drawer that provided access to several medications opened. The anesthetist inadvertently removed an ampule of digoxin rather than **BUP**ivacaine, prepared the dose, and administered it intrathecally. The anesthetist did not scan the barcode or read the label aloud to another staff member prior to administration. Anesthesia staff then recognized that the patient was not getting the anticipated **BUP**ivacaine effects and thought that it had been injected into the wrong space. They called the covering anesthesiologist for assistance, and a second dose was administered. The cesarean team delivered a healthy baby. However, shortly after the birth, the patient complained of dizziness, blurred vision, and a severe headache with left facial drooping and left-sided weakness. She began losing her ability to communicate and then experienced apnea and complete paralysis. She was intubated and transferred to the intensive care unit. During an OR ADC medication count, a nurse found that a digoxin ampule was missing. Inadvertent digoxin administration into the intrathecal space was suspected, and a digoxin level was ordered and detected. The team determined that the patient was brain dead, and she died shortly thereafter.

While the manufacturer names for the ampules were not reported to us, **BUPIVACAINE SPINAL** (preservative-free **BUP**ivacaine for intrathecal use) and digoxin are both available in 2 mL ampules (**Figure 1**). Since medications are not often provided in ampules, this can heighten the risk of mix-ups between the two drugs. We have previously received reports about cases in which digoxin had been accidentally administered via a neuraxial route (e.g., epidural, intrathecal) instead of the intended **BUP**ivacaine or **BUP**ivacaine with **EPINEPH**rine. One review (Patel S. Cardiovascular drug administration errors during neuraxial anesthesia or analgesia-a narrative review. *J Cardiothorac Vasc Anesth.* 2023;37[2]:291-8) analyzed inadvertent neuraxial cardiovascular medication administration errors reported between 1972 and 2022. Among the 33 events reported, digoxin was the medication most commonly administered in error and was associated with paraplegia and encephalopathy in eight patients.

Figure 1. Examples of ampules of **BUP**ivacaine Spinal by Hospira (NDC 0409-3613-11) (top) and digoxin by Hikma Pharmaceuticals (NDC 0641-1410-31) (bottom).

Safe Practice Recommendations: Given the repeated number of serious mix-ups between digoxin ampules and local anesthetics, the US Food and Drug Administration (FDA) should take steps to have manufacturers package digoxin in vials. In the meantime, organizations should consider the following recommendations:

- Review which medications (with special attention to ampules) are available in each unit-specific ADC location, anesthesia tray, and medication kit. Remove those that are not needed (considering typical diagnoses).

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SAFETY briefs

Promotional materials can be confused with medicinal products. A hospital pharmacy department received a carton of unfrozen ice pops in assorted flavors labeled **EMERPHED** (**Figure 1**, page 2), presumably as a promotion by Nexus for its e**PHED**rine sulfate injection. The pops were shipped in a container reading, "Chill out with EMERPHED" (**Figure 2**, page 2). Product prescribing information was also included in the package. While there is little concern that these might be confused with real Emerphed injection vials or prefilled syringes, we agree with the reporter who stated that promoting a product in this way is a poor marketing choice.

While we like treats like these as much as anyone else, we have received multiple reports about confusion between promotional materials and drug products over the years. In one case, a dermatologist gave a patient what he thought was a sample tube of a company's ointment, but it was a magic marker that was shaped to look like the ointment tube. A young woman then applied the "ointment" (purple ink) all over her face to treat her facial contact dermatitis/eczema. She later visited an emergency department to treat a local reaction to the ink.

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Quarterly ISMP Resources and Services Highlights

What does ISMP have to offer you? Check out our quarterly highlighted educational webinars and workshops, professional development opportunities, and **FREE** medication safety tools. The summer edition is now available as a convenient webpage; please visit: www.ismp.org/node/61994.

> **Digoxin instead of BUPivacaine** — continued from page 1

- Evaluate whether digoxin needs to be stocked in your OR and labor and delivery unit or if it can be requested from the pharmacy, as needed.
- Employ individual locked pockets or segregated storage, especially for high-alert medications like digoxin, or medications given via the spinal route, such as preservative-free **BUP**ivacaine.
- Use barcode scanning upon selection in the pharmacy and when stocking medications in the ADC to ensure it is placed in the correct drawer or pocket.
- Avoid stocking medications in ampules when possible or store them far apart, and never store more than one medication in an ampule in an open matrix drawer.
- In the OR, order **BUP**ivacaine for patients and scan the barcode prior to administration. Read labels aloud, as would typically occur at handoffs between the circulating and surgical nurse.
- Establish policies and procedures for returning unused medications. Require staff to return unused, non-refrigerated medications with intact packaging into a secure one-way return bin in the ADC, that is maintained by the pharmacy. Otherwise, return these items to the original secure locked-lidded pocket if it is a non-controlled substance. This process should be guided by barcode verification. Practitioners should return unused refrigerated medications to the designated ADC refrigerated return bin, which should be checked regularly by pharmacy staff.
- Educate staff (e.g., anesthesia personnel, nurses, pharmacists, pharmacy technicians) and conduct regular competency assessments about the safe use of ADCs during orientation and annually.
- Share this event with staff and discuss lessons learned. In addition, conduct regular reviews and discussions of medication events and close calls reported in your organization and by outside organizations such as ISMP.

For additional recommendations, review the following resources:

- ISMP ***Guidelines for the Safe Use of Automated Dispensing Cabinets*** (www.ismp.org/node/1372)
- ISMP ***Guidelines for Safe Medication Use in Perioperative and Procedural Settings*** (www.ismp.org/node/31601)
- ECRI. Automated dispensing cabinet setup and use errors may cause medication mishaps [ECRI Exclusive Hazard Report]. *ECRI Alerts*. February 8, 2017. Accession No. H0365

Worth repeating...

Tranexamic acid wrong route errors continue

We recently became aware of a state medical board order against a physician who accidentally used tranexamic acid injection instead of **BUP**ivacaine injection while administering spinal anesthesia prior to knee surgery. The incident occurred in December 2020, just 3 weeks after the US Food and Drug Administration (FDA) released a warning about tranexamic acid errors (www.ismp.org/ext/1138). According to the medical board's ruling, signed on March 21, 2023, the physician was fined and reprimanded. FDA had asked Pfizer, the product's sponsor, to update the label on their **CYKLOKAPRON** (tranexamic acid injection) to prominently state

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>*SAFETY* briefs

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Figure 1. Unfrozen ice pops labeled "EMERPHED (ephedrine sulfate injection)" made by Nexus.

Manufacturers sometimes promote medications with items that look like the drug product itself but serve some other purpose. This also creates a potential for medication errors. For example, when **GLIADEL** wafers (carmustine implant) were first marketed, we received complaints about a marketing campaign in which the chocolate candy wafers were packaged to look like the real Gliadel, which is implanted intracranially for malignant glioma.

Figure 2. Shipping containers also provide promotional material for Emerphed injection.

Given that patients and healthcare professionals could be confused by such promotional tools, we believe marketing campaigns such as this should not be permitted. In the past, the US Food and Drug Administration (FDA) has been involved in requesting that manufacturers stop such promotions. ISMP has contacted FDA in the hope they will address this one as well.

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"Intravenous Use Only," which they did (**Figure 1**). Generic manufacturers should have done the same; however, not all have followed through.

Figure 1. The current Cyklokapron (tranexamic acid injection) label by Pfizer prominently states "Intravenous Use Only" in a black box with reverse print.

Tranexamic acid is an antifibrinolytic that is used in a variety of hemorrhagic conditions to control bleeding, including postpartum hemorrhage. It works by preventing the breakdown of fibrin, thus promoting clotting. When accidentally administered via a neuraxial route, tranexamic acid injection is a potent neurotoxin with a mortality rate of about 50% and is almost always harmful to the patient. Survivors of intraspinal tranexamic acid often experience seizures, permanent neurological injury, and paraplegia (www.ismp.org/ext/1139).

ISMP has repeatedly warned against errors with tranexamic acid, including in a feature article in the May 23, 2019, ***ISMP Medication Safety Alert!*** (www.ismp.org/node/8706). ISMP also published a ***National Alert Network (NAN)*** warning on September 9, 2020 (www.ismp.org/node/20154). At that time in the United States, some **BUP**ivacaine, **ROP**ivacaine, and tranexamic acid products were packaged in vials with the same blue color cap (**Figure 2**). While label colors and vial sizes are now different, mix-ups related to cap color can still happen when the vials are stored upright near each other.

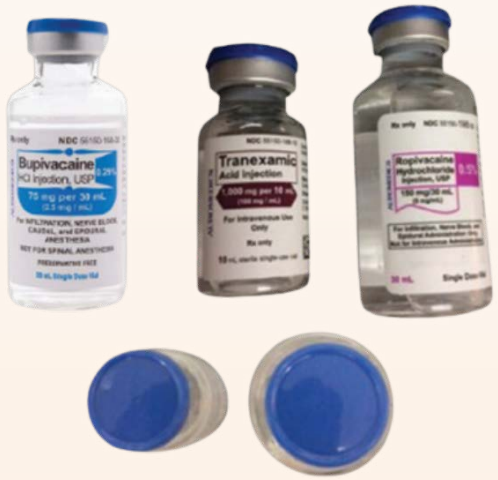

Figure 2. While label colors and vial sizes are different, the **BUP**ivacaine, tranexamic acid, and **ROP**ivacaine vials may have the same cap color and could lead staff to select the wrong vial based on cap color, without completely reading the label, especially if the vials are stored upright with only the caps showing.

Currently, the Cyklokapron vial by Pfizer has a yellow cap and there are a number of generic manufacturers with various cap colors. We have also received a report where a practitioner selected and administered tranexamic acid rather than rocuronium. Both vials had yellow caps. Practitioners have also reported concerns with confusing tranexamic acid and succinylcholine vials that both have red caps. In addition, outside the United States, tranexamic acid and local anesthetics often are available in ampules with labels on clear glass that are difficult to read, and also can be mistaken.

To make matters worse, these drugs are often found in areas where barcode scanning may not have been implemented or is not routinely utilized (e.g., perioperative areas, labor and delivery, emergency department). So, practitioners are less likely to detect mix-ups. Unfortunately, the literature has numerous reports of serious medication errors due to mix-ups between tranexamic acid and **BUP**ivacaine or **ROP**ivacaine during regional anesthesia (www.ismp.org/ext/1151).

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Infuvite vials 1 and 2 have the same NDC and barcode. INFUVITE ADULT, manufactured by Sandoz Canada and distributed by Baxter, is a multivitamin injection. Each carton contains 10 vials (five of vial 1 and five of vial 2) that must be combined and further diluted in intravenous (IV) fluids prior to infusion (**Figure 1**). An organization reported that a pharmacy technician used two of the same vials, both labeled "vial 1," to prepare an infusion. Both vial 1 and vial 2 had the same National Drug Code (NDC 54643-5649-1), so the IV workflow management system (IVWMS) did not capture the error during barcode scanning. A pharmacist reviewed the compounded product and recognized the error prior to it leaving the sterile compounding room.

We reached out to the US Food and Drug Administration (FDA) and the manufacturer to notify them of this error and recommend assigning unique NDCs and barcodes to each vial (vial 1 and vial 2) for all Infuvite products. To help prevent this error from happening, review how your electronic health record (EHR), IVWMS, and master compounding formulation are set up for Infuvite, and ensure instructions specify the use of "vial 1" and "vial 2" to prepare the final product. Also, educate staff that the contents of the two vials are different and that one of each must be used. Consider adding signage where the vials are stored, or store one of each vial together, as an additional reminder.

Figure 1. A carton of Infuvite Adult contains 10 vials, five of "vial 1" and five of "vial 2." To prepare an infusion, one vial of each (vial 1 and vial 2) must be combined and further diluted.

>*Worth* repeating

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To help prevent these types of errors, some key points are ***Worth* repeating**.

- Meet with key stakeholders (e.g., anesthesiologists, certified registered nurse anesthetists [CRNAs], surgeons, surgical staff) to review their workflow when ordering and administering tranexamic acid.
- Do not store tranexamic acid in an anesthesia tray.
- Determine if tranexamic acid can be ordered through an order set and sent by the pharmacy.
- Separate or sequester tranexamic acid in storage locations (e.g., pharmacy, clinical areas). Consider the use of signage, shelf talkers, or other warnings such as labels that state, "**Contains Tranexamic Acid**" to place over the vial caps and in storage locations. Avoid storing local anesthetics and tranexamic acid near one another.
- To prevent misidentifying medications by viewing only the vial caps, avoid storing injectable medication vials such as tranexamic acid in an upright position, especially when stored in a bin or drawer below eye level. Store them in a way that always keeps their labels visible.

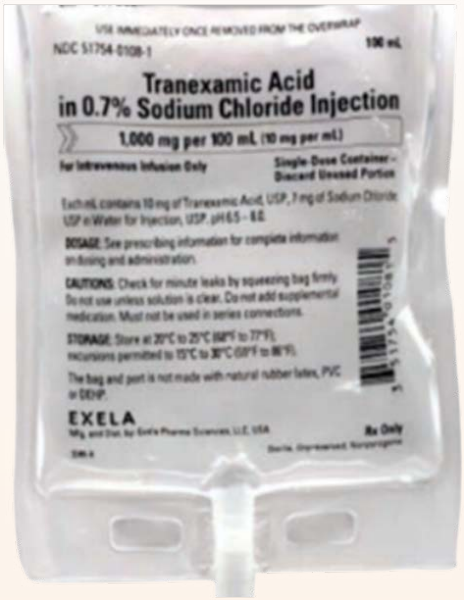

Figure 3. A commercially available premixed container of IV tranexamic acid in a sodium chloride solution for injection (NDC 51754-0108-1) made by Exela Pharma Sciences.

- Conduct a review to identify any look-alike ampules or vials (including caps) and determine if the risk of a mix-up will be reduced by purchasing them from different manufacturers. If so, purchase them that way.
- Employ barcode scanning in surgical and obstetrical areas to confirm medication/solution selection prior to dispensing and administration.
- When appropriate, use premixed intravenous (IV) tranexamic acid in sodium chloride injection, 1 g/100 mL (10 mg/mL) (**Figure 3**), which is less likely to be confused with local anesthetics in vials. While approved to reduce or prevent hemorrhage for patients with hemophilia undergoing tooth extraction, some organizations use this product off-label to treat other forms of bleeding. However, vials of tranexamic acid may still be needed since loading doses may be required prior to infusion (or a smart infusion pump loading dose feature could be used that automatically switches to a continuous infusion once the loading dose has been delivered). In addition, the off-label use of tranexamic acid topically and locally for hemorrhage may still require vials to be available.
- If not using commercially available premixed containers of tranexamic acid (e.g., during drug shortages), consider pharmacy-prepared intravenous infusions for surgical areas, to avoid confusion with vials of other medications.

Device and technology resources available through HII-Tech

Did you know that ISMP's affiliate, ECRI, has unique expertise in the design, proper use, and maintenance of medical devices and healthcare technology? The **Healthcare Incident Investigation and Technology Consulting (HII-Tech)** team of experts can help organizations prevent known device-related hazards before they occur, respond appropriately in the wake of an adverse event or close call, address specific healthcare technology concerns, and provide targeted education designed to improve the event investigation process.

Over the last 40 years, the HII-Tech team has conducted over 2,000 unbiased, third-party incident investigations involving a variety of medical devices and procedures. During these investigations, the team utilizes a systems approach, looking at devices, technology, users, patients, and the environment of care. After determining what went wrong and why, this team provides guidance on developing and implementing strategies, procedures, and safeguards to prevent future incidents.

With their unique expertise, this team can provide tailored consulting services to help organizations make biomedical engineering operations more efficient through data standardization, service history reviews, and biomedical benchmarking. HII-Tech can also work with organizations to develop long-term plans for equipment purchases (such as smart infusion pumps), which can increase safety and efficiency across the healthcare system and drive down costs. In addition, they can use their expertise to solve unique healthcare technology issues.

Organizations should also be aware of the HII-Tech team's online course that is intended to educate risk managers, biomedical engineers, and other healthcare providers on how to manage and investigate healthcare incidents. The **Healthcare Incident Management and Investigation (HIMI)**

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Remembering Lawrence (Larry) Trissel, BS Pharm, FASHP

We were saddened to learn of the passing of our friend, **Lawrence Trissel**, on August 11, 2023. Larry was a public health advocate, pharmacist, and scientist who held various positions at the National Institutes of Health (NIH), the US Food and Drug Administration (FDA), and the National Cancer Institute (NCI). He also served as the Director of Clinical Pharmaceutics Research, Division of Pharmacy at the University of Texas, M.D. Anderson Cancer Center, where he ran a research laboratory for many years.

Larry was the author of a series of editions of the *Handbook on Injectable Drugs*, as well as multiple other publications, including hundreds of research papers. Much of his work focused on drug stability in parenteral solutions, including when a drug is combined with other drugs. Healthcare professionals worldwide have relied on "Trissel's" (now *ASHP Injectable Drug Information*) whenever drug compatibility and stability information are needed. He served on the USP Sterile Compounding Committee where he was active with <797> until this past November.

Among Larry's many significant contributions to medication safety is the original work on the stability of vin**CRIS**tine after dilution in a minibag of intravenous (IV) fluid (Trissel LA, Zhang Y, Cohen MR. The stability of diluted vincristine sulfate used as a deterrent to inadvertent intrathecal injection. *Hosp Pharm*. 2001;36[7]:740–5). This laid the groundwork for the concept of dispensing vin**CRIS**tine diluted in a minibag to avoid syringe preparation and inadvertent fatal intrathecal injection. Dispensing vin**CRIS**tine in a syringe has been a set-up for mix-ups with drugs that are supposed to be injected intrathecally via syringe and has led to 150 known deaths worldwide. Thanks in large part to Larry's work, current FDA labeling calls for vin**CRIS**tine to only be dispensed in a minibag, not a syringe.

Larry was the 2011 ISMP **Cheers Lifetime Achievement** awardee. During his acceptance speech, he held the audience spellbound as he pointed out how fewer and fewer studies on drug storage, stability, compatibility, and beyond-use dating are being conducted in the United States. He noted how this entire area of study and research has undergone a transformation, "withering into near non-existence." Key product information that could promote safer pharmaceutical compounding, reduce medication errors, and lessen the impact of drug shortages has become scarce (www.ismp.org/node/693). In fact, the prescient pharmacist was one of few to publicly warn of the dangers ahead. The New England Compounding Center tragedy (www.ismp.org/node/653) began in the fall of 2012, not even a year after he spoke.

Healthcare professionals and pharmacists worldwide will be forever grateful for Larry's work and dedication. We will greatly miss Larry Trissel and offer our deepest condolences to his wife and others in his family.

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course (www.ismp.org/ext/1225) consists of six 20-minute interactive modules. In each module, a case study, based on a real-life device investigation, is presented to teach participants how to utilize ECRI's seven-point Incident Management and Investigation (IMI) plan.

For more information about the services and educational products provided by the HII-Tech team, please visit: www.ismp.org/ext/1226.

Special Announcements

Increase your medication safety knowledge

Pharmacists, pharmacy technicians, and nurses can earn 41 continuing education (CE) hours by completing the ***ASHP/ISMP Medication Safety Certificate*** online self-guided program. Medication Safety Officers Society (MSOS) members will be able to purchase the program at the discounted ASHP member price through **December 31, 2023**. For more information, visit: www.ismp.org/node/770.

Virtual MSI workshops

Do not miss the opportunity to register for one of our unique 2-day, virtual ***ISMP Medication Safety Intensive (MSI)*** workshops. Join us for one of our next sessions, scheduled for **October 4-5**, and **November 30 & December 1, 2023**. For more details about the program and additional workshop dates, please visit: www.ismp.org/node/127.

To subscribe: www.ismp.org/node/10

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