Mix-Ups Between Epidural Analgesia and IV Antibiotics in Labor and Delivery Units Continue to Cause Harm

Hospital Pharmacy
2019, Vol. 54(3) 155–159
© The Author(s) 2019
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/0018578719825730
journals.sagepub.com/home/hpx

Michael R. Cohen¹ and Judy L. Smetzer¹

Within weeks of each other this past fall, 2 hospitals reported mix-ups between epidural analgesia and intravenous (IV) antibiotics in labor and delivery (L&D) units. These mix-ups mimic previously published events and have similar contributing factors including look-alike infusion bags, overlooked warning labels, and a point-of-care barcode medication administration (BCMA) system that was not fully engaged. However, unlike the prior events, drug shortages also played a role in the most recent errors.

Recent Errors

Epidural FentaNYL With Bupivacaine Administered IV

An obstetrician prescribed IV penicillin G 5 million units for a woman in labor along with an order to “prepare the patient for an epidural.” Although the patient was experiencing few contractions, the L&D nurse obtained infusion bags of IV penicillin G and epidural fentaNYL (2 µg/mL) with bupivacaine (0.125%) from the automated dispensing cabinet (ADC) and placed them in the patient’s room on the counter, with the pharmacy labels face down.

The pharmacy label was on the same side as the manufacturer’s primary label. A red “Epidural Use Only” warning label was on the front of the fentaNYL with bupivacaine bag, but from the back, the bag looked nearly identical to the penicillin G bag. The epidural tubing was stored in the patient’s room, but it was not near the bag of fentaNYL with bupivacaine. Both infusions had been prepared by the pharmacy in 50-mL bags of 0.9% sodium chloride, although the penicillin G bag contained a total of 50 mL, and the fentaNYL with bupivacaine bag contained a total of 100 mL, so it looked a bit overfilled.

Prior to the event, the pharmacy had been purchasing larger 100-mL bags of epidural fentaNYL with bupivacaine from an outsourcer, which had a bright yellow label. However, due to the recent drug shortage of both bupivacaine and 100-mL bags of 0.9% sodium chloride, the pharmacy had been compounding the epidural solution using bupivacaine vials taken from epidural and patient-controlled analgesia kits. The bupivacaine and fentaNYL were mixed in a 50-mL bag of 0.9% sodium chloride, and then additional diluent was added to reach a total volume of 100 mL. The

pharmacy applied its standard white label to the fentaNYL with bupivacaine bags, like other pharmacy-prepared infusions, along with a red epidural auxiliary warning label. However, L&D nurses had not been informed about the changes in bag size and label colors. So, at the time of the event, they expected epidural infusions to be in 100-mL bags with a yellow label.

The nurse picked up the wrong bag from the counter, not realizing that she had fentaNYL with bupivacaine in hand instead of the intended penicillin G. Although a BCMA system had been fully implemented in other areas, information technology staff were still working with the L&D unit to implement the technology in this last patient care unit. One of the barriers to implementation had been the requirement for pharmacy to verify all medication and solution orders before the system was operational. However, epidural infusions were typically ordered and documented after anesthesia staff started the infusion.

Soon after receiving the wrong medication, the woman began having seizures and experienced respiratory arrest. A responding anesthesiologist noticed the error after reading the label on the infusing IV bag and immediately administered IV naloxone and a bolus of lipid emulsion, with an IV lipid emulsion infusion to follow. The baby was delivered via emergency cesarean section and had a low Apgar score that improved over time. Fortunately, both mother and baby appear to be without long-term adverse effects.

IV Gentamicin Administered Epidurally

An anesthesia practitioner administered 450 mg of IV gentamicin via the epidural route to a woman in labor instead of bupivacaine (0.125%). The pharmacy-prepared gentamicin infusion had been removed from an ADC instead of the intended bupivacaine infusion. Earlier, a pharmacy technician had incorrectly loaded 1 bag of the IV gentamicin in the bin holding the epidural bupivacaine infusions.

¹Institute for Safe Medication Practices, Horsham, PA, USA

Corresponding Author:

Michael R. Cohen, President, Institute for Safe Medication Practices, 200 Lakeside Drive, Suite 200, Horsham, PA 19044, USA.
Email: mcohen@ismp.org

Due to a drug shortage of bupivacaine, the hospital was no longer able to purchase compounded bupivacaine infusions from an outsourcer. Pharmacy staff had just begun mixing bupivacaine infusions in 100-mL bags of 0.9% sodium chloride and were also mixing gentamicin infusions (not available commercially) in 100-mL bags. Similar-looking pharmacy labels had been applied to the front of the bags, and a red "Epidural Use Only" label had been affixed to the front of the bupivacaine bag. Although barcode scanning was used when refilling the ADC, only the first product in a batch loaded into each bin was scanned. In this case, the technician scanned 1 of the correct bupivacaine infusions but did not notice that 1 of the 5 similar-looking bags loaded in that bin contained gentamicin. Several days later, an anesthesia practitioner removed the gentamicin bag from the ADC and did not notice the error. Although nurses in L&D employed a BCMA system routinely prior to administering medications, the technology was not used at all by anesthesia practitioners. Thus, the anesthesia practitioner administered the gentamicin by the epidural route, believing the bag contained bupivacaine.

The patient complained of significant pain during labor and delivered her baby 2 hours later. The mother was stable post delivery, and the baby had high Apgar scores. The error was finally noticed when a nurse discontinued the epidural solution post delivery; however, 69 mL of gentamicin had infused. The anesthesia practitioner administered normal saline via the epidural route for 10 hours to dilute the gentamicin in the epidural space.

Prior Errors

Since 2000, Institute for Safe Medication Practices (ISMP) has described more than a dozen errors that occurred in the United States and the United Kingdom involving the IV administration of epidural bupivacaine in L&D units, including 5 deaths of young mothers.¹⁻⁵ Prior errors involving epidural administration of IV antibiotics have also occurred. Most of the fatalities occurred with IV administration of epidural bupivacaine before IV lipid emulsion therapy was recommended as an antidote by the American Society of Regional Anesthesia and Pain Medicine (ASRA).⁶ Events occurring before (2006) and after (2016) widespread knowledge of lipid emulsion therapy as an antidote are provided as examples.

2006 Event

A 16-year-old woman in labor died after accidental IV administration of fentaNYL with bupivacaine instead of penicillin G.³ The L&D workflow favored collection of all supplies at the start of labor or induction. Therefore, the epidural medication had been brought into the patient's room before it was prescribed so it was ready for anesthesia staff when needed. The bag of penicillin G was also in the room. Both infusions had been prepared in 150-mL bags, and both bags were labeled with the same orange-colored pharmacy

labels. A large pink warning label, "For Epidural Use Only," was on the front of the epidural bag, and a small pink label was on the back. However, the nurse misread the pharmacy label, and the warning labels did not catch her attention. Her perception of risk was not high, as she thought she had penicillin G in hand, not an epidural infusion.

Several weeks before the event, the hospital's L&D unit had implemented a BCMA system. However, most of the L&D patients bypassed the admissions department, where identification (ID) bands were typically applied, and were admitted directly to the unit without an ID band. Therefore, the patient did not have an ID band on when the nurse was administering what she thought was penicillin G. Thus, the BCMA system was not used. Within minutes of infusing the fenta NYL with bupivacaine IV, the patient experienced cardiovascular collapse. Although a healthy infant was delivered by cesarean section, the medical team was unable to resuscitate the mother.

2016 Event

A healthy 21-year-old woman in labor received IV fentaNYL with bupivacaine instead of penicillin G.⁵ Shortly after epidural placement, the patient began experiencing perioral numbness and tinnitus followed by stupor, seizures, hypotension, and tachycardia. It was quickly noticed that the nurse had mistakenly grabbed and administered a 100-mL bag of epidural fentaNYL (2 µg/mL) with bupivacaine (0.25%), thinking it was penicillin G. Naloxone and an IV bolus of lipid emulsion was administered, followed by a lipid emulsion infusion, with patient improvement in just a few minutes. Fetal heart rate never dropped below 130 beats per minute, and the patient delivered a healthy infant with high Apgar scores. It was prompt recognition followed by prompt administration of the IV lipid emulsion that saved this young woman and her infant.

Safe Practice Recommendations

Due to the risk of mix-ups between epidural analgesia and IV antibiotics in L&D settings, consider the following recommendations.

Prescribing.

Initiate and verify orders. If a patient requires IV antibiotics and/or epidural analgesia, require the physician or anesthesia professional to initiate the required orders and have a pharmacist verify the orders before either infusion is brought to the patient's bedside.

Consider less toxic anesthetics. When appropriate, consider the use of other local anesthetics for epidural analgesia that may be less cardiotoxic than bupivacaine (e.g., ropivacaine), in case the epidural analgesia is inadvertently administered IV.⁷

Dispensing

Inform all practitioners about changes. When products or preparation processes change due to drug shortages or other reasons, let frontline practitioners (e.g., nurses, anesthesia staff) know about any differences in the appearance, labeling, container sizes, concentrations, products, or directions for administration of infusions before dispensing the alternative. If time permits, conduct a failure mode and effects analysis (FMEA) before making the change to identify and mitigate risks with the alternative product.

Differentiate epidural bags. If possible, use a different size or shape container, or colored overwraps, for epidural analgesia to differentiate it from IV medications and infusions.

Apply auxiliary warnings. Apply distinctive, *large* warning labels that state, “**For Epidural Use Only,**” in a standard color on *both sides* of an epidural analgesia bag. Apply a warning label over the seal of the access port used to spike an infusion bag.

Dispense with epidural tubing. Have pharmacy dispense epidural analgesia along with the required yellow-striped epidural tubing to promote administration by the correct route. The analgesia bag can be spiked with the tubing only if administration is imminent.

Scan each bag. When stocking an ADC, scan each epidural infusion individually before placing it in the correct storage location (when technology allows).

Preparing patient for epidural analgesia

Define patient “readiness.” Define how nurses should prepare patients for epidural analgesia. Include a timeline and checklist to guide the process (similar to an operating room readiness checklist) with steps to accomplish before calling anesthesia staff.

Administration

Limit access to epidural analgesia. Require the practitioner who will be administering the epidural analgesia to bring the medication to the patient’s bedside immediately before use. This avoids a handoff between nurses and anesthesia staff and limits the potential for confusion with other IV medications and infusions in the patient’s room. If epidural analgesia and IV infusions must be brought into the patient’s room together, establish separate and secure drug storage locations for each phase of the L&D process, thereby separating epidural analgesia and IV antibiotics (and other medications/infusions).

Reduce interruptions. Establish a quiet zone in the patient’s room or anteroom for getting medications and

solutions ready for administration. Advise the patient and family when the nurse needs to move to the quiet zone and the importance of minimizing interruptions. Require the setup of epidural analgesia to be a separate, dedicated process conducted immediately prior to the start of the infusion. Except in urgent/emergent situations, medications should be readied in the quiet zone, not at the bedside.

Fully employ BCMA. Establish an admission process that ensures L&D patients have a barcoded ID band applied shortly after arrival and before nonemergent medications or solutions are administered. Require full use of the BCMA system by all practitioners, including anesthesia staff. Remedy any system or labeling problems that limit full compliance and run compliance reports regularly to ensure widespread use over time.

Conduct a time-out. Conduct a time-out immediately before starting the epidural infusion, which includes reading aloud the drug name and concentration from the container label to verify the epidural infusion.

Trace Lines. Trace lines from their respective sources (and infusion pump) to the patient’s access into the body before making connections or administering medications or solutions.

Mitigate harm

Consider a medication error. If a patient expresses concern about a medication or experiences unexpected symptoms, evaluate the medications and solutions the patient has received and investigate the possibility of a medication error.

Establish toxicity treatment protocol. Establish a protocol to identify and treat local anesthetic toxicity.⁵⁻⁹ Make the protocol and required medications (i.e., lipid emulsion) readily accessible on code carts or with other secured emergency supplies.

Staff awareness and planning

Educate staff. Alert practitioners to the risk of mix-ups between epidural analgesia and IV antibiotics in L&D settings and how to recognize and treat local anesthetic toxicity.

Plan for neuraxial connectors. All medical devices that connect to the neuraxial route will eventually use a unique neuraxial connector. Although epidural infusion bags will still be able to be spiked with IV tubing and thus misconnected despite special epidural connectors, hospitals should plan to transition to these connectors when they become available to prevent other types of neuraxial/IV misconnections. For details and helpful tools to prepare for the new neuraxial connectors, visit www.ismp.org/ext/100.

Filtering EPINEPHrine Withdrawn From Glass Ampoules?

The ISMP *Guidelines for Safe Practice of Adult IV Push Medications* recommend using a filter needle when drawing medications from glass ampoules. While some glass fragments may enter the solution when the ampoule neck is snapped, there is little evidence of patient harm from glass ampoule particles (www.ismp.org/ext/129). Nevertheless, the use of a filter needle was supported by a consensus of summit participants during development of the ISMP Guidelines (www.ismp.org/ext/130) after consideration of its potential impact on safety and its ability to be implemented in most organizations.

At least 1 manufacturer, Belcher, sells EPINEPHrine in a glass ampoule. But are filters needed when EPINEPHrine doses for a severe allergic reaction or anaphylaxis are withdrawn from ampoules and administered subcutaneously or intramuscularly (IM)? We were asked this recently and decided NOT to recommend using a filter needle for subcutaneous or IM EPINEPHrine injections. Our reasoning is that it adds another step in the dose preparation process during an emergency, even if anaphylaxis kits are supplied with a filter needle. Requiring the use of a filter needle will incorporate a multistep process of possibly removing a needle from a syringe, replacing it with a filter needle, preparing the dose, then removing the filter needle, and reattaching a needle for injection. Without a kit, staff may have trouble locating a filter needle (or straw), and most clinics, doctor's offices, and community pharmacies (where vaccines are administered) may not have filter needles on hand, even if they stock EPINEPHrine in glass ampoules.

Keep in mind, most doses of EPINEPHrine for treating anaphylaxis will be given subcutaneously, or preferably IM, with a subcutaneous or IM needle, not IV, where glass particles are more likely to reach the systemic circulation. The risk of harm from injecting glass particles into subcutaneous tissue or muscle is less than the risk of delaying a life-saving dose. Another factor is that small bore 25- or 27-gauge needles are typically used to administer EPINEPHrine, which would likely prevent glass from being drawn into the syringe. A study showed that larger bore, unfiltered needles increase the risk of aspirating glass and other particles than smaller bore, unfiltered or filtered needles (www.ismp.org/ext/131).

We recommend using EPINEPHrine autoinjectors to treat an allergic reaction or anaphylaxis (www.ismp.org/node/245) because it avoids the issue altogether. Another reason that we favor autoinjectors is that we have received occasional reports of EPINEPHrine overdoses in which clinicians have administered, sometimes by the IV route, the full 1 mg amount in an ampoule rather than a 0.15 to 0.5 mg dose. There are now generic autoinjectors available, so the cost has decreased compared with previously.

Perioperative Area Needs Barcode Scanning!

The perioperative area is vulnerable to medication errors because it typically operates with fewer medication safety strategies in place than other patient care units. Medications are often prepared and administered by the same person without an independent double check or pharmacy review of an order, and without the benefit of information technology to provide clinical decision support. In addition, barcode scanning is not widely used in these areas.

We recently heard from an anesthesiologist who accidentally administered lidocaine 2% IV instead of fentanyl. While the container labels on the vials do not look similar, both products are available in small vials with light blue caps (Figure 1). Light blue is used as a standard color for opioids with user-applied labels in anesthesia (Figure 2). However, there is no standard color used for commercially manufactured medication vials. Still, according to the person who reported this event, light blue is a color that many anesthesia providers have come to associate with opioids, including fentanyl. Also, both vials were stocked in the anesthesia medication tray in an upright position so only the caps were showing before removal.

In 2010, the Anesthesia Patient Safety Foundation (APSF) released consensus recommendations to improve the practice and safety of patients in the surgical suite (www.ismp.org/ext/106). These recommendations include a section on the standardization and storage of medications along with the use of technology. Specifically, APSF recommends setting up anesthesia carts or ADCs so that vial labels are readily visible to the user rather than storing the vials in an upright position, which could foster reliance on cap color when selecting a medication. APSF also recommends not storing look-alike vials near one another, a strategy the reporting institution is implementing to reduce the risk of similar errors. However, the strongest recommendation by both APSF and ISMP is to employ barcode scanning systems to identify medications before drug preparation and administration.

Look-Alike, Sound-Alike Caution

Migalastat (GALAFOLD) was approved in August 2018 for the treatment of adult patients with Fabry disease, an inherited disorder due to a dysfunctional enzyme that leads to a buildup of globotriaosylceramide, a fat. This eventually causes pain in the hands and feet, discolored spots on the skin, a reduced ability to sweat, and other disorders, some life-threatening (www.ismp.org/ext/123). Migalastat works by stabilizing the enzyme.

Unfortunately, migalastat looks and sounds very much like miglustat (ZAVESCA), which was approved several years ago for the treatment of adults with mild or moderate type 1 Gaucher disease (www.ismp.org/ext/124). Individuals with Gaucher disease also have a defect in an enzyme that

Figure 1. Although these vials are somewhat different in overall appearance, the light blue cap color contributed to the medication mix-up.

Figure 2. This label color is the standard American Society for Testing and Materials (ASTM) color for opioids.

normally breaks down certain fatty substances that can build up in some organs and cause problems in the liver, spleen, bone, and blood. Both drugs are associated with enzymes and fat disorders.

In addition to name similarity, migalastat and miglustat are both only available in a capsule dosage form; migalastat comes as a 123-mg capsule and miglustat as a 100-mg capsule. Because only 1 strength is available for either medication, the strength may be omitted when ordering the drug in some circumstances. With similarities in names, single strengths, and oral capsule formulations, omitting the

strength increases the risk of an error. It is also possible that the odd 123-mg strength of migalastat may be viewed as a dosing mistake.

To prevent errors, neither medication should be prescribed, dispensed, or refilled without verifying the proper patient diagnosis. If you have both medications in your organization, consider adding an alert during order processing to warn about possible mix-ups or require a hard stop to verify the patient's diagnosis. Also refer to these medications using brand names when possible. Barcode scanning should be employed during product selection and administration, and we recommend storing the medications apart from one another. We are considering tall man letters (e.g., migALastat and migLUstat) to help differentiate these drugs on computer screens and in other presentations. We will inform you if we add this drug name pair to our list of drug names with tall man letters.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Institute for Safe Medication Practices. Epidural-IV route mix-ups: reducing the risk of deadly errors. *ISMP Medication Safety Alert!* 2008;13:1-3.
2. Institute for Safe Medication Practices. Root cause analysis published. *ISMP Medication Safety Alert!* 2010;15:4.
3. Smetzer J, Baker C, Byrne FD, Cohen MR. Shaping systems for better behavioral choices: lessons learned from a fatal medication error. *Jt Comm J Qual Patient Saf.* 2010;36:152-163.
4. Institute for Safe Medication Practices. Another fatal event with IV bupivacaine. *ISMP Medication Safety Alert!* 2010;15:2.
5. Institute for Safe Medication Practices. More on lipid rescue. *ISMP Medication Safety Alert!* 2016;21:4-5.
6. Neal JM, Bernards CM, Butterworth JF, et al. ASRA practice advisory on local anesthetic systemic toxicity. *Reg Anesth Pain Med.* 2010;35:152-161.
7. Guo S, Li B, Gao C, Tian Y. Epidural analgesia with bupivacaine and fentanyl versus ropivacaine and fentanyl for relief in labor: a meta-analysis. *Medicine (Baltimore).* 2015;94:e880.
8. Weinberg G, Ripper R, Feinstein DL, Hoffman W. Lipid emulsion infusion rescues dogs from bupivacaine-induced cardiac toxicity. *Reg Anesth Pain Med.* 2003;28:198-202.
9. Rosenblatt MA, Abel M, Fischer GW, Itzkovich CJ, Eisenkraft JB. Successful use of a 20% lipid emulsion to resuscitate a patient after a presumed bupivacaine-related cardiac arrest. *Anesthesiology.* 2006;105:217-218.