

Medication Handling and Compounding Errors in the Operating Room.

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The Case

A 62-year-old man was undergoing a vitrectomy procedure for repair of a macular hole. Indocyanine Green (ICG) dye and 50% dextrose were retrieved from the medication dispensing machine and compounded by the circulating nurse (who had limited eye surgery training and experience, and was not familiar with the surgeon's documented "preference card"). During preparation, the nurse followed protocol by reading and showing the label of the medication (ICG) and its expiration date to the scrub technician. A label was then created for the compounded medication ("ICG in 50% dextrose") by the scrub technician on the sterile field. When requested by the attending surgeon, the scrub technician verbally confirmed the medication ("ICG in D50") being handed to the surgeon. The surgeon injected the medication to stain the eye. Soon after administration, the macula turned white. The ICG was immediately washed out of the eye and the macula returned to its normal color. The surgery was completed without further events. It was recognized soon after the surgery that the ICG had been prepared using 50% dextrose, rather than the requested 5% dextrose, because the medication dispensing machine did not have any 5% dextrose. The effect of this error on the patient's eye and vision is unknown at the current time.

The Commentary

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[Medication errors](#) are a well-known cause of patient harm and can occur at any time that medications are prescribed, transcribed, prepared, dispensed, administered, or documented in the hospital.¹⁻³ Medication errors not only lead to potential patient harm and longer hospital stays but can be very expensive, with reports of costing the US economy more than \$177 billion per year.² The perioperative area, specifically within operating rooms, provides a unique setting in which providers can prescribe and administer various

medications for immediate administration using a one-step process and may create an environment where errors can occur.⁴ [One study](#) in the perioperative setting reviewed 3,671 medication administrations and found a total of 153 medication errors or roughly one error in every 20 medication administrations.³ Leading contributing factors to medication errors within the operating room include distractions, improper syringe labeling, provider fatigue, look alike medication vials/ampules, and compounding when premade products are not available.^{1,4} Furthermore, the risk for errors is exacerbated in this setting by the limited safety resources available including inconsistent access to another provider for a double check, lack of electronic clinical decision support, and limited pharmacy oversight.^{4,5} This commentary focuses on immediate-use compounding and how the process creates situations in which medication errors can occur.

As demonstrated in the case, the surgical setting requires use of medications that may not be readily available as premade products, resulting in a need to [reconstitute or compound](#).⁴ It should be noted that there is a distinction between compounding and reconstitution of a medication. The FDA states that compounding is the act of combining, mixing, or altering ingredients to create a medication that is specific to an individual patient.⁶ Reconstitution of a medication, however, is following a manufacturer-provided package insert that details the diluent and volume required to reconstitute a powder or dilute to a lower concentration prior to administration.^{6,7} Using the FDA definitions, mixing a powdered cefazolin 1 gram vial with 2.5mL sterile water for injection (SWFI) to create a concentration of 330 mg/mL and administering as an IV push over 3 to 5 minutes, in accordance with cefazolin's package insert, is considered reconstitution.^{7,8} Per the package insert, it would also be considered reconstitution if the powdered cefazolin 1 gram vial was mixed with 2.5mL SWFI and then diluted in 50 or 100mL of a compatible solution (e.g. D5W or normal saline) and infused over 30 or 60 minutes.^{7,8} By contrast, using the same powdered cefazolin 1 gram vial reconstituted with 2.5mL SWFI as stated in the package insert, but then diluting it further into a 1-liter bag of normal saline for irrigation, represents compounding.⁹ Because such an order is not consistent with the instructions in cefazolin's package insert, adding the reconstituted vial of cefazolin to a 1-liter bag for irrigation changes the classification of the preparation from reconstitution to compounding.^{8,9} This type of compounding falls under the definition of immediate-use compounding, whether completed in the operating room or in a patient's room.^{5,9,10}

Immediate-use compounding of medications introduces unique safety and regulatory compliance concerns including erroneous calculations that can lead to an unintended final concentration and inappropriate aseptic technique putting patients at risk for infection.^{4,5,10} In the perioperative setting, registered nurses (e.g., circulating nurses) handle medications as a standard practice. They assist the surgeon with procedural medications by assessing each surgeon's preference card for the planned surgery and preparing the required medications if needed, either through reconstitution or compounding.⁶ The standardized steps include:

1. The circulating nurse reads the label in the presence of the surgeon and announces its expiration date to the scrub technician.
2. The scrub technician creates a label verbatim of what was read by the circulating nurse and repeats it out loud.
3. The circulating nurse dispenses the medication in the labeled container on the sterile field. The scrub technician draws up the medication in a syringe and places the label on the syringe.

4. Upon the surgeon's request for the medication, the scrub technician reads the label aloud once again before handing the surgeon the labeled syringe.

The above outlined process performed by the surgical team ensures that the correct medications are selected and administered to the patient. Due to staffing constraints, it is often challenging to train specialized teams to know the unique needs of each individual surgeon or procedure. Therefore, nurses regularly consult preference cards that serve as a guide to prepare for surgery, and those preference cards include lists of required medications and how they should be prepared.

In this case, the nurse was compounding (not reconstituting) because the recommended diluent in the package insert was sterile water, but the order instead required the use of 5% dextrose to mix with the indocyanine green dye.¹¹ The circulating nurse had limited ophthalmology experience, which may have contributed to the errors that followed. First, the nurse did not consult the surgeon's preference card while retrieving the requested dextrose, but instead trusted that the medication dispensing machine serving the ophthalmology operating room would only be stocked with the correct dosage of dextrose. However, only 50% dextrose was available in the medication dispensing machine, so the nurse mixed indocyanine green dye with 50% dextrose. The nurse correctly read the label in the presence of the surgeon, who may have been distracted, and the scrub technician created the label as it was read. Because the label was correct on the container, the surgical team was able to identify the error quickly once the macula turned white.

This case illustrates how it can be challenging to ensure that the correct diluent is selected for either compounding or reconstitution in the operating room.¹² Medications in the operating room are typically prepared ahead of time or at the time of the procedure. Additional issues with preparing medications in the operating room include the frequent need to remove multiple medications from the manufacturer packaging for delivery to the sterile field, a lack of standardized medication labeling and documentation, and distractions during medication preparation.¹² In the case above, the circulating nurse prepared ICG utilizing D50 instead of D5W. Some potential contributing factors included the presence of multiple medication syringes within the work area, improper communication or lack of understanding on how to prepare the ICG, ready availability of D50 during preparation of ICG, improper labeling of medications that had been removed from manufacturer packaging, and/or distraction while receiving the verbal order or preparing the ICG. In this case, there were two contributing factors to the use of D50 instead of D5W. First, the circulating nurse did not review the surgeon's preference card, which stated that D5W should be used. Second, the nurse presumably assumed that the only diluent available in the medication dispensing machine should be used, an example of confirmation bias (evidence that confirms a belief without seeking other information).

As mentioned previously, the surgical setting allows for immediate local medication administration. This process bypasses the safety check that results from having multiple healthcare providers assess an order before it is administered to a patient.^{4,5} Omitting this step when compounding medications in the operating room may lead to instances in which the safety and effectiveness of one or both components (medication or diluent) of the compounded medication is not verifiable.^{4,5} Upon initial review, the request for ICG to be diluted with D5W may appear to be an odd request to those unfamiliar with ophthalmology procedures. The use of ICG for staining the epiretinal membrane (ERM) in macular hole surgery allows for improved visualization of the ERM during removal, leading to improved visual outcomes.^{11,13} However, there have been concerns raised regarding the toxicity of ICG, and mitigation strategies have been studied to address

this concern.¹³⁻¹⁵ The usage of D5W as a solvent for ICG has been shown to be just as effective and safe as sodium-based fluids for macular hole surgery.¹⁵ The addition of D5W has been shown to reduce the concentration of ICG at the retinal surface, decrease ICG toxicity, shorten the total operating time, and ensure complete removal of the epiretinal membrane, leading to improved visual outcomes.¹³⁻¹⁵

Compounding Safety

Due to the nature of procedural areas, many required medication or dosage forms cannot be purchased commercially, resulting in a continued need for compounding.⁵ The question of who is responsible for compounding has been debated and addressed by several regulatory bodies. The American Nurses Association does not define the scope of practice for nurses on a national level, and instead defers to definitions set by state regulations, resulting in nurses' ability to compound varying from state to state or even year to year.¹⁶ The [Institute for Safe Medication Practices](#) (ISMP) also addressed who can compound in the perioperative area in a recently published set of OR-specific guidelines for improved medication safety, with the recommendation that pharmacy take on the role of compounding medications when commercially available products are not available.⁵

From a regulatory standpoint, compounding is considered to be a "fundamental part of pharmacy practice" and is tightly regulated by each state's Board of Pharmacy and by a national standard known as US Pharmacopeia (USP) Chapter <797>.^{9,10,17} Hospital pharmacy personnel complete extensive training on how to properly compound sterile and nonsterile products and may not start compounding until they have been assessed and signed off for proper aseptic technique. For example, at our institution, when new pharmacy personnel are hired, they are assigned online learning modules that include compounding and mathematical competencies. After successful completion of these modules and associated tests, the new hire is directly assessed for their ability to compound aseptically.⁹

Proper aseptic compounding requires competency in four domains to ensure each product has minimal microbial contamination: quality, environment, personnel activities, and control processes.^{5,9,10} These four common themes are not typically standardized or tracked in the perioperative setting; however, all are required for sterile compounding in a hospital pharmacy and are enforced by each state's board of pharmacy when licensing or reviewing a sterile compounding pharmacy.^{9,10} There will continue to be a push for pharmacy services to absorb compounding activities from the perioperative area due to the rigorous licensing and accreditation requirements that improve safety in the compounding pharmacy setting.⁵

Approach to Improving Safety & Patient Safety Target

As a low-level intervention, an inexperienced specialty circulator nurse should be onboarded and precepted by an experienced nurse. At minimum, there should be a checklist for the circulator nurse that includes a requirement to review the surgeon's preference card first and to be prepared to discuss all medications prior to the start of an operation.¹⁸ The opportune time to ensure that correct medications are available is during the pre-procedure huddle. This huddle is conducted to confirm the availability of all relevant documentation, information, supplies, and equipment prior to the start of the procedure. The anesthesia team, the surgical team, the operating room nurse, and the scrub technician all can ask questions and

voice concerns during this time. During the pre-procedure huddle, the scrub technician states what medications are on their sterile back table. The surgical team at this point should request any additional needed medications. It is critical for patient safety to discuss medications with zero distractions and interruptions. The team should agree that the circulating nurse and scrub technician should call out to the surgeon audibly and purposely when they are reading the drug label. The surgeon should be supportive in active listening and the other team members should be aware to not distract the surgeon during that time.

As a high-level intervention, system changes should be addressed and implemented to improve patient safety. Such changes can include implementing recommended safety features into the surgical area such as barcode scanning, utilizing premade products whenever possible, or taking a broader approach to move compounding from the perioperative space to the inpatient pharmacy.⁵

Systems Change Needed/Quality Improvement Approach

Moving perioperative compounding to the inpatient pharmacy poses its own challenges. A primary limitation is the variation of products preferred by each surgeon.¹⁹ One facility tackled this problem after a concern was raised by The Joint Commission when the compounding of a variety of irrigation solutions was observed in the perioperative setting.¹⁹ This facility performed a detailed analysis of each of its 50 surgeons' preference cards and had multiple in-depth conversations with the surgeons and clinical leaders to narrow the list to three standardized options. The facility also educated every member of the perioperative staff and now requires everyone to complete a competency assessment for available irrigation solutions.¹⁹

At our practice site, the perioperative space sees numerous patients within a single day, requiring approximately 34 different sterile compounds behind the "red line" daily. The task of absorbing compounding of sterile products for the perioperative setting into pharmacy workflows was discussed with surgeons along with clinical leadership and is currently a work in progress. We have reviewed the available preference cards and medication administrations used by each surgical team over a 4-month period. The most commonly used products were chosen, and literature was assessed to find stability data to create a master formulation record for those compounds. Products with validated stability data are currently being built into order entry options in our electronic health record by our Information Technology team in partnership with the Pharmacy Department. Once these builds are completed, education will be provided to all perioperative staff to ensure that these compounded sterile products are ordered before planned operations.

Loop Closure

For this specific case, important patient safety issues were identified. First, the circulating nurse not reading the surgeon's preference card resulted in the incorrect selection of the D50 that was available in the medication dispensing machine. That machine did not include the diluent (D5W) that would be needed for that operation, despite the fact that the operation was presumably scheduled in advance. The nurse's actions were considered compounding based upon the ICG package insert stating the medication should be reconstituted with the manufacturer-provided SWFI. Hospitals must verify whether compounding is included in the nurses' scope of practice as it is not allowed in every state. If this case occurred in a state

that does not allow nurses to compound, education is required for the whole surgical team to address educational gaps regarding nursing scope of practice. Regardless of the state this case occurred in, emphasis must be placed on the need for surgical teams to follow established systems to prevent errors, such as review of surgeon preference cards, preoperative discussion of the medications needed, and standardized physician order entry options. Institutions should consider discussion on perioperative compounding responsibility, with the goal of pharmacy absorbing responsibility for most compounding, with support to ensure a smooth transition.

Take Home Points

- All circulating nurses should receive appropriate onboarding and oversight for each specialty area. At a minimum, there should be a written checklist to guide best practices particularly for medication safety.
- Medication errors can be reduced by following standardized processes and working together as an interdisciplinary team to support those processes.
- Compounding is the mixing of two or more drugs and/or diluents together in the absence of specific manufacturer instructions (i.e., ICG dye and D5W instead of sterile water), while reconstituting is medication preparation in accordance with the product's package insert (i.e., reconstituting cefazolin powder with sterile water for injection).
- Compounded medications should follow USP <797> standards on sterility, handling/storage, and beyond use dating regardless of whether compounding occurs at bedside or within a compounding pharmacy.
- Whether perioperative compounding is absorbed by pharmacy or remains at the bedside, a careful review and consolidation of the physician preference cards is warranted and would benefit from interdisciplinary collaboration to minimize variation in practice and resultant potential errors.

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