

# To Dilute or Not Dilute: Drug Errors and Consequences in the Operating Room

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## The Case

A 78-year-old woman with a history of hypertension, hyperlipidemia, coronary artery disease, and macular degeneration presented for a pars plana vitrectomy (PPV) under monitored anesthesia care (MAC) with an eye block. She had undergone a similar procedure 4 weeks earlier and tolerated it well. In the preoperative holding area, the anesthesia team took the patient's history and performed a brief physical examination. The patient's daughter accompanied her for support and help with translation. Nothing had changed in her physical status since her prior procedure. She was bit slow to reply to questions, but this finding was attributed to the language barrier, as she had no reported history of cognitive impairment. The procedure was discussed with the patient and her daughter, and they agreed to proceed with the same MAC anesthetic that she had received during her prior procedure.

?This was one of many eye cases during a busy day at a large academic medical center. The anesthesia team consisted of an attending anesthesiologist and a resident from another specialty. At this academic center, eye cases under MAC are typically performed with an eye block by the surgeon after the anesthesiologist has administered some short-acting sedation, commonly with remifentanil. For this purpose, the pharmacy typically stocks 2 mL syringes with a prediluted mixture of remifentanil 50 mcg/mL in the "eye rooms." On this day, there was a shortage of premixed remifentanil. The only remifentanil available was a vial of 1 mg in powder form. The resident, who was unfamiliar with the process of drug dilution, assumed that this should be diluted into 2 mL to mimic the premade syringes, and mixed 1 mg of remifentanil powder into a syringe of 2 mL saline at a concentration of 500 mcg/mL.

The patient was brought into the operating room and monitors were applied. After the pre-induction briefing was completed, the patient received 1 mL of the remifentanil solution. Shortly thereafter, she became unresponsive, hypotensive, and apneic. After multiple attempts to stimulate her, an overhead code was called. The attending anesthesiologist verified with the resident that only 1 mL of Remifentanil had been administered, and checked the record to confirm that this dose had been well tolerated by the patient in the

past. Vasoactive drugs were administered to recover the blood pressure and the patient was ventilated with an ambu-bag. A neurological exam confirmed that the pupils were equal and reactive, albeit pinpoint. The possibility of a stroke was discussed, and a computed tomography (CT) scan was ordered “stat.” After approximately 30 minutes of resuscitation, the patient was hemodynamically stabilized, regained her respiratory function, and became increasingly responsive. She was transported to the recovery room in stable condition and examinations by the neurology and cardiology consultation teams were unremarkable.

After the patient recovered, the case was reviewed. The process of dilution of the remifentanil was discovered to have yielded a 10-fold stronger concentration than anyone had realized at the time. Instead of 50 mcg, the patient had received 500 mcg of remifentanil, which explained the hypotension, apnea, and loss of consciousness.

## The Commentary

*By Robin Aldwinckle, MD and Edmund Florendo, MD*

### Background

In the United States, it is estimated that about 100,000 to 400,000 patients die annually due to a preventable medical error.<sup>1</sup> About 10-15 percent of these errors are due to a medication error, and the true incidence is likely even higher as many go unreported.<sup>2</sup> Not only do these medication errors cause morbidity and mortality, but they also contribute to a significant financial burden with \$40 billion each year spent to treat medication-related errors.<sup>2</sup>

In the hospital, medications are typically prescribed by physicians, prepared by pharmacists, and then administered by nurses. By the time the medication has reached the patient, several healthcare personnel have checked that the medication, dosing, and route are all correct.<sup>3,4,5</sup> In addition to human verification, electronic and engineering safety checks exist between these steps to catch errors. However, the operating room (OR) is a unique environment where the anesthesiologist is the only provider involved in the entire process of prescribing, dispensing, formulating, administering, and documenting the medication. This practice is problematic as it bypasses the multi-level safety checks otherwise implemented in the hospital setting.<sup>3,4,5</sup> In addition, rapid changes in the patient’s condition require the anesthesiologist to prepare and administer medications in a very short period. As a result, the OR is vulnerable to medication errors that may cause serious harm to the patient.

According to the Anesthesia Closed Claims Project, about 4% of claims against anesthesia providers are due to medication errors.<sup>6</sup> Most of these errors occurred when the wrong dose (31%) or wrong drug (24%) was administered.<sup>6</sup> In this case, the error occurred when the wrong concentration of drug was prepared, and therefore the wrong dose was given. In the OR there is typically no checking of the dilution of the drug concentration, unless another provider is immediately present. Undiluted remifentanil in the OR’s automated medication dispensing system comes in a 1 mg powdered form, which is mixed in a 20 ml solution to make a concentration of 50 mcg/ml. However, in this case, the 1 mg was diluted into a 2 ml syringe instead and made a 500 mcg/ml concentration. As a result, the patient received ten times the intended dose and experienced overdose complications (hypotension, apnea, loss of consciousness).

Drawing up and diluting medications is a standard but error-prone practice in the OR. Examples of common drugs that are diluted for each surgical case are local anesthetics, sedatives, antibiotics, opioids and vasoactive medications. A concentrated form of the medication, in either powdered or liquid form, is mixed into a solution of normal saline or sterile water to achieve a desired diluted concentration. Different drugs require different concentrations, and a typical anesthetic case requires the use of at least four medications. [7](#) A study that measured the concentration of diluted drugs in the OR revealed that the measured concentration was >10% of the target concentration in 70% of the samples and >30% of the target concentration in 23% of the samples.[8](#) To complicate this process even more, desired common drug concentrations can be expressed in different terms, depending on the drug. For example, concentrations of local anesthetics, such as lidocaine, are commonly expressed in percentages (e.g., 1% lidocaine) and can be mixed with epinephrine that is expressed in ratios (e.g., 1:200,000 epinephrine). Some drugs require serial dilution and may come in different units of weight (e.g., mcg/ml vs mg/ml). Thus, it is important for the person performing the dilution to be familiar with the process as well as the desired drug concentration to avoid making errors. Medication errors are not always reversible and can cause permanent damage or death; therefore, our focus should be on preventing these occurrences.

### **Approach to Improving Safety**

Medication administration in the perioperative environment possesses a unique challenge as it bypasses the safety checks established in other parts of the hospital. Societies such as the Anesthesia Patient Safety Foundation (APSF), Association of Anesthetists, the Society for Intravenous Anesthesia, and the Safe Anesthesia Liaison Group (SALG) and Australian and New Zealand College of Anesthetists (ANZCA) have suggested strategies on how to prevent medication errors. These strategies include pharmacy assistance, use of technological solutions, and standardization.[5](#)[9](#)[10](#) Some of these strategies directly address errors that can be made from diluting medications.

To minimize drug dilution errors, one solution is to supply pre-mixed syringes or vials that already contain the desired concentration of the drug.[1](#)[5](#)[9](#) These premade syringes can be made by the pharmacy or purchased from a third-party supplier. This approach is likely to reduce drug errors as the syringe already has both the desired dose and concentration of the drug. It also saves time in the OR and minimizes the risk of a nosocomial infection from contamination during the dilution procedure. However, premixed medications are sometimes 2-3 times more expensive and may have availability constraints. In the case described, the hospital had premixed 2ml syringes of remifentanyl in the desired concentration of 50 mcg/ml, but this product was not available on the day when the error occurred.

Another solution is to have a convenient way to reference drug dilutions.[1](#) This goal could be accomplished by having an instruction manual in the OR or in the electronic health record, with simple detailed instructions on how to dilute medications (e.g., put X mg of drug to Y ml of normal saline to make X/Y concentration). A pharmacist could also serve as a resource on how to dilute medications or verify the drug concentration.

Many operating rooms are now equipped with barcode medication labeling machines.[1](#)[5](#)[9](#) These machines scan the medication vial and print stickers with the drug name and concentration that can be placed on the syringe. This approach verifies the drug as well as the concentration in the vial. There is also an option on

the machine to specify dilution, in which case it will print the label with the desired concentration. This label can be used as a reference when diluting, although it does not guarantee that the medication is correctly diluted.

Standardization of drug concentrations can also be effective in reducing dilution errors.[1:5:9](#) Having one or two concentrations within the institution and standardizing concentrations in weight/volume vs percentage or ratios can minimize potential confusion.

Human factors of training and culture must also be considered. A [2013 survey](#) of 604 anesthesiology trainees reported a greater incidence of medical errors with negative consequences for patients and medication errors among trainees who had less supervision by faculty. Another study<sup>11</sup> found that both anesthesiology residents and faculty erred frequently on a computational test, with junior residents and faculty with more experience committing errors more frequently. Residents committed serious errors twice as frequently as faculty. These studies suggest that trainees are prone to computational errors, and patient harm may be increased by less supervision of trainees.

Finally, the culture within the institution should be supportive and protective of personnel who report medication errors or near-misses.[1:5:9](#) Staff should be encouraged to report these occurrences and a follow-up should occur in a timely manner to allow for measures that could prevent these errors in the future. Also, patient safety should always be the priority in the OR and should not be jeopardized by the time pressure of OR scheduling.

## Take-Home Points

- The operating room is a unique environment where the anesthesiologist is the only provider involved in the entire process of prescribing, dispensing, formulating, administering, and documenting the medication.
- Having premixed syringes or vials prepared by the pharmacy can reduce dilutional errors.
- Simple instructional manuals or pharmacy assistance can help decrease uncertainties when diluting medications.
- Barcode labeling machines can be used to verify the drug and concentration.
- Trainee supervision and institutional culture should encourage error reporting and prioritizing patient safety.

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## References

1. Wahr JA, Abernathy JH 3rd, Lazarra EH, et al. Medication safety in the operating room: literature and expert-based recommendations. *Br J Anaesth*. 2017;118(1):32-43. [[Free full text](#)]
2. Tariq RA, Vashisht R, Sinha A, Medication Dispensing Errors and Prevention. In: *StatPearls*. Treasure Island; FL: StatPearls Publishing; July 25, 2021. [[Free full text](#)]
3. Kothari D, Gupta S, Sharma C, et al. Medication error in anaesthesia and critical care: a cause for concern. *Indian J Anaesth*. 2010;54(3):187-192. [[Free full text](#)]
4. Glavin RJ. Drug errors: consequences, mechanisms, and avoidance. *Br J Anaesth*. 2010;105(1):76-82. [[Free full text](#)]
5. Eichhorn JH. APSF hosts medication safety conference: consensus group defines challenges and opportunities for improved practice. *APSF Newsletter*. Spring 2010;25(1):1,3-8. [[Free full text](#)]
6. Bowdle TA. Drug administration errors from the ASA Closed Claims Project. *ASA Newsletter*. 2003;67(6):11-13. [[Available at](#)]
7. Smith G, D'Cruz JR, Rondeau B, Goldman J. General anesthesia for surgeons. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing; October 12, 2021. [[Free full text](#)]
8. Welte JF, Desgranges FP, De Queiroz et al.. Medication errors in paediatric anaesthesia: the hidden part of the iceberg. *Br J Anaesth*. 2017;118(5):797-798. [[Free full text](#)]
9. Nimmo AF, Absalom AR, Bagshaw O, et al. Guidelines for the safe practice of total intravenous anaesthesia (TIVA): Joint Guidelines from the Association of Anaesthetists and the Society for Intravenous Anaesthesia. *Anaesthesia*. 2019;74(2):211-224. [[Free full text](#)]
10. Australian and New Zealand College of Anesthesiologists and the Faculty of Pain Medicine. Guideline for the Safe Management and Use of Medications in Anesthesia. Australian and New Zealand College of Anesthesiologists; April 2021. [[Free full text](#)]
11. Black S, Lerman J, Banks SE, et al. Drug calculation errors in anesthesiology residents and faculty: an analysis of contributing factors. *Anesth Analg*. 2019;128(6):1292-1299. [[Free full text](#)]

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