Smart pump custom concentrations without hard “low concentration” alerts—A perfect storm for patient harm

Last month marks the tenth anniversary of our very first newsletter article about a “new and emerging technology” we coined back then as “smart” infusion pumps (“Smart” infusion pumps join CPOE and bar-coding as important ways to prevent medication errors. February 7, 2002. www.ismp.org/Newsletters/acute care/articles/20020207.asp). Since then, smart infusion pump technology has evolved considerably, and its application has spread substantially throughout US hospitals. Based on results from our 2011 ISMP Medication Safety Self-Assessment for Hospitals, about half of the respondents now use smart pump technology throughout the organization to intercept and prevent errors due to misprogramming or the miscalculation of doses or infusion rates. Another quarter of hospitals use smart infusion pumps in some patient care units. Yet, preventable errors associated with the misprogramming of smart infusion pumps still occur, sometimes causing serious harm to patients.

Failing to employ available dose error-reduction software (DERS) as intended and failing to heed important clinical alerts are common contributors to these errors. In particular, the misuse of custom concentration options (i.e., user must enter the concentration) that do not employ a hard (requires reprogramming) minimum concentration limit is a prime example. This issue contributes largely to preventable errors with smart pumps given the counterintuitive, inverse relationship between concentration and volume. More concentrated drugs require less volume to deliver a specified dose; less concentrated drugs require more volume to deliver a specified dose. When using “fill-in-the-blank” custom concentrations, the concentration must be programmed into the pump so it can calculate the volume needed to deliver the prescribed dose. If the programed concentration is input incorrectly, the concentration that is programmed into the pump may result in an incorrect concentration being programmed. This misprogramming in the absence of a hard minimum concentration limit and DERS has resulted in patient harm.

What’s wrong with “ketofol”? In a word, plenty!

The term “ketofol” is becoming common in many hospitals. It’s a term used to describe a combination of ketamine (KETALAR) and propofol (DIPRIVAN). The admixture is used for procedural sedation. The combination of these two drugs has been favored because it is said to preserve sedative efficacy while minimizing each of their respective adverse effects. The combination of drugs is believed to result in less toxicity than administering either drug alone because their complementary effects enable the use of lower doses of each drug. A combination of these two drugs is not available commercially so the drugs are mixed within a single syringe prior to administration.

While studies have shown that “ketofol” appears to be effective and safe for procedural sedation before painful procedures, a few important safety issues linger.

Sterility. For efficiency, “ketofol” admixing often takes place in non-sterile areas such as procedural units and the emergency department. Since propofol has inherent sterility issues, this bears close monitoring to assure the following: the admixture occurs under sterile conditions, single-dose vials are not punctured multiple times, the appropriate expiration date is applied to the syringe, and the medication is properly discarded upon expiration.

Caution: drug names that end with the letter “L.” A nurse transcribed an order for lisinopril 2.5 mg PO daily for a patient who was transitioning from the emergency department (ED) to an inpatient area by copying the prescriber’s orders that were previously on hold. However, the nurse read the dose as 12.5 mg PO daily (Figure 1), seeing the final “L” in lisinopril as the number one (1). Usually, the attending physicians who admit patients from the ED at this hospital ask the nurses for an assessment of the patient’s condition, medications, diagnostic tests, and other clinical features. They then generally order the continuation of the medications, which have been written pending the patient’s admission. In reality, nurses rarely read back all of these medication orders, which is probably why the mistake was not recognized. The patient received several incorrect doses and eventually developed hypotension, which required special monitoring. Drug names that end with the letter “L” have occasionally been the subject of overdoses reported to ISMP. ISMP’s List of Error-Prone Abbreviations, Symbols, and Dose Designations (www.ismp.org/Tools/errorproneabbreviation.spdf) mentions this problem, and we also wrote an article in our June 2010 newsletter (www.ismp.org/Newsletters/nursing/Issues/ NurseAdviseERR201006.pdf) on misidentification of alphanumeric symbols in handwritten and computer-generated information. Please advise prescribers to leave sufficient space between the numeric dose and the drug name, and to ensure that the last letter of the drug name is not separated from the rest of the drug name with a space (as seen in Figure 1). This also applies to electronic prescribing and standard order sets since errors can occur if sufficient space is not provided between the drug name and strength (e.g., lisinopril2.5 mg).
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grammed concentration is lower than the actual concentration in the infusion bag or syringe, the pump will deliver an overdose. If the programmed concentration is higher than the actual concentration in the bag or syringe, the pump will deliver an underdose. Without a hard minimum concentration limit, the former scenario has led to life-threatening events, such as those described below.

A physician prescribed IV HYDROMORPHINE 20 mg/100 mL (0.2 mg/mL) to infuse at 2.5 mg/hour. In this hospital, the standard concentration for this infusion was 0.1 mg/mL, so the custom concentration of 0.2 mg/mL had to be entered into the smart pump. The nurse selected the custom concentration option, and then mistakenly entered 2.5 mg/100 mL as the concentration instead of 20 mg/100 mL. Given the erroneously programmed concentration of 0.025 mg/mL, the pump issued a soft (can be overridden) low concentration alert. The nurse overrode the warning, mistakenly believing the warning was inconsequential. Based on the erroneous concentration, the smart pump infused the drug at a rate of 100 mL/hour, while the intended rate was 12.5 mL/hour. The pump delivered the entire bag of HYDROMORPHINE 20 mg to the patient in 1 hour. The outcome of the patient was not reported.

An infusion of IV furosemide 10 mg/hour was prescribed. When programming the smart pump, a nurse selected the custom concentration option and then accidentally entered the concentration as 10 mg/100 mL (0.1 mg/mL) instead of 100 mg/100 mL (1 mg/mL). The pump had a soft low concentration limit set at 0.2 mg/mL, so a soft alert was issued. The nurse bypassed the alert, and the entire bag containing 100 mg of furosemide infused in 1 hour instead of 10 hours. Fortunately, the patient was not harmed.

MILRINONE IV was prescribed to infuse at 2.5 mg/hour. The pharmacy dispensed a 20 mg/100 mL (0.2 mg/mL) MILRINONE infusion bag. Using the custom concentration option, a nurse set the concentration as 0.2 mg/100 mL. The entire bag containing 20 mg infused in a matter of minutes instead of infusing over 8 hours. The patient required a bolus of IV fluids to treat hypotension, but no changes in the patient’s heart rhythm were reported.

If a soft low concentration alert is provided, the significance of the alert may not be fully appreciated. Since the primary emphasis on averting IV errors is often on doses that exceed maximum limits, it appears that “low concentration” soft alerts may be misinterpreted as being similar to “low dose” alerts. Pharmacists responsible for building and maintaining smart pump libraries also may not fully appreciate the significance of “low concentration” alerts and the importance of making them hard alerts, particularly for high-alert drugs.

Other serious smart pump-related errors have occurred when practitioners have unnecessarily selected a custom concentration option—and then entered the wrong concentration—even though a standard concentration option for the drug was available in the pump library. In these cases, programming errors would have resulted in a hard clinical alert (requiring reprogramming) had the standard concentration pathways been employed rather than the custom concentration pathways. Examples of this type of error follow.

A physician prescribed IV heparin to infuse at 800 units/hour. The pharmacy dispensed the heparin in a 250 mL bag (25,000 units/250 mL). This option was available in the smart pump library, but the nurse selected the custom concentration option and erroneously entered the heparin concentration as 800 units/250 mL. Given the erroneously programmed concentration of 3.2 units/mL, the smart pump infused the drug at a rate.

To reduce the risk of harmful errors associated with nonstandard and custom concentrations that are infused via smart infusion pumps:

- **Educate staff**. Educate staff regarding the inverse relationship between concentration and volume and the significance of low concentration alerts.
- **Consider the infusion rate**. For all infusions, assess the final infusion rate to be sure it falls within an expected range. Entering an erroneous, low concentration can result in a high, atypical infusion rate, which should serve as a signal to re-verify the pump settings.
- **Match MAR and label to pump settings**. The medication administration record (MAR) and the infusion label should present the drug and concentration (and infusion rate, if provided) in the same manner required when programming the pump, with specific instructions for custom concentrations. Detailled information for pharmacy technicians who prepare an infusion should not be on the final product label.
- **Verify pump programming**. For infusions with key high-alert medications (e.g., patient controlled analgesia, insulin), require an independent double-check of the product label, MAR, and pump settings. Employ barcode scanning technology to verify patients and infusions, as well as interoperable electronic medical records or other technology that can automatically populate required pump fields (as this functionality becomes available).
- **Standardize concentrations**. When possible, use a single, standard concentration for each drug infusion. If more than one concentration is necessary, limit the number of standard concentrations to two, and avoid concentrations that differ by a factor of 10 (e.g., 0.1 mg/mL and 1 mg/mL, 1 mg/mL and 10 mg/mL) which could be confused. Use of custom concentrations should be curtailed and, when possible, restrict continued on page 3—Check it out!
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of 250 mL/hour, not the intended rate of 8 mL/hour. The pump delivered the entire 25,000 units of heparin to the patient in 1 hour. The patient required treatment with IV protamine but did not experience significant bleeding.

A physician prescribed morphine patient-controlled analgesia with a demand dose of 1.5 mg, a lockout of 10 minutes, and a basal rate of 1.5 mg/hour. The pharmacy dispensed a 60 mL syringe containing morphine 55 mg/55 mL. Instead of using the standard concentration (1 mg/mL) option in the library, the nurse entered a custom concentration of 1.5 mg/55 mL, which resulted in a concentration of 0.027 mg/mL. Given the basal rate of 1.5 mg/hour, the patient received the entire 55 mg of morphine within an hour and was transferred to an intensive care unit for treatment. No outcome was reported.

Some of the above-cited errors appear to be mental mix-ups in which the “per mL” concentration was paired with the total infusion volume—for example, a 1 mg/mL concentration of morphine in a 25 mg/25 mL syringe ends up as a 1 mg/25 mL concentration. Sometimes, the way the concentration is expressed on labels—particularly if the label includes technician instructions for admixture—has also contributed to mistaken concentrations.

Residual custom concentrations that inadvertently remain in the drug library after a limited number of standard concentrations have been added are another factor associated with these errors. This problem has been reported with pediatric drug infusions for which standard concentrations have more recently been established. Custom concentrations may be required for some medications that are dosed according to body weight or surface area. But leaving the option open to enter the concentration that has since been standardized needlessly increases the risk of patient harm.

There are several lessons to be learned from the events described above to maximize safety when using smart infusion pumps. You can assess your hospital’s vulnerability to programming errors related to the use of multiple standard concentrations and custom concentration options by evaluating the level of implementation of the recommendations listed in the “Check it out” column to the right (which starts on page 2).

New Resource

Tubing Misconnections Self Assessment for Healthcare Facilities

Catheter and tubing misconnections are a serious problem in healthcare. While new international standards are being developed to address this issue, ISMP has been collaborating with Baxter Healthcare’s Clinical Center of Excellence on the development of a self assessment for healthcare facilities. Hospitals completing the assessment will be able to better identify products and practices that pose a risk of inadvertent tubing misconnections, with the goal of mitigating potentially known risks. The tool guides users through a modified risk assessment that evaluates current delivery systems and mating devices, rates ease of connection and potential for patient harm, and assigns a risk priority score. A brief tutorial can be accessed from ISMP’s website (www.ismp.org/selfassessments/tubingMisconnections), and the full assessment and tutorial can be accessed from Baxter’s Clinical Center of Excellence website (www.baxter.com/healthcare_professionals/clinical_center_of_excellence/connections_portfolio/programs/tubing_misconnection_index.html). We believe this is a major first step toward helping hospitals mitigate the risk of tubing misconnections.

**Check it out! cont’d from page 2**

- **Eliminate unnecessary options.** Remove custom concentration options from the pump library when a standard concentration for that drug has been established and entered into the library.

- **Set hard minimum concentration limits.** For each drug that allows a custom concentration option in the smart pump drug library, set a hard minimum concentration limit that requires reprogramming to avoid a catastrophic overdose. This is especially important for infusions with high-alert medications.

- **Distinguish custom concentrations.** Should a custom concentration be unavoidable, ask pharmacy to make the container label distinctive and to affix auxiliary labels as appropriate.

- **Require doses to be expressed in the drug’s metric weight.** Protocols and prescribers’ orders for infusions should include a metric weight per time period (mg/hour, mcg/kg/hour, etc.). Orders with just the infusion rate (eg., mL/hour) should not be accepted, even if only one standard concentration of the drug is being used hospital-wide. As appropriate, handwritten orders for infusions should not be prescriptive regarding the concentration—only the patient’s dose (mg/hour, mcg/kg/min, etc.) should be specified to avoid the risk of variable concentrations. Standardized order sets and electronic prescribing systems should allow the prescriber to select only the standard concentration(s) when applicable.

- **Analyze data.** Routinely evaluate quality reports that are available with smart pumps to identify soft alert overrides and other vulnerabilities to errors, and take action to reduce identified risks. Be sure to identify any issues associated with why nurses would use a custom concentration option to program an infusion dispensed in a standard concentration, which is also available in the drug library.
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Nomenclature. Another problem with this combination is its name. “Ketofol” is a contrived name, so you will not find the admixture listed in any official compendia or most commonly employed drug references. This may present problems for people unfamiliar with the contrived name. There is also a potential for drug mix-ups if “ketofol” is misread or misinterpreted as Ketalar alone.

Compatibility. There is very little information available regarding the compatibility of these drugs with other drugs and solutions. Drug information resources list Y-site compatibility for ketamine and propofol for up to 1 hour.1 However, two recent studies show that this combination is stable as an admixture for at least 3 hours in two different concentrations (1:1 and 3:7).2,3

Standardization. The concentrations and volumes of the two products used to mix “ketofol” are not standardized. Different ratios (percent of each drug in the syringe) have been used. Therefore, ordering “ketofol” or labeling a syringe as “ketofol” at one institution (or on one unit) may mean a 1:1 ratio of ketamine to propofol, while at another institution (another unit), “ketofol” may indicate a 1:4 ratio. A further problem with differing ratios is that the stability of any ratio other than 1:1 and 3:7 is not known.

Visual similarity. A syringe containing “ketofol” looks very similar to a syringe containing propofol. So, with “ketofol,” there is now a syringe containing “the other white stuff”—as an ISMP staff member overheard another practitioner say when referring to “ketofol.” We have received enough reports of mix-ups between other white substances—IV lipids, propofol, Rotaglide (a fat-based lubricant used during procedures)—to know that “ketofol” will likely add to the problem.

If you use a combination of ketamine and propofol for sedation, consider conducting a failure mode and effects analysis to identify risks, including those discussed above. Work with your pharmacy department to take steps to promote sterility during admixture, and establish a standard ratio to guide the mixing process. Although it will no doubt be an uphill battle, we recommend not using the term “ketofol.” Many hospitals appropriately require that each drug’s official name be designated—such should be the case for a combined ketamine and propofol product. The syringe label should also include both product names and their doses.

References:

https://secure.muhealth.org/~ed/students/articles/AnnEM_49_p0023.pdf

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