May 21, 2020 ▪ Volume 25 Issue 10

ISMP An ECRI Affiliate

Acute Care ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Subtherapeutic heparin infusions: Is your organization at risk of bypassing soft low-dose alerts?

Problem: We recently received a report from a large health system about a trend related to misprogramming continuous intravenous (IV) heparin infusions administered via smart infusion pumps. The misprogramming resulted in significant subtherapeutic doses of heparin for multiple patients, increasing their risk of serious thromboembolic complications. In this health system, more than 90% of all continuous IV heparin infusion doses are weight-based, using standardized, indication-based heparin protocols to determine the patient's initial bolus dose and infusion rate, as well as any required dose changes based on regular blood coagulation measurements (e.g., aPTT, anti-Factor Xa). A typical heparin starting dose might include a bolus dose of 60 to 80 units per kg followed by an infusion rate of 12 to 18 units per kg per hour, depending on the indication.

Interoperability not implemented in the ED and surgical/procedural areas

About a year ago, this health system had implemented interoperability between its electronic health record (EHR) (Epic) and smart infusion pumps (BD Alaris). However, the misprogrammed heparin infusion events had occurred in the two patient care areas where interoperability had not been initiated—the emergency department (ED) and surgical/procedural areas. Interoperability had not been implemented in surgical/procedural areas due to technical incompatibilities between the EHR order workflow and the pump interoperability platform. The necessary workflow for practitioners to use barcode scanning to associate the smart pump with a medication infusion order, and then to send the order parameters to the pump, had not been developed. In the ED, interoperability had not been established initially due to limitations in the EHR, which have since been corrected. More recently, the primary barrier to interoperability in the ED is an inadequate supply of smart infusion pumps and channels for administration of all IV plain solutions and non-critical medications via a smart pump.

Smart infusion pump-EHR interoperability enables the infusion parameters ordered by the prescriber, which have been reviewed by a pharmacist, to pre-populate the smart

continued on page 2 — Soft low-dose alerts >

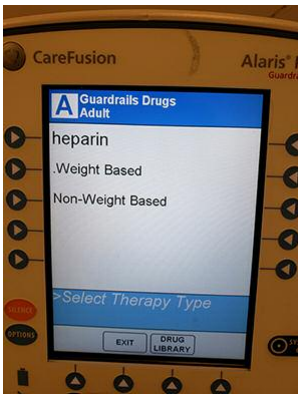

Figure 1. When programming a heparin infusion, users must select whether the dose is "weight based" or "non-weight based."

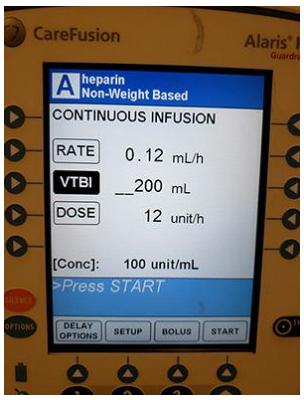

Figure 2. Selecting "non-weight based" heparin in error has resulted in delivery of heparin as units per hour instead of units per kg per hour.

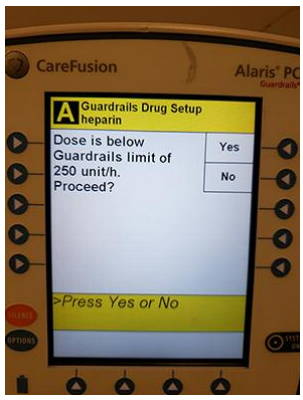

Figure 3. A soft low-dose alert may be issued if heparin is programmed as units per hour instead of units per kg per hour; however, the soft alert can easily be overridden.

SAFETY briefs

Confusion with Venclexta unit dose package label continues. In our November 7, 2019 newsletter, we described several dispensing errors with **VENCLEXTA** (venetoclax) related to confusion with the packaging and labeling of the unit dose product. We recently received another report of a dispensing error. For a patient who was supposed to receive Venclexta 20 mg, pharmacy dispensed 40 mg (two 20 mg unit dose packages) because the product's 20 mg unit dose package was mistakenly believed to hold just 10 mg. The hospital noted that this error has happened on several occasions.

Figure 1. Venclexta 20 mg unit dose package is labeled as 10 mg (top). Each tablet is 10 mg (bottom).

Confusion exists because each Venclexta unit dose package actually contains two 10 mg tablets, but the label lists the strength as 10 mg (**Figure 1**). Venclexta is an oral B-cell lymphoma 2 (BCL-2) inhibitor indicated for the treatment of adult patients

continued on page 2 — SAFETY briefs >

> Soft low-dose alerts — continued from page 1

infusion pump screen, thereby reducing the risk of manual programming errors.[1] The pump settings must then be confirmed by a nurse or other user prior to starting the infusion. Interoperability also facilitates the automatic documentation of infusion data in the EHR. According to analysis of infusion pump errors submitted to the ECRI Patient Safety Organization (PSO), up to three-quarters of the pump programming errors associated with primary infusions could have been averted with successful pump interoperability, as long as the associated pump warnings were heeded.[2]

Misprogrammed heparin infusions

A pharmacist from one hospital in the health system had received a report of an error with a heparin infusion that had occurred in the ED, where nurses needed to manually program smart infusion pumps. During the event investigation, it was found that once "heparin" was selected within the drug library, the nurse was presented with a screen for selecting whether the heparin infusion would be "weight based" or "non-weight based" (**Figure 1**, page 1). The misprogramming error began at this initial step, with selecting a "non-weight based" heparin infusion instead of a "weight based" heparin infusion. This resulted in a significant subtherapeutic dose: the pump was programmed to deliver only 12 units per hour (**Figure 2**, page 1) for an 80 kg patient who was supposed to receive heparin 12 units per kg per hour (960 units per hour). Because the dose error-reduction system (DERS) was engaged, the smart infusion pump issued a soft low-dose alert (**Figure 3**, page 1), which was overridden by the nurse. Unlike maximum dose alerts and low concentration alerts, low-dose alerts cannot be configured as hard stops within the BD Alaris (CareFusion) pumps. Thus, the heparin infused at a low rate of 12 units per hour (0.12 mL per hour).

Trend identified

The pharmacist investigating this error remembered a similar programming error with heparin that had happened recently. She asked rotating student pharmacists to help conduct a small study to identify similar errors that may be happening systemwide. The students ran a basic systemwide smart infusion pump data report to identify all adult heparin infusions that were initially infused at a rate less than 1 mL per hour (100 units per hour), since these low-rate infusions all represented errors. The data report identified more than 70 low-rate infusions within a 2-month period. Further analysis showed that users had initially selected "non-weight based" heparin in error and entered a low dose per hour. They then overrode the soft warning about the low dose. Within a minute, however, two-thirds of the users realized their error and reprogrammed the pump to correctly deliver the prescribed heparin dose.

The pharmacist and students then reviewed all cases in which the subtherapeutic heparin dose (less than 1 mL [100 units] per hour) continued for at least 20 minutes. In a 2-month period, they identified 25 cases in 3 hospitals in which the heparin infusion ran for at least 20 minutes as units per hour instead of units per kg per hour. The longest subtherapeutic heparin infusion continued for more than 28 hours. Because the pump data were not linked to specific patients, the pharmacist and students were unable to determine if the patients who received these subtherapeutic doses were harmed. However, heparin is a high-alert medication, and both under- and overdoses can lead to significant patient harm.

Safe Practice Recommendations: To reduce the risk of heparin infusion errors related to the misprogramming of a smart infusion pump, consider the following recommendations:

Review smart pump data. If you permit both weight-based and non-weight-based dosing of heparin infusions within the same drug library, analyze your smart infusion pump data to determine if similar programming errors have occurred in your facility. Organizations that employ smart infusion pumps should provide dedicated time and

continued on page 3 — Soft low-dose alerts >

> SAFETY briefs

cont'd from page 1

with chronic lymphocytic leukemia (CLL), small cell lymphocytic lymphoma (SLL), or acute myeloid leukemia (AML).

The manufacturer, AbbVie, told us that it recently made changes to the label to indicate the package holds 10 mg "per tablet." They are also working with the US Food and Drug Administration (FDA) and Health Canada on further updates to clarify that the package contains a total of 20 mg. Hopefully, these additional changes will be seen this year. Meanwhile, we advise dispensing the 20 mg unit dose package with a clarifying auxiliary label noting that each packet contains 20 mg (2 x 10 mg tablets).

Also, in previous reports, practitioners noted that, when scanning the manufacturer's barcode, nurses were prompted to scan a second package, as the first scan indicated only a partial dose. If testing of the manufacturer's barcode shows that the package only contains 10 mg, consider affixing a new barcode that would indicate each package contains 20 mg, or at least warn nurses that the manufacturer's barcode will identify just 10 mg.

HIGH-ALERT

Barcode scan workaround leads to error. A mix-up was reported between heparin 25,000 units in 250 mL and ropivacaine 400 mg in 200 mL. The patient had an order for a heparin infusion, 25,000 units in 250 mL, which was stocked in the unit's automated dispensing cabinet (ADC). However, a ropivacaine bag had been misplaced in the same bin as heparin, and the nurse retrieved the ropivacaine bag in error. Prior to administration, the nurse scanned the empty heparin bag that was still hanging on the pole instead of the replacement bag, which contained ropivacaine. Had she scanned the replacement bag she intended to administer, the scanning system would have identified that a medication error was about to take place. Ropivacaine is associated with acute central nervous system and cardiovascular toxicity, which could occur after inadvertent intravascular injection or a dosing error (www.ismp.org/ext/474).

Workarounds like the one described above bypass the immense value of barcode scanning for preventing medication errors. More than 10 years ago, Koppel et al. developed

continued on page 3 — SAFETY briefs >

> Soft low-dose alerts — continued from page 2

resources for regular review and analysis of pump data (at least quarterly) to assess how medications (e.g., heparin) and solutions are being administered, and to improve overall medication safety.[1,3]

Heparin weight-based dosing. Standardize to only weight-based dosing for heparin infusions. Eliminating non-weight-based dosing of heparin will reduce the risk of inadvertently administering infusions as *units per hour* instead of *units per kg per hour*. If there are specific indications for which standard weight-based heparin dosing is not feasible, limit the non-weight-based heparin infusion programming choice to the appropriate care area/profile where it is needed.

Configure heparin low-dose hard stops (when possible)**.** Establish a hard stop for low-dose alerts with heparin if your smart infusion pump allows such configuration. The health system that noted a trend with subtherapeutic heparin infusion dosing has shared its smart infusion pump study data with BD Alaris and asked the company to allow a hard stop for minimum doses of certain high-alert medications, including heparin. ISMP has also been in contact with BD to request this capability. In the meantime, educate nurses about the potential significance of low-dose alerts and to consider the consequences of subtherapeutic heparin doses. Low-dose alerts may signal a programming error and should trigger a full review (and independent double check—see below) of the pump programming before proceeding. At least quarterly, all overridden smart pump alerts (high- and low-dose limits) should be reviewed for appropriateness.[1]

Implement interoperability. Implement bi-directional (i.e., auto-programming and auto-documentation) smart infusion pump interoperability with the EHR. See the ***ISMP Guidelines for Optimizing Safe Implementation and Use of Smart Infusion Pumps***[1] for comprehensive recommendations associated with adopting interoperability. Also ensure that an adequate supply of smart infusion pumps (and channels) is available for use in all clinical areas, including in the ED and surgical/procedural areas. Organizations that have implemented interoperability in the ED have excluded "out of scope" medications/infusions that are emergent in nature, such as those used during code blues, rapid responses, or trauma care, and timely thrombolytics for stroke patients. After managing these emergencies, the infusion is then linked to the EHR. Use of interoperability in the surgical and procedural areas is supported by some EHRs and pump interoperability platforms but may not be feasible in your facility at this time depending on restrictions with existing workflow, space, and technology platforms. However, please see our March 12, 2020, newsletter[3] regarding implementation of smart infusion pumps with an engaged drug library in the operating room as a first step towards interoperability in the surgical setting.

Independent double check for user-programmed heparin infusions. If user-programming of infusion pumps is necessary, consider requiring an independent double check of all programming parameters (as well as verification of the patient, patient's weight, drug [concentration and dose rate], line attachment, and lab values upon which dosing is based) before administering heparin infusions. For hospitals that may not have a second nurse readily available to perform an independent double check, a pharmacist could be called instead to confirm all calculations and dosing, and to verbally review all concentration, dose, and rate settings, as they appear on the pump screen, with the nurse.

References

1) ISMP. Guidelines for optimizing safe implementation and use of smart infusion pumps. 2020. www.ismp.org/ext/485
2) ECRI. Guidance article. Infusion pump integration. *Health Devices.* 2013;42(7):210–21.
3) ISMP. Do you know what doses are being programmed in the OR? Make it an expectation to use smart infusion pumps with DERS. *ISMP Medication Safety Alert!* 2020;25(5):1-5. www.ismp.org/node/14833

> SAFETY briefs

cont'd from page 2

a typology of clinician workarounds when using barcode medication administration (BCMA) systems (www.ismp.org/ext/354). The authors shadowed nurses at several hospitals, interviewed staff, and attended meetings where the barcode system was discussed. Although the specific workaround above was not listed, more than 15 other types of barcode scanning workarounds were identified during all phases of the medication use process, not just during drug administration. The point is, safety leaders need to be aware of workarounds that represent at-risk behaviors that can adversely affect medication safety. We are not aware of any system issues (e.g., hard-to-scan barcode) that might have led the nurse to scan the old rather than the new bag. However, we urge organizations to create a safe environment for discussions about BCMA workflow and possible issues with barcoding so the underlying system issues or practice patterns can be remedied.

HIGH-ALERT

Lidocaine cardiac dose given instead of analgesic dose. A trauma patient awaiting an inpatient bed was being held in the emergency department (ED) when the trauma team ordered intravenous (IV) lidocaine for pain. In the ED, the multimodal order set for pain management called for lidocaine 800 mg in 200 mL of IV fluid (4 mg per mL) to be administered over 4 hours at a dose of 200 mg (50 mL) per hour. However, instead of the pain dose for lidocaine, the prescriber accidentally ordered a 2 g lidocaine bag, which is used to treat cardiac arrhythmias.

The patient's nurse, who was expecting a bag of lidocaine to treat pain, called the pharmacy to verify the order and request the medication. The pharmacist verified the cardiac lidocaine order and sent a bag of lidocaine 2 g in 500 mL of 5% dextrose (lidocaine 4 mg per mL). The nurse administered this lidocaine based on the multimodal pain order set (200 mg or 50 mL per hour) for 3 hours until a pharmacist who was present in the ED recognized the lidocaine 2 g bag, realized the error, and intervened.

Because the lidocaine concentration was the same for both indications, and the administration rate was set correctly at

continued on page 4 — SAFETY briefs >

Nymalize formulation and packaging change

A recent change to the formulation and new unit dose packaging for **NYMALIZE** (ni**MOD**ipine) oral solution might present new challenges when treating patients with ENFit feeding tubes or pediatric patients. The drug, used to reduce the incidence and severity of ischemic deficits in adult patients with subarachnoid hemorrhage (SAH), is only administered orally or enterally. The drug is also used off-label in children for the prevention of cerebral vasospasm after intracranial aneurysm rupture or after cerebral trauma (www.ismp.org/ext/489). Nymalize is the only commercially available ni**MOD**ipine oral solution.

Errors with niMODipine gel capsules

ISMP has been a proponent of the oral solution since it was first marketed. Prior to Nymalize, only liquid-filled gel capsules of ni**MOD**ipine were available. Errors sometimes occurred when the drug was withdrawn from the liquid-filled gel capsules with a parenteral syringe and needle to facilitate administration of the liquid orally or through a feeding tube. Unfortunately, the drug withdrawn from the gel capsules was sometimes accidentally administered intravenously (IV). Intravenous injection can cause profound hypotension, sometimes leading to fatalities (www.ismp.org/ext/488).

Change in packaging and concentration

Recently, the manufacturer, Arbor Pharmaceuticals, announced several changes for Nymalize. First, the company has changed the concentration from 3 mg per mL to 6 mg per mL to require less volume per dose. Second, the product will now only be available in prefilled oral syringes of 30 mg per 5 mL or 60 mg per 10 mL (**Figure 1**). The product will no longer be marketed in 10 mL or 20 mL unit dose cups or a 473 mL (pint) bottle.

Concerns with new packaging

One concern with the new packaging is how the drug will be administered to patients with feeding tubes who may not be able to swallow. Not all feeding tubes will easily accommodate an oral syringe. Also, some hospitals have converted to ENFit tubing, which is not compatible with oral syringes. Only ENFit syringes will connect to ENFit tubing, but the product is not available in an ENFit syringe. Also, the Global Enteral Device Supplier Association (GEDSA) has announced that member manufacturers will begin phasing out the manufacturing of legacy feeding tubes, administration sets, and transition adapters over the next year. It appears that ni**MOD**ipine oral syringes may need to be repackaged for compatibility with ENFit.

Pediatric use of the oral syringe in the current syringe sizes is also of concern. For children, the drug requires weight-based dosing at 1 mg per kg every 4 hours (www.ismp.org/ext/489). Given the 30 mg or 60 mg oral syringe sizes and lack of the previously available 473 mL (pint) bottles, only portions of the oral syringe will be needed to prepare and administer a dose. For example, a 10 kg child might need 10 mg for each dose, or 1.67 mL of the 6 mg per mL solution. Given the risk of severe adverse effects from dosing errors, storage of syringes in automated dispensing cabinets (ADCs) and preparation on nursing units is strongly discouraged. Instead, patient-specific doses for children should be prepared in the pharmacy by withdrawing the dose from the newly available oral syringes.

ISMP has discussed the situation with Arbor and the US Food and Drug Administration (FDA). Arbor cannot comment on pediatric use of the drug since it is not FDA-approved for such use. However, the company is considering ISMP's concern, with an aim to establish a resolution to the ENFit incompatibility issue. We will provide additional information as it becomes available.

Figure 1. Nymalize will only be available in oral syringes of 60 mg per 10 mL (left) and 30 mg per 5 mL (right).

> SAFETY briefs cont'd from page 3

200 mg per hour, the patient did not receive an overdose. However, had the nurse programmed the infusion pump to deliver the full volume to be infused (500 mL), the patient would have received a 2 g dose, not the prescribed 800 mg dose.

As a result of the error and to reduce confusion when selecting these drugs from computer screens, the hospital has now added "**for CARDIAC use only**" to the description for lidocaine 2 g per 500 mL. Because the use of lidocaine for pain is growing, organizations should ensure they have applicable order sets and appropriate settings in the smart pump library.

Special Announcement

ISMP survey on Best Practices open

Due to the COVID-19 pandemic, our survey on the level of implementation of the two new **2020-2021 Targeted Medication Safety Best Practices** (TMSBPs) **for Hospitals** was put on hold. As crisis mode begins to diminish, we would appreciate your participation in this survey regardless of whether you have implemented the Best Practices. You can view all the TMSBPs by going to: www.ismp.org/node/160. The survey is available at: www.ismp.org/ext/350 and will be open through **July 17, 2020**. Since we are only conducting the survey on the two new Best Practices, it should only take you about 5 minutes.

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

ISMP An ECRI Affiliate

ISMP Medication *Safety Alert!* Acute Care (ISSN 1550-6312)

Report medication and vaccine errors to ISMP: Please call 1-800-FAILSAF(E), or visit our website at: www.ismp.org/MERP or www.ismp.org/VERP. ISMP guarantees the confidentiality of information received and respects the reporters' wishes regarding the level of detail included in publications.