Small Effort, Big Payoff: Automated Maximum Dose Alerts With Hard Stops

Matthew Grissinger, RPh, FASCP

Automated alerts can provide an effective means of communicating essential information about a drug and patient to clinicians who prescribe, dispense, and administer medications. These alerts are intended to support clinical decisions about the safety and efficacy of the drug therapy. Alerts are typically communicated through warning messages that pop up on a screen. These alerts can cause either a soft stop or a hard stop.

A soft stop provides information to the clinician about a potential drug safety or efficacy problem and may offer alternative suggestions for the clinician to consider. However, minimal or no action or acknowledgment of the alert is required on the part of the user to proceed. A hard stop halts the progress of prescribing, dispensing, or administering a medication that would likely be dangerous to a patient. Further execution of the order is blocked. A nearly hard stop may allow continuation of the process if significant action is taken by the user, such as requiring a prescriber to call the pharmacy to discuss the order.

Studies have shown that soft stops are often overlooked or quickly overridden without careful consideration of the warning for a variety of reasons, including alert fatigue and poor design of the warning.1-4 Hard stops and nearly hard stops have been shown to be much more effective in capturing the user’s attention and getting the user to change the prescription, re-enter the drug, or reprogram a device.5-7

As we describe errors with amphotericin B, methotrexate, and fentanyl, keep in mind that a well-designed alert with a hard stop could have prevented these harmful errors.

Amphotericin B

In one reported event, amphotericin B conventional was prescribed in a dose reserved for the lipid-based product. A patient with acute myeloblastic leukemia and a recent bone-marrow transplant developed pulmonary aspergillosis. Using a computerized prescriber order-entry (CPOE) system, the patient’s physician entered an order for amphotericin B conventional 375 mg intravenous (IV) every 24 hours. Based on the patient’s weight of 75 kg, the patient received 5 mg/kg of amphotericin B conventional while the maximum safe dose for this product is 1.5 mg/kg per day. This higher dose would have been appropriate for one of the lipid-based products, but it was more than three times higher than the maximum dose recommended for conventional amphotericin B. Within three hours of administration, the patient suffered a cardiac arrest and died.

During prescriber order entry of the drug, a warning had popped up on the screen asking the prescriber to verify that the dose did not exceed 1.5 mg/kg. However, the CPOE system did not require acknowledgment of the warning or action by the prescriber. The alert quickly disappeared after hitting the Enter key and was bypassed without consideration. The pharmacist also missed an opportunity to capture the dosing error. Although the screen accessed by the pharmacist when verifying the order revealed that amphotericin B conventional “equivalent to Fungizone” had been prescribed, the pharmacist misunderstood the order as the lipid-based product and even obtained a required approval from an infectious disease prescriber to dispense AmBisome. However, the pharmacy label that printed resulted in preparation of the conventional amphotericin B. The nurse who administered the drug did not notice the error, as she was not aware of the dosing differences between the conventional and lipid-based forms of the drug.

Numerous risk-reduction strategies might have helped to prevent or detect this error, such as including brand names when prescribing the lipid-based forms of the drug. However, a computer alert with a hard stop for doses of conventional amphotericin B greater than 1.5 mg/kg for both the CPOE and pharmacy system is a key strategy, the importance of which should not be minimized. While the Institute for Safe Medication Practices (ISMP) recommends entry of patient weights in all order-entry systems, if this does not occur consistently at your practice site, you may want to establish a catastrophic dose limit for a hard-stop alert. Such an alert would not be designed to ensure an appropriate dose, but rather to force a time-out and protect against a massive overdose.

Methotrexate

In 2004, we published a study of methotrexate errors over a four-year period that resulted in 25 deaths and 48 serious outcomes, many due to daily dosing.8 The latest reported event happened at a compounding pharmacy, but the same type of error has occurred in hospitals. In this case, the compounding pharmacy received a telephone order to prepare an oral liquid preparation of methotrexate 12 mg/mL, with instructions to administer 6 mg (0.5 mL) once a week for a 19-month-old child with juvenile dermatomyositis. A pharmacist transcribed the order incorrectly and entered it into the pharmacy computer with a dosing frequency of daily. The pharmacy compounded the solution using methotrexate powder, and labeled the medication with instructions to take 0.5 mL daily instead of weekly. The pharmacist handling the order was unfamiliar with methotrexate dosing and did not recognize that a daily dose would be toxic. Also, the pharmacy had never filled a prescription for oral liquid methotrexate before the event. The child received a daily dose for seven days before the error was noticed by the prescriber. The child was undergoing diagnostic laboratory tests to determine the adverse effects of this overdose when the event was reported to ISMP.
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Again, this is an ongoing error that could easily be prevented by a hard stop in the pharmacy computer for daily dosing of oral methotrexate (or if filling frequent oncology orders, for daily doses without a stop date after five days or less).

Fentanyl

A fentanyl dosing error occurred with a 2-month-old infant who had been admitted to the hospital for a pyeloplasty. The anesthesia team started a fentanyl infusion (200 mcg in 20 mL of 5% dextrose) to be delivered at 1 mcg/kg per hour during the surgical procedure. However, the infant received the entire 200 mcg of fentanyl in less than an hour because the smart infusion pump had been misprogrammed to deliver 1 mcg/kg per minute instead of 1 mcg/kg per hour. The infant became hypotensive for a short interval but tolerated the procedure and was breathing spontaneously after surgery. As with the other events, numerous risk-reduction strategies could help prevent infusion-pump programming errors, but one key intervention in this case includes a hard stop during pump programming that would not allow the programming of such a catastrophic dose to continue. A hard stop in this case would have required reprogramming of the pump in accordance with preapproved dosing guidelines.

Conclusion

The errors described above demonstrate specific situations with amphotericin B, methotrexate, and fentanyl in which hard stops would have protected patients from harmful medication errors. While some clinicians may complain that hard stops potentially delay order completion or slow the dispensing and administration process, the intent is to allow for a brief period of investigation to ensure safety. Clearly for drugs like amphotericin B, methotrexate, and fentanyl, the risk of a potentially fatal dosing error far outweighs any risk of a slight delay in therapy. Another barrier may be that some clinicians find hard stops objectionable, noting that decision support should not replace the clinician’s responsibility for patients.1,9

However, when relatively simple actions such as thoughtfully placed hard stops could prevent harmful events and clinicians do not implement them, they are clearly not upholding their responsibility to keep patients safe from unreasonable risk. While organizations need to address any clinicians’ concerns about hard stops and to make every effort to minimize any unintended effects, we suggest that all organizations place the issue of hard stops for certain drugs, including the three described above, and other preventable clinical situations on the top of their safety agenda.

REFERENCES