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PATIENT SAFETY NETWORK

Crossed Coverage

February 1, 2007
Kayser SR. Crossed Coverage. PSNet [internet]. 2007.
https://psnet.ahrq.gov/web-mm/crossed-coverage

The Case

A 27-year-old woman with a history of congenital heart disease was admitted for cardiac transplantation evaluation. She had already undergone multiple surgeries, including aortic valve replacement for which she was on warfarin with a goal international normalized ratio (INR) level of 2.0–3.0.

On admission, her hemoglobin level was normal and her INR was 2.6. At the admitting hospital, a formal policy required that all inpatient orders for warfarin be rewritten each day to prevent overdosing. The intern caring for the patient ordered her usual outpatient dose of 15 mg x 1. On hospital day two, the patient's INR had risen to 3.6. The intern did not write the order for warfarin for hospital day two and clearly outlined in the daily progress note that the warfarin was to be held.

After the shift change, the evening nurse noted that the daily warfarin order had not been written. She was puzzled, as she distinctly remembered from signout that the patient was on warfarin for the prosthetic aortic valve. Without checking the progress notes or the laboratory values for that day, she paged the night float intern (not the primary intern caring for the patient) who was cross-covering. Having not received a verbal signout from the primary intern, the cross-covering intern reviewed the written signout on the patient and noted that warfarin was listed as one of the patient's medications. As it turns out, the primary intern had not updated the written signout that day, and warfarin was still listed as an active medication. Without checking the progress notes or the patient's INR level for the day, the cross-covering intern gave the nurse a verbal order to give the patient one dose of warfarin, 15 mg.

The pharmacy dispensed the medication, and the patient received 15 mg of warfarin. The next day, the patient's INR was 5.6; 3 days later, it peaked at 7.7. Oral vitamin K was given to counteract the effects of the warfarin. The patient had a minor nosebleed but no other adverse consequences.

The Commentary

Anticoagulant drugs are among the most common agents responsible for adverse events in hospitalized patients as well as a frequent cause of medication errors.(1) Warfarin, in particular, can be quite

dangerous—the narrow therapeutic index and its variable pharmacologic response require careful dosing and management.

Efforts to improve the quality and safety of warfarin administration include publishing standardized guidelines, enforcing institutional dosing policies, and using computerized physician order entry (CPOE) with clinical decision support. Although distributing evidence-based guidelines for anticoagulant medication administration resulted in a trend toward a decrease in anticoagulant-associated adverse events in one study (2), these interventions are generally unsuccessful, as they are only advisory in nature and require no action on the part of the provider. Proper and safe dosing requires the provider to refer to the guidelines and subsequently use them appropriately. An example of a warfarin dosing guideline is shown in the Table.

Many hospitals have implemented institutional warfarin dosing policies that require the medication to be prescribed and dispensed in a specifically described manner. One example is a policy that eliminates standing orders for warfarin and requires the order to be rewritten each day as a one-time order. A similar policy was in place at the admitting hospital in the case described, but it clearly did not prevent the error. For high-risk drugs like warfarin, another policy that potentially could reduce errors would mandate a specific order when the intent is to discontinue or withhold a dose (as opposed to when the intention is to give the medication). Such a policy could have helped prevent the error in this case. Lastly, warfarin is traditionally dosed in the evening. Requiring morning administration could prevent errors since more staff members (including the primary team responsible for a patient's care) are in the hospital at this time and available to clarify orders.

Although not widespread, many hospitals have implemented CPOE with clinical decision support to aid in the dosing and management of warfarin. An alert triggered by the association of warfarin with an INR that exceeds a certain value (e.g., greater than 3.5) and supported by a management algorithm might have prevented the error that occurred in this case. A system designed to consider conflicting medications and comorbidities that influence warfarin might be able to recommend specific doses. However, with just computerized order entry, medication errors persist. In one hospital where CPOE has been in place for a number of years, anticoagulants accounted for 7.2% of all medication errors, with warfarin accounting for 21.5% of these.(1) Of the anticoagulant-related adverse events, 6.2% required medical attention and 1.5% resulted in prolonged hospital stay. The most common errors were missed or extra doses.(1)

One alternative strategy to enhance the quality and safety of inpatient anticoagulation administration is the active engagement of inpatient pharmacists. For example, pharmacy-managed inpatient anticoagulation consultation services have been demonstrated to improve the use of anticoagulants, including a reduction in the number of supratherapeutic INRs and a decrease in bleeding incidents and the use of transfusions.(3) In most inpatient anticoagulation services, the pharmacist provides a chart note with specific recommendations about dosing, which is then reviewed by the physician who can either accept or reject the recommendation. Although this kind of service can prevent many errors, it may not have prevented the error in this case, since the chart was not consulted and the pharmacist's note is only advisory in nature.(4) On the other hand, a program of direct anticoagulation management by the pharmacist upon the request of a physician may have prevented the error in this case. Most of these programs are voluntary, so the availability of this service also might not have prevented the error.(5)

The majority of preventable adverse drug events occur at the time of either ordering or administration.(6) The pharmacy is in an ideal position to prevent errors at both junctions, since the nurse depends on pharmacy processing to be able to access the medication and administer it. Policies could be established that require the dispensing pharmacy to check the laboratory data for each patient prior to processing an order. In this case, such a policy would have led the pharmacist to observe that the INR rose acutely (2.6 to 3.6) and to contact the physician to intervene. A more comprehensive program would establish a pharmacy-directed anticoagulation dosing service on a 24-hours-a-day, 7-days-a-week basis that includes all patients receiving warfarin.(7)

Another potential solution is using electronic laboratory alerts based upon certain rules, which are directed to a dedicated anticoagulation pharmacist prior to the dispensing of the medication.(8,9) For example, when any two consecutive INR levels differed by more than 0.4 units, an alert could be forwarded to the pharmacist for review and potential intervention. The use of alerts during medication ordering has met with variable success. In a setting of patients residing in an academically affiliated long-term care facility, alerts directed to physicians resulted in only a slight increase in the likelihood of taking appropriate action (although alerts related to warfarin were the most likely to result in an action).(10) In the case under discussion, an alert associated with a "rule" that was linked to the laboratory result might have caught the warfarin error. Our institution uses such a system, in which an electronic laboratory alert is generated for certain anticoagulation-related laboratory values and directed to a dedicated anticoagulation pharmacist, and it works well.(11)

Overall, multiple failures of communication occurred in this case. When the nurse noticed that no warfarin order was written, as part of her scope of practice, she should have reviewed the progress note to see if the omission was intentional. The primary intern should have updated the written signout or provided a better verbal signout to the cross-covering intern. Enforcement of a no verbal order policy might have led the cross-covering intern to look at the chart prior to writing the order. The covering intern should have reviewed the laboratory results prior to ordering the medication.

Although there were many human errors, a better system probably would have prevented this error. Institutional policies requiring an order when warfarin is to be discontinued or held, or requiring that it be ordered only in the morning, may have helped. A clinical decision support component of CPOE might have prevented the error if it were designed to respond to either a threshold INR or change in INR of a predetermined magnitude.(12) Finally, a dedicated, pharmacist-managed anticoagulation service available 24 hours a day, 7 days a week, with or without computer clinical decision support, is most likely to prevent these types of adverse reactions. This type of service could also deal with other anticoagulant-related issues that may arise.

Take-Home Points

- When a medication, especially a high-risk one, is not ordered, the chart should be reviewed by physicians, nurses, and pharmacists to inquire if it was intentional.
- A no verbal order policy should be strongly considered.
- Mandatory review of laboratory data should be required with warfarin dosing.
- Pharmacy-directed anticoagulation services should be considered.

Steven R. Kayser, PharmD Professor of Clinical Pharmacy School of Pharmacy University of California, San Francisco

References

1. Fanikos H, Stapinski C, Koo S, et al. Medication errors associated with anticoagulant therapy in the hospital. Am J Cardiol. 2004;94:532-535. [go to PubMed]

2. Schumock GT, Blackburn JC, Nutescu EA, et al. Impact of prescribing guidelines for inpatient anticoagulation. Ann Pharmacother. 2004;38:1570-1575. [go to PubMed]

3. Bond CA, Raehl CL. Pharmacist-provided anticoagulation management in United States hospitals: death rates, length of stay, Medicare charges, bleeding complications, and transfusions. Pharmacotherapy. 2004;24:953-963. [go to PubMed]

4. Dager WE, Branch JM, King JH, et al. Optimization of inpatient warfarin therapy: impact of daily consultation by a pharmacist-managed anticoagulation service. Ann Pharmacother. 2000;34:567-572. [go to PubMed]

5. Mamdami MM, Racine E, McCreadie S, et al. Clinical and economic effectiveness of an inpatient anticoagulation service. Pharmacotherapy. 1999;19:1064-1074. [go to PubMed]

6. Bates DW, Cullen DJ, Laird N, et al. Incidence of adverse drug events and potential adverse drug events. Implications for prevention. ADE Prevention Study Group. JAMA. 1995;274:29-34. [go to PubMed]

7. Burns N. Evaluation of warfarin dosing by pharmacists for elderly medical in-patients. Pharm World Sci. 2004;26:232-237. [go to PubMed]

8. Hartis CE, Gum MO, Lederer JW Jr. Use of specific indicators to detect warfarin-related adverse events. Am J Health Syst Pharm. 2005;62:1683-1688. [go to PubMed]

9. Lederer J, Best D. Reduction in anticoagulation-related adverse drug events using a trigger-based methodology. Jt Comm J Qual Patient Saf. 2005;31:313-318. [go to PubMed]

10. Judge J, Field TS, DeFlorio M, et al. Prescribers' responses to alerts during medication ordering in the long term care setting. J Am Med Inform Assoc. 2006;13:385-390. [go to PubMed]

11. Comprehensive Hemostasis and Antithrombotic Service (CHAS), UCSF Medical Center.

12. Nebeker JR, Hoffman JM, Weir CR, Bennett CL, Hurdle JF. High rates of adverse drug events in a highly computerized hospital. Arch Intern Med. 2005;165:1111-1116. [go to PubMed]

Table

Guidelines for Warfarin Dosing

Warfarin orders must be written daily (i.e., no standing orders).

INR must be monitored daily.

An INR increase of 0.2–0.3 units per day represents an optimal response to initiation of warfarin. Any increase in INR greater than or equal to 0.4 units per day should result in warfarin dose reduction or holding warfarin dose.

INRs should not be assessed when activated partial thromboplastin time (aPTT) is >100 seconds, due to the contribution of unfractionated heparin's effect to INR. Wait until aPTT is

For INRs significantly above the therapeutic range, hold warfarin until INR falls within range prior to restarting warfarin.

Factors that may impact the INR: drug interactions, malnutrition, alcohol, concomitant disease (e.g., thyroid dysfunction, liver disease, fever), medication adherence.

Algorithm for *Initiating* Warfarin in Hospitalized Patients [Baseline prothrombin time (PT)/INR, partial thromboplastin time (PTT), and platelet count must be obtained prior to initiation of warfarin.]

Day	INR	Action
1		5 mg (2.5 or 7.5 mg in select populations)
2	Less than 1.5	Continue dose
	Greater than or equal to 1.5	Decrease or hold dose*
3	Less than or equal to 1.2	Increase dose*
	Greater than 1.2 and less than 1.7	Continue dose
	Greater than or equal to 1.7	Decrease dose*
4 (or until therapeutic)	Daily increase is less than 0.2 units	Increase dose*
	Daily increase is 0.2–0.3 units	Continue dose
	Daily increase is 0.4–0.6 units	Decrease dose*
	Daily increase is greater than or equal to 0.7 units	Hold dose

*In general, dosage adjustments should not exceed 2.5 mg or 50%.

Factors to Consider When Initiating Warfarin

Usual initiation dose = 5 mg (NOT 10 mg)

Consider higher initial dose (e.g., 7.5 mg) in the following populations:

1. Weight >85 kg
2. African-American patients
3. Clinical hypothyroidism
4. Concomitant medications

Consider lower initial dose (e.g., 2.5 mg) in the following populations:

1. Frail or advanced age (older than 75)

2. Asian patients
3. Hepatic insufficiency
4. Malnutrition/poor PO intake
5. Clinical hyperthyroidism
6. High bleeding risk
7. Concomitant medications

This project was funded under contract number 75Q80119C00004 from the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services. The authors are solely responsible for this report's contents, findings, and conclusions, which do not necessarily represent the views of AHRQ. Readers should not interpret any statement in this report as an official position of AHRQ or of the U.S. Department of Health and Human Services. None of the authors has any affiliation or financial involvement that conflicts with the material presented in this report. *View AHRQ Disclaimers*