Oral Anticoagulants: A Review of Common Errors and Risk Reduction Strategies

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ABSTRACT

Oral anticoagulants, a class of high-alert medications, are widely used in the United States for varying indications, including treatment after deep-vein thrombosis or pulmonary embolism as well as prevention of stroke in valvular and non-valvular-related atrial fibrillation. Analysts reviewed medication error reports submitted from July 2013 through June 2014 through the Pennsylvania Patient Safety Reporting System (PA-PSRS) involving four oral anticoagulants: warfarin, apixaban, rivaroxaban, and dabigatran. Of the 831 errors related to oral anticoagulants analyzed from PA-PSRS, the most common event types were drug omissions (32.5%, n = 270), other (18.5%, n = 154), and extra doses (11.7%, n = 97). Medication errors categorized as "other" involved problems related to prescribing, wrong dose, wrong patient, and inaccurate medication lists. Risk reduction strategies include establishing functional hard-stop drug alerts during order entry, establishing an anticoagulant management service program, and providing continuous education for staff on anticoagulant use. (Pa Patient Saf Advis 2015 Jun;12[2]:54-61.)

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INTRODUCTION

Oral anticoagulants have been identified as one of the most commonly implicated drug classes in adverse drug events.[1,2] In fact, anticoagulants and cardiovascular agents, when compared with other medications, are more likely to cause potentially preventable adverse events that result in or prolong hospital stays.[3,4]

The Institute for Safe Medication Practices (ISMP) considers oral anticoagulants high-alert medications, as they bear a heightened risk of harm if used in error.[5] ISMP has written on risks associated with the use of anticoagulants, such as duplicate or concurrent therapy, accidental stoppage of therapy, dosing errors during transition of care, and monitoring problems.[6] The National Quality Forum (NQF) endorsed two warfarin-related measures from the Centers for Medicare and Medicaid Services to help identify problems and prevent adverse events.[7] Newer oral anticoagulants do not have as long a track record of data, including event reports; however, proactive efforts, targeted education, and error mitigation efforts should be encouraged to prevent errors.[8] Furthermore, the Joint Commission continues to designate careful oral anticoagulant use as part of the National Patient Safety Goals.[9]

In a retrospective, hospital-specific, five-year study by Piazza et al., the investigators found that 48.8% (n = 226) of all adverse drug events involved anticoagulant-related medication errors.[10] In the study, the 30-day mortality rate was increased in the 11% of patients who experienced an anticoagulant-associated adverse drug event. Retrospective studies on emergency hospitalizations for adverse drug events in older Americans implicated warfarin (Coumadin®) as the leading (33.3%) medication contributing to hospitalization.[11] It is important to note that at that time, warfarin was the only available oral anticoagulant, so future data will likely include newer agents.

Prior to 2010, warfarin was the only approved oral anticoagulant agent. Since then, several new oral anticoagulants, also referred to as target-specific anticoagulants, have been introduced into the market. Among them are apixaban (Eliquis®), dabigatran (Pradaxa®), and rivaroxaban (Xarelto®). Another agent, edoxaban (Savaysa®), received final US Food and Drug Administration (FDA) approval in January 2015.

Not all oral anticoagulants are approved and labeled for use for all of the same indications. Warfarin, a vitamin K antagonist, works by altering the clotting mechanism via protein C and S as well as factors II, VII, IX and X.[12] Target-specific oral anticoagulants, except dabigatran, work by inhibiting platelet activation and fibrin clot formation via selective and reversible inhibition of both free and clot-bound factor Xa.[13,14] Dabigatran works by reversibly inhibiting both free and fibrin-bound thrombin, resulting in reduced thrombin-mediated platelet aggregation.[15]

Unlike warfarin, target-specific oral anticoagulants cannot be monitored using international normalized ratio (INR) or other blood tests and do not require dietary modifications.[16] Although all target-specific anticoagulants are shown to be safe and effective for the indications for which they are approved, data in elderly patients or those with chronic illness is limited.[16] Also, many prescribers are still not quite versant on how to deal with target-specific oral anticoagulants in cases of trauma, surgery, and sudden emergencies requiring conversion from oral to intravenous anticoagulants such as heparin or argatroban.[17] Anticoagulants need to be monitored closely to avoid serious adverse effects (e.g., bleeding, thrombosis) that may result from inappropriate use.[16] Unlike warfarin, which can be reversed with phytonadione (vitamin K), there is still no FDA-approved antidote for the newer agents.

Time needed for oral anticoagulant agents to reach full therapeutic effect also varies. Warfarin does not reach full therapeutic effect until five days after treatment initiation. The target-specific oral anticoagulants can reach full effect in less than 24 hours. Both warfarin and the target-specific oral agents have significant drug-drug interactions that should not be overlooked. Warfarin's dosing and monitoring is also complicated by consumption of foods containing vitamin K, such as spinach and kale.[12] Also, target-specific anticoagulants are highly protein-bound, making it quite difficult to remove them with dialysis.[13-15]

METHODS

Analysts queried the Pennsylvania Patient Safety Authority's Pennsylvania Patient Safety Reporting System (PA-PSRS) database for medication error reports involving each of the approved oral anticoagulant products. Specifically, the "medication prescribed" and "medication administered" fields in medication error event reports were queried by the brand and nonproprietary names of the approved oral anticoagulants apixaban, dabigatran, rivaroxaban, and warfarin. Categorization of the reports by harm score was adapted from the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) Index for Categorizing Medication Errors.[18]

RESULTS

Pennsylvania healthcare facilities submitted 831 medication error reports associated with oral anticoagulants to the Authority from July 2013 through June 2014. The highest number of errors were reported as drug omissions (32.5%, n = 270), "other" (18.5%, n = 154), and extra doses (11.7%, n = 97) (see the Table). Approximately 2.5% (n = 21) of the events reported as "other" did not include enough detail to determine what occurred or factors contributing to the event. While the analysts were unable to separately categorize these reports, these errors remained in the analysis to be categorized based on harm score and demographics such as patient age, medication involved, and patient care area. Medical-surgical units were identified as having the highest incidence of errors at 24.1% (n = 200), followed by telemetry 9.9% (n = 82) and then rehabilitation units 9.4% (n = 78).

Of the oral anticoagulants, warfarin was predominantly reported (81.5%, n = 677), followed by rivaroxaban (11.9%, n = 99), dabigatran (3.6%, n = 30), and apixaban (2.2%, n =18). Of the reported errors, 78.7% (n = 654) involved adults age 60 or older. Over a third of the medication errors (34.4%, n = 286) involved adults age 80 or older, whose risk of adverse drug events is increased because of declining liver and renal function, greater propensity for drug interactions due to polypharmacy, and other comorbidities.

After categorization of reports by harm score using the NCC MERP index,[18] it was noted that nearly a third of the cases (29.4%, n = 244) were reported as having a harm score of D to F. This means that not only did the error reach the patient, but it also required, at minimum, intervention to prevent harm as well as further monitoring of the patient. A large number of events (44.0%, n = 366), grouped as having a harm score of C, reached the patient but did not cause

Table. Number of Oral-Anticoagulant-Related Medication Errors, by Event Type, Reported to the Pennsylvania Patient Safety Authority, July 2013 through June 2014 (N = 831)

EVENT TYPE	n	%
Dose omission	270	32.5
Other (specify)	154	18.5
Extra dose	97	11.7
Wrong dose/overdosage	50	6.0
Monitoring error: clinical (lab value, vital sign)	46	5.5
Wrong time	40	4.8
Unauthorized drug	34	4.1
Wrong dose/underdosage	28	3.4
Wrong patient	23	2.8
Medication list incorrect	22	2.6
Prescription/refill delayed	20	2.4
Wrong drug	14	1.7
Monitoring error: drug-drug interaction	8	1.0
Wrong duration	5	0.6
Wrong strength/concentration	5	0.6
Wrong technique	5	0.6
Monitoring error: other (specify)	5	0.6
Wrong dosage form	2	0.2
Wrong route	1	0.1
Monitoring error: drug-disease interaction	1	0.1
Monitoring error: deteriorated drug/biologic	1	0.1

harm. Additionally, 1.8% (n = 15) of the reported events contributed to temporary harm to the patient (harm score E). There were no reports categorized as harm score G to I.

It should be noted that warfarin has been the mainstay of anticoagulant therapy for decades, while the other oral anticoagulants have been introduced over the past few years. Therefore, throughout this analysis, it was expected that the number of events involving warfarin would be greater than the number of events involving newer anticoagulants.

ANALYSIS

Dose Omissions

An omission of an anticoagulant, especially if that omission occurs for multiple doses, places the patient at risk of a thromboembolic event. Based on the analysis of event descriptions, the reasons for dose omissions involving anticoagulants varied, and different sources of the origin of the errors were identified, ranging across the medication-use continuum from breakdowns in prescribing to not administering an anticoagulant. Errors of omission (n= 270) resulted from medications not being ordered (35.9%, n = 97), orders not being administered (31.5%, n = 85), and orders being processed incorrectly (27.8%, n = 75).

It is worth noting that a small number (1.5%, n = 4) of patients did not receive their medications because the pharmacy could not provide them. These four cases involved target-specific anticoagulants. As with many newer medications, which lack generic equivalents, it is possible that these agents were not included in the hospital formulary.

In the analysis, 88.5% (n = 239) of dose omissions involved warfarin. It is common practice for institutions to order warfarin on a daily basis as a "one time" dose after evaluating the patient's INR for that day. This is unlike the administration of other oral anticoagulants, which are independent of INR results and can be prescribed with a fixed dosing schedule. In the example below, an oral anticoagulant dose was missed after the procedures, but it is unclear who was supposed to write the order. Note that the details of the PA-PSRS event narratives in this article have been modified to preserve confidentiality.

> *Upon assessment of patient, it was noted that warfarin daily order was to be obtained for an INR of 1.9 (target INR goal = 2 – 3), but the dose was missed the previous day. Upon review of the chart to determine the dose the patient received the previous day, it was noted that following the TEE [transesophageal echocardiogram] and cardioversion, no warfarin was ordered.*

Problems have also been reported in which medication orders are temporarily "held" for scheduled tests or procedures but are not restarted as intended once the procedure is completed.[19] Most hospitals have established standard times for the administration of oral anticoagulants, which primarily affects warfarin, as the dose depends on receiving and responding to INR results. Unfortunately, if transfer or movement of patients occurs during the standard administration times, breakdowns in communication among members of the healthcare team might lead to dose omissions.

In 6.7% (n = 18) of reported omission-related events, doses were omitted during transitions of care. In most instances, one provider expected another provider to order the medication. In other cases, a patient was transferred from one unit to another without receiving a scheduled dose for the day or arrived in another care location and providers in the receiving care area were not aware of the omission, as shown in the following example.

> *Upon reviewing the most current warfarin doses, it was noted that there was no warfarin ordered or given for one day. Reviewed the initial postoperative orders, which indicated "medicine" [medical service] was to dose. Hospitalist consulted and will be following the case.*

Nurses play an important role in the medication-use process to ensure that the correct medication and appropriate dose are administered to the patient. However, breakdowns in medication administration processes can include forgetting to call for orders, signing off on lab results and not notifying the prescriber to place an order, and not ensuring that the patient actually takes the medication, such as leaving the medication with the patient to self-administer without supervision. In some cases it was unclear whether the ordered medications were received from the pharmacy or why they were not given to the patient if they were supplied, as shown in the following examples.

> *Patient [presented] to the ED [emergency department] complaining of dizziness, blackouts, and one-sided body pain from waist down into leg. Past medical history of DVT [deep-vein thrombosis]. Warfarin and Lovenox® (enoxaparin) ordered but not given. Error discovered by staff after patient was discharged from the ED. Patient called and asked to return to the ED for medication. Patient did return and received both warfarin and Lovenox. No immediate harm to patient.*

> *The patient has an order to receive rivaroxaban 20 mg PO [by mouth] daily. During the daily cart exchange, one dose was remaining in the patient's drawer. A review of the MAR [medication administration record] showed the previous dose was signed off as given. No apparent harm to patient noted. Patient and physician notified.*

Drug omissions also originated during order processing. Errors occurred when written orders either were not faxed or

scanned to the pharmacy or were written with parameters such as pending laboratory results but laboratory tests were scheduled for the next day. Another issue included situations when orders were scanned after the hospital's standard administration times and the dose was scheduled to start the next day. Hospitals that use standardized times may risk a dose omission if the system defaults to the next standardized time and no alert is presented to the pharmacist during order entry. The following examples highlight multiple opportunities for a dose being missed.

> *Physician notified me that she placed an order for warfarin 4 mg PO every night at 1930. The patient did not receive dose that night because the medication time for evening is 1800 and the system automatically scheduled the first dose at 1800 on the next day. The patient's first dose was delayed 24 hours.*

> *Pharmacy overlooked profiling time. Patient was ordered a one-time warfarin dose. Patient did not have an INR drawn; order was placed as conditional and pharmacy requested INR result be called to pharmacy. INR was not entered or drawn until the morning. Warfarin dose was missed. Pharmacist did not follow up when INR results were not called. No adverse outcome reported due to omission.*

Extra-Dose Errors

When patients receive extra doses of anticoagulants, they are placed at an increased risk for bleeding events. As previously stated, nearly 12% (n = 97) of the reports involved extra doses of anticoagulants. In the following example, the error stemmed from not holding an order of warfarin after an elevated INR. Care should be exercised, as hold orders without specific instructions on when to resume or who restarts them, may lead to dose omissions after the INR stabilizes.

> *Patient was admitted for acute DVT of the left lower extremity and was receiving daily warfarin. Due to elevated INR results earlier in the day, patient's daily dose of warfarin was to be held in the evening. This was not done, and warfarin was given. The INR the next morning was elevated to 8.5, and 3 units of FFP [fresh frozen plasma] were ordered and administered to the patient. An additional unit of FFP was given the next day. The patient did not experience any active bleeding during this time.*

Extra doses were also administered when an order to discontinue an existing anticoagulant was missed, as in the following example.

> *Patient admitted for pulmonary embolism and placed on heparin protocol. The resident ordered rivaroxaban 15 mg by mouth BID [twice daily] to start that evening. At about 1800, I instructed the evening shift nurse to stop heparin drips right before rivaroxaban was given. The next day, the medical resident indicated that the heparin drips had been continued by the nurse until the following morning. Patient received both rivaroxaban and heparin for several hours, which placed her at an increased risk of bleeding.*

Unfortunately, a break in care that results from a change in clinicians may lead to unintended extra-dose errors. While shift change is an opportunity to communicate the patient's clinical status to the next practitioner, completing a thorough review of the each patient's MAR may not be plausible. In addition, though not always evident, patient preferences might also conflict with the hospital's preferred times for medication administration. If daily oral anticoagulant status is not properly communicated (i.e., given versus not given) or if clinicians do not thoroughly review the patient's MAR, errors can happen, as shown in this example.

> *An order was placed for 10 mg of warfarin to be given at night, which the patient received in the morning. At 2100, a resident rounded on the patient and noted that there was no order for warfarin and placed another order for a one-time dose of 10 mg of warfarin. The patient received the medication. His INR rose to 7. The patient was monitored without any bleed. He also received 10 mg of PO vitamin K, with INR decreased to 1.9 on the day of discharge.*

Error Type "Other"

Analysis of events submitted as "other" (n = 154) revealed similar errors that could have been classified as more specific event types, such as errors related to prescribing, wrong dose, wrong patient, inaccurate medication list, or omission errors. Prescribing errors (29.2%, n = 45) comprised the largest subcategory, followed by incomplete medication list (13.0%, n = 20). During prescribing, errors primarily involved duplication of therapy.

Patients receiving oral anticoagulants either at the time of admission or after admission would not need additional prophylaxis medications for DVT, unless there was a break in therapy. In the following example, a prescriber ordered a target-specific oral anticoagulant but did not discontinue subcutaneous heparin for DVT prophylaxis.

> *The patient was receiving heparin 5,000 units [subcutaneously] every 8 hours for DVT prophylaxis. Later in the day, apixaban 5 mg BID was also prescribed. The heparin was not discontinued. Therefore, the patient received subcutaneous heparin while receiving therapeutic anticoagulation with apixaban.*

When starting warfarin therapy, it takes several days for the INR to reach the target or therapeutic goal ranges. As a result, practitioners follow "warfarin bridging" practices. This method of giving an oral anticoagulant together with heparin is used to ensure the patient stays anticoagulated enough to avoid clot growth or re-thrombosis as the INR level rises to a therapeutic level. Medication error reports, such as the following example, revealed problems with prescribers ordering multiple anticoagulants including both oral and injection formulations.

> *Physician wrote orders for dabigatran, subcutaneous Lovenox, and warfarin. The medications were not administered, and all orders were discontinued by the physician except for the Lovenox.*

Warfarin and target-specific oral anticoagulant agents ordered concurrently, as in the following example, also reflects a duplication of therapy.

> *The patient was on rivaroxaban 15 mg PO BID for treatment of PE [pulmonary embolism]. Five days later, warfarin 10 mg by mouth one dose was ordered and profiled. The warfarin was given that evening. The additional prescription was noted by the clinical pharmacist the next day. The attending physician and nurse were notified, and the warfarin was stopped. The patient was discharged and continued on rivaroxaban anticoagulation only.*

As previously noted, incomplete medication lists were the second most common source of error identified in the "other" reports. Unfortunately, incomplete medication lists continue to be a problem, particularly during transitions of care, when a patient is admitted to the hospital, transferred from one care area to another, or discharged from the hospital. The Joint Commission's National Patient Safety Goal 03.06.01 states that organizations have to "maintain and communicate accurate patient medication information."[9] When all (N = 831) oral anticoagulant medication errors are considered, the rate of incomplete medication lists is approximately 5.2% (n = 43).

RISK REDUCTION STRATEGIES

Organizations and healthcare facilities can strive to identify system-based causes of errors involving oral anticoagulant agents and implement effective types of risk reduction strategies to prevent harm to patients. Education relies heavily on individual performance. System-based improvements such as constraints and standardization are more effective.[20,21] Consider the strategies described below, which are based on a review of current literature, events submitted to the Authority, and observations from ISMP.

Constraints

- Oral anticoagulants are sometimes involved in complex drug regimens, with risks for drug interactions or duplications. A pharmacist's review of each medication order prior to dispensing could help with verifying the drug and dose against therapeutic indication.[6]
- Functional drug alerts, such as hard stops, that prevent a provider from ordering two anticoagulants at a time without giving a reason may prevent duplication of therapy.[6]
- Verbal orders can be misinterpreted, misunderstood, or not transcribed correctly.[22] Organizations can strive to eliminate the use of verbal orders unless in emergency situations. If verbal orders have to be used, consider a "read back" method, such that the nurse first documents the order in writing (or electronically) and then reads it back to the prescriber, versus a "repeat back" method, in which there may be a gap, and potentially interruptions, before order entry is completed.

Standardization

Prescribing

- The dose of some of the target-specific agents requires adjustment based upon patient characteristics (e.g., renal function, body weight). Therefore it is important to standardize the baseline information, such as weight in kilograms and serum creatinine function, needed during the ordering of oral anticoagulants.[6] Also, having a standardized process for updating computer systems and healthcare records is important. Displaying the current calculated creatinine clearance during electronic prescribing is helpful to prevent errors.[6,23,24]
- Elderly patients may require lower starting doses for oral anticoagulants, depending on the agent ordered, because of reduced renal function or, in some instances, lower body weight.[6]
- Dose omissions that were seen often were in part a result of orders that were held and not reinstated. Establishing a standard process and following a strategy for handling "hold" orders is vital. Having an active order or reminder listing the drug, route, and frequency, with clear annotation on the records to ensure that a dose is prescribed each day according to lab values in both the pharmacy and MARs, may help minimize omissions.[19,25]
- Organizations are encouraged to establish anticoagulation management service (AMS) programs for dosing and monitoring, as well as for teaching patients about their therapy.[26-28] The first step in developing AMS programs is to assess current practices associated with anticoagulation safety. The self-

assessment process allows facilities to identify ways in which to provide safer care while improving patient outcomes.[28] The Authority has accessible resources to help organizations interested in establishing an AMS program as well as an anticoagulant organization assessment (available at http://patientsafetyauthority.org/EducationalTools/PatientSafetyTools/ams/Pages/Home.aspx).[29] AMS programs help to centralize care of the patient and provide agreed-upon interdisciplinary treatment and monitoring guidelines.

- Standard protocols for rapid or emergency reversal of anticoagulation and expected restarting of anticoagulants can be useful tools for use in institutions. The effects of some reversal agents such as phytonadione continue for up to a week; therefore, use of national guidelines for guidance on restarting anticoagulation if indicated may be helpful.[6]
- The Joint Commission addresses incomplete and "blanket" orders, even in electronic prescribing, such as "resume all meds," and recommends they not be used.[30] Standardized processes for the medication reconciliation process during handoffs or at any transition of care can help ensure appropriate anticoagulant ordering takes place.
- "NOAC" has been used in medical literature as an abbreviation for the target-specific, or "novel," oral anticoagulants. Unfortunately, this abbreviation has been misunderstood as "no anticoagulation" and may contribute to unintended discontinuation of the medication, leading to dose omissions.[31] ISMP recommends the abbreviation be prohibited, as it is prone to error and misinterpretation.

Dispensing and Administration

- Administration of warfarin at a standard time allows for a thorough review of daily laboratory results and any necessary dose adjustments before administration; however, coordination of laboratory data and dose administration is important.[6]
- Most organizations will only stock one medication per therapeutic class to streamline costs by reducing inventory and carrying costs. However, due to the uniqueness of each of the newer oral agents, this might not be the best strategy for these medications. If only a limited selection of medications is added to the formulary, define policies and procedures for therapeutic substitution or ways to approve use of a patient's own medication to avoid missed doses.[8]

Redundancies

- Strategically placed independent double checks—such as a pharmacist check of stock medications for units and of automated dispensing cabinets (ADCs) before leaving the pharmacy or a nurse verification of a dose for new starts as well as one-time orders for anticoagulants—may avoid anticoagulant-related errors.[6]
- Clinical decision support in computerized order entry and pharmacy information systems may help avert dosing errors and duplication of orders by firing alerts to users.[29]
- Bar-code scanning during stock replenishment of ADCs may reduce stocking errors.[32] In addition, bar-code scanning during administration may help ensure the correct drug and dose is administered.[33]

Therapeutic Monitoring

- When an oral anticoagulant is indicated, baseline lab test results such as renal function tests need to be available in two hours or less to help guide therapy.[6]
- Process control charts can be used to display trends in INR values for patients and to assist with dosing oral anticoagulants, especially warfarin.[6]

Education and Information

Staff Education

- Annual competence assessments for clinicians who prescribe, dispense, or administer oral anticoagulants help to ensure clinicians understand different oral anticoagulant medications and their uses in therapy.[6]
- When a new anticoagulant is added to the organization's formulary, notify staff using tools like newsletters and in-services. Studies show that even with continuous offerings for educational programs on therapeutic agents, healthcare professionals find it difficult to keep completely up to date through independent effort. Therefore, providing relevant and reliable information may be helpful.[34]
- When a new oral anticoagulant is added to the organization's formulary, ensure underlying protocols, including oral anticoagulant reversal protocols, are up to date. Organizations may consider proactively developing protocols even if the product is not on formulary in anticipation of a patient being admitted on a target-specific anticoagulant.
- Combining oral anticoagulants with oral antiplatelet agents such as clopidogrel, although potentially useful in some situations, increases bleeding risk, and expertise in therapy management is critical.[35]

Patient Education

- Patient counseling and education provides an opportunity to empower patients to recognize, intercept, and prevent errors. At the onset

of therapy and prior to discharge, provide education to patients who are on anticoagulants. Some of the oral anticoagulants have complex dosing and the potential for serious drug-drug interactions, so it is extremely important for a patient to understand how to take the medication.[16,36] Remind patients that the risks of anticoagulants include bleeding but that there are also risks of clotting from the underlying condition due to inadequate anticoagulation when doses are missed.[16] Tools exist, such as ISMP's patient counseling sheets, which can be shared with patients to help prevent errors with warfarin.[36]

- The patient's ability to afford and purchase oral anticoagulant agents can impact adherence to therapy. Consider involving case management services prior to discharge to prevent situations in which a patient is forced to omit a dose for financial or other reasons.
- Hospitals providing discharge process education also noted it was better for the patient and the hospital team to not delay discharge education until the day of discharge. Organizations are encouraged to plan teaching a couple of days prior to discharge to ensure the care team has adequate time to review and make suggestions for the patient's therapy without being rushed. In addition, this provides the patient with an opportunity to review and ask questions prior to discharge.[37]

Monitoring of Adverse Drug Events

- When errors happen, investigating and sharing them with other clinicians raises awareness on issues surrounding oral anticoagulants.
- Prior potential, near-miss, and harmful event reports may help facilities identify possible errors and areas for improvement.
- Defined adverse drug event triggers such as INR greater than 6, sudden decline in renal function, bleeding, or hypercoagulability may help monitor patients and identify the potential or actual onset of new adverse drug events.[38] Administration of reversal agents such as vitamin K1 and protamine are additional triggers that can be used to identify adverse events during chart review processes.[37]

CONCLUSION

Oral anticoagulants are considered high-alert medications because, when used in error (e.g., dose omission, inappropriate administration), there is a heightened risk of causing significant patient harm (i.e., failure to prevent life-threatening thrombosis, contribution to life-threatening bleeding). While the approval of new oral anticoagulants has provided clinicians and patients with more therapeutic options, the target-specific agents have varied indications and mechanisms of action, and this complexity introduces more opportunities for errors. The errors noted in this article reflect errors that can happen during any stage of therapy, from prescribing through administration. Extra precautions and risk reduction strategies provided in this analysis may help hospitals minimize the occurrence of oral-anticoagulant-related adverse events.

NOTES

1. Office of Inspector General (OIG). US Department of Health and Human Services. Adverse events in hospitals: national incidence among Medicare beneficiaries [online]. Report no. OEI-06-09-00090. 2010 Nov [cited 2015 Apr 10]. http://oig.hhs.gov/oei/reports/oei-06-09-00090.pdf
2. Budnitz DS, Pollock DA, Weidenbach KN, et al. National surveillance of emergency department visits for outpatient adverse drug events. JAMA 2006 Oct 18;296(15):1858-66.
3. Davidsen F, Haghfelt T, Gram LF, et al. Adverse drug reactions and drug non-compliance as primary causes of admission to a cardiology department. *Eur J Clin Pharmacol* 1988;34(1):83-6.
4. Bordet R, Gautier S, Le Louet H, et al. Analysis of the direct cost of adverse drug reactions in hospitalised patients. *Eur J Clin Pharmacol* 2001 Mar;56(12):935-41.
5. Institute for Safe Medication Practices. ISMP list of high-alert medications in acute care settings [online]. 2014 [cited 2014 Dec 15]. http://www.ismp.org/Tools/institutionalhighAlert.asp
6. Institute for Safe Medication Practices. High-alert medication feature: anticoagulant safety takes center stage in 2007. [online]. ISMP Med Saf Alert Acute Care 2007 Jan 11 [cited 2014 Dec 15]. http://www.ismp.org/Newsletters/acutecare/articles/20070111.asp
7. National Quality Forum. Patient safety measures [online]. 2014 [cited 2014 Dec 15]. http://www.qualityforum.org/ProjectMeasures.aspx?projectID=73701
8. Dunn SP, Kazmi H. New oral anticoagulants: implications for health systems [online]. Pharmacy Times 2013 Jul 22 [cited 2014 Dec 15]. http://www.pharmacytimes.com/publications/health-system-edition/2013/July2013/New-Oral-Anticoagulants-Implications-for-Health-Systems
9. Joint Commission. National Patient Safety Goals effective January 1, 2015 [online]. 2015 Jan 1 [cited 2015 Jan 2]. http://www.jointcommission.org/assets/1/6/2015_NPSG_HAP.pdf
10. Piazza G, Nguyen TN, Cios D, et al. Anticoagulation-associated adverse drug events. *Am J Med* 2011 Dec;124(12):1136-42.

11. Budnitz DS, Lovegrove MC, Shehab N, et al. Emergency hospitalizations for adverse drug events in older Americans. *N Engl J Med* 2011 Nov 24;365(21):2002-12.
12. Bristol-Myers Squibb. Coumadin® (warfarin sodium) [prescribing information online]. 2011 Oct [cited 2014 Dec 15]. http://packageinserts.bms.com/pi/pi_coumadin.pdf
13. Janssen Pharmaceuticals, Inc. Xarelto® (rivaroxaban) prescribing information [online]. 2014 Sep [cited 2014 Dec 15]. http://www.xarelto hcp.com/sites/default/files/pdf/xarelto_0.pdf
14. Bristol-Meyers Squibb. Eliquis® (apixaban) [prescribing information online]. 2014 Aug [cited 2014 Dec 15]. http://packageinserts.bms.com/pi/pi_eliquis.pdf
15. Boehringer Ingelheim Pharmaceuticals, Inc. Pradaxa® (dabigatran etexilate mesylate) [prescribing information online]. 2014 Sep [cited 2014 Dec 15]. http://bidocs.boehringer-ingelheim.com/BIWebAccess/ViewServlet.ser?docBase=renetnt&folderPath=/Prescribing%20Information/PIs/Pradaxa/Pradaxa.pdf
16. New oral anticoagulants for acute venous thromboembolism. *Med Lett Drugs Ther* 2014 Jan 6;56(1433):3-4.
17. Darves B. No antidote: reversal strategies for newer anticoagulants [online]. 2013 May [cited 2014 Dec 15]. http://www.todayshospitalist.com/index.php?b=articles_read&cnt=1671
18. National Coordinating Council for Medication Error Reporting and Prevention. NCC MERP index for categorizing medication errors [online]. 2001 Feb [cited 2014 Dec 15]. http://www.nccmerp.org/medErrorCatIndex.html
19. Hold on to these orders. PA PSRS Patient Saf Advis [online] 2006 Mar [cited 2014 Dec 15]. http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2006/Mar3%281%29/documents/33.pdf
20. Cohen MR, Smetzer JL, Tuohy NR, et al. High-alert medications: safeguarding against errors. Chapter 14. In: Cohen MR, ed. *Medication errors*. 2nd ed. Washington (DC): American Pharmacists Association; 2007.
21. Institute for Safe Medication Practices. Medication error prevention "toolbox." *ISMP Med Saf Alert Acute Care* 1999 Jun 2;4(11):1.
22. Cohen MR. Preventing prescribing orders. Chapter 9. In: Cohen MR, ed. *Medication errors*. 2nd ed. Washington (DC): American Pharmacists Association; 2007:190-2.
23. Galanter WL, Didomenico RJ, Polikaitis A. A trial of automated decision support alerts for contraindicated medications using computerized physician order entry. *J Am Med Inform Assoc* 2005 May-Jun;12(3):269-74.
24. Michaels AD, Spinler SA, Leeper B, et al. Medication errors in acute cardiovascular and stroke patients: a scientific statement from the American Heart Association. *Circulation* 2010 Apr 13;121(14):1664-82.
25. Cohen MR. Preventing prescribing orders. Chapter 9. In: Cohen MR, ed. *Medication errors*. 2nd ed. Washington (DC): American Pharmacists Association; 2007:187.
26. Streiff MB, Kraus PS, Pronovost P. Pennywise, pound-foolish? Highmark Medicare Services' proposal for anticoagulation clinic reimbursement. *Ann Pharmacother* 2010 Apr;44(4):733-6.
27. Ansell J, Hirsh J, Hylek E, et al. Pharmacology and management of the vitamin K antagonists. *Chest* 2008 Jun;133(6 Suppl):160S-198S.
28. Anticoagulation management service: safer care, maximizing outcomes. Pa Patient Saf Advis [online] 2008 Sep [cited 2014 Dec 15]. http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2008/Sep5(3)/Pages/81.aspx
29. Pennsylvania Patient Safety Authority. Pennsylvania Hospital Engagement Network: organization assessment of safe anticoagulant practices [online]. 2014 [cited 2015 Jan 7]. http://www.patientsafetyauthority.org/EducationalTools/PatientSafetyTools/ams/Documents/assessment.pdf
30. Joint Commission. Standard MM.04.01.01. In: *Comprehensive accreditation manual for hospitals*. Update 2. Oakbrook Terrace (IL): Joint Commission Resources; 2015 Jan.
31. Institute for Safe Medication Practices. Use of "NoAC" abbreviation. *ISMP Med Saf Alert Acute Care* 2013 Dec 12;18(25):2-3.
32. Institute for Safe Medication Practices. Guidance on the interdisciplinary safe use of automated dispensing cabinets [online]. 2008 [cited 2015 Apr 9]. http://www.ismp.org/tools/guidelines/ADC/ADC_Guidelines_Final.pdf
33. Medication errors occurring with the use of bar-code administration technology. Pa Patient Saf Advis [online] 2008 Dec [cited 2015 Apr 9]. http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2008/Dec5(4)/documents/122.pdf
34. Routledge PA, O'Mahony MS, Woodhouse KW. Adverse drug reactions in elderly patients. *Br J Clin Pharmacol* 2004 Feb;57(2):121-6.
35. Holmes DR Jr, Kereiakes DJ, Kleiman NS, et al. Combining antiplatelet and anticoagulant therapies. *J Am Coll Cardiol* 2009 Jul 7;54(2):95-109.
36. Institute for Safe Medication Practices. Medication safety tools [online]. 2014 [cited 2014 Dec 15]. http://www.consumermedsafety.org/tools-and-resources/medication-safety-tools-and-resources
37. Martin ES 3rd, Overstreet RL, Jackson-Khalil LR, et al. Implementation of a specialized pharmacy team to monitor high-risk medications during discharge. *Am J Health Syst Pharm* 2013 Jan 1;70(1):18-21.
38. Rozich JD, Haraden CR, Resar RK. Adverse drug event trigger tool: a practical methodology for measuring medication related harm. *Qual Saf Health Care* 2003 Jun;12(3):194-200.

PENNSYLVANIA PATIENT SAFETY ADVISORY

This article is reprinted from the Pennsylvania Patient Safety Advisory, Vol. 12, No. 2–June 2015. The Advisory is a publication of the Pennsylvania Patient Safety Authority, produced by ECRI Institute and ISMP under contract to the Authority.

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