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Improving Heparin Safety

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National Conference on Heparin Safety

The ninth invitational conference at the CareFusion Center for Safety and Clinical Excellence in San Diego, held on March 13 through 14, 2008, brought together more than 40 anticoagulation experts and practitioners to share information, offer perspectives and address issues on the topic of improving heparin safety. The day and a half of presentations and round-table discussions included individuals representing The Joint Commission, United States Pharmacopoeia, the Institute for Safe Medical Practices, academic institutions, large health care systems and small hospitals. This conference report summarizes 21 presentations by nationally recognized experts on the types and frequency of heparin errors, National Patient Safety Goals, impact of smart infusion technology, laboratory and nursing issues and identified opportunities to improve heparin safety. The proceedings were edited by Philip J. Schneider, MS, FASHP; at time of conference: Clinical Professor and Director, Latiolais Leadership Program, College of Pharmacy, The Ohio State University, Columbus, OH; at time of publication: Clinical Professor and Associate Dean, University of Arizona College of Pharmacy, Phoenix Biomedical Campus, Phoenix, AZ.

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PROCEEDINGS

Medication Errors Involving Heparin: Findings from a National Reporting Program

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Key points

- *Heparin has been one of the most commonly reported products involved in errors and one of the leading medications involved in harmful errors.*
- *The majority of heparin errors originate during administration and nursing staff were most frequently involved.*
- *Compared to the general error data set, there are fewer problems with prescribing heparin therapy but more problems with preparing/dispensing or administering the correct dose.*
- *Frequently occurring problems included:*
  - *Incorrect infusion rates as a result of incorrectly programming an intravenous (IV) infusion pump*
  - *Infusion rate switches with another large-volume infusion*
  - *Order incorrectly entered by pharmacy*
  - *Staff unfamiliar with heparin protocols*
  - *Incomplete documentation on medication administration record*
  - *General IV pump programming errors*
- *Any discussion of implementing new policies, procedures or protocols for heparin use should evaluate their potential for increasing the opportunities for error events.*

Medication errors involving anticoagulants, especially heparin, are common[1-3]. Heparin has been one of the most commonly reported products involved in errors overall and one of the leading medications involved in harmful errors, according to previous MEDMARX® reports published by the United States Pharmacopeia (USP)[4-6].

USP MEDMARX® data findings

More than 17,000 heparin medication errors were reported to the USP's MEDMARX® program during a five-year period from 2003 to 2007. Of these, 556 errors (3.1%) resulted in harm to patients, including seven deaths (Table 1). The average percentage of harm for error reports submitted to MEDMARX® has been approximately 1.5%, indicating that when heparin is involved, it may be twice as likely to result in harm.

Analysis of the reported heparin errors provided information about where in the medication use process they originated and the most frequent types and causes associated with these events. The majority (47.6%) of heparin errors originate in administering the medication, followed by 18.8% in transcribing the order, 14.1% in prescribing the product, 13.9% in dispensing functions and 5.4% in patient/laboratory monitoring activities. Nursing staff were most frequently involved with heparin errors (60%), followed by pharmacy staff (14%) and prescribers (13%).

The three most frequently reported types of error were wrong dose, omission and prescribing error, comprising nearly 70% of all

Table 1. Severity of heparin errors

Error Category [a]	% [b]
Potential error	
Category A (n=628)	3.5
Error, no harm	
Category B (n=5,130)	28.5
Categories C-D (n=11,661)	64.9
Error, harm	
Categories E-I (n=556) (7 fatalities)	3.1

a. For complete definitions of the NCC MERP Error Category Index, see www.nccmerp.org
b. Based on 17,975 records for the period of Jan. 2003 – Dec. 2007.

Table 2. Most frequently reported types of error involving heparin[a]

Type of Error[a]	n	%[b]	MEDMARX® Overall %[c]
Wrong dose/quantity	6,482	36.5	21.7
Omission error	4,203	23.7	20.7
Prescribing error	2,259	12.7	18.4
Unauthorized/wrong drug	1,926	10.8	12.2
Extra dose	1,018	5.7	5.3
Wrong time	992	5.6	6.3
Wrong administration technique	627	3.5	1.4
Wrong patient	575	3.2	4.7
Drug prepared incorrectly	423	2.4	2.8
Wrong route	355	2.0	1.4
Wrong dosage form	233	1.3	2.5

a. USP's MEDMARX® program tracks 14 different types of error. Only the 10 most frequently reported involving heparin are shown.
b. Based on 17,756 records for the period of Jan. 2003 – Dec. 2007
c. Based on 1,108,803 records for the period of Jan. 2003 – Dec. 2007

error type selections (Table 2). These error types are also frequently among the leading types of error in the general MEDMARX® data set. There were, however, differences between the general error data set and the sub-set of heparin errors for several types including wrong dose (21.7% vs. 36.5% for heparin errors) prescribing error (18.4% vs. 12.7% for heparin errors) and wrong administration technique (1.4% vs. 3.5% for heparin errors). This suggests there are fewer problems with prescribing heparin therapy, but more problems either in the pharmacy or by nursing staff with preparing/dispensing or administering the correct dose. Many of the wrong administration technique errors involved problems with programming and using an intravenous (IV) infusion pump.

Most patient safety experts agree that error events are the result of multiple causes. Among the nearly 70 different causes of errors tracked in the MEDMARX® program, the leading causes associated with heparin errors were performance deficit, procedure/ protocol not followed and communication (Table 3). Performance deficit is often cited in combination with procedure/ protocol not followed, indicating a logical inter-connection between them. Contributing factors such as distractions, inexperienced staff and workload increase are often cited in reports when performance deficit or procedure/protocol not followed are listed as error causes. This may explain their high ranking among the numerous possible causes that a reporter may select.

Other causes frequently reported with heparin errors were knowledge deficit, documentation and transcription inaccurate/omitted. These findings point to areas where safety improvements are needed. Discussions of implementing new procedures/protocols on heparin use should examine errors associated with failing to follow current procedures/ protocols and communications between prescribers, nurses and pharmacists, to avoid introducing new error opportunities.

Selected heparin error reports

Case #1:

A patient being administered a heparin infusion at 1,000 units/hr via an IV pump was transported to radiology for an MRI. The nurse in radiology discontinued use of the pump and regulated the heparin infusion with a manual flow device but inadvertently altered the heparin infusion rate so that the patient received 20,000 units (8,000 units/hr). A stat-activated partial thromboplastin time was performed and the heparin infusion held.

Table 3. Most frequently reported causes of error involving heparin[a]

Cause of Error[a]	n	%[b]
Performance Deficit	7,845	43.1
Procedure / Protocol not followed	5,175	28.4
Communication	2,578	14.2
Knowledge deficit	2,078	11.4
Documentation	1,900	10.4
Transcription inaccurate/omitted	1,776	9.8
Computer entry	1,681	9.2
Calculation error	1,301	7.1
Monitoring inadequate/lacking	1,191	6.5
Pump, improper use	980	5.4

a. USP's MEDMARX® program tracks nearly 70 different types of error. Only the 10 most frequently reported involving heparin are shown.
b. Based on 17,572 records submitted to MEDMARX® during the period Jan. 2003 – Dec. 2007

Fortunately, the patient did not experience any significant sequelae.

Case #2:

A patient returned from a procedure in the cardiac catheterization laboratory arrived on the nursing unit with an infusion of tissue plasminogen activator and heparin. Heparin (50 units/mL) was ordered at a rate of 16 mL/hr but was found to be infusing at a rate of 166 mL/hr (8,300 units/hr). The physician was contacted and the heparin infusion held for one hour and then resumed at the ordered rate. Partial thromboplastin time three hours later was 182. The error led to temporary harm and the primary cause was improper use of the IV pump.

Case #3:

A patient presented in the emergency room, was given a heparin bolus and started on a heparin infusion. The patient was transferred to the coronary care unit where a physician, unaware that the patient was on a heparin infusion, ordered enoxaparin. Later an on-call physician, unaware that the patient was receiving the enoxaparin, ordered another dose of the heparin infusion. The nurse who received the physician's call did not inform him of the patient's other medications. The patient received both heparin and enoxaparin for 15 hours, leading to a drop in the patient's hemoglobin and hematocrit, shortness of breath and rales. The patient was given a blood transfusion and placed on a ventilator. The causes of error were reported as failures in communication and not following procedures and protocols.

Common error scenarios

Based on a review of several hundred reported error events, frequently occurring problems included:

- Incorrect infusion rates (generally by a factor of 10) as a result of incorrectly programming an IV pump (e.g., 60 units/hr vs 6 units/hr)
- Infusion rate switches with another large-volume infusion (e.g., heparin rate and a standard hydration infusion), especially during patient transfers from their primary unit to other areas such as radiology or the cardiac catheterization laboratory
- Order incorrectly entered by pharmacy, leading to an incorrect concentration being prepared and infused
- Staff unfamiliar with heparin protocols, leading to inadequate monitoring
- Incomplete documentation on medication administration record (MAR), leading to unclear or omitted information on rate, when infusion started, among others
- General IV pump programming errors

Conclusion

Heparin therapy is commonly associated with safety problems and the potential for medication errors. Data submitted to the USP's MEDMARX® program can help identify where safety risks exist and how current practices contribute to error events. Any discussion of implementing new policies, procedures or protocols for heparin use should evaluate their potential for increasing the opportunities for error events.

References

1. Fanikos J, et. al. Medication errors associated with anticoagulant therapy in the hospital. *Am J Cardiol* Aug 15 2004;94(4):532-5.
2. Winterstein AG, et. al. Identifying clinically significant preventable adverse drug events through a hospital's database of adverse drug reaction reports. *Am J Health Syst Pharm* Sep 15 2002;59(18):1742-9.
3. Errors Involving Drug Products Used to Treat Cardiovascular Diseases: Part III. USP *CAPSLink Newsletter*. May 2005. Retrieved on June 30, 2008 from http://www.usp.org/pdf/EN/patientSafety/capsLink2005-05-01.pdf.
4. Hicks RW, Becker SC, Cousins DD. MEDMARX® data report. A report on the relationship of drug names and medication errors in response to the Institute of Medicine's call for action. Rockville, MD: Center for the Advancement of Patient Safety, US Pharmacopeia; 2008.
5. Hicks RW, Becker SC, Cousins DD. MEDMARX® data report: A Chartbook of Medication Error Findings from the Perioperative Settings from 1998-2005. Rockville, MD: Center for the Advancement of Patient Safety, US Pharmacopeia; 2006.
6. Santell JP, Hicks RW, Cousins DD. MEDMARX® data report: A Chartbook of 2000-2004 Findings from Intensive Care Units and Radiological Services. Rockville, MD: Center for the Advancement of Patient Safety, US Pharmacopeia; 2005.

PROCEEDINGS

The Joint Commission's Anticoagulant-related National Patient Safety Goals

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Key points

- *In 2008, the Joint Commission added a requirement to the National Patient Safety Goals (NPSG 3E, renamed NPSG 03.05.01) that organizations implement a defined anticoagulation management program to individualize care provided to each patient receiving anticoagulation therapy.*
- *NPSG 03.05.01 is currently limited to warfarin, heparin and the low-molecular-weight heparins and does not address anti-platelets, heparinoids or other anticoagulants.*
- *Implementation of NPSG 03.05.01 is effective as of January 1, 2009 and organizations will be scored on 9 elements of performance related to this goal.*
- *NPSG 03.05.01 will be evaluated and scored by Joint Commission surveyors and results will be publicly disclosed on the Joint Commission's website.*

In 2008 the Joint Commission added a requirement to the National Patient Safety Goals (NSPG 3) that organizations implement a defined anticoagulation management program to individualize care provided to each patient receiving anticoagulation therapy (Table 1). There are nine elements of performance (EPs) associated with this requirement that will be evaluated and scored by Joint Commission surveyors. To meet NPSG 03.05.01, an organization must be in compliance with all nine EPs as of January 1, 2009. Detailed interpretations of the EPs can be found in the FAQs on the Joint Commission website[1].

This article includes a discussion of Joint Commission goals and standards and a brief review of the EPs for NPSG 03.05.01 for anticoagulation therapy, particularly unfractionated heparin and low-molecular-weight heparin (LMWH).

Goals and standards

The Joint Commission's Comprehensive Accreditation Manual for Hospitals contains 16 NPSGs and approximately 475 standards. A primary focus in health care organizations should be on complying with the goals. Each NPSG but not every standard is reviewed on every survey. In addition, compliance with each NPSG is publicly disclosed on the Joint Commission's website, but not performance with each standard. A NPSG is sometimes retired, usually because satisfactory compliance has been demonstrated with accredited organizations, at which point, the NPSG is integrated into the standards.

The NPSGs undergo a multi-committee approval process with extensive input from frontline practitioners. The goals are very prescriptive; however, an organization can propose an alternative approach to meet the intent of the goal. Proposed alternatives are reviewed on a case-by-case basis by the same expert panel that developed the goal.

NPSG 03.05.01

This new requirement applies only to organizations that provide anticoagulation therapy. This usually includes most hospitals. An ambulatory care organization in which anticoagulant medications are not pre-

Table 1. National Patient Safety Goal 3: Improve the safety of using medications

- Requirement 03.05.01: Reduce likelihood of patient harm associated with the use of anticoagulant therapy
- Elements of Performance (EPs); surveyors' score
- FAQs: interpret and refine EPs
- Must be reviewed on every survey (unlike standards)
- Results are publicly disclosed
- Effective January 1, 2009

scribed, dispensed or administered is not subject to the goal, even though patients who are being treated with warfarin may be cared for and have a clinical pharmacist who is responsible for monitoring therapy. Requirement 03.05.01 is currently limited to warfarin, heparin and LMWH and does not include anti-platelets, heparinoids or other anticoagulants. The focus is on the therapeutic use of anticoagulants, not catheter flushes or short-term prophylactic use of these medications, where the intent is to keep laboratory tests within the normal range.

NPSG 03.05.01: EPs

For any NSPG requirement, the first and last EPs serve as bookends that begin with program implementation and end with program evaluation.

1. *The organization implements a defined anticoagulation management program to individualize care provided to each patient receiving anticoagulation therapy.*

For NSPG 03.05.01, the first EP is that a hospital has a defined program; that is, a written description of the program.

2. *To reduce compounding and labeling errors the organization uses ONLY oral unit-dose products, prefilled syringes and pre-mixed infusions when these products are available*.

For inpatients, the Joint Commission requires the use of a unit-dose product when it is commercially available from a manufacturer in that form. The pharmacy must purchase the manufacturer's product; the only exception is when all medications are packaged by a robot. When available, the use of infusions premixed by the manufacturer are also required. For example, a pharmacy cannot prepare a 10,000-unit/L bag, because that product is commercially available. Except for pediatrics, the manufacturer's prefilled syringe must be used, but only if the dose ordered is equivalent to the dose in the syringe.

3. *The organization uses approved protocols for initiation and maintenance of anticoagulation therapy appropriate to the medication used, to the condition being treated, and to the potential for drug interactions.*

The Joint Commission has received many questions about how specific protocols need to be. Protocols should allow for variability in clinical decision making, but have standardization of practices, such as how treatment is monitored, when and by whom. The protocol should be viewed as a guideline, and is similar to a standardized sliding scale for insulin therapy, with additional components for laboratory testing, monitoring activities, etc. The goal of the protocol is to reduce adverse drug events. The protocol should include the roles of nurses and pharmacists, not just physicians. The protocol should also address rescue and response to adverse drug reactions.

4. *For patients being started on warfarin a baseline international normalized ratio (INR) is available and for all patients receiving warfarin therapy, a current INR is available and is used to monitor and adjust therapy.*

This EP specifies the use of the INR to monitor warfarin therapy. Pharmacists cannot dispense warfarin unless there is a baseline INR or current INR to determine that the dose is appropriate for a particular patient. Note: the Joint Commission considers a baseline INR as an INR taken before the patient is being treated with warfarin. It does not mean an admission INR, when the patient is already being treated with warfarin. The organization needs to define how current an INR is required before admission to be used in allowing warfarin dosing.

5. *When dietary services are provided, the service is notified of all patients receiving warfarin and responds according to its established food-drug interaction program.*

If there is a dietary service (specifically clinical dietitians), they must be notified of all patients being treated with warfarin, regardless of whether the dietary department responds with diet changes or not.

6. *When heparin is administered intravenously and continuously, the organization uses programmable infusion pumps.*

Although most hospitals use programmable pumps, many dial-a-flow and gravity pumps are still used in home care.

7. *The organization has a policy that addresses baseline and ongoing laboratory tests that are required for heparin and LMWH therapies.*

Organizations are allowed to specify which tests they use to monitor heparin and LMWH. Use of anti-Xa activity to monitor LMWH is not required. Small and rural hospitals often do not have that capability and may use platelets or complete blood counts to monitor LMWH therapy. The medical staff will decide about the laboratory tests that will be used at each organization. The expectation is that tests are available and a written policy defines how they are to be used and how anticoagulant therapy is to be monitored.

8. *The organization provides education regarding anticoagulation therapy to prescribers, staff, patients and family.*

An organization must ensure that prescribers are well informed about the latest developments in anticoagulation therapy and their protocols. Staff members including nurses, dietitians and pharmacists should receive in-service training and patients and families should receive appropriate education including the importance of follow-up monitoring, compliance issues, dietary restrictions, and potential for adverse drug reactions (ADRs) and interactions. Preprinted education materials need to be reviewed for inclusion of these components. If missing, supplemental information may be needed.

9. *Organization evaluates anticoagulation safety practices, takes appropriate action to improve its practices and measures the effectiveness of those actions on a regular basis.*

The final EP is to have a process for ongoing measurement and assessment of the quality of anticoagulant therapy and a continuous improvement program.

Related NPSGs

Other NPSGs related to anticoagulation therapy are shown in Table 2. NPSG 01.01.01 requires identifying the patient before giving the medication by using two unique patient identifiers, not just the room number. Surprisingly often, this is not done. NSPG 02.02.01 requires that a verbal order for heparin be read back to the prescriber.

Using medical abbreviations (NPSG 02.02.01) is one of the most frequent areas of non-compliance. One organization was certain they had solved their medication abbreviation problem and challenged the Joint Commission surveyor to find one "U" anywhere in their charts. About 500 "U"s were found.

Organizations are required to define the timeframe for reporting a critical test result (NPSG 02.03.01). For example, if an INR were extremely abnormal, how quickly can the physician be notified? A program to measure, assess and approve the timeliness of reporting must be implemented. This is the most frequent non-compliant NPSG.

Organizations also are frequently non-compliant with NPSG 02.05.01, which requires using a standardized approach to ensure hand-off communications including medications, especially if a patient is being treated with heparin.

NPSG 03.03.01 addresses medications that look and/or sound alike. There are other medications that look like or have names that sound similar to heparin and organizations are required to have these medications on a list of such agents to have interventions to prevent errors.

NPSG 03.04.01 requires organizations to label all medication solutions in procedural areas. Non-compliance is frequently observed in cardiac catheterization laboratories, such as flush solutions that are drawn from a bag of heparin and syringes that are not labeled.

Medication reconciliation is required by NPSG 8. Finally, NPSG 13 requires that patients be encouraged to be involved in their own safety and to report any issues they see.

Table 2. Related NPSG Requirements

- NPSG 01.01.01: Use at least two patient identifiers.
- NPSG 02.01.01: Read back of verbal orders.
- NPSG 02.02.01: Do not use abbreviations (e.g., "U" for units, leading or trailing zero).
- NPSG 02.03.01: Report critical tests and critical test result values in a timely manner.
- NPSG 02.05.01: Use a standardized approach to handoff communications, including an opportunity to ask and respond to questions.
- NPSG 03.03.01: Annual review a list of look-alike, sound-alike drugs used by the organization and take action to prevent errors involving the interchange of these drugs.
- NPSG 03.04,01: Label all medications and solutions in procedural areas.
- NPSG 8: Accurately and completely reconcile medications across the continuum of care.
- NPSG 13: Encourage the patient's active involvement in their own care as a patient safety strategy.

Summary

The aim of NPSG 03.05.01 is to reduce the likelihood of patient harm associated with anticoagulant therapy and is effective January 1, 2009. This new requirement has nine EPs, which are explained in the Joint Commission's online FAQs and will be evaluated and scored by Joint Commission surveyors. The results of these surveys will be publicly disclosed on the Joint Commission's website. Among the related NPSGs, hospitals are most often non-compliant with NPSG 02.02.01, 02.03.01 and 02.05.01.

Reference

1. www.jointcommission.org

PROCEEDINGS

Heparin Medication Errors: Failure Modes Associated with Administration

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Key points

- *The Institute for Safe Medication Practices (ISMP) receives and analyzes reports of medication errors, helps develop practice recommendations and advocates for necessary changes to improve patient safety.*
- *High-profile reports of heparin overdoses will likely stimulate changes in product labeling, use of barcode systems and other medication safety technologies.*
- *Based on an analysis of medication error reports, there are many well known reasons for heparin errors.*
- *The **ISMP Medication Safety Self Assessment® for Antithrombotic Therapy for Hospitals** allows hospitals to assess safety and compare their performance to other organizations.*
- *Being proactive in addressing heparin medication issues is important to improving the safety and quality of therapy.*

The Institute for Safe Medication Practices (ISMP) operates a unique national voluntary reporting program for medication errors. Front-line practitioners and consumers can contact ISMP to tell their story. ISMP analyzes not data but stories, and uses the information to help develop evidence-based, peer-reviewed practice recommendations. With ongoing communication with practitioners, regulatory authorities and the pharmaceutical industry, ISMP advocates for necessary changes to improve medication use and safety.

ISMP also works with a unique mandatory state reporting program, the Pennsylvania Patient Safety Reporting Program. State statute mandates that all hospitals, birthing centers, surgery centers and other facilities submit incident reports. ISMP receives all the medication-related reports and can contact the facilities, as necessary. This allows the investigation of anecdotal reports and data to identify issues in ways that cannot be done with a voluntary practitioner reporting program. As partners in the Food and Drug Administration's (FDA) MedWatch program, ISMP also shares narrative and other forms of information with the FDA.

Recent events such as the heparin overdose administered to the infant twins of actor Dennis Quaid and his wife received extensive media attention and will likely affect the entire industry by stimulating changes in product labeling and the acquisition of barcode systems to help to prevent product mix-ups. The use of other technologies such as smart pumps and computerized prescriber order entry (CPOE) also continues to grow. In 2007, more than 40% of hospitals now had acquired smart pumps and about 22% had barcode systems[1].

The Quaids decided to sue the pharmaceutical manufacturer for providing containers that allegedly looked alike—this was the first time that a pharmaceutical company was sued specifically for this reason. That this was not the first such incident undoubtedly played a role in their decision to sue. Today, there has been a significant change in the appearance of the higher-concentration heparin vial (Figure 1). The FDA is now requesting that other heparin manufacturers adopt enhanced labeling, which will probably be requested for other medications, as well. These changes, along with barcoding, should help to reduce a problem that has been talked about for years.

A major issue is the need to be proactive, not reactive. After the first incident at an Indiana hospital, the pharmaceutical company had sent out a "Dear Pharmacy Director" letter and ISMP had issued warnings and written about this potential for potentially life–threatening error. Necessary information is available from many sources. Not paying attention, not acting on this information is, unfortunately, all too often the norm. This is an important issue in addressing the problems seen today.

Root causes

Look-alike labeling is not the only issue when product mix-ups occur. ISMP analysis has identified the following as some of the root causes of common errors and those that have led to fatalities.

Failed check systems

High-risk medication errors are also related to failures in medication distribution, storage, check systems and documentation. Issues such as poor lighting, e.g., working in dark areas, have contributed to difficulties in reading labels. Whether the medication was stored in an automated dispensing cabinet or satellite pharmacy, the check system failed.

Confirmation bias

In at least one of the recent heparin incidents, confirmation bias was a major issue. An area of the automated dispensing cabinet had always held the appropriate 10 unit/mL vials and confirmation bias led the clinician to see what was expected, not what was there.

Preparation of critical medications on the nursing unit

These issues also reinforce the need to stop preparation of critical medications, especially high-alert drugs, on the nursing units, except in extreme emergencies. However, when ISMP is called to respond to a sentinel event or to consult at hospitals, drug preparation on the nursing units is frequently seen, despite recommendations by ISMP and the Joint Commission that discourage the practice.

Duplicate or concurrent therapy

This is still a serious problem, even though it has been lessened by medication reconciliation and safety software such as CPOE. People still come into the emergency room, receive LMWH and about an hour later upon transfer to an inpatient area are placed on heparin, which has led to fatal hemorrhages. One reason is that the emergency department's (ED) software is separate from the rest of the hospital. Even if the ED uses automated dispensing cabinets and the charge is captured, that information is not sent to the pharmacy computer system, so no alert is generated for duplicate therapy. Medication reconciliation appears to have reduced this danger. Improved software and 23-hour admissions that use the pharmacy computer system are very helpful. Recommendations for addressing duplicate therapy are shown in the Table.

Accidental discontinuation of therapy

Medication reconciliation is an important aspect for addressing this issue. Many hospitals regularly print out a list of medications the patient is receiving, but medical staff does not understand how important it is to review this information. Pushing for greater compliance in this regard could help prevent this type of error.

Look-alike vials or syringes

These types of errors include mix-ups among various concentrations of heparin packaged in vials or bags, mix-ups between heparin vials and other look-alike vials (e.g., insulin, saline), mix-ups between heparin flush syringes and other look-alike syringes (e.g. saline flush, low molecular weight heparin [LMWH]) and confusion between look-alike bags of IV heparin, lidocaine and Hespan (hetastarch). Different concentrations of other drugs are also confused as the result of problems in labeling, similar colors and similar look to the rubber target. The ISMP has used findings from the reporting program to go to the pharmaceutical companies and advocate for change, which, over the years, has resulted in major changes in labeling and packaging of both syringes and IV bags (Figure 2).

Table. Addressing Duplicate Therapy

- Computer alerts for duplicate therapy
- Carefully consider current and recent drug therapy before ordering, dispensing and administering any heparin product.
- Protocols, guidelines and standard order forms (including those used for cardiac catheterization) should prominently remind practitioners to assess all drug therapy to avoid concomitant use.
- One hospital told us that they affix alert stickers stating, "Patient on low molecular weight heparin," to the front of the chart to help communicate this information to all who provide care to the patient.

Figure 1. Old and New Labeling: Hep-Lock 10 units/mL and Heparin 10,000 units/mL

Packaging-related problems

A former packaging concept used by some manufacturers was a specially designed IV bag that separates the active drug from the diluent to avoid stability problems with dextrose. To treat patients with pulmonary embolism or deep vein thrombosis, a clinician had to fracture a piece of plastic to allow the drug to go into the diluent. If this is not done, only plain diluent goes to the patient.

Syringes such as those for Lovonox are

Figure 2. Old and New Labeling for IV Heparin

packaged as unit doses, e.g., 30 mg, but do not have any scale to use in administering a partial dose, which has led to errors.

IV admixture errors have occurred when the hospital standard concentration of a commercially available product is not used. Dosing charts and smart pumps can help eliminate many serious problems with this issue, but in some organizations nurses continue to mix heparin on the patient care unit.

Unsafe abbreviations

Use of "U" for "unit" can lead to 6U being confused with 60, 4U with 44 and 25cc/hr with 25 units/hr (Figure 3). Confusing 1000U with 10,000 can easily lead to a 10-fold overdose. This type of mistake can be prevented by use of a smart pump drug library.

Verbal order not read back

"Read back" is one of the National Patient Safety Goals. The order shown in Figure 4 was transcribed so that "10U" was legible as "10 units," but the order was not read back to the prescriber. Read back, it would have been apparent that for a patient with a blood sugar of 324, the correct medication would be insulin, not heparin.

Nomenclature issues

Confusing "HEPARIN" and "HESpan" is common. Hetastarch, the generic name for Hespan, can be confused if the product is referred to as Hespan. The "h," "e" and "p" are all in the same sequence. If a bag of heparin is accidentally placed in the storage location for hetastarch (Hespan), which is used for volume replacement for shock, selection of the wrong bag could lead to a fatal error. A patient who needs hespan can be in shock because of hemorrhaging. Administering heparin to such a patient is fatal. The error has also happened the other way around, i.e., hetastarch administered in place of heparin.

Insulin-heparin mix-ups

Vials of 100-unit heparin flush and 100-unit insulin are often found together on top of medication carts and counters, contributing to mix-ups. Someone could mistakenly pick up the wrong vial, causing a fatal event. There is a need to minimize or eliminate the availability of heparin flushes, to use unit-dose heparin syringes and to standardize on a single concentration for newborns where it is used for vascular catheter patency, e.g., a 1-unit syringe.

Figure 4. This is your Brain on Call

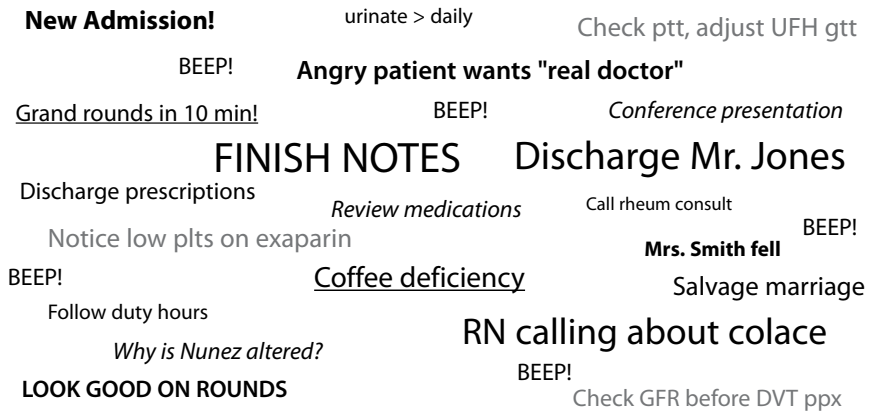


Figure 3. Use of Abbreviation "U" for "units"

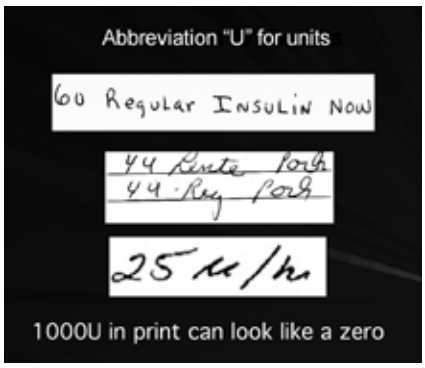
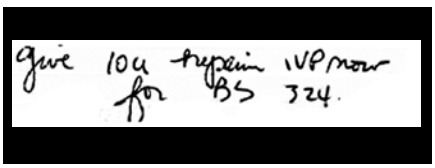


Figure 4. Telephone order not read back



Improper manufacturer labeling

A label can show the concentration of drug per mL but not indicate the total amount of drug in the vials. If a 10-mL vial is labeled "5,000 units/mL," a nurse may read this as a 5,000 unit total, when it actually totals 50,000 units.

Preservatives

Heparin containing benzyl alcohol as a preservative has caused toxicity in newborns.

Dosing errors

Dosing errors can occur if patient weight is not estimated or not verified or if an incorrect nomogram used, e.g., acute cardiac syndrome vs. DVT vs. stroke.

Many calculation errors are listed in the reports sent to ISMP. These include mathematical errors in determining the volume of heparin to use for a bolus or the rate of infusion and miscalculation of the amount of heparin to add to total parenteral nutrition (TPN) solutions.

Dosing errors with infusion pumps can occur when an infusion pump is used to deliver a bolus dose and then not adjusted to a continuous infusion rate, (e.g., administering a 5,000- to 10,000-unit bolus by increasing the infusion rate but forgetting to change the rate back to a 1,000 unit/hr infusion). Other pump programming errors include programming concentration or rate incorrectly. Fortunately, the introduction of smart pumps has helped to address these types of errors.

ISMP Medication Safety Self Assessment®

A free ISMP Medication Safety Self Assessment® for Antithrombotic Therapy for Hospitals is available at www.ismp.org[2]. More than 400 hospitals completed this self-assessment during the first quarter of 2008. The self-assessment was put together with experts from all over the country in hematology, pharmacy practice and nursing. The text lays out the system enhancements that need to be in place, system issues that need to be addressed in order to deliver heparin safely. Hospitals can enter their data, monitor it over time and compare their performance to organizations nationwide.

Conclusion

Heparin errors are both common and a matter of public concern. There are many ways to improve the safety of heparin use in hospitals. The healthcare industry needs to be proactive, not reactive, in taking action to address the many issues that contribute to heparin errors. The necessary information is available from many sources. Paying attention and acting on this information will play a major role in addressing problems and improving the safety and quality of heparin therapy and patient care.

References

1. Pederson CA, Gumpper KF: ASHP National survey on informatics: Assessment of the adoption and use of pharmacy informatics in US hospitals. *Am J Health Syst Pharm*, 2008; 65:2244-64.
2. ISMP Medication Safety Self Assessment for Antithrombotic Therapy in Hospitals. Retrieved October 22, 2008 from http://www.ismp.org/selfassessments/asa2006/Intro.asp.
3. ISMP websites: http://www.ismp.org and http://www.consumermedsafety.org.

PROCEEDINGS

Heparin Medication Safety: Impact of Smart Infusion Technology

John Fanikos, RPh, MBA, Assistant Director of Pharmacy, Brigham and Woman's Hospital, Boston, MA

Key points

- *Adverse drug event surveillance at Brigham and Women's Hospital (BWH) showed that in cardiovascular patients, anticoagulants are the drug class most frequently associated with adverse drug reactions and the second most frequent cause of medication errors.*
- *Unfractionated heparin (UFH) was associated with the greatest number of anticoagulant medication errors, with infusion pump and parenteral delivery problems as the most frequent causes of these errors.*
- *Of the anticoagulant errors, 1.5% of the events prolonged hospitalization and 6.2% required medical intervention.*
- *Continuous quality improvement (CQI) data from smart infusion devices showed that averted UFH overdoses accounted for 29.0% of intercepted UFH medication errors. Dosing errors ranged from 30-999 mL/hr (3,000-99,900 units/hr). Averted UFH underdoses accounted for 20.6% of intercepted UFH medication errors. Dosing errors ranged from 0.1-2.7 mL/hr (10-270 units/hr).*
- *Almost two-thirds of UFH averted errors occurred between noon and 4 p.m., or close to the time of the principal nursing-shift change at 3 p.m. Averted errors were less common on Fridays and during weekends.*
- *For those facilities using smart pump technology, CQI data of infusion-related medication errors should be reviewed promptly to identify opportunities to improve anticoagulant medication safety.*

Adverse drug events (ADE) consist of adverse drug reactions (ADR) and medication errors that result in harm. ADEs can increase costs, generate adverse publicity, compromise patient trust and demoralize hospital staff[1-7]. Analysis of ADEs in specific disease-state populations or medication classes in the hospital setting has been limited[8-12]. Anticoagulation in the hospitalized patient is cited as frequently being associated with medication errors[3-5].

As part of the Drug Safety Surveillance Program at BWH, ADEs in cardiovascular patients were reviewed, errors with anticoagulant medications analyzed and the impact of smart pump technology evaluated[12-14]. Smart pumps with dose-error-reduction software (DERS) may reduce the number of these medication errors.

Overall medication errors vs. anticoagulant errors

In the cardiovascular patients reviewed, ADRs and medication errors occurred with equal frequency (51.1% and 49.1%, respectively). Anticoagulants were the drug class most frequently associated with ADRs including elevations in laboratory monitoring tests, thrombocytopenia and hemorrhage. Anticoagulants were the second most frequent source of medication errors[12]. A review of all anticoagulant errors showed that anticoagulants accounted for 1.72 medication errors per 10,000 patient days[13]. Anticoagulation therapy accounted for 67% of anticoagulant medication errors, while 33% were associated with prophylaxis.

Anticoagulant errors

Among anticoagulant drugs, unfractionated heparin (UFH) was associated with the greatest number of events followed by warfarin, low molecular weight heparin (LMWH), argatroban and lepirudin. The medication error rate for anticoagulants in general was 1.67 per 1,000 patients treated and for UFH, 1.27 events per 1,000 patients treated. Wrong rate or frequency were the most commonly reported errors associated with anticoagulant administration, and most of these were associated with UFH administration.

Infusion pump and parenteral delivery problems were the most frequent proximate cause of anticoagulant medication errors (Figure 1). These errors were only associated with heparin administration. While no deaths were attributed to any of the anticoagulant errors, 1.5% of the events prolonged hospitalization and 6.2% required medical intervention. Many events required an increase in laboratory monitoring but caused no patient harm.

Averted programming errors

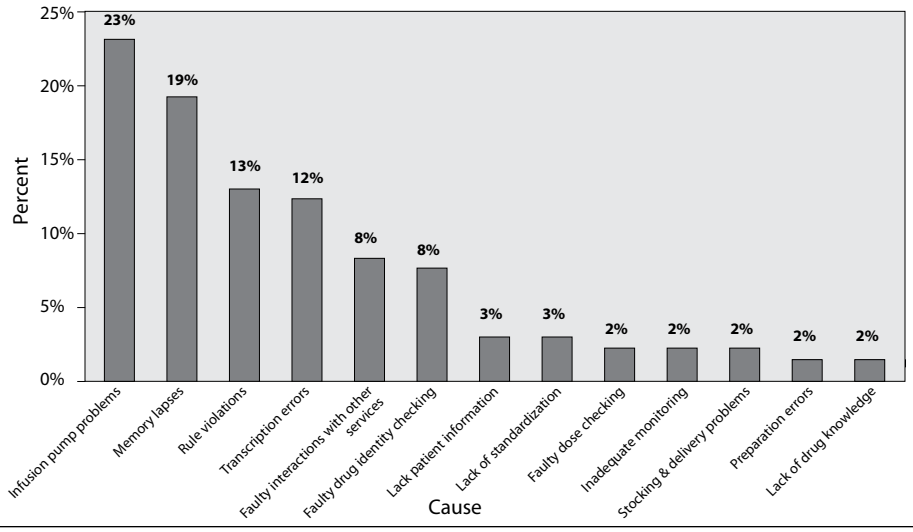
The Alaris® System with Guardrails® software from CareFusion Health (formerly known as the Medley™ Medication Safety System) was implemented at our hospital. This is a smart (computerized) infusion device with a hospital-determined drug library and dose-error-reduction software (DERS). The software drug library contains a list of parenteral medications, their admixture concentrations and approved dosage ranges. If an infusion were programmed for an IV infusion rate or dose that exceeded approved ranges, the software would generate an alert that must be addressed before infusion could begin.

Averted errors were identified by continuous quality improvement (CQI) data showing that a clinician responded to an alert by reprogramming or cancelling and infusion. Over a 16-month period, CQI logs in the safety software documented 7,395 averted errors, 858 (11.6%) of which were triggered by anticoagulant therapy[14]. Of 14,012 heparin doses administered to 3,674 patients, UFH infusion programming in 246 patients generated 501 alerts that were subsequently reprogrammed or the infusion cancelled, i.e., averted errors. "Dose Above Maximum" overdoses accounted for 29.0% of UFH averted errors, and "Dose Below Minimum" underdoses, for 20.6%. UFH averted overdoses ranged from 30-999 mL/hr (3,000-99,900 units/hr) and averted underdoses from 0.1-2.7 mL/hr (10-270 units/hr).

The infusion safety software captured all cases of reprogramming in response to an alert (Figure 2). CQI data showed a 100-fold potential overdose in 40 averted errors (28.5%), 10-fold potential overdose in 40 averted errors (28.5%) and a greater-than-100-fold potential overdose in 10 (6.5%) averted errors. A 100-fold potential underdose would have occurred in 39 (25.2%) and a 10-fold potential underdose in 26 (16.8%) averted errors. Programming errors were frequently duplicated. In 72.8% of averted errors, one alert was sufficient to have the user reprogram the device. However, in 27.2% of averted errors, the user repeated the error in response to the alert, i.e., reprogrammed the device with the same incorrect entry.

The highest percentage (18.2%) of averted errors occurred between 2 p.m. and 4 p.m., and the next-highest (12.7%) between noon and 2 p.m. (Figure 3). These periods coincide with the nursing shift change at 3 p.m. Averted errors were equally common during weekdays Monday through Thursday and had the lowest occurrence on Fridays and during weekends.

Figure 1. Causes of Anticoagulant Errors



Discussion

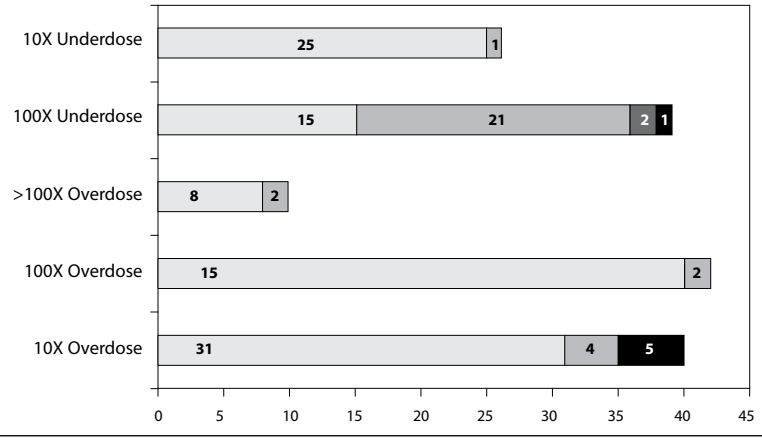
Among cardiovascular patients, ADRs and medication errors are most commonly associated with routinely utilized medications. Anticoagulant therapy, specifically UFH, was a common culprit and perhaps the best target for error-prevention strategies and early recognition of ADRs and medication errors. UFH's broad indications, widespread use, laboratory monitoring and frequent dosing changes make ADEs a common occurrence[9-10].

CQI data showed that heparin medication errors occurred most commonly during drug administration. Infusion device programming errors were identified as the most frequent cause of heparin errors, which influenced the decision to purchase smart infusion devices. Following implementation of these devices, CQI data generated by the safety software showed that programming errors involving incorrect infusion rates or doses are common. Possible explanations for incorrect programming included transcription errors associated with misplaced zero(s) and/or decimal points, and transposition of rate and dose. CQI data showed that smart infusion technology helped to avert such errors, thereby reducing opportunities for anticoagulation over- or underdosing.

A recent study has shown the difficulties in achieving and maintaining therapeutic anticoagulation with UFH[15]. Smart infusion technology may help to achieve these goals by helping to alert staff to incorrect infusion rates and doses. A recently published, prospective, randomized, time-series trial assessed infusion safety devices in critically ill patients. Investigators concluded that the smart pumps could detect IV medication errors and potential ADEs[16].

Averted errors most frequently occurred between 2 p.m. and 4 p.m., a period associated with a relatively high rate of admissions and transfers, nursing shift change and typically the height of medical staff prescrib-

Figure 2. Dosing Errors and their Magnitude



ing. Averted errors occurred with equal frequency during weekdays but with less frequency on Fridays and during weekends. Past studies have found higher medication error rates at the time of hospital admission and during transfer between facilities.[17-18]

Recent studies have suggested a higher patient mortality rate on weekends and correlated nurse staffing levels to quality of care.[19-20] More research is required to determine possible associations between these variables and effective drug use, especially with complex medications such as anticoagulants.

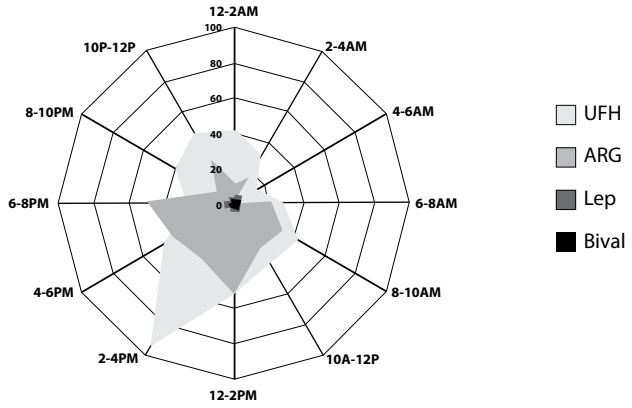
Conclusion

CQI data from BWH smart pumps provide a real-life illustration of IV UFH-related potential ADEs occurring during the routine care of patients and may provide guidance for resource allocation to improve practice to prevent or avoid future events. Smart pump CQI data on infusion medication errors should be reviewed promptly to identify opportunities for rapid response to improve anticoagulant medication safety.

References

1. Bates DW, Cullen DJ, Laird N, et al. Incidence of adverse drug events and potential adverse drug events. *JAMA* 1995;274:29-34.
2. Chyka PA. How many deaths occur annually from adverse drug reactions in the United States? *Am J Med* 2000;109:122-30.
3. Johnson JA, Bootman JL. Drug –related morbidity and mortality: A cost of illness model. *Arch Intern Med* 1995;155:1949-56.
4. Bates DW, Spell N, Cullen DJ, et al. The cost of adverse drug events in hospitalized patients. *JAMA* 1997;277:307-11.
5. Claussen DC, Pestotnik SL, Evans RS, et al. Adverse events in hospitalized patients. Excessive length of stay, extra costs and attributable mortality. *JAMA* 1997;277:301-6.
6. Grant SM. Who's to blame for tragic error? *Am J Nurs* 1999; 99 (9).
7. Brink S. 1995 best hospitals. Tragedy at Dana-Farber. *US News & World Report* 119(4): 53-4, 56, 1995 Jul 24.
8. Landrigan CP, Rothschild JM, Cronin JW, et al. Effect of reducing interns' work on serious medical errors in intensive care units. *N Engl J Med* 2004;351:1838-48.
9. Kaushal R, Bates DW, Landrigan C, et al. Medication errors and adverse drug events in pediatric inpatients. *JAMA* 2001; 285:2114-20.
10. Simpson JH, Lynch R, Grant J, et al. Reducing medication errors in the neonatal intensive care unit. *Arch Dis Child Neonatal Ed* 2004;89:480-2.
11. Mehta RH, Alexander JH, Van de Werf F, et al. Relationship of incorrect dosing of fibrinolytic therapy and clinical outcomes. *JAMA* 2005; 293:1746-50.
12. Fanikos J, Cina JL, Baroletti S, et al. Adverse events in hospitalized cardiac patients. *Am J Cardiol* 2007; 20:1465-9.
13. Fanikos J, Stapinski C, Kucher N, et al. Medication errors associated with anticoagulant therapy in the hospital. *Am J Cardiol* 2004; 94:532-5.
14. Fanikos J, Fiumara K, Baroletti S, et al. Impact of smart infusion technology on administration of anticoagulants (unfractionated heparin, argatroban, lepirudin, and bivalirudin . *Amer J of Cardiol* 2007;(99);7:1002 - 5.
15. Hylek EM, Regan S, Henault LE, et al. Challenges to the effective use of unfractionated heparin in the hospitalized management of acute thrombosis. *Arch Intern Med* 2003;163:621-7.
16. Rothschild JM, Keohane CA, Cook EF, et al. A controlled trial of smart infusion pumps to improve medication safety in critically ill patients. *Crit Care Med* 2005;33:522-40.
17. Cornish PL, Knowles SR, Marchesano R, et al. Unintended medication discrepancies at the time of hospital admission. *Arch Int Med* 2005; 165:424-9.
18. Boockvar K, Fishman E, Kyriacou CK, et al. Adverse events due to discontinuation in drug use and dose changes in patients transferred between acute and long-term care facilities. *Arch Int Med* 2004; 164:545-50.
19. Bell CM, Redelemeier DA. Mortality among patients admitted to hospitals on weekends as compared with weekdays. *N Engl J Med* 2001;345:663-8.
20. Needleman J, Buerhaus P, Mattke S, et al. Nurse-staffing levels and the quality of care in hospitals. *N Engl J Med* 2002;346:1715-22.

Figure 3. Alerts by Time of Day



PROCEEDINGS

Pooled Data from Smart IV Pumps: Review of Heparin Averted Errors and Variability

Tim Vanderveen, PharmD, MS, Vice President, Center for Safety and Clinical Excellence, San Diego, CA

Key points

- *Smart pumps help avert high-risk intravenous (IV) medication errors and provide previously unavailable data on IV medication use.*
- *Wireless networking increases the usefulness of smart pump technology.*
- *Analysis of pooled smart-pump data from many hospitals has identified patterns of errors and unnecessary variability in IV medication practices.*
- *Heparin safety concerns include:*
  - *Mixing dosing units*
  - *Switching from weight-based load/continuous dosing to non-weight based protocols*
  - *Interchanging rates and doses*
  - *Allowing the use of many different heparin concentrations*
  - *Not complying with smart pump use policies*
  - *Bolus dosing from continuous infusion bag (without bolus feature on smart pump)*
  - *Setting smart pump limits that are too narrow*
  - *Delayed restarting of infusions after an order is placed on hold.*
- *Hospitals need to allocate sufficient resources to educate and train staff, maintain system software and identify opportunities to improve IV-medication safety.*

The introduction of smart pumps (computerized intravenous [IV] infusion systems) has helped clinicians avert errors with high-risk IV infusion medications and collect previously unavailable data about IV medication use. Analysis of pooled data from many hospitals makes it possible to identify problems and trends that might not be apparent at individual institutions. These include unnecessary or undesirable variability with IV medication use that increases complexity and opportunities for error. This article presents a brief overview of averted errors, variability and other safety issues associated with the use of IV heparin.

Smart pumps

Traditional infusion pumps can be programmed to deliver any dose at any rate. Smart pumps with dose-error-reduction-software (DERS) allow hospitals to create customized drug libraries with standardized concentrations and pre-established dosage limits based on best practices for infusion of IV medications. If infusion programming is outside drug-library limits, the software generates an alert that must be addressed before infusion can begin.

The software also logs when a clinician reprograms or cancels an infusion in response to an alert (averted error). Analysis of these data for continuous quality improvement (CQI) efforts identifies opportunities to improve drug library datasets, best practices and quality of care. In 2007, it was estimated that 44% of US hospitals had implemented smart pump technology[1].

Implementation of wireless networking further increases the clinical usefulness of this technology. CQI data can be downloaded in close to real time and reported in a variety of formats (Figure 1) to help clinicians more easily identify problem areas and opportunities for improvement. Changes to drug library parameters can quickly be uploaded wirelessly to all devices throughout a hospital. Although no survey has reported the adoption rate of wireless connectivity, it is estimated from marketing data that approximately 400 hospitals have implemented wireless connectivity[2].

Averted errors

Aggregated smart pump data from 52 hospitals show that heparin was second only to propofol in the number of alerts for infusion programming outside hospital-established limits and was associated with the greatest number of "low dose" alerts (Figure 2)[2]. Figure 3 shows two typical examples of "good catches" in which the initial heparin dosage was multiple times the reprogrammed dose. In the first example 800 units/Kg/hr was reprogrammed to 8 units/Kg/hr, which suggests that initially the number for the total units/Kg the patient was supposed to receive

(assuming a 100 unit/mL concentration) was inadvertently entered as the dose. The second example in Figure 3 shows that 240 units/Kg/hr was reprogrammed to 9.2 units/Kg/hr, which suggests that the volume of the container was initially entered as the dose. Figure 4 shows a typical distribution of how many "times the limit" heparin doses were initially programmed. In some cases, the incorrectly programmed dose was 50 times the hospital's limit for a continuous heparin infusion[4]. Data such as these can greatly increase staff awareness of IV medication errors and provide compelling evidence of the need to improve IV medication practice.

Variability

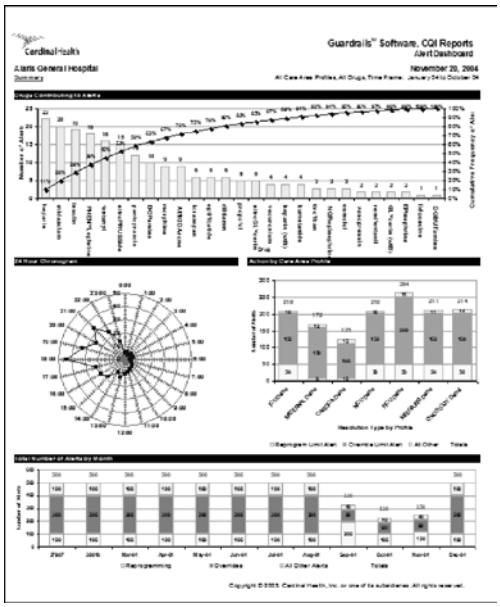
After the introduction of smart pumps, a sample drug library was developed based on evidence and consensus reports to help hospitals more quickly develop their customized data sets. Hospital pharmacists reported they could not simply adapt the sample library to their institutions because of the high degree of variability among institutions.

This experience prompted Bates et al.[3] to compare the smart pump drug libraries of 100 hospitals to assess the number of drug names used and the variation in concentrations, dose units, dose limits and administration practices. Investigators concluded that "…[s]ubstantial unnecessary variation in IV medication practices is likely associated with increased risk of harm. Standardization has the potential to substantially improve IV medication safety."[3] This is particularly true with heparin.

Drug names

For drugs such as heparin, hospitals had been encouraged to incorporate descriptors into the drug library that would reflect the way of using a particular drug. Pooled data from 207 hospitals showed that a total of 191 different names were used for heparin (examples, Table 1)[2].

Figure 1. Smart pump CQI data reports[2]



Concentrations

Although heparin is available from IV solution manufacturers in standard concentrations, analysis of data from 207 hospitals with smart pump drug libraries identified a surprising and troubling lack of standardization[2]. Fifteen unique heparin concentrations were included, with eight in pediatric care units and seven in adult care units (Table 2)[2]. Recent media reports have highlighted tragic errors resulting from confusion between 1 unit/mL heparin concentrations used to flush IV catheters and 1000 units/mL used to anticoagulate patients.

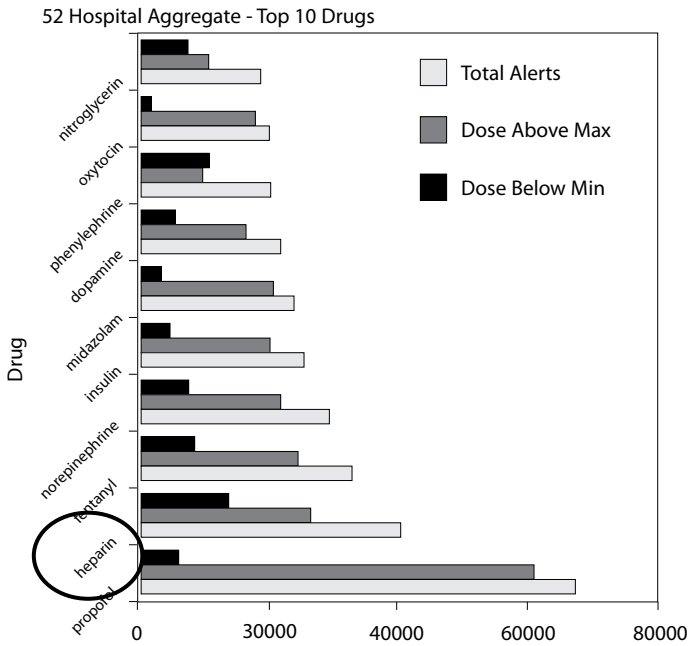
Mixed dosing units

Analysis of data from 54 hospitals showed that while most hospitals used only units/Kg/hr or units/hr, 29% allowed the use of both weight-based and non-weight-based dosing[2]. In hospitals where drug libraries had both dosing units, smart pump alerts resulting in reprogrammed doses were two to four times more frequent (Table 3)[2]. This suggests that standardizing on one method of ordering and programming doses could dramatically reduce the potential for heparin programming errors.

Table 1. Names used for heparin: examples[2]

Heparin		
Heparin	heparin (DBL)	heparin (protocolWt)
heparin–units/hr	heparin (dilute)	heparin (standard)
heparin–wt based	heparin (DOUBLE STR)	heparin (STD)
Heparin Drip	heparin (DOUBLE)	Heparin (STROKE)
Heparin Drip TRAIN	Heparin (Drip)	heparin (unit/h)
1/4NS heparin 1:1	heparin (DS)	heparin (units/hr)
A –heparin–units/hr	Heparin (DVT/PE)	heparin (universal)
A –heparin–wt based	heparin (Flush)	heparin (WB)
Art Line w Heparin	Heparin (IV drip)	heparin (weight)
D10 1/8NS w/heparin	Heparin (Lines)	heparin (wgt based)
hepaBAR -u/hr	heparin (MAX)	Heparin + 1/2 NS IV
HEParin 2.5-4.9 kg	Heparin (NICU)	heparin NEO UV
heparin (>40 kg)	heparin (NURSERY)	Heparin NICU FLUSH
Heparin (2x)	Heparin (Ped ArtLine	heparin NON PROTOCOL
heparin (Art Line)	Heparin (pedi)	Heparin NON WEIGHT
Heparin (CARDIO)	Heparin (Peds)	heparin PEDS
heparin (CARDIOLOGY)	heparin (premix)	heparin PROTOCOL
heparin (DBL conc)	heparin (Protocol)	heparin sodium

Figure 2. 52 hospital aggregated smart pump data – Top 10 drugs[2]



Other opportunities for error arise when patients are started on a weight-based bolus and weight-based continuous infusion (units/Kg/hr) and subsequent orders are written to decrease heparin by 100 units/hr based on laboratory results. Making this switch requires complicated, error-prone computation. This is particularly likely in hospitals that use both types of dosing unit.

Additional heparin safety issues

Programming rates and doses interchangeably

Smart pumps allow clinicians to enter either a rate or a dose. CQI data show many mismatches between rates and doses, which can lead to 100-fold under-or overdose with a 100 units/mL concentration. It would be possible to eliminate rate-setting from pump programming; however, nurses report that often they want to enter the rate or to be able to know what the rate is while administering a dose.

Lack of a single standard concentration

Despite the Joint Commission requirement for standardizing and limiting the number of drug concentrations available, many organizations still use many different concentrations. Over time, the Joint Commission's requirement will help move organizations to select a single concentration as the standard, thereby decreasing opportunities for error.

Bolus (loading) dosing from continuous infusion bag

When bolus dose programming is not available or a clinician does not use the bolus feature, administration of loading or bolus doses from the continuous infusion bags is not a safe practice. Since the continuous infusion containers typically contain many hours of heparin, a calculation or programming error can lead to a very large overdose. To improve safety, many hospitals have changed drug library limits on high-risk drugs to hard limits that cannot be overridden, so that clinicians are forced to use the bolus feature with its safety limits.

Table 2. Heparin concentrations on smart pump libraries: 207 hospital analysis[2]

Heparin		
0.5 unit/1mL	**25unit/1mL**	**100unit/1mL**
0.5unit/1mL	2500unit/100mL	100unit/1mL
25unit/50mL	6250unit/250mL	2000unit/20mL
50unit/100mL	**40unit/1mL**	2500unit/25mL
250unit/500mL	20000unit/500mL	5000unit/50mL
500unit/1000mL	**50unit/1mL**	10000unit/100mL
1unit/1mL	50unit/1mL	25000unit/250mL
1unit/1mL	1500unit/30mL	30000unit/300mL
50unit/50mL	2500unit/50mL	50000unit/500mL
250unit/250mL	12500unit/250mL	**200unit/1mL**
500unit/500mL	25000unit/500mL	4000unit/20mL
2unit/1mL	**60unit/1mL**	5000unit/25mL
2unit/1mL	15000unit/250mL	10000unit/50mL
1000unit/500mL	**80unit/1mL**	20000unit/100mL
6unit/1mL	80unit/1mL	50000unit/250mL
3000unit/500mL	20000unit/250mL	**400unit/1mL**
10unit/1mL	40000unit/500mL	400unit/1mL
10unit/1mL		**500unit/1mL**
5000unit/500mL		1000unit/20mL

Table 3. Heparin CQI analysis– 54 hospital sample[2]

Dosing Units	Ave # Averted Errors	Total Alerts
Units/hr 48%	64 (2x)	26%
Units/kg/hr 23%	32 (x)	12%
Both 29%	123 (4x)	62%

Smart pump limits that may be too tight

Drug library limits that are too tight can result in inconsequential, nuisance alerts that lead to "alert fatigue" whereby clinicians begin to disregard all alerts. The introduction of wireless networking makes it much easier for an institution to recognize this situation and quickly change the drug library in all smart pumps across an institution. To facilitate the fine-tuning of dose limits, it is essential that the CQI data from smart pump use be analyzed frequently to identify current practices.

Delayed restarting of infusions on hold

Smart pumps cannot now alert a clinician that an infusion is still on hold, even after several hours.

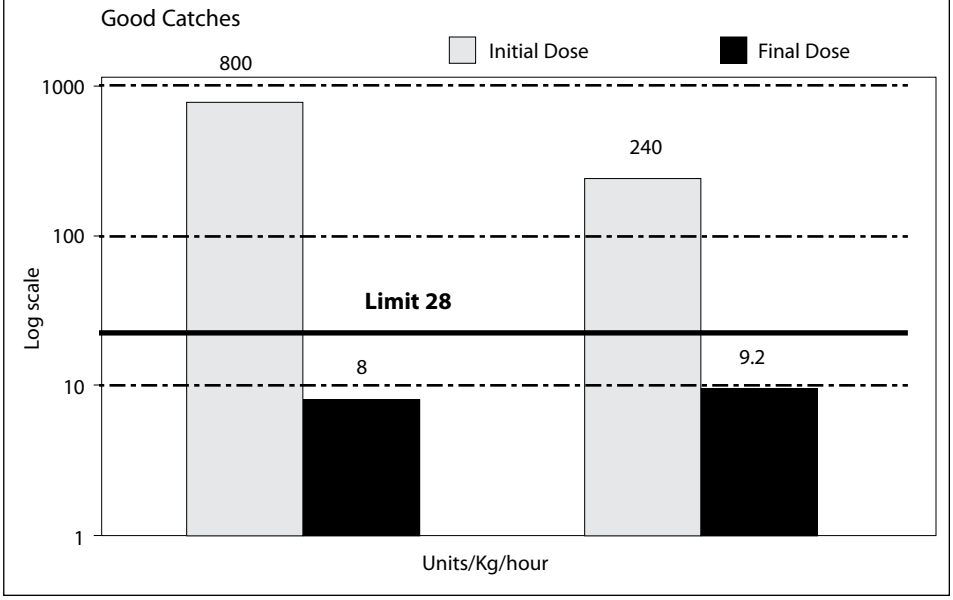
Compliance with smart pump use

Experience has shown that after smart pump implementation, there is a need to ensure continuing education, training and monitoring with regard to smart pump use to realize the full benefits of this technology.

Summary

Smart pumps originally were designed to help avert medication errors associated with the highest risk of harm (i.e., IV medication administration errors at the point of care). After their introduction, it rapidly became apparent that the previously unavailable data provided by smart pumps could play an equally important role in improving IV medication safety. To obtain full benefit of the safety improvements possible with this technology, it is critically important that sufficient resources be allocated to maintain staff education and training, maintain and update system software and identify and act on opportunities for IV medication best practice improvements.

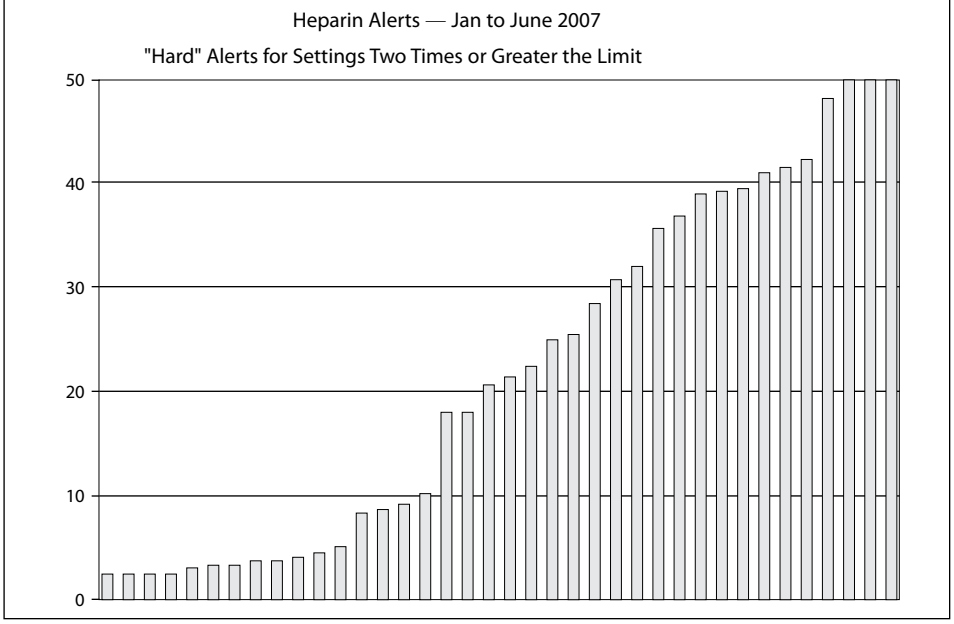
Figure 3. Heparin averted errors[2]



References

1. Pederson CA, Gumpper KF: ASHP National survey on informatics: Assessment of the adoption and use of pharmacy informatics in US hospitals. *Am J Health Syst Pharm*, 2008; 65:2244-64.
2. Data on file, CareFusion, San Diego, CA.
3. Bates DW, Vanderveen T, Seger DL, et al. Variability in intravenous medication practices: implications for medication safety. *Jt Comm J Pt Safety Qual* 2005;31(4):203-10.
4. Data on file, CareFusion Performance Analytics Service.

Figure 4. Smart pump alerts for programming ≥ 2X "hard" limits[2]



PROCEEDINGS

Using Smart Infusion Continuous Quality Improvement (CQI) Data to Improve Anticoagulation Management

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Key points

- *In 2001 St. Joseph's/Candler Health System, Inc. (SJCHS) determined that intravenous (IV) medication errors were associated with the greatest risk of patient harm and began implementation of a smart infusion system with dose-error-reduction software (DERS)[2,3]*
- *Wireless networking of the infusion devices improved the efficiency and timeliness of process interventions based on continuous quality improvement (CQI) data collected by the devices.*
- *Failure mode and effects analyses (FMEA) before and after smart system implementation showed a reduction in IV heparin administration risk score from 210 to 56, primarily achieved by improved detection of infusion programming errors[2].*
- *Nine-month CQI data showed that heparin accounted for 42% of averted overdoses with the highest potential for patient harm, the great majority of which occurred in non-critical care settings[4].*
- *Heparin CQI data analyses in 2004 and 2006 resulted in:*
  - *Standardization of IV heparin concentrations to 50 units/mL*
  - *Elimination of three time-consuming dose-calculation steps*
  - *Elimination of infusion-rate calculations by nurses and pharmacists by using dose-based pump programming in units/Kg/hr*
  - *Addition of bolus parameters to infusion-system drug library*
  - *Extensive computer-based re-education of nurses and pharmacists*

St. Joseph's/Candler Health System, Inc (SJCHS) is a multi-hospital, community-based, tertiary care referral health system located in Savannah, GA. It consists of two acute care and one rural hospital; the two Savannah hospitals are St. Joseph's and Candler Hospitals, together equaling 644 beds. These facilities provide primarily adult care, including all medical and surgical specialties except solid organ transplantation. There are about 500 physicians and surgeons on staff. SJCHS is a teaching site for students in all health disciplines except post-graduate medicine and is affiliated with several public and private universities throughout Georgia.

After an extensive internal analysis of various issues related to medication safety, in 2001 SJCHS elected to implement technology that reduced the likelihood of intravenous (IV) medication errors, since these errors are ones most often associated with patient harm[1]. As a result of this decision, SJCHS began a process of implementing a smart infusion system with dose-error-reduction software (DERS) that extended over several years[2,3]. The computerized system generates an alert whenever infusion programming exceeds pre-established drug library limits. Data from this system have been used for continuous quality improvement (CQI) of our medication use processes[2]. CQI has been tremendously aided by the implementation of wireless networking of the infusion devices, which allows more rapid downloading of smart-system data and uploading of drug library revisions.

Risk score reduction

Before implementation of the smart infusion system, a failure mode and effects analysis (FMEA) demonstrated a risk score of 210 for IV administration of heparin. This risk score was driven predominantly by a lack of a second check of the pump setting by nurses before starting the infusion. FMEA after implementing the smart infusion system resulted in a risk score of 56, a 4-fold reduction achieved primarily by improved detection of heparin infusion programming errors[2].

Averted infusion programming errors

An in-depth analysis of CQI data from a nine-month period showed that 245 infusion system alerts resulted in a programming change or canceled infusion representing averted errors[4]. Of these, 166 averted overdoses were felt to represent the greatest

potential for harm. Heparin represented 23 (14%) of 166 potentially harmful overdoses[4].

Further analysis using the IV Medication Harm Index[5] demonstrated that heparin accounted for a significant number of averted overdoses with the highest potential for harm. The IV Medication Harm Index is an analytic tool that characterizes the magnitude of potential harm based on three sub-scales: 1) drug risk and magn itude of overdose; 2) level of care and patient acuity and 3) detectability of adverse event. It has a range of values of 3.5 to 14.0[5]. In our analysis, heparin accounted for 42% of those overdoses with risk scores equal to or greater than 11.0 on the IV Medication Harm Index[4]. Most patients who would have received these overdoses were treated in non-ICU medical/surgical nursing units[4].

Table 1. Averted Overdoses: Risk for Harm/Patient Care Types[4]

Patient Care Type	Smart Pumps (n=426)	Total Averted Overdoses (n=166)	Highest-Risk Averted Overdoses* (n=33)		
			Total (n=33)	Propofols (n=10)	Heparin (n=14)
ICU Critical Care	332 (78%)	140 (84.3%)	16 (48.5%)	10 (100%)	1 (7%)
Non-ICU	67 (22%)	26 (15.7%)	17 (51.5%)	—	13 (93%)

* Averted overdoses with scores ≥ on the IV Medication Harm Index16 (drug risk overdose range, level of care /acuity and detectability).

Process and practice improvements

Wireless network connectivity of smart infusion devices allows the opportunity to evaluate aggregated data from the system and identify medication-use processes that need improvement. Analysis of heparin data in 2004 demonstrated a need to assess and redesign SJCHS weight-based heparin protocols[2]. As a result of this analysis:

- Multiple IV heparin concentrations were standardized to 50 units/mL
- Three time-consuming steps in dose calculation were eliminated
- Infusion rate calculations by nurse or pharmacist were eliminated by implementing dose-based pump programming in units/Kg/hr
- Extensive computer-based re-education of nurses and pharmacists was conducted

Additional analysis in 2006 demonstrated continued problems with pump programming for bolus dosing of heparin infusions (Table 2). To correct these problems, bolus parameters were defined in the infusion-system's software drug library and additional nurse and pharmacist education was implemented using case scenarios in computer-based learning modules.

Recent SJCHS medication-use data indicate that more than 75% of parenteral anticoagulant use is low molecular weight heparins (LMWH); unfractionated heparin (UFH) is administered to a minority of patients who require anticoagulation. Although UFH use is declining, it is unlikely that it will be totally replaced by other anticoagulants in the near future. LMWH may be a safer alternative to UFH in those patients who are appropriate candidates for its use.

Table 2. Examples of SJCHS 2006 Heparin CQI Data

Date	Profile	Initial Dose	Final Dose	Multiple of Max Limit	Times Intended Dose
1/4/06	Adult Critical Care	80 units/kg/hr	18 units/kg/hr	2	4.4
1/12/06	Adult Critical Care	80 units/kg/hr	18 units/kg/hr	2	4.4
2/1/06	Adult Med Surg	80 units/kg/hr	18 units/kg/hr	2	4.4
3/26/06	Adult Med Surg	80 units/kg/hr	12 units/kg/hr	2	6.7

Summary

Smart infusion systems provide actionable data that can be used to improve medication use processes for many IV-administered drugs, including heparin. Although heparin is administered in both intensive care unit (ICU) and non-ICU settings, patients who receive the drug outside of the ICU may be at greater risk for harm, because the level of monitoring for adverse events is less intense in these settings. Wireless network communication with infusion devices significantly improves the efficiency and timeliness of process interventions based on CQI data collected by the devices.

References

1. Communication with D.W. Bates, M.D., M.Sc. of Brigham & Women's Hospital in Boston, October 2001.
2. Williams CK, Maddox RR. Implementation of an i.v. safety system. *Am J Health-Syst Pharm* 2005: 62:530-6.
3. Maddox RR, Williams CK, Oglesby H, et al. Clinical experience with patient-controlled analgesia using continuous respiratory monitoring and a smart infusion system. *Am J Health-Syst Pharm* 2006; 63:157-64.
4. Williams CK, Maddox RR, Heape E, et al. Application of the iv medication harm index to assess the nature of harm averted by "smart" infusion safety systems. *J Patient Saf* 2006; 2:132-9.
5. Sullivan J. IV medication harm index: results of a national consensus conference. In: Schneider PJ, ed. Infusion safety: addressing harm with high-risk drug administration. *Hosp Health Netw* 2004; 78(5suppl):29-31. Retrieved September 9, 2005 from: www.cardinalhealth.com/clinicalcenter/materials/conferences/index.asp.

PROCEEDINGS

Heparin Safety and the Coagulation Laboratory

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Key points

- *National Patient Safety Goal Requirement 3E requires hospitals to reduce the likelihood of patient harm associated with the use of anticoagulation therapy.*
- *Unfractionated heparin (UFH) therapy is usually monitored with a clot-based test, activated partial prothrombin time (aPTT).*
- *A laboratory can change aPTT reagents every 12 to 16 months, depending on its manufacturer-determined stability, and the new therapeutic range may need to be determined using the new reagent lot.*
- *The aPTT result can be affected by variations among testing devices and reagents, patient physiology and pathophysiology, concurrent medications, improper blood collection and plasma preparation and delay in centrifuging or testing a sample.*
- *Test results vary among POC devices and typically do not match laboratory aPTT results because of differences in sample type, clot detection method and sample-reagent incubation period.*
- *Sharing knowledge about the potential shortcomings of aPTT testing to monitor UFH therapy and the possible need to change the therapeutic range can help reduce the likelihood of harm and improve the care of patients receiving anticoagulation therapy.*

In 2008, the Joint Commission's new National Patient Safety Goals included Requirement 3E: Reduce the likelihood of patient harm associated with the use of anticoagulation therapy[1]. This applies to patients receiving either oral or intravenous (IV) anticoagulation therapy. The most frequently used IV anticoagulant is heparin.

Safe and effective heparin use requires frequent monitoring to ensure that drug levels are maintained within a narrow therapeutic window. Unfractionated heparin (UFH) therapy is usually monitored with a clot-based test, activated partial prothrombin time (aPTT). Other clot-based tests such as thrombin time are infrequently used but can be useful in situations such as patients with lupus who have elevated baseline aPTT levels. Other approaches are to measure levels of heparin or anti-Xa activity. Heparin levels are most commonly measured by chromogenic methods, although protamine titration is still used. Activated clotting time (ACT) is widely used outside the clinical laboratory setting.

In this manuscript, the laboratory's role in monitoring continuous infusion UFH using aPTT testing and some of the associated problems will be discussed.

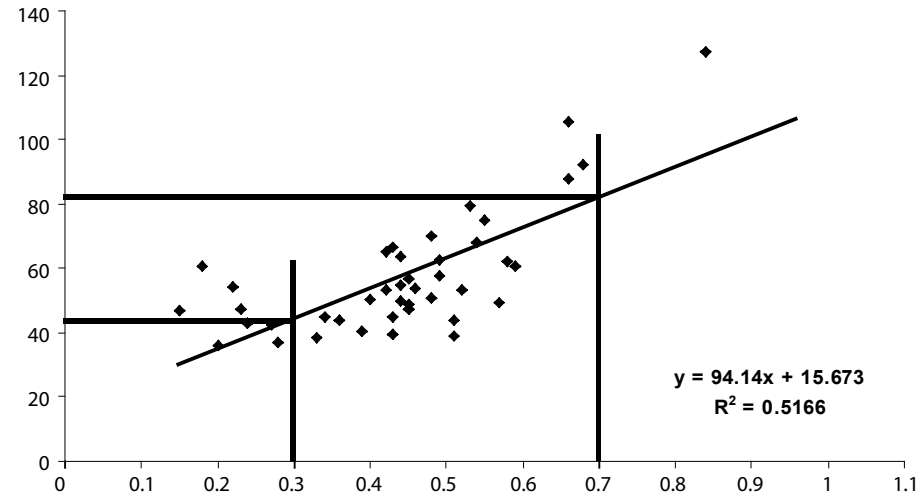
Background

The College of American Pathologists (CAP) is one of the organizations that certify clinical laboratories. For UFH monitoring, CAP requires that each laboratory have a documented system for determining and validating an aPTT-based heparin therapeutic range using an appropriate technique[1,2]. The most common approach is to use the method described by Brill-Edwards, et al. to compare heparin levels with aPTT values[3]. When chromogenic methods are used, a regression analysis is done between levels of aPTT and heparin. The therapeutic range is determined by drawing intercept lines between 0.3-0.7 units/mL heparin levels and aPTT values (Figure 1).

A laboratory can change aPTT reagent every 12 to 16 months, depending on its manufacturer-determined stability. CAP suggests that at least 30 UFH patients be tested, with no more than two samples per patient[4]. After concurrent testing of new and existing lots, CAP recommends using the differences between aPTT means and summation of mean differences over past evaluation periods. In either case, if the difference between the aPTT means of the new lot and either the existing lot or cumulative difference is <5 seconds, then no action is necessary and the change may not be noticed by clinicians. If either difference is >7 seconds, then a new therapeutic range must be determined.

To minimize the possibility of having to create a new therapeutic range, a laboratory

Figure 1: Determination of heparin therapeutic range



Heparin therapeutic range comparing chromogenic heparin levels (X axis) to corresponding aPTT values in patients receiving therapeutic UFH. A regression line is drawn, and then intercept lines between 0.3-0.7 units/mL UFH and the aPTT axis. In this example the therapeutic range would be 42-82 seconds.

can request that a reagent manufacturer supply a new lot with similar heparin responsiveness. A laboratory could also obtain multiple lots for evaluation and select the lot that more closely matches results for the existing lot. Another option is to save plasma samples from UFH-treated patients throughout the year for future testing. This allows even the smallest laboratory to have enough samples for comparison testing. Any UFH samples that are frozen should be validated, for reasons discussed below. It is not acceptable to determine the therapeutic range using UFH-spiked plasma, because this approach tends to overestimate the therapeutic range.

Pre-analytical variables can affect aPTT results, and mechanisms to ensure proper blood collection and plasma preparation are required. Testing should be performed on unclotted, 3.2% sodium citrate, platelet-poor plasma (<10,000/mm^3) within 4 hours of collection[5]. For monitoring UFH therapy, the aPTT sample should centrifuged within one hour and tested within four hours of collection[5]. The citrate tube should be nearly full to avoid an improper citrate:plasma ratio that could falsely increase clotting times. At our institution, before analysis every coagulation sample is rimmed with applicator sticks to check for macroscopic clots. The processing centrifuge is checked daily to assure that platelet-poor plasma is created. For citrated samples to be saved for later testing, the plasma is removed from the primary collection tube and placed into a secondary tube and re-centrifuged. After the second centrifugation, the plasma is then aliquoted into freezer-safe capped vial(s) prior to freezing at -70^{o}C.

New lot evaluation of aPTT reagents—UC Davis Health System protocol

At our institution, two to three different lots of aPTT reagent with similar UFH sensitivity are requested from the manufacturer for initial evaluation. The coagulation analyzers are set up to reflex patient testing on new lot aPTT reagents if they meet established criteria for evaluation: 1) aPTT within current therapeutic range with current lot aPTT reagent, and 2) normal INR. After testing is complete on the new and current lots of reagents, the samples are saved at -70^{o}C for possible future analysis. Although CAP recommendations allow up to two samples per patient, we prefer to use a patient only once for data analysis. Access to electronic medical records (EMR) allows the staff to review UFH dosing to determine whether therapeutic doses have been given. Regression analysis and bias plots are used to determine which new-lot aPTT reagents are preferable. At least 40 UFH-treated patients are evaluated to determine whether a new therapeutic range is warranted. Data are shared with pharmacists to alert them to potential bias areas when transition to a new reagent lot occurs.

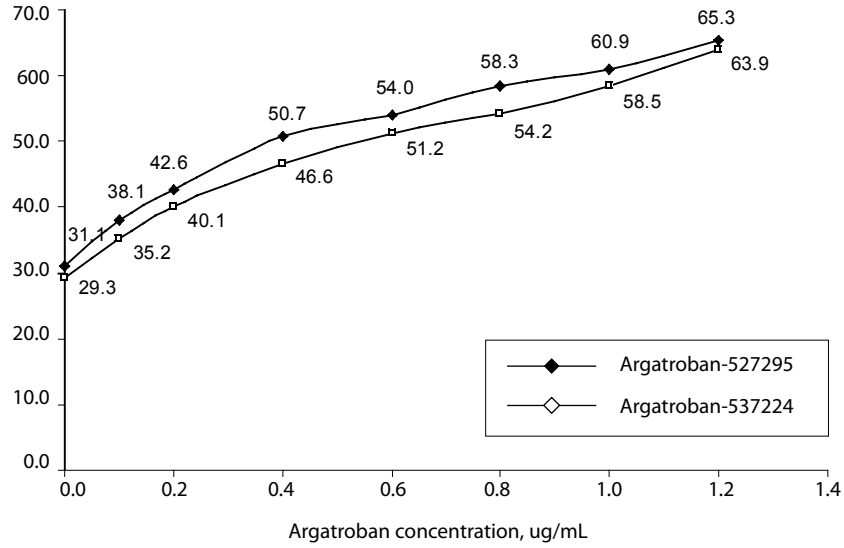
Establishing rapport between laboratory staff and the pharmacy staff is prudent. Sharing information facilitates smooth transition if new therapeutic ranges are required and allows the clinical staff to address any issues surrounding the data. New therapeutic ranges most likely will require a change in dosing orders, so a lead time (one month, at our facility) before new-lot transition would allow new dosing orders to be approved and disseminated for the new reagent lots. If the therapeutic range is changed, a concrete transition day and shift must be established and appropriate pharmacy and clinical staff notified.

Direct thrombin inhibitors (DTI) are also monitored using the aPTT. Informing clinical staff about the impact of new reagent lots on DTI therapy is strongly recommended, to ensure that they can assess potential issues (Figure 2). Secondly, since aPTT testing is also used in settings such as hemophilia screening or lupus anticoagulation, informing the clinical staff about the performance characteristics of a new aPTT reagent lot would be beneficial.

aPTT testing: ancillary issues

Many pre-analytical and analytical variables affect the accuracy of aPTT results. Probably the most important variable is the

Figure 2: Differences between new and existing reagent lots



Example of pooled plasma spiked with varying concentrations of argatroban. The two lines represent existing-lot aPTT reagent (527295) and new-lot aPTT reagent (537224). These spiked samples could be stored at -70°C for future analysis of new-lot aPTT reagents.

blood-acquisition (phelebotomy) technique. In healthy individuals, blood is usually drawn from the antecubital fossa using vacutainer-type blood collection tubes without major problems. When drawing blood presents a problem, technique may affect results. The use of small-bore needles (<23 gauge), entry into small veins and increased force in drawing back the syringe plunger may result in lysis of red blood cell (RBC) and the release of phospholipids that may initiate the coagulation process. Cell lysis may not be not readily apparent until the blood is processed in the laboratory.

The use of syringes for venipuncture also presents other challenges. Blood is activated by exposure to negatively charged surfaces such as glass or plastic and delays of >60 seconds in transferring freshly collected blood into vacutainer tubes containing appropriate anticoagulants may also effect test results. Other problems include tourniquet time, improper blood-to-anticoagulant ratio, improper anticoagulant uses (different colored blue top tubes), improper clearing of indwelling catheters prior to blood collection for testing, improper storage of sample once collected and delays in getting samples to the laboratory. The effects of poorly phlebotomized blood may not become apparent until the sample reaches the laboratory (clotted sample) or during the analytical (testing) phase (decreased clotting time) or post-analytical phase, when samples are saved for future testing.

A properly collected citrated sample must be sent to the laboratory immediately. As noted above, platelet-poor plasma should be processed within one hour of collection[5].

Analytical variables, e.g., differences between instruments and reagents, may not be evident within a laboratory or consortium of laboratories that use like reagents and instruments, but may become apparent when samples are compared to other laboratories. While the largest variable is different reagents, instruments also differ in the endpoint measurement of the test. Different types of activator and the concentration and type of phospholipid in the reagent will yield different results, even if samples are analyzed concurrently on the same instrument[6,7].

Physiological variations will also affect aPTT results. The aPTT measures the functional ability of nine coagulation factors and, to a lesser degree, fibrinogen. Decreased factor levels or activity can increase aPTT, and increased factor levels or activity can decrease aPTT. Especially in UFH monitoring, elevated levels of fibrinogen and factor VIII, both acute-phase reactants, may falsely decrease the aPTT and suggest "heparin resistance"[2,8]. Unintended effects of other drugs such as thrombolytics, Xigris® and NovoSeven® may also increase or decrease aPTT results. Pathologic states such as antiphospholipid antibody syndrome, vonWillebrand disease, immune causes of factor deficiency, among others, may also affect the aPTT result.

Variation among laboratories

CAP survey results highlight the problems of aPTT testing for UFH monitoring. CAP requires each clinical laboratory to dem-

Table 1. 2007 CAP survey of aPTT proficiency testing

Survey Sample ID	Number of Labs submitting results	Mean	Median	CV (%)	Low	High
2007 CG2-07	984	67.4s	70s	18.3	45s	104s
2007 CG2-12	1064	34.7s	35	8.8	26s	43s

Sample results of 2007 CAP survey of aPTT proficiency testing. Each data set represents cumulative results for all reporting sites using 8 different reagents and 16 different instrument combinations.

onstrate proficiency compared to its peers for each laboratory test used in patient care. Typically, aPTT proficiency is determined using lyophilized samples distributed by CAP to each clinical laboratory in the U.S. Each laboratory tests the blinded samples and submits results to CAP for evaluation. The blinded samples may be normal, contain anticoagulants or have decreased factor levels. In 2007, CAP sent three sets of five blinded samples each to participating laboratories. In the second survey, sample CG2-07 contained "therapeutic levels of fractionated heparin," but 0.5% (5/984) of participating laboratories interpreted their findings as normal (Table 1).

Table 2. 2007 CAP survey of heparin-level proficiency testing

Survey Sample ID	Number of Labs submitting results	Mean Range (U/mL)	CV (%) Range	CV (%)	Low
2007 CG2-07					
LMWH	195	0.26-0.70	23-34	0.10	1.24
UFH	105	0.38-0.48	13-24	0.20	0.64
2007 CG2-12					
LMWH	208	0.07-0.30	40-68	0.0	0.54
UFH	107	0.09-0.19	27-52	0.0	0.30

Samples results of 2007 CAP survey of heparin-level proficiency testing. Each data set represents range results for all reporting sites using 3 different reagents combinations generated from either LMWH or UFH standard curves. Range results are the spread of calculated results between the different reagent combinations.

The CAP survey also evaluated heparin-level testing without informing laboratories whether a sample contained UFH or low-molecular-weight heparin (LMWH). The data showed marked differences between results obtained by extrapolating from a UFH or a LMWH curve (Table 2, Figure 3). For laboratories using LMWH curves, results ranged from 0.0-0.54; for laboratories using UFH curves, results ranged from 0.0-0.30 (Table 2). In some cases, samples containing no UFH were reported to have UFH levels up to 0.30 Anti-Xa activity. These findings underscore the importance of using the appropriate calibration curve for reporting results and for generating heparin therapeutic ranges.

From the CAP survey, it is unclear how the calibration of the heparin test was performed, which may account for the bias seen. There have been many reports of variability between reagent methods for determining heparin levels[9-11]. This most likely is due to manufacturer-kit differences, including whether the patient's plasma is supplemented with antithrombin (AT) prior to measuring residual factor Xa. The addition of AT to test plasma may increase the reported heparin level in patients with decreased in-vivo AT levels.

Heparin testing is a little more robust than aPTT testing, with few variables that can affect the result. There is better precision with heparin assays and minimal interferences with increased factor activity levels. However, it is important that the correct calibration curve be used for the correct drug monitoring, as there may be an over or underestimation of the heparin levels if an inappropriate curve is used (Figure 3).

Figure 3. Differences in testing results using UFH or LMWH curves

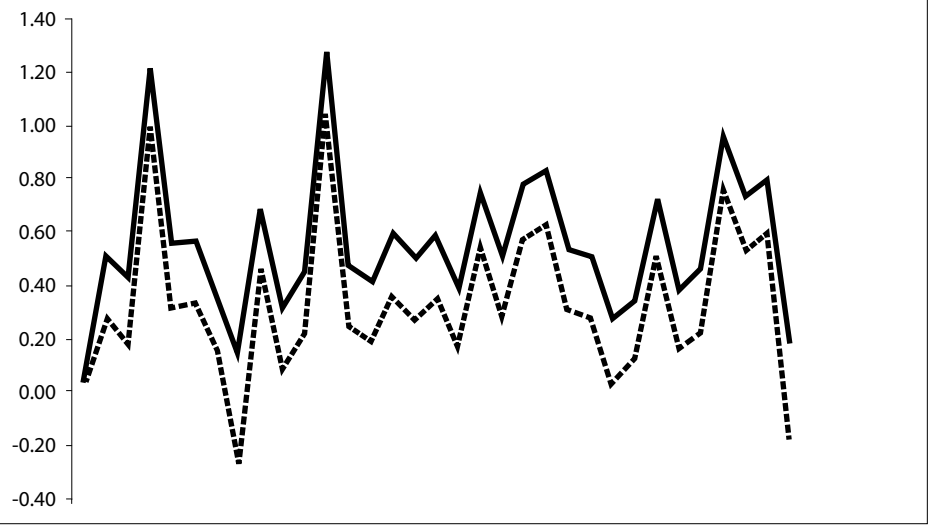
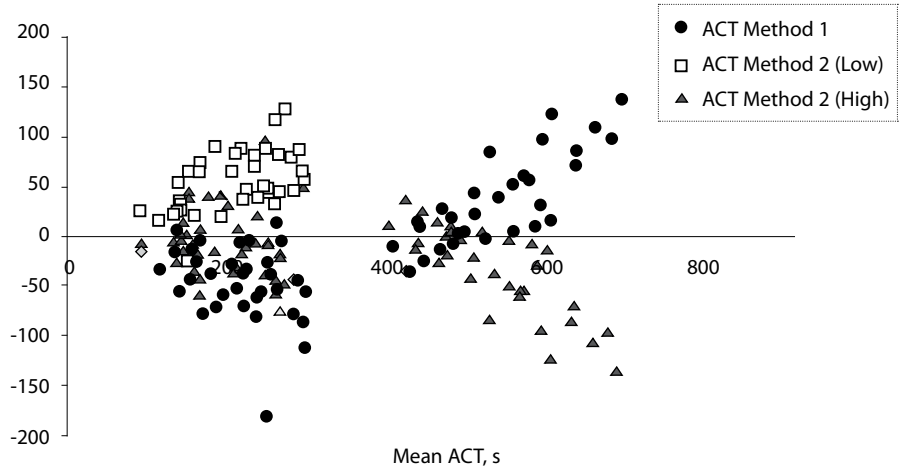


Figure representing concurrent testing of samples on two different heparin-assay curves. The dashed line represents heparin-activity (anti-Xa activity) results generated from an UFH curve. The solid line represents testing of the same samples but with heparin-activity results generated using an enoxaparin curve.

Effect of freezing samples

CAP allows for freezing of samples from patients on UFH to minimize the difficulty in acquiring an adequate number or UFH patient samples for generating heparin therapeutic ranges even in smaller institutions. Freezing plasma samples slightly increases the aPTT[12]. A recent internal study at our institution unexpectedly showed that freezing was not a viable option. aPTT results from frozen samples averaged 8% higher, but were as much as 85% higher, than results from fresh samples. Overall, 23% of the frozen samples tested higher than the acceptable accuracy threshold (<15%) between fresh and frozen sample results. Using fresh samples for aPTT results, the UFH therapeutic range was 47-65

Figure 4: Biases among ACT reagents in UFH testing

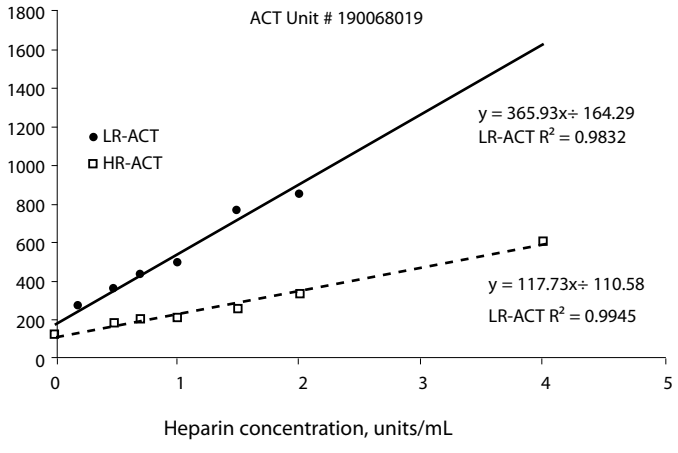


Bias plot comparison between baseline/UFH anticoagulated samples tested with two different ACT instruments using 3 different ACT cartridges. This graph demonstrates the biases that exist between ACT reagents.

seconds, while using frozen samples for aPTT results, the therapeutic range was 55-87 seconds. This would result in dramatically different therapeutic ranges, if frozen plasma were used for testing.

Laboratory practice requires checking each sample for clots (swirling each sample with applicator sticks to detect fibrin/clot), using a double-spin technique prior to freezing and daily monitoring of centrifuge for platelet-poor plasma generation. Nonetheless, there appeared to be problems with the patient plasma that were not readily apparent during the pre-analytical and analytical phase of testing. Filtering plasma collected from selected patients results in multiple filter use, suggesting fibrin/platelet aggregate formation. Filters also remove von Willebrand's factor/Factor VIII complexes, yielding increased aPTTs—another reason why filtering plasma for future aPTT testing is not an acceptable practice.

Figure 5. ACT cartridges in low-dose UFH anticoagulation monitoring



This graph represents the response between ACT cartridges for low-dose UFH anticoagulation. Note the more sensitive response of the low-dose ACT cartridge compared to the high-dose ACT cartridge.

Point of care testing

A few point of care (POC) devices are available for monitoring UFH treatment. Most use activated clotting time (ACT), but aPTT and heparin concentrations are also used. Creating a therapeutic range using these devices is more challenging than with laboratory testing because of sample type (whole blood used). Test results vary among POC devices and typically do not match laboratory aPTT results, because of differences in sample type, clot detection method and sample-reagent incubation period.

ACT is the most commonly used method for POC testing. Differences in methodology include type of activator (kaolin, celite), heparin dosing (low dose 0.1-2.0 units/mL and high dose >2.0 units/mL) and use for either citrated or freshly collected whole blood samples. There are also differences between ACT manufacturers and between ACT cartridge types (Figure 4). UFH anticoagulation may be underestimated if high-dose ACT cartridges are used in patients with lower UFH infusion rates (Figure 5).

Summary

Safe and effective anticoagulation therapy requires accurate monitoring, typically using laboratory aPTT testing. Differences among aPTT reagents and instruments, the effects of pre-analytical variables and difficulties in determining the UFH therapeutic range are primary reasons why a strong working relationship between pharmacy and laboratory staff should be encouraged. Sharing knowledge about the potential shortcomings of UFH therapeutic range determinations and coagulation testing, in general, can help reduce the likelihood of harm associated with the use of anticoagulation therapy and improve patient care.

References

1. College of American Pathologists Laboratory Accreditation Program (LAP) Checklist. Hematology-Coagulation Checklist Revision 09/27/2007. Northfield, IL.
2. Olson JD, Arkin CF, Brandt JT, et al. College of American Pathologists Conference XXXI on laboratory monitoring of anticoagulant therapy: laboratory monitoring of unfractionated heparin therapy. *Arch Pathol Lab Med* 1998;122(9):782-98.
3. Brill-Edwards P, Ginsberg JS, Johnston M, et al. Establishing a therapeutic range for heparin therapy. *Ann Intern Med* 1993;119(2):104-9.
4. College of American Pathologists Laboratory Accreditation Program (LAP) Checklist. 2007 Participant Survey CG2-B. Pages 6-8.
5. Clinical and Laboratory Standards Institute H21-A4—Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays; Approved Guideline 4th Edition 2003.
6. Kitchen S, Cartwright I, Woods TA, et al. Lipid composition of seven APTT reagents in relation to heparin sensitivity. *Br J Haematol* 1999;106(3):801-8.
7. Kitchen S, Jennings I, Woods TA, et al. Wide variability in the sensitivity of APTT reagents for monitoring of heparin dosage. *J Clin Pathol* 1996;49(1):10-4.
8. Hirsh J, Raschke R. Heparin and low-molecular-weight heparin: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004;126(3 Suppl):188S-203S.
9. Kitchen S, Theaker J, Preston FE. Monitoring unfractionated heparin therapy: relationship between eight anti-Xa assays and a protamine titration assay. *Blood Coagul Fibrinolysis* 2000;11(2):137-44.
10. Kovacs MJ, Keeney M. Inter-assay and instrument variability of anti-Xa results. *Thromb Haemost* 2000;84(1):138.
11. Kovacs MJ, Keeney M, MacKinnon K, et al. Three different chromogenic methods do not give equivalent anti-Xa levels for patients on therapeutic low molecular weight heparin (dalteparin) or unfractionated heparin. *Clin Lab Haematol* 1999;21(1):55-60.
12. Adcock D, Kressin D, Marlar RA. The effect of time and temperature variables on routine coagulation tests. *Blood Coagul Fibrinolysis* 1998;9(6):463-70.

PROCEEDINGS

Issues in Heparin Management

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Key points

- *In the treatment of venous thromboembolism (VTE), weight-based dosing that achieves activated partial thromboplastin time (aPTT) values in the target range within 24 hours has been associated with a reduction in recurrent thromboembolism.*
- *The use of heparin dosing and monitoring guidelines usually is necessary to optimize medication safety and therapeutic outcomes.*
- *Problems that can lead to incorrect heparin dosage adjustments include phlebotomy technique, bolus dosing, differences in aPTT reagent sensitivity and confusion in interpreting laboratory results.*
- *Making dosing guidelines available electronically allows for easy access by clinicians and rapid updating to reflect revisions, corrections and follow-up observations.*
- *Standardized procedures to initiating, monitoring and adjusting continuous infusions of heparin and an anticoagulation oversight process can help improve safety and quality of care.*

Despite the availability of newer parenteral anticoagulants as preferred alternatives to heparin, a shorter-acting, reversible agent still is needed in certain clinical situations, such as when bleeding risks are high or an invasive procedure requires rapid adjustments in anticoagulation intensity. In the treatment of venous thromboembolism (VTE), weight-based dosing that achieves activated partial thromboplastin time (aPTT) values in the target range within 24 hours has been associated with a reduction in recurrent thromboembolism[1-4]. When the risk of bleeding is high and thromboembolism low (no acute thromboembolism is present), a lower intensity of anticoagulation (lower value in the aPTT range) and avoidance of bolus dosing may be considered.

Standardized dosing and monitoring guidelines

Usually the use of heparin dosing and monitoring guidelines is necessary to optimize medication safety and therapeutic outcomes. Since continuous heparin infusions are used in different clinical settings, different guidelines may be needed to individualize therapy. For example, because of alterations in cardiac output and concurrent use of antiplatelet agents, heparin infusion rates may be lower in patients with acute coronary syndrome (ACS) than those being treated for VTE (Table). When treating a patient with a stroke, clinicians may wish to avoid heparin bolus dosing to minimize bleeding risks.

Laboratory testing issues

Several factors should be considered when aPTT or activated clotting time (ACT) results are used to help determine heparin dosage adjustments. Drawing serum samples from IV lines increases the risk of hemidilution, which may lead to unexpectedly high aPTT (and INR) values. A large bolus dose of heparin may affect subsequent aPTT values for more than six hours (Figure). For example, an aPTT result for four hours after a 5,000-unit heparin bolus may suggest adequate heparinization, but a subsequent result that reflects only the continuous infusion may be below the target range.

Delays in establishing an aPTT in the target range or confusion in interpreting test results can make initiating heparin therapy challenging. Anti-Xa has been suggested as an alternative test; however, potential drawbacks include variability among anti-Xa testing methods in reported results or in comparisons to the aPTT. Anti-Xa testing may reduce variability associated with aPTT but may also reduce accuracy in measuring antithrombotic intensity.

The influence of antithrombin (AT) on test results should also be considered. Indirect inhibitors of factor Xa activity such as unfractionated heparin, low-molecular-weight-heparin and fondaparinux enhance the activity of AT. Acute reductions in AT resulting from disseminated intravascular coagulation (DIC), large clots, renal disease, trauma, liver disease

or hereditary factors may diminish response to these agents. Low AT levels also have been associated with an increased incidence of thromboembolism[5]. Lack of an aPTT response at heparin rates above 25units/Kg/hr may suggest AT deficiency (or high factor VIII, high fibrinogen). The method by which an assay measures anticoagulation activity should also be considered, e.g., an anti-Xa activity assay that adds AT may not detect low AT activity.

Unlike INR for prothrombin ratio, standardization of the aPTT has not been achieved, despite several attempts. Different aPTT assays can yield different target ranges for a given infusion of heparin. Changes in an aPTT reagent may necessitate changes in established dosing and monitoring guidelines. To ensure that clinical practice reflects any such changes, open communication between laboratory and clinical staff is essential.

Table. Unfractionated Heparin: Dosing

Is a bolus needed?

How much?

- 50-80 units/Kg
- 2-3,000 units max
- Stroke: None
- ACS: 1 units/Kg
- LMWH on board
- INR > 2

Maintenance Dosing: units/Kg

- ACS: 12 units/Kg/hr
- Stroke: 15 units/Kg/hr
- DVT/PE: 18 units/Kg/hr
- Prophylaxis

How many protocols?

- ECMO
- Dialysis/CRRT
- Pediatrics/Neonates
- CT surgery

Laboratory reagent issues

Differences among aPTT reagents should also be considered in determining therapeutic ranges and dosing guidelines. For example, a clinical trial may have been done using a more sensitive aPTT reagent that leads to a higher aPTT target range when calibrated to anti-Xa activity. In clinical practice, use of the higher aPTT target range but a less-sensitive aPTT reagent (lower aPTT results) may lead to systematic overdosing of heparin. Conversely, if a there is a change to a more sensitive reagent, then continued use of previously established guidelines may result in heparin underdosing. Any changes in reagents should be reviewed in advance, new target ranges established and dosing guidelines adjusted.

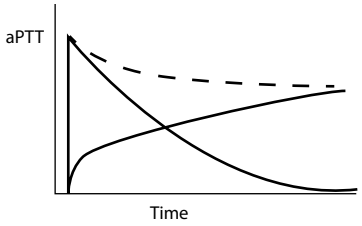
Electronically available guidelines

Maintaining all dosing guidelines in electronically available formats allows the dosing guidelines to be easily accessed by a clinician when ordering a heparin infusion and rapidly updated to reflect any revisions or corrections. The use of pre-printed forms can result in delayed and incomplete implementation of updated guidelines. Electronically available heparin orders can also be adjusted, as necessary, based on follow-up observations.

Figure. Unfractionated Heparin: Monitoring

Monitoring (aPTT)

- Time for no effect from bolus: 6-8 hr
- No bolus given: 4-6 hr
- Kearon et al Arch Intern Med 1998
  - Warfarin: INR ↑ 1.0 = ~ 16 sec aPTT ↑
- Monitoring Xa ? 03-07 in DVT
  - Double Lumen Catheter Draw



Anticoagulation oversight

In addition to standardizing approaches to initiating, monitoring and adjusting continuous infusions of heparin, establishment of an oversight process that involves clinicians with in-depth understanding of anticoagulation therapy can help improve outcomes. Individuals involved in oversight may include the responsible physician, bedside nurse, pharmacist and laboratory technician, with one practitioner designated to be responsible for adjusting dosages for patients receiving anticoagulation therapy. Pharmacist-provided anticoagulation management has been associated with statistically significant reductions in death rates, length of stay, cost of therapy and bleeding complications[6].

Conclusion

Given the complexity of intravenous heparin therapy, institutions should consider developing a multidisciplinary approach to anticoagulation management that considers the goals of therapy and addresses the many factors that may influence monitoring, dosage adjustments and eventual treatment outcomes. These factors include variability in the laboratory testing used to monitor heparin, the appropriate use of the results from labo-

ratory testing, standardizing the dosing and monitoring heparin therapy and the method by which the standardized approach is made available to clinician prescribing and monitoring therapy. Addressing these issues by involving clinicians with knowledge of the laboratory and clinical aspects of heparin therapy can improve treatment outcomes for patients receiving this high-risk medication.

References

1. Raschke RA, Reilly BM, Guidry JR, et al. The weight-based dosing nomogram compared with a "standard care" nomogram. A randomized controlled trial. *Ann Intern Med* 1993;119:874-1.
2. Hull RD, Raskob GE, Brant RF, et al. Relation between the time to achieve the lower limit of the APTT therapeutic range and recurrent venous thromboembolism during heparin treatment for deep vein thrombosis. *Arch Intern Med* 1997 Dec 8-22;157(22):2562-8.
3. Anand S, Ginsberg JS, Kearon C, et al. The relation between the activated partial thromboplastin time response and recurrence in patients with venous thrombosis treated with continuous intravenous heparin. *Arch Intern Med* 1996 Aug 12-26;156(15):1677-81.
4. Anand SS, Bates S, Ginsberg JS, et al. Recurrent venous thrombosis and heparin therapy: an evaluation of the importance of early activated partial thromboplastin times. *Arch Intern Med* 1999 Sep 27;159(17):2029
5. Owings J, Bagley M, Gosselin R, et al. Effect of critical injury on plasma antithrombin activity: low antithrombin levels are associated with thromboembolic complications. *J Trauma* 1996 Sep;41(3):396-405
6. Bond CA, Raehl CL. Pharmacist-provided anticoagulation management in United States hospitals: death rates, length of stay, Medicare charges, bleeding complications and transfusions. *Pharmacother* 2004 Aug;24(8):953-63.

PROCEEDINGS

Venous Thromboembolism: Improving Safety and Outcomes of Heparin Therapy

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Key points

- *Serious medication errors related to the administration of heparin are common in clinical practice.*
- *Correctly dosing heparin to attain a therapeutic activated partial thromboplastin time (aPTT) within 24 hours significantly reduces the risk for recurrent venous thromboembolism (VTE), yet without the use of a standardized protocol, this outcome is achieved only 37% of the time.*
- *Use of a weight-based heparin protocol significantly increased the percent of patients that reached the therapeutic aPTT threshold within 24 hours and significantly reduced the risk of recurrent VTE.*
- *The sensitivity of aPTT testing devices can vary greatly among testing instruments, reagents, and even reagent lots.*
- *Failure to account for variable sensitivity in aPTT can lead to systematic over- or underdosing of heparin.*
- *The therapeutic aPTT range should be calculated at each institution using the recommended methodology and updated whenever the reagent or lot of reagent is changed.*

Errors involving treatment with unfractionated heparin (UFH) are among the most common and serious in clinical practice. Some recent examples witnessed by the author include administering heparin in response to an order for a Hespan® (hetastarch) bolus, giving therapeutic doses of heparin and enoxaparin simultaneously and administering heparin to a patient with known heparin-induced thrombocytopenia.

Practice variability

Unnecessary variation in heparin dosing is a less dramatic but more pervasive type of error that occurs when protocols for heparin management are not used. Studies have shown that attaining a therapeutic aPTT within 24 hours significantly reduces the risk for recurrent venous thromboembolism (VTE), yet non-protocol-driven practice achieves this outcome only 37% of the time[1]. In a published survey of physician management of heparin in the treatment of VTE, initial heparin infusion rates for a 70-kg patient ranged from 500 to 1500 units/hr (7 to 21 units/Kg/hr). Only half of the respondents said they would administer another bolus dose and increase the heparin infusion rate in response to subtherapeutic aPTT values.

The survey showed wide variability in aPTT therapeutic ranges, which were not based on valid calculation in the coagulation laboratory[3]. Widespread and unnecessary variation in physician practices increase opportunities for errors in aPTT interpretation and heparin dosing. To reduce this unnecessary and deleterious variability, a weight-based heparin protocol was developed (Table 1)[2].

Weight-based heparin protocol

A randomized, controlled trial (RCT) was conducted at three hospitals that included 115 patients receiving therapeutic-dose hep-

Table 1. Weight-based Protocol[2]

- Initial: 80 units/Kg bolus, 18 units/Kg/hr

aPTT value:	change:
1.2 x control	bolus, ↑ 4 units/Kg/hr
1.2 - 1.5	bolus, ↑ 2 units/Kg/hr
1.5 - 2.3	no change
2.3 - 3.0	↓ 2 units/Kg/hr
> 3.0	hold 1 hr, ↓ 3 units/Kg/hr

arin. A standard-care protocol was compared to a weight-based protocol. The weight-based protocol started heparin treatment with a bolus dose of 80 units/Kg and an infusion of 18 units/Kg/hour. Use of the weight-based protocol increased the percent of patients that reached the therapeutic aPTT threshold within 24 hours from 77% to 97% (p=0.002) and significantly reduced the risk of recurrent VTE (RR 0.2, p=0.02)[2].

Laboratory test variability

The ability to generalize the weight-based protocol in other institutions was hindered by variability in laboratory methodology used to measure the aPTT. Many different aPTT thromboplastin reagents and instruments are in use in the United States. Each has a unique sensitivity to the effect of heparin (akin to the different sensitivities of prothombin time reagents that necessitate calculation of the INR). Thus, in one hospital a sample might be interpreted as subtherapeutic and the heparin dose increased, and in another hospital the same sample might be interpreted as supratherapeutic and the heparin dose decreased.

Even when a single reagent is used, clinically significant changes in the sensitivity can occur from lot to lot. The responsiveness of different lots of the same thromboplastin reagent used at BGSMC varied over time (Table 2, Figure 1). If this variable responsiveness were unaccounted for in calculation of the aPTT therapeutic range, systematic errors would occur in which large numbers of patients would be either under- or overdosed with heparin, depending on whether the reagent were more or less responsive.

The use of aPTT ratios (such as 1.5-2.5 times control) does not ameliorate this problem. Studies have shown that aPTT therapeutic ratios vary from 1.6-2.7 times control to 3.7-6.2 times control when the therapeutic range is appropriately determined by anti-Xa measurement[4,5].

Recommendations

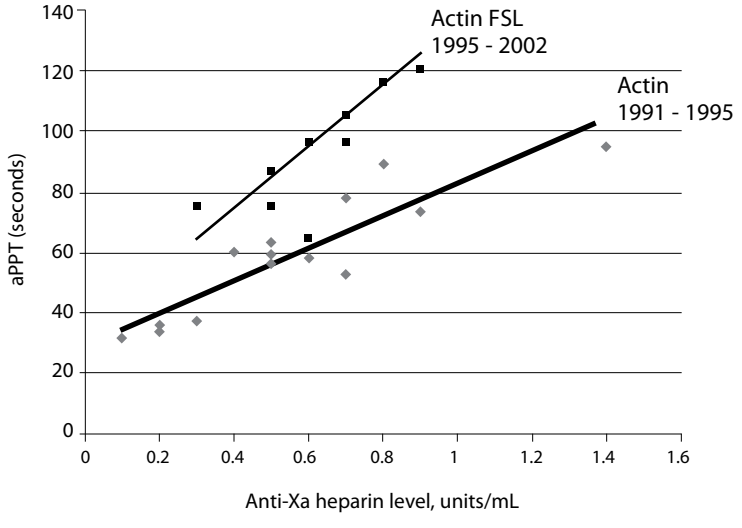
To account for the unique responsiveness of the thromboplastin reagent and laboratory instrumentation, the College of American Pathologists (CAP) and the American College of Chest Physicians (ACCP) Consensus Conference on Antithrombotic Therapy therefore recommend that the aPTT therapeutic range be independently validated at each institution. This is accomplished most easily by taking plasma from at least 30 patients receiving heparin therapeutically and simultaneously measuring anti-Xa heparin levels and aPTT results. The valid aPTT therapeutic range can then be calculated using simple linear regression to correlate the aPTT values with heparin levels of 0.3 to 0.7 anti-Xa units/mL. Figure 1 shows the results of using this technique when a change in thromboplastin reagent at BGSMC altered the therapeutic range from 45 to 65 seconds to 70 to 105 seconds. Failure to recognize this change would have resulted in systematic underdosing of the vast majority of patients receiving intravenous heparin at that institution.

Unfortunately, laboratory-specific validation of the aPTT therapeutic range is often overlooked. A review of 15 RCTs comparing UFH and low-molecular-weight heparin for the treatment of VTE showed that only three studies used appropriately validated aPTT therapeutic ranges and 11 used ranges that were known to be subtherapeutic for the thromboplastin reagents they employed[6]. Failure to use validated aPTT therapeutic ranges was a significant potential source of bias in these studies, since it would be expected to lead to systematic underdosing of heparin. It also demonstrates the pervasiveness of this problem, even in academic medical centers.

Table 2. Actin FS: Change in Therapeutic aPTT Range at BGSMC

Ther. aPTT	Ther. aPTT ratio	Year
60-85	1.8-2.5	1989
66-109	2.2-3.6	1990
79-105	2.3-3.0	1991
64-112	2.2-3.9	1997
55-78	1.9-2.7	1998
81-185	2.6-6.0	1998
72-119 to 98-165	2.6-4.3 to 3.7-6.2	2001

Figure 1. Change in aPTT therapeutic range following reagent change at BGSMC



Pseudo heparin resistance

The aPTT therapeutic range may also require recalculation in rare patients with abnormalities such as increased circulating levels of coagulation factor VIII. The plasma of these patients attenuates the sensitivity of the aPTT response, yielding a lower aPTT result at any given plasma heparin concentration. Therefore, the patient demonstrates pseudo heparin resistance in which unnecessarily high doses of heparin may be erroneously administered to overcome the blunted aPTT response. This diagnosis may be suspected when patients require unusually high heparin infusion rates and can be confirmed by comparing a set of the patient's aPTT values with simultaneous anti-Xa heparin levels. Persistently subtherapeutic aPTTs are observed despite therapeutic or even supratherapeutic anti-Xa heparin levels. Patients with pseudo heparin resistance can be treated using a protocol based on anti-Xa heparin levels, if that test result is available with acceptable timeliness.

Conclusions

Implementation of a weight-based heparin protocol can be expected to lead to improved intermediate outcomes (such as time until achievement of therapeutic aPTT) and a reduction in recurrent VTE[2]. The use of a protocol with an invalid aPTT therapeutic range may actually be counterproductive. The therapeutic aPTT range at each institution should be calculated by the recommended methodology and updated whenever the reagent or lot of reagent is changed.

References

1. Cruickshank MK, Levine MN, Hirsh J, et al. A standard heparin nomogram for the management of heparin therapy. *Arch Intern Med* 1991;151:333-7.
2. Raschke RA, Reilly BM, Guidry JR, et al. The Weight-based Heparin Dosing Nomogram Compared with a "Standard Care" Nomogram. *Ann Internal Med* 1993;119(9):874-81.
3. Reilly B, Raschke R, Sandhya S. et al. Intravenous heparin dosing: patterns and variations in internists' practices. *J Gen Intern Med* 1993 Oct;8(10):536-42.
4. Brill-Edwards P, Ginsberg JS, Johnston M, et al. Establishing a therapeutic range for heparin therapy. *Ann Intern Med* 1993;119:104-9.
5. Bates SM, Weitz JI, Johnston M, et al. Use of a fixed activated partial thromboplastin time ratio to establish a therapeutic range for unfractionated heparin. *Arch Intern Med* 2001;161:385-91.
6. Raschke R, Hirsh J, Guidry JR. Suboptimal monitoring and dosing of unfractionated heparin in comparative studies with low-molecular-weight heparin. *Ann Intern Med* 2003;138:720-3.

PROCEEDINGS

The Epidemiology and Outcomes of Patients Treated With Heparin During Hospitalization

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Key points

- *Current National Patient Safety Goals call for hospitals to reduce the likelihood of patient harm associated with the use of anticoagulation therapy.*
- *A recent study examined the epidemiology, length of stay and occurrence of bleeding or other complications in non-surgical patients treated with heparin infusions during hospitalization.*
- *A total of 1443 non-surgical cases treated with heparin for at least 24 hours during hospitalization from January 2004 to June 2007 were analyzed retrospectively.*
- *Based on serum activated partial thromboplastin time (aPTT) results at 6 and 24 hours, cases were categorized as subtherapeutic (< 50 seconds), therapeutic (50-75 seconds), above therapeutic (76-99 seconds) and supra-therapeutic (≥100 seconds).*
- *One in 3 cases treated with heparin had a subtherapeutic aPTT at 24 hours and these cases had increased hospital length of stay.*
- *Clinicians responsible for assuring anticoagulation safety should incorporate strategies to monitor subtherapeutic aPTT results as diligently as supra-therapeutic results.*

Introduction

Anticoagulant use is a frequent cause of medication errors in hospitalized patients. A review of published studies found that guidelines recommended by American College of Cardiology/American Heart Association for weight-based heparin therapy are not commonly used[1,2]. This review also noted a higher rate of bleeding events in patients who received excess bolus and infusion heparin doses. A study by Fanikos et al. of smart pump technology found that the most common alerts were for underdose (59.8%), followed by overdose (31.3%)[3]. The Joint Commission has issued a Sentinel Event Alert to help hospitals prevent errors associated with commonly used anticoagulants[4]. In this brief report the epidemiology, activated partial thromboplastin time (aPTT) response and outcomes of patients receiving therapeutic doses of heparin are described.

Methods

Study population

Data for this analysis were obtained from the CareFusion Outcomes Research Database, a large, multi-institutional database of US acute care hospitals[5]. Data collected included patient-level information regarding diagnosis and procedures (all principal and secondary diagnoses and procedure codes), severity of illness on admission, length of hospital stay (LOS), hospital charges and clinical variables such as laboratory results and vital signs. Eligible patients were drawn from four hospitals that electronically provided pharmacy orders and laboratory results for an entire hospital stay from January 2004–June 2007. The current study was conducted in compliance with the New England Institutional Review Board/Human Subjects Research Committee (Wellesley, MA), federal regulations and the Health Insurance Portability and Accountability Act. All data were de-identified in a manner that did not allow for direct or indirect identification of patient-specific information.

Case definitions

Cases with a heparin order were screened for route and dosing. All cases older than 18 years old receiving intravenous (IV) heparin for more than 24 hours were included in the analysis and were defined as those with a second IV heparin infusion order at least 24 hours after first order, or with an aPTT laboratory order at least 24 hours after first IV heparin infusion order. Cases were grouped based upon their principal discharge diagnosis (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]) and further categorized as surgical or medical. aPTT results at 6 hours and at 24 hours post heparin initiation were grouped into the following categories: sub-therapeutic aPTT (< 50 seconds), therapeutic aPTT (50-75 seconds), above therapeutic aPTT (76-99 seconds) and supra-therapeutic aPTT (≥ 100 seconds). Retrospective analysis identified 1,443 medical cases that received IV heparin infusions as described.

Adverse and clinical outcomes

Clinical outcomes analyzed included in-hospital mortality, LOS, bleeding or other complications. Bleeding or other complications were identified by the presence of a ICD9 diagnosis code for bleeding at time of admission or by meeting any of the following criteria within 7 days of IV heparin infusion initiation: (1) presence of a ICD9 procedure code for transfusion, (2) thrombocytopenia defined as (a) initial platelet ≥ 150,000 and lowest platelet <150,000, or (b) decrease in platelet count > 50% from baseline; and (3) decreased hemoglobin of ≥ 10% or 4 gm/dL from baseline.

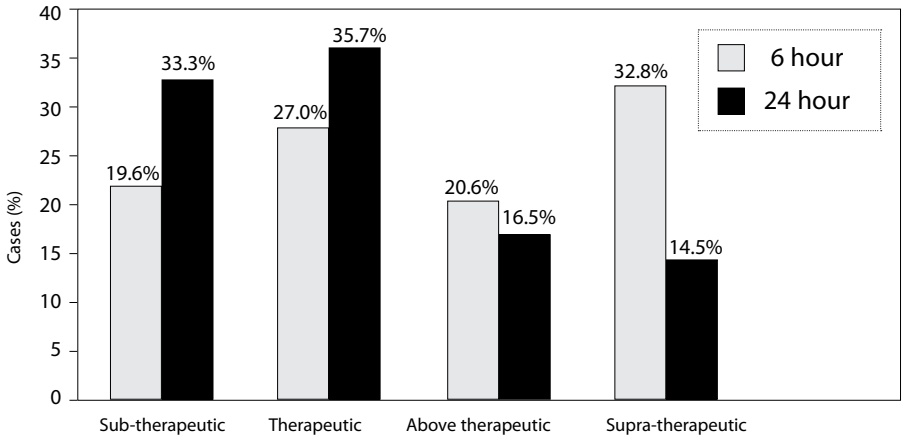
Data analysis

Of the 1,443 medical cases, 216 that did not have an aPTT measured at 24 hours post heparin initiation were excluded. Univariate analysis was performed on the four aPTT categories for mortality, LOS and the presence of bleeding or other complications. Observed and expected mortality and LOS ratios were calculated with previously described predictive models that use demography, comorbidities and laboratory results to stratify risk in the peri-admission period[5]. These models were recalibrated on the study population to account for differences in predicted mortality among disease groups. All statistical analyses were performed using Statistical Analysis Software (SAS; version 9.01, SAS Institute Inc., Cary, NC). P values <0.05 were considered statistically 2.17^ significant.

Results

For 1,443 medical admissions that received IV heparin for at least 24 hours, the median age was 70 years, 50.5% were men and the crude mortality was 3.7%. An aPTT was not done within 24 hours of starting IV heparin infusion in 15.0% of cases. Of all cases, 82% were admitted within 15 disease conditions, with the five most common causes of admission being non-hemorrhagic stroke, acute myocardial infarction, heart failure, pulmonary embolism and arrhythmia.

Figure 1. aPTT results at 6 and 24 hours medical cases only



Approximately 1 in 5 cases and 1 in 3 cases were sub-therapeutic at 6 and 24 hours, respectively. At 6 and 24 hours the percent of cases in the therapeutic category increased from 27.0% to 35.7% and those in the supra-therapeutic category decreased from 32.8% to 14.5% (Figure 1).

By the fourth hospital day 90.2% of cases were started on IV heparin infusion. Cases were further stratified by those started on IV heparin infusion within 4 days and beyond 4 days from admission. Cases on heparin beyond 4 days had a significantly higher ratio of actual to predicted mortality within each aPTT category and a higher ratio of actual to predicted LOS that was not significant (Table 1). Differences were also noted with bleeding or other complications.

Given these differences and to account for a more homogenous population, further analysis was done for cases started on IV heparin infusion within 4 days of admission. Results for these cases showed that the actual

Table 1. Outcomes for heparin start day† medical cases only

	Sub therapeutic		Therapeutic		Above therapeutic		Supra therapeutic	
	≤ 4 days	> 4 days	≤ 4 days	> 4 days	≤ 4 days	> 4 days	≤ 4 days	> 4 days
Cases (n)	360	49	413	25	182	20	165	13
Actual LOS (avg)*	7.3	18.0	5.8	13.5	5.8	13.1	6.1	11.8
Predicted LOS (avg)*	7.5	8.3	6.6	8.7	6.6	7.8	6.7	7.3
Ratio act/predict LOS	0.97	2.17^	0.88^	1.55^	0.88^	1.67^	0.90^	1.62^
Mortality %	4.7	12.2	3.1	16.0	1.6	0.0	1.2	15.4
Predicted mortality %	4.3	6.7	3.3	5.5	3.2	4.4	2.8	5.1
Ratio act/predict mortality	1.11	1.82	0.95	2.93	0.52	0.00	0.44	3.04
Bleeding diagnosis code	13.9	26.5	11.6	28.0	12.1	35.0	12.1	7.7
Transfusion procedure (%)	8.3	2.0	6.1	12.0	5.5	0.00	7.9	0.0
Thromboycytopenia (%)	6.9	14.3	6.3	16.0	2.7	15.0	3.0	23.1
Decreased hemoglobin (%)	26.1	46.9	23.2	36.0	18.1	45.0	17.0	38.5

† Mortality and LOS recalibrated for all medical cases receiving heparin in ≤ and > 4 days* excluding deaths, ^ p < 0.05

Table 2. Outcomes for heparin started within first 4 days medical cases only

Characteristic	1-SUBTHP	Groups 2,3,4†
Cases (n)	360 (32.1)	760 (67.9)
Acutal LOS (avg)*	7.3	5.9
Predicted LOS (avg)*	6.8	6.1
Ratio Act/Predict LOS	1.07 (p=.12)	0.96 (p=.07)
Mortality %	4.7%	2.4%
Predicted Mortality %	3.7%	2.7%
Ratio Act/Predict Mort (95% CI, p value)	1.28 (0.84-2.71) p=.37	0.87 (0.61-1.50) p=.61
Total Charges (ave $)	28,389	18,876

† 2 = therapeutic, 3 = above therapeutic, 4 = supra-therapeutic; * excluding deaths

LOS was higher for sub-therapeutic cases than for all other aPTT groups combined (7.3 days vs. 5.9 days, $p < 0.05$). The ratio of actual to predicted LOS was higher for sub-therapeutic cases (1.07, p=0.12) than for all other aPTT groups combined (0.96, p = 0.07) (Table 3). Although these actual to predicted results did not reach statistical significance, there may be a trend in the direction of the ratio that indicates that sub-therapeutic cases have a higher LOS.

The results of regression analysis of risk factors for bleeding or other complications showed that severity of illness on admission (OR = 2.55) and cases started on heparin beyond 4 days (OR = 2.55) had significantly higher rates of bleeding or other complications (Table 3).

Discussion

Results of a retrospective analysis of four-hospital data found that sub-therapeutic aPTT results were common. Even in the subset of medical cases in which IV heparin infusion was initiated early in the hospitalization (within 4 days) these rates persist. It is noteworthy that at 6 hours the percent of sub-therapeutic cases (19.6%) was lower than the percent of supra-therapeutic cases (32.8%); however, at 24 hours the percent of sub-therapeutic cases (33.3%) was higher than the percent of supra-therapeutic cases (14.5%) (Figure 1). The higher predicted mortality of sub-therapeutic cases (Table 1) may indicate that clinicians were being more cautious with heparin dosing in patients with a higher severity of illness. A substantial fraction of cases (15.0%) lacked evidence of measured aPTT.

When risk-adjusted outcomes were compared, the sub-therapeutic cases had higher ratios of actual to predicted LOS and mortality, although the differences were not statistically significant for cases started on heparin within 4 days of admission. Differences in complication rates between the groups appear to be related to underlying patient severity of illness. The limitations of this analysis are the retrospective nature of the study, hospital specific therapeutic aPTT was not available and bleeding was not confirmed by clinical case review.

Table 3. Complication model for medical patients receiving heparin

Variable	OR (95% CI)	p	c statistic
Aggregated severity on admission	2.55 (1.95, 3.35)	<.0001	0.8272
1st heparin order >3 days	2.55 (1.28, 5.05)	0.0075	0.8307
Above therapeutic	0.35 (0.10, 1.25)	0.1069	0.8373
No PTT	0.66 (0.26, 1.68)	0.3802	0.8382
Supra-therapeutic	0.62 (0.20, 1.92)	0.4081	0.8410
Sub-therapeutic	1.05 (0.54, 2.07)	0.8836	0.8414

Note: Therapeutic as reference

Conclusions

The differences observed in this analysis may be important for hospitals evaluating performance of IV heparin infusion protocols. Given the outcomes and complication differences seen in this analysis, when conducting hospital-specific analysis it may be important to stratify cases by early and late initiation of heparin and possibly by severity of illness. Given the high rate of sub-therapeutic cases at 24 hours and their associated worse outcomes, it may be important to evaluate both sub- and supra-therapeutic cases.

Further research should examine differences in aPTT response to understand if physician preference or patient risk characteristics are influencing heparin therapeutic ranges and subsequent outcomes. Hospital-specific evaluation of aPTT response to IV heparin infusion therapy may also provide insights to help clinicians improve heparin use.

References

1. Melloni C et al. Unfractionated heparin dosing and risk of major bleeding in non-ST-segment elevation acute coronary syndromes. *Am Heart J* 2008;156:209-15.
2. Hirsh J, et al. Parenteral Anticoagulants. American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *CHEST* 2008; 133:141S-59S.
3. Fanikos J, et al: Medication errors associated with anticoagulant therapy in the hospital. *Am J Card*, 2004, 94:532-5.
4. The Joint Commission. Sentinel Event. Retrieved May 5, 2009 from http://www.jointcommission.org/SentinelEvents/SentinelEventAlert/sea_41.htm.
5. Tabak YP, Johannes RS, Silber JH. Using automated clinical data for risk adjustment: development and validation of six disease-specific mortality predictive models for pay-for-performance. *Medical Care* 2007; 45(8): 789-805.

PROCEEDINGS

A Systematic Approach to Improving Anticoagulation Safety

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Key points

- *Anticoagulation therapy is a complicated process that includes at least 51 opportunities for failure, which can all lead to serious patient harm.*
- *Three principles for ensuring medication safety include designing systems to prevent errors and harm, making errors that do occur visible to staff and having procedures in place to mitigate harm.*
- *The following steps should be taken to improve the safety of heparin use:*
  1. *Write pre-typed protocols*
  2. *Develop a heparin dosing service*
  3. *Use low molecular weight heparin (LMWH) rather than unfractionated heparin (UFH)*
  4. *Use pre-mixed bags and a single concentration of heparin*
  5. *Limit floor stock*
  6. *Prohibit override access from automated dispensing cabinets*
  7. *Minimize stock in pharmacy*
  8. *Use saline flush to maintain line patency*
  9. *Use "TALLman" lettering*
  10. *Duplicate drug checking*
  11. *Use anticoagulation flow sheets*
  12. *Ensure competency of staff*
  13. *Use smart pumps*
  14. *Use barcoding*
  15. *Use computer alerts/pages for high aPTT values*
- *By understanding the complexity of heparin therapy, managing every step and taking action to identify and eliminate every source of error, significant progress can be made towards achieving the goal of "do no harm."*

The medication process has seven core steps: evaluating a patient, ordering a drug, transcribing the order, preparing and dispensing a drug, administering a drug to a patient and monitoring patient response. There is no single owner of this process. While physicians, nurses, pharmacists and patients each own certain sub-elements of the process, a safe and effective overall process requires each discipline to consider their role in the context of others.

With anticoagulant therapy, there are at least 51 opportunities for failure. A failure at any one of the steps can lead to serious patient harm.

Errors may include:

Evaluation:

1. Insufficient information about other drugs a patient is taking
2. Insufficient information about past dose-response relationships
3. Insufficient drug information
4. Insufficient laboratory information
5. Insufficient allergy, pregnancy or other patient information
6. Incorrect diagnosis
7. Home medication lists are not reconciled

Decision:

1. Incorrect drug selected
2. Incorrect dose selected
3. Incorrect route selected
4. Parameters incorrect; too rapid of a titration schedule
5. Regimen too complex

Ordering:

1. Illegible handwriting
2. Order not transmitted to pharmacy
3. Overlapping scales

4. Failure to account for changing conditions of diet, total parenteral nutrition (TPN) or enteral feedings
5. Wrong route prescribed
6. Use of the letter U or other unsafe designations
7. Untimely orders (e.g. the nurse must call the physician for orders but the time delay is prolonged)
8. Wrong dose prescribed

Transcription:

1. Misreading of order
2. Incorrect entry into pharmacy computer or computerized prescriber order entry (CPOE) system due to a slip or picking error
3. Illegible transcription

Dispensing:

1. Incorrect drug or concentration selected
2. Patient information unavailable
3. Drugs that look or sound alike
4. Label incorrect, ambiguous or applied incorrectly
5. Infusion prepared incorrectly
6. Incorrect dose drawn into syringe
7. Incorrect mapping to automated dispensing cabinet
8. Floor stocking error

Administration:

1. Improper storage and lighting
2. Look-alike labeling
3. Incorrect syringe used
4. Administered via incorrect route
5. Failure to chart correctly or in a timely manner
6. Medication administration record misread
7. IV pump issues:

   A. Changing concentrations

   B. Non-standard concentration

   C. Pump programming error

   D. Bag inserted into incorrect channel

   E. Over-reliance on smart technology

   F. Line swaps

   G. Free flow pump

Monitoring:

1. Incomplete or insufficient monitoring; patient not observed for bleeding
2. Blood tests not ordered
3. Blood tests ordered incorrectly
4. Blood test results unavailable
5. Blood test results communicated incorrectly
6. Mislabeled specimens
7. Fragmented care

Nolan has described three principles for system design to improve patient safety[1]. The first principle is to design systems that prevent errors and harm. Knowing that best efforts cannot prevent 100 percent of all errors or harm, errors must be made visible to staff. Finally, procedures must be in place to mitigate harm.

Based on these principles, the following steps should be taken with regard to heparin.

P = prevention
M = mitigation
D = detection

16. *Write pre-typed protocols (P, M).* Handwritten protocols are unquestionably prone to error. Dosing or monitoring parameters may be illegible, ambiguous or incorrect. Different instructions for different patients can lead to confusion and patient mix-ups. Use of simple pre-typed protocol enables pre-typed or pre-prepared medication administration records, eliminates handwriting problems and provides clarity and consistency for staff. A well-designed protocol also includes clear instructions for managing an out-of-range laboratory test or medication error.
17. *Develop a heparin dosing service (P, D, M).* Despite the use of protocols, clinical judgment needs to account for the nuances of patient conditions and dose:response relationships. Investing accountability in a heparin dosing service comprising a small group of highly trained experts (usually pharmacists) can help standardize practice while allowing for patient variability. This service also increases early detection of adverse events and rapid intervention should an adverse event or error occur.
18. *Use low molecular weight heparin (LMWH) (P).* There is no question that LMWH is safer than unfractionated heparin UFH). For most clinical situations, a LMWH is as effective as UFH and prescribing, administration and monitoring are far simpler. Thus, conversion from UFH to LMWH will improve the safety of anticoagulation. The main barrier to this conversion has been cost: the acquisition cost of LMWH is significantly higher than UFH. A more complete assessment shows that when the use of IV lines, IV pumps, laboratory testing and labor of dose changes and related functions are taken into account, the costs of the two products begin to equalize.
19. *Use pre-mixed bags and a single concentration of heparin (P).* The process of mixing IV solutions is highly prone to error. Use of more than one concentration of heparin creates a risk that the two formulations may be confused. Hospitals

can help reduce the risk of errors by purchasing heparin in a ready-to-use form from one of several manufacturers and by standardizing to a single concentration for all patient populations. Under no circumstances should IV heparin solutions be prepared outside the pharmacy department.

20. *Limit floor stock (P).* Emergency use of heparin is seldom needed outside of areas such as interventional cardiology or radiology, the operating room and perhaps the emergency department. Therefore, its availability should be limited to carefully selected areas of the hospital. Heparin should be stocked in unit-of-use formulations with the fewest possible strengths and types. Other than for emergency purposes, heparin should be dispensed in patient-specific form directly from the pharmacy.

21. *Prohibit override access from automated dispensing cabinets (P).* Except for emergency situations and the departments described above, access to heparin should be limited to patients with an active order for that form of heparin. This ensures pharmacy screening of the order and helps reduce medication errors such as selecting an incorrect formulation or administering heparin to an incorrect patient.

22. *Minimize stock in pharmacy (P).* Heparin is available in many concentrations and sizes, including vials, pre-filled syringes and large-volume infusion bags. The greater the variety of products available on the shelf, the greater the likelihood of dispensing errors. Limiting what is available on pharmacy shelves can help to minimize these errors.

23. *Use saline flush (P).* There is little, if any, evidence that heparin is more effective than saline for maintaining the patency of peripheral or arterial lines. The use of saline solution to flush lines avoids the risk of confusing heparin formulations and the risk of heparin-induced thrombocytopenia.

24. *Use "TALLman" lettering (P).* There have been many reports of mix-ups between heparin and Hespan™ (a brand of hetastarch). Most authorities recommend differentiating product names by the use of "TALLman" lettering that capitalizes the distinguishing features of words. For example, HEParin or HeSPAN should be used on shelf and pharmacy labels and in the electronic health record.

25. *Duplicate drug checking (P).* The pharmacy computer software and electronic health record should be configured to check for duplicate anticoagulants and for drugs such as thrombolytics that influence the response to heparin, and to alert practitioners so appropriate modifications can be made. Checking should include LMWH and other agents that may not be active at the time the heparin order is placed. For example, a one-time dose of enoxaparin may have been administered in the emergency department but not be considered active when the heparin order is written on the inpatient unit. The system should also check for discontinuation of agents that could require the dose of heparin to be increased. Ideally, the system will minimize nuisance alerts such as a heparin infusion and bolus dose or a heparin infusion and line flush.

26. *Use anticoagulation flow sheets (P,D).* When multiple loading and bolus doses are given, infusion rates may change and laboratory tests be received up to four times daily. Understanding dose-response relationships or locating a patient's dosing history can be daunting and lead to incorrect decisions. Use of a flowsheet can greatly simplify the process of adjusting dosages and reduce the likelihood of error.

27. *Ensure competency of staff (P).* Heparin use is highly complex. Safe use of this medication requires that all practitioners fully understand the pharmacology of the drug, dosing considerations and the use of site-specific systems designed to minimize the risks of error and harm.

28. *Use smart pumps (P, D).* Smart pumps are infusion devices that are designed to deliver dosages within pre-established parameters. The standard concentration of the drug is preloaded into the device software along with upper and lower dosage limits. If a nurse attempts to infuse a dose outside these limits, the safety software generates an alert. If a nurse overrides an alert and proceeds with the original programming, an icon or other message on the pump's screen alerts staff that the drug is infusing outside of usual limits. Some smart pumps also have hard limits—limits that cannot be overridden. Smart pumps help to reduce pump programming errors such as 10-fold overdoses. However, they do not detect programming errors within established limits, line swaps or if a nurse has selected heparin but hung a bag of insulin or another medication. Despite these limitations, smart pumps should be considered a minimum standard for infusing high-risk medications such as heparin.

29. *Use barcoding (P, D).* Barcoded medication administration helps detect and prevent administration of a drug to an incorrect patient by alerting the nurse that the drug is not on a patient's profile or not due for administration. Barcoding can also help ensure accuracy in replacing drugs in automated dispensing cabinets and in stocking drugs received from the wholesaler or other sources. Barcoding is not fool-proof and practitioners often find ways to bypass the system; as such, its use needs to be carefully managed and monitored.

30. *Use computer alerts/pages for high aPTT (D).* When an aPTT or other laboratory test reaches a certain level, it is important to respond in a timely fashion. Too often, a laboratory report comes to a person such as a unit secretary who is not in position to take action and needs to track down a decision-maker. In some hospitals, laboratory values are automatically sent by computer or page directly to the decision-maker.

Conclusion

It is commonly believed that because of the complex nature of anticoagulation it is simply not possible to eliminate all errors or adverse events. Such fatalistic perspective will defeat excellence. By understanding the complexity of heparin therapy, managing every step and taking actions to identify and eliminate every source of error, significant progress can be made towards achieving the goal of "do no harm."

Reference

Nolan TW. System changes to improve patient safety *Brit Med J* 200 Mar 18; 320(7237):771-3.

PROCEEDINGS

A Coordinated Inpatient Anticoagulation Program: Part of the Heparin Solution?

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Key points

- *Comparison of data from 955 hospitals shows that those with heparin services have lower death rates, length of stay, Medicare charges and bleeding complication rates, compared with hospitals that do not have this service.*
- *The Fairview Southdale model for heparin dosing specifies that all patients receiving heparin are managed by pharmacy and all dosing and titrations are weight-based and customized to the disease state being managed.*
- *St. Mary's Medical Center (SMMC) experienced four serious warfarin-related events with a few months, which underscored the need to improve anticoagulation therapy.*
- *A hospital-wide anticoagulation program eliminated sentinel events for warfarin, low molecular weight heparin (LMWH) and direct thrombin inhibitors (DTI) and showed that 80% to 90% of heparin errors could also be prevented.*
- *Anticoagulation program data helped convince senior leadership of the need for smart infusion pumps; work on incorporating heparin into the anticoagulation program continues.*

This article includes a brief review of the successful anticoagulation program at St. Mary's Medical Center (SMMC) in Duluth, MN that improved medication safety of warfarin, low molecular weight heparin (LMWH) and direct thrombin inhibitor (DTI) therapies and a discussion of continuing efforts to incorporate heparin management into the program.

Need for improved anticoagulation medication safety

Anticoagulation therapy involves the use of high-risk medications and complex protocols that increase the likelihood of error. The demands of increasingly complex environments and staff shortages can overwhelm even the most professional nurse's capacity to follow a complex protocol correctly. Pharmacists are able to assist in managing complex heparin dosing more efficiently and accurately. The Fairview Southdale model in use at many hospitals reflects the type of system change that is needed. With this model, all patients on heparin are managed by pharmacy and all dosing and titrations are weight-based and customized to the disease state being managed.

The impact of pharmacist management of heparin and warfarin was evaluated by Bond and Raehl in 2004[1]. Using 1995 Medicare and the National Clinical Pharmacy Services Databases from 955 hospitals, they compared data from hospitals that do and do not have anticoagulation services. Results showed that, when compared with hospitals that have heparin services, hospitals without such services had higher death rates, length of stay, Medicare charges and bleeding complication rates (Table 1)[1].

St. Mary's Medical Center

St. Mary's Medical Center (SMMC) is a 380-bed, tertiary care hospital, the flagship of the SMDC Health System with 20 clinics, hospitals and specialty care facilities located in northern Minnesota, Wisconsin and Michigan. In 2003 SMMC faced the emergency situation of four serious warfarin-related events with a few months, which focused attention on the need to manage anticoagulant therapy in the hospital and outpatient setting. An interprofessional team was formed to deal with this.

Chaired by the Vice President of Medical Affairs, the team included primary and specialty physicians, outpatient clinic administrators, information technology personnel, nurses and a pharmacist clinical coordinator. A hospital-wide anticoagulation program, focusing its efforts on improving the safe and effective use of warfarin, was implemented and no sentinel events involving warfarin occurred in program patients. The program went on to create one of the first computer programs specifically designed for use by an inpatient anticoagulation service. LMWH and DTI were added to the program and no sentinel events occurred with these agents[2].

Incorporating heparin into the program

The anticoagulation program was then focused on heparin errors. The existing protocol had called for a floor nurse to adjust infusion dosing and led to errors such as those shown in Table 1. The pharmacist anticoagulation program chair worked with pharmacy students who were on acute care rotations to evaluate heparin medication usage and identify opportunities to improve heparin use at SMMC.

Table 1. Heparin errors

Example 1. Heparin gtt (drop) was increased at 0600 to 1800 units/hr. A new bag was hung at 0815 because the previous bag was empty. The previous pump settings were not changed when the new bag was hung. At 0930 the pump was alarming for air because the bag was dry. At 0930, a nurses inspected the pump and settings and discovered that the rate was set at 18,000 units/hr rather than 1800 units/hr.

Example 2. Patient was on a heparin drip. Day shift received PTT results and should have decreased heparin by100 units/hr. Heparin was accidently increased by100 units/hr.

Example 3: Patient returned from dialysis with the infusion pump shut off. His heparin gtt bag was dry and he had blood backed up about 12 inches in his intravenous (IV) tube, which was difficult to flush. Patient had left the floor around 0700. Dialysis was called to ask why they had not called for a heparin drip bag. They replied that the bag had gone dry right before transport so they shut it off and sent the patient back to the nursing unit. At 0600, the PTT for this patient was 70 and the drip rate was 1500 units/hr. At 1405, blood was drawn for a stat PTT, which was 33. The heparin drip rate needed to be increased by 200 units/hr and a bolus of 40 units/Kg was administered per heparin protocol, instead of restarting the heparin dose the patient was already stabilized on.

Results showed that partial thromboplastin time (PTT) values were not obtained as scheduled to ensure accurate use of the protocol, the protocol was not always interpreted correctly and platelets were not consistently monitored as intended in the protocol to watch for heparin-induced thrombocytopenia (HIT). Even though a system was in place, heparin therapy was not being delivered as specified.

Analysis of data over a two-year time period by the anticoagulation team showed that between 80% and 90% of heparin errors could be prevented by the adoption of two strategies: 1) have pharmacists actively manage the dosing of heparin infusions and 2) implement smart (computerized) infusion pump technology. The anticoagulation team successfully used data about heparin errors to obtain administrative approval to purchase smart infusion pumps, which will be implemented for heparin this year.

Table 2. If a hospital did not have a heparin service[1]

- Death rates were 11.41% higher
  - 6.37% vs. 7.19%
- Length of stay was 10.05% higher
  - 7.79 days vs 8.66 days
- Medicare charges were 6.6% higher
  - $1145 more per patient
- Bleeding complications were 3.1% higher
  - 8.84% vs 9.12%

Continuing efforts

Important questions still need to be answered at SMMC. Should pharmacists begin to actively manage all patients on heparin therapy? Should the anticoagulation program be modeled after the Fairview Southdale service? As was done for other anticoagulants, computerizing the monitoring system for heparin is needed but raises issues of resource allocation and staff acceptance.

If the primarily nursing-driven model continues, how can compliance with the anticoagulation program be assured? The Joint Commission National Patient Safety Goal (NPSG) 3E requires hospital to improve the safety of anticoagulation therapy. To meet this mandate, clinicians need to function as a multidisciplinary team. Does the current SMMC model meet this standard?

Addressing large issues of heparin management remains difficult. However, NPSG 3E has prompted more focus on this issue. The two-year data analysis of heparin errors can be used to raise concern about this issue with administration. Shared learning with clinicians from other hospitals dealing with these issues can help advance heparin medication safety efforts.

Summary

Implementation of an inpatient anticoagulation program virtually eliminated warfarin, LMWH and DTI sentinel events; however, eliminating heparin errors continues to be a challenge. Anticoagulation program data helped convince senior leadership of the need for smart infusion pumps. Work continues on defining how to incorporate heparin into the anticoagulation program.

References

1. Bond CA, Raehl CL. Pharmacist-provided anticoagulation management in United States hospitals: death rates, length of stay, Medicare charges, bleeding complications, and transfusions. *Pharmacother* 2004; 24(8): 953-63.

2. Schneider BL, Gulseth MP, Cusick M. et. al. A computer program for a pharmacy managed inpatient warfarin dosing service. *Am J Health-Syst Pharm* 2005; 62:2393-6.

PROCEEDINGS

Reducing Heparin Errors: The Indianapolis Coalition for Patient Safety

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Key points

- *The Indianapolis Coalition for Patient Safety (ICPS) was established to improve patient safety among the six major health systems in Indianapolis.*
- *ICPS has standardized procedures for surgical-site verification, established a standardized list of unsafe abbreviations and collaborated on the Institute for Healthcare Improvement (IHI)* 100,000 Lives *campaign.*
- *The ICPS anticoagulant workgroup, working with the Institute for Safe Medication Practices (ISMP), completed a safe-practices self-assessment of all organizations, developed a universal anticoagulant metric, created a library of documents related to anticoagulant use and assessed how well hospital computer systems alerted clinicians to anticoagulant safety concerns.*
- *Institutions reported the percent of partial thromboplastin time (PTT) values that were therapeutic, sub-therapeutic, high or super-therapeutic.*
- *Analysis of computerized prescriber order entry (CPOE) and pharmacy computer systems revealed variations in alerts with regard to providing anticoagulant safety alerts.*
- *The ICPS workgroup educated coalition members about systems and processes so that more educated questions could be asked and further work done to improve anticoagulant safety city-wide. Identifying outliers within the group enabled members to answer the question: How do I compare?*

Indianapolis Patient Safety Coalition

The Indianapolis Coalition for Patient Safety (ICPS) is one of a handful of citywide coalitions in the United States focusing on patient safety. The coalition was formed in 2003 to provide a forum for Indianapolis-area hospitals to share information about best practices and to work together in a non-punitive setting to solve the patient safety issues of most concern in Indianapolis hospitals. ICPS membership includes Wishard Health Services, which has a level-one trauma center, burn unit and 10 community healthcare centers; the Richard L. Roudebush Veterans Administration Medical Center; St. Francis Hospitals and Health Centers and St. Vincent Health, both faith-based organizations; Clarian Health; Community Health Network and Suburban Health Organization hospitals. An executive director was hired in 2006.

Primary membership includes all chief executive officers (CEOs), chief nursing officers (CNOs), chief medical officers (CMOs), safety officers and pharmacy leaders. Meetings are held every two months, and the work of the coalition is presented to the CEOs at a semi-annual meeting. Several task forces and work groups have been developed, including one focused on anticoagulant safety.

Successes

Several successes illustrate the coalition's effectiveness. For example, ICPS first worked to standardize surgical-site verification for all coalition hospitals. Many of these are teaching hospitals and residents circulate from hospital to hospital. Establishing uniform procedures for surgical site verification and other processes can greatly increase compliance by the medical group. ICPS established one list of unsafe abbreviations for hospitals throughout the city. A letter outlining the rationale for the list was signed by the CEO of every hospital and sent to the medical staff at all hospitals sending a very powerful message. ICPS hospitals participated in a collaborative project aimed at reducing rates of methicillin-resistant Staphylococcus aureus (MRSA) infections in Indianapolis hospitals. The project helped improve preventive practice adherence and resulted in a significant reduction in MRSA infection rates on study units.

Staff recognition has also been an important aspect of the coalition's work. Every year, each hospital awards a patient safety hero award to an individual or team in the hospital that has done the best work to promote patient safety. ICPS also collaborated with the Institute for Healthcare Improvement (IHI) *100,000 Lives* campaign. Each of the health

systems took ownership for one part of the IHI campaign and formed work groups among all the hospitals to work on that issue.

Anticoagulant workgroup

The goal of the anticoagulant workgroup is to improve anticoagulant medication safety in Indianapolis health systems. The workgroup included 12 pharmacists and one registered nurse. Each organization completed the Institute for Safe Medication Practices (ISMP) failure mode and effects analysis (FMEA) to identify areas of vulnerability. After that, members completed best-practice self-assessments and agreed to share and compare data.

The group began work in February 2007, met every two or three weeks through the summer, and identified four major tasks to complete. The first task was a self-assessment of all organizations using a list of safe practices provided by ISMP. Other tasks were to develop a universal anticoagulant metric among participating hospitals, create a library of documents related to anticoagulant use for hospitals to share and assess how well hospital computer systems were alerting physicians, pharmacists and others about anticoagulant safety concerns.

Assessing safe practices

The ISMP list of safe practices includes 14 universal practices that all hospitals should have in place, including having "U" on the list of "Do not use" unsafe abbreviations, having a standardized heparin concentration and using a manufacturer-prepared solution whenever possible.

Other core practices included ensuring that computerized prescriber order entry (CPOE) and pharmacy systems provided drug interaction warnings and that medication reconciliation was done. There were also four "stretch" goals resulting in a total of 18 core practices.

Grids were developed with cells representing each of the core and target safe practices for each of the six hospitals. Medication reconciliation was assessed at admission, transfer and discharge, which required more cells for each of the stages. Cells were color-coded to show assessment results: green meant that a hospital was completely compliant with that core practice; yellow meant there was still work to do; red meant that work had not begun.

The majority of core practices were green, some were yellow and very few were red. Core safe practice that needed improvement included having functional drug interaction warnings for CPOE and pharmacy systems and compliance with medication reconciliation for anticoagulants. Compliance with target safe practices indicated more challenges, including dispensing of all anticoagulant doses from pharmacy, independent double checks and monitoring service for all anticoagulants by pharmacists.

Universal metric

A universal metric was developed to measure the impact of safety strategies that were implemented. The goal was to avoid laborious chart reviews and automate measurement as much as possible, have results be meaningful from a safety standpoint and be able to compare results across systems.

Discussions with ISMP and IHI led to the use of partial thromboplastin time (PTT) as the universal metric. Because institutions used different therapeutic ranges, each organization did not report PTT values, but the percent of PTTs that were therapeutic (within the target range), sub-therapeutic, high or super-therapeutic (two or more times the upper therapeutic limit).

The first question was whether an institution had a weight-based protocol in place. Electronic data already available from hospital laboratories were used to separate PTT results into the four categories. Results for all were compared.

Anticoagulation library

The coalition created a library comprising studies, protocols, nomograms and other information related to anticoagulant safety. The documents were scanned and compiled in a CD library that was distributed to every member organization to allow everyone to learn from existing practices.

Computer systems test

The last task was to evaluate how well the CPOE and pharmacy computer systems were alerting clinicians to therapeutic duplication, disease-drug and drug-drug interactions. Two pharmacists who specialized in the use of anticoagulants and had run an anticoagulant outpatient clinic created an assessment tool that tested 19 different scenarios for both CPOE and pharmacy alerts. While it later became apparent that the tool could be more complete, the first version provided a starting point.

All coalition hospitals used the assessment tool to evaluate their CPOE and pharmacy systems to see what alerts were provided. Every time an alert occurred the screen was printed so that alerts could be measured and compared. Alert fatigue and the need for meaningful alerts were also discussed.

A grid comparing all systems showed that one CPOE system provided no alerts. Further investigation revealed that the hospital had just installed their CPOE system and did not want a too many alerts so that physicians might be deterred from using it. Physicians knew that the pharmacy system screened for the same potential problems and they were relying on the pharmacist to correct these problems. Two hospitals used the same system, but each provided different alerts because the alerts had been customized for each institution.

In addition to data, the printed screens were also shown to CEOs, CNOs and CMOs in the coalition so they could see the actual screens that practitioners see to recognize and understand alerts. Screens were often overloaded with information and difficult to read. Senior leadership might have thought that the existing systems would catch all problems, but when they examined what users saw, they realized that the value of providing alerts was not as straightforward as one might think.

Results of this study underscored the need for standardization. CEOs and CMOs discussed that a physician could enter an order at one hospital and get an alert and then go to another hospital, enter the exact same order for the exact same patient and not get an alert.

Lessons learned

ICPS evaluations revealed many process variations. Five systems had a weight-based heparin protocol, one did not. Results for all were compared. Anticoagulant safety issues among the different hospitals were similar. Correlating actions with outcomes was difficult. The experience and results from this project educated coalition members about systems and processes so that better questions could be asked.

Summary and conclusions

ICPS representatives from six hospital systems developed a consensus about safe practices for anticoagulant use. Four targeted actions were implemented to assess and improve anticoagulant safety but data-based conclusions were difficult to reach and more questions were raised. The next steps are to reconvene the ICPS to complete another self-assessment to determine whether any progress has been made and to determine if initiatives such as computer alerts have continued to progress at ICPS health systems. If goals are not met, they will be the subject of further investigation. ICPS is now considering how to expand the coalition to include suburban hospitals and others in Indiana.

PROCEEDINGS

Heparin Safety in Children

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Key points

- *Medication errors are at least as common in children as in adults.*
- *Infants in neonatal intensive care units (ICUs) and older children with complicated chronic illnesses or severe trauma are at greatest risk.*
- *Root causes of pediatric medication errors include:*
  - *The complexity of the medication use process*
  - *Variability in the size of pediatric patients, dosing regimens and medication concentrations*
  - *Patients' inability to self-advocate*
  - *Limited research*
  - *Insufficient training and customization of treatment and safety technologies*
  - *Inadequate patient safety culture*
  - *Look-alike/sound-alike medications*
  - *Reliance on individual vigilance rather than on systems and technology*
- *Medication errors are a system issue and require a system response.*
- *Government, professional organizations, regulatory bodies, researchers, hospital senior leadership, clinicians and industry need to work together to create systems that maximize medication safety in children.*

National Initiative for Children's Healthcare Quality

National Initiative for Children's Healthcare Quality (NICHQ) is an action-oriented organization whose mission is to improve child health. NICHQ's current improvement agenda focused on four areas: equity, childhood obesity, chronic illness and patient safety. During the past three years NICHQ coordinated the Pediatric Affinity Group of the Institute for Healthcare Improvement's (IHI) *Five Million Lives* Campaign, working together with the American Academy of Pediatrics, the National Association of Children's Hospitals and Related Institutions, and the Child Health Corporation of America.

Pediatric medication errors

Medication errors in children are at least as common in children as in adults[1]. Studies based on reviews of medical records show that the frequency of medication errors in children is the same as it is for adults[2]. More sensitive tools such as the trigger tool recommended by IHI and modified for pediatric patients show that the frequency of medication errors is somewhat higher in children than in adults[3]. The youngest and oldest pediatric patients are at highest risk, namely, infants in neonatal intensive care units (ICUs) and older children with complicated chronic illnesses or severe trauma. The ICU setting is the highest-risk environment[4].

Causes of pediatric medication errors

Although several root causes of medication errors in children are similar to those in adults, several characteristics of children and their health care raise additional concerns.

- *Comparable complexity.* The complexity of the medication use process, from diagnosis and prescribing medicines to administration and documentation of the dose, is the most common underlying cause. The medication use process involves many steps with the potential for error at any step. As in the adult setting, attention traditionally has focused on vigilance rather than on the system as the strategy for addressing this issue in the pediatric setting.

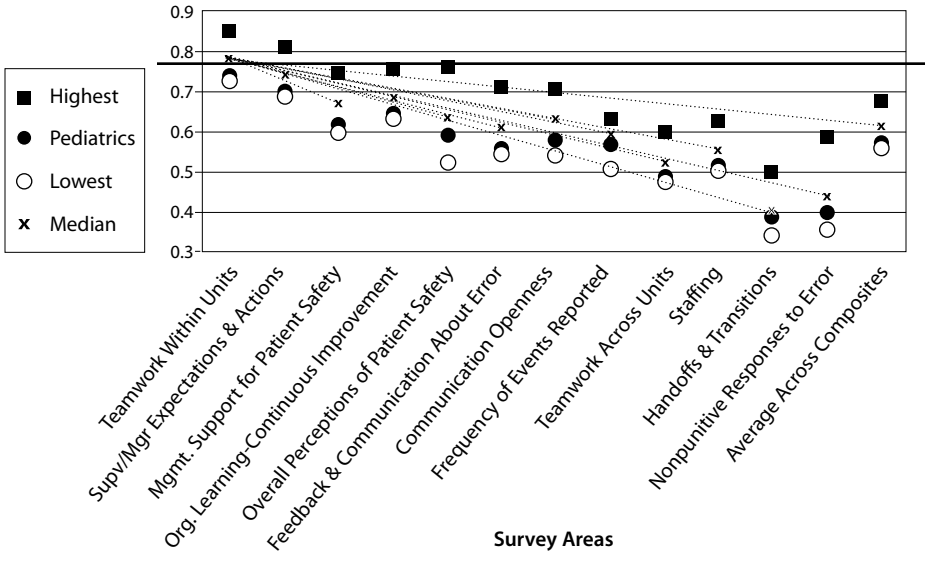
- *Greater variability.* Pediatric patients range in size from the smallest premature infant to adult-sized adolescents. This presents major challenges with regard to medication use. Dosing regimens and medication concentrations used for pediatric patients are therefore highly variable. There is also a lower margin for error with infants and young children compared to adults.
- *Lack of self-advocacy.* Young children are not able to advocate for themselves or ask questions about their medication. A healthy parent may ask questions, so it difficult to determine whether this increases or decreases a child's risk of harm.
- *Less research.* Pediatric patients represent a smaller market for pharmaceutical companies, and there are fewer studies of the safety of medications for this population. Changes in the pediatric drug laws have improved but not resolved this situation.
- *Insufficiently customized technology.* Some medication safety technologies such as computerized prescriber order entry (CPOE) and medication administration systems initially were not sufficiently customized for the variable sizes of pediatric patients.
- *Insufficient training and customized treatment*. Anecdotal evidence suggests that hospitals with both adult and pediatric patients and mixed systems may not have the same level of specialized training, treatments and formulary for pediatric patients that might be found in children's hospitals.
- *Inadequate patient safety culture.* Differences in patient safety culture may also increase the risk of medication errors in children. An NICHQ analysis of data from the first Agency for Healthcare Research and Quality's Patient Safety Survey[5] shows that staffs who work on pediatric units report lower levels of patient safety practices in areas such as teamwork and management support for patient safety issues (Figure 1). These results did show improvement in the 2008 survey, suggesting that the increased attention to safety and quality in hospital settings serving children may be improving the safety culture.
- *Look-alike/sound-alike medications*. The widely publicized issue that medication vials look alike is another cause of pediatric medication errors, specifically with regard to tragic heparin-related incidents during the past two years. Two vials of heparin may look similar but contain 1,000-fold different concentrations. In these cases, nurses on the pediatric care unit used adult-strength heparin to prepare flushes for intravenous catheters instead of using the low-concentration heparin. The hospitals also relied on the vigilance of individuals to avert medication errors rather than use technology to match patient to medication. For example, barcoding systems could have been used when stocking the automated dispensing cabinet and when medicines were administered to patients.

Responsibility

Some difficult questions experts are often asked are: why, after the first incident, did the same error pediatric medication error happen again? Who was responsible and why was the system not fixed? A failure mode effects analysis (FMEA) performed by the Institute for Safe Medication Practices showed that no single person is responsible for these errors. Medication errors are a system issue and require a system response.

There are many places where responsibilities lie. There is a responsibility to regulate the pharmaceutical industry. Look-alike or sound-alike medications are not permissible. In keeping with the Joint Commission's efforts, there need to be hospital standards to ensure patient safety through the use of technology and staff training. Hospitals must be provided with resources to implement these changes. Financial incentives need to be aligned. An example of an emerging alignment of incentives to improve patient safety is the Medicare policy of not paying a hospital for the care of a condition resulting from a medication error.

Figure 1. Patient Safety Culture Composite—Percentage Responding Favorably



At the individual hospital there is also responsibility at the executive governance level. This is suggested in the concept of "Getting the Board on board" in the IHI *Five Million Lives* campaign[6]. IHI also emphasizes the importance of having a learning culture. If a major adverse drug event happens, senior leaders in a healthcare organization are responsible for finding out about that event and making sure that it could not occur in their organization. NICHQ believes that if a hospital is committed to caring for children, there is a need to employ every means available to ensure those children will be safe. In a smaller institution it may be particularly difficult for senior leadership to devote the necessary resources for its pediatric patients.

Professional responsibility is also involved. A serious medication error often attracts media attention and criticism. Nurses may be criticized for not demonstrating appropriate professional responsibility in carrying out their duties. While professionalism is important, organizations need to ensure appropriate training, supervision and staffing that enable professionals to perform to the best of their capacities and desires.

Organizations that fund and publish research have a responsibility to support research into pragmatic questions such as whether a specific medication, such as heparin, needs to be administered in a specific setting. The study of medication safety systems is still underfunded.

Conclusion

Government, professional organizations, regulatory bodies, researchers, hospital senior leadership, clinicians and industry need to work together to create a future that maximizes medication safety in children. Developing specific policies and practices is essential to safeguarding children against medication errors. NICHQ is committed to working collaboratively to promote the development and widest possible dissemination of these practices.

References

1. Kaushal R, Bates DW, Landrigan C, et al. Medication errors and adverse drug events in pediatric inpatients. *JAMA*. 2001;285:2114-20.
2. Woods D, Thomas E, Holl J, et al. Adverse events and preventable adverse events in children. *Pediatrics*. 2005;115:155-60.
3. Takata GS, Mason W, Taketomo C, et al. Development, testing, and findings of a pediatric-focused trigger tool to identify medication-related harm in US children's hospitals. *Pediatrics*. 2008;121:e927-35.
4. Sharek PJ, Horbar JD, Mason W, et al. Adverse events in the neonatal intensive care unit: development, testing, and findings of an NICU-focused trigger tool to identify harm in North America. *Pediatrics*. 2006;118:1332-40.
5. Agency for Healthcare Research and Quality. Hospital Survey on Patient Safety Culture. 2007. Retrieved January 9, 2009 from http://www.ahrq.gov/qual/hospsurveydb/.
6. Institute for Healthcare Improvement. Getting Boards on board. Retrieved January 9, 2009 from http://www.ihi.org/IHI/Programs/Campaign/BoardsonBoard.htm.

PROCEEDINGS

Improving Heparin Safety: A Pharmacy Perspective

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Key points

- *Extra efforts are necessary to improve patient safety with high-risk medicines such as anticoagulants.*
- *Heparin therapy is particularly susceptible to errors because of the use of units for dosing, variability in ordering, the need to prepare patient-specific doses and monitor patient response to therapy.*
- *The activities needed for heparin therapy at each of the critical steps in the medication-use system should be analyzed.*
- *Efforts to standardize heparin dosing need to involve representatives from multiple departments, including surgical services and interventional radiology where heparin is frequently used during critical procedures.*
- *The need for heparin to flush intravenous (IV) catheters for in pediatric and neonatal patients should be assessed, and preparations used for this purpose should be provided to these patient care areas from the pharmacy.*

The medication-use system consists of a continuum of critical steps, including the selection and storage of medications, ordering, transcribing, preparing, dispensing and administering medications for patients and monitoring patient response. Though attention to detail is expected by all who are involved in the use of drugs, extra efforts are necessary to improve patient safety with high-alert medications such as anticoagulants.

Heparin therapy is particularly susceptible to errors because of the use of units for dosage, variability in ordering using or not using weight-based dosing, the need to prepare patient-specific doses and the need to monitor patient response to therapy. The impact of heparin on each of the critical steps in the medication-use system should be analyzed.

Strategies to consider for improving the safety of heparin therapy include:

- Selection
  - Identify and evaluate all stock of heparin used, including vials, premixed infusions and components of prepared trays.
  - Only pharmacy should select the heparin products for therapeutic use.
  - If departments such as materials management or dialysis order heparin in any form for catheter flushing (such as in a prepared tray), pharmacy must provide oversight of the selection and storage of the supplies.
  - Only concentrations and vial and syringe sizes appropriate for the indications and patient population should be selected.
- Storage
  - Pharmacy should approve all storage locations.
  - Storage outside of the pharmacy department should be limited.
  - Prominent warning stickers and other visual cues should be used to minimize the possibility of selecting an incorrect dosage unit.
  - The availability of heparin before pharmacist review of an order should be avoided.
  - Vials of 10,000 units/mL concentration should not be stocked outside of the pharmacy.
- Ordering
  - Medical staff-approved protocols should be used whenever possible.
  - The order sheet listing the approved protocol should be examined by pharmacy, medical records and other appropriate departments to ensure that hospital policies are followed, no

prohibited abbreviations are used, only standard concentrations are listed and other hospital policies are followed.

- Each protocol should be reviewed annually and the evaluation documented.

- Dispensing
  - Pharmacy should dispense unit-of-use, patient-specific doses. Ideally, each dose should be available from a profile-driven automated dispensing cabinet, with appropriate warnings available provided by the device in the most expedient manner.
- Administration
  - Nursing should receive each ready-to-use dose before the administration time.
  - If in an urgent situation a dose needs to be obtained before pharmacist review (an override), an independent double-check with two qualified staff members should be required.
  - Appropriate laboratory data should be available to the nurse or other healthcare professional administering the dose.
- Monitoring
  - Hospital-defined parameters should be established.

Most organizations have standardized heparin bolus doses and premixed IV solutions in general– and critical care patient units. Other departments including Surgical services, interventional radiology, cardiac catheterization laboratory and dialysis often use heparin during procedures. These areas often have not been involved in efforts to control and standardize heparin dosing. Attention needs to be paid to these areas to ensure patient safety during these critical procedures.

Pediatric and neonatal units often need concentrations of heparin flush solutions that are not commercially available in the volume or dosage form required. Use of the agent should be assessed, and preparations provided for these areas by pharmacy.

Many organizations have eliminated heparin for flushing peripheral IV catheters. Saline is generally the preferred agent.

Conclusion

Heparin is a high-alert medicine that should be evaluated throughout the medication-use system within the entire healthcare organization.

PROCEEDINGS

A Nursing Perspective on Heparin Safety

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Key points

- *The combination of a high-volume, high-risk process with many interruptions greatly increases the risk of an unintentional medication error.*
- *Administration of heparin is particularly challenging because of the narrow therapeutic range, complex dosage regimens and potential for patient harm.*
- *An unprecedented combination of factors greatly increases the probability of potentially life-threatening heparin errors.*
- *Challenges affecting heparin administration include:*
  - *Labels that look alike*
  - *Complex dosage calculations*
  - *Variation in the accuracy of obtaining patient weight*
  - *Perceived "need for speed" that can lead to poor compliance with safety technology*
  - *Lack of standard protocols*
  - *Difficulties recognizing over-anticoagulation and heparin-induced thrombocytopenia*
- *Ensuring the safety of highly complex heparin administration requires a multidisciplinary approach in which nursing concerns and front-line observations are heard and respected in advocating for a culture of safety, nurses' rights and, most importantly, keeping patient safety at the forefront.*

Medication administration is a primary function of nursing, and it often causes stress to nurses because of the complexities and potential for patient harm. A nurse may administer up to 50 medications during a single shift, often being distracted and interrupted[1,2]. This increases the risk that a nurse will make an unintentional medication error. The Joint Commission and the United States Pharmacopeia report that medication errors continue to be a leading cause of sentinel events and the majority of medication errors occur at the point of administration[7]. The safe administration of heparin is particularly challenging because of the narrow therapeutic range, extremely complex dosage regimens, frequent dosage adjustments and high potential for patient harm associated with heparin therapy.

Nurses have been educated on the 5 Rights of medication administration: right drug, right patient, right dose, right time and right route. These rights have evolved to the 7 Rights of medication administration that also include right reason and right documentation[3].

For nurses to consistently practice these 7 Rights, they also have other rights that need to be met. Cook and the Massachusetts Nurses Association published the "Nurses' Six Rights for Safe Medication Administration" as guidelines to assist nurses[4]. These include:

1. The right to a complete and clearly written order.
2. The right to have the correct drug route and dose dispensed.
3. The right to current information and resources on medications.
4. The right to access medication administration policies.
5. The right to administer medications safely and to identify problems in the system.
6. The right to stop, think and be vigilant when administering medications.

Along with reliable systems, multidisciplinary partnerships are necessary to ensure that both the 7 Rights and Nurses' 6 Rights are achieved in the interest of patient safety. This is particularly true with regard to heparin.

A perfect storm for errors

Currently nursing is in the midst of a perfect storm for heparin errors. There is an unprecedented combination of factors that greatly increase the probability of potentially life-threatening errors. One of the conditions creating this circumstance is the nursing

shortage that affects many practice settings in the United States, including the medical-surgical and critical care units where heparin is frequently used. Nurses are challenged by higher patient acuity, unrelenting pressures to decrease cost and improve patient outcomes and increasingly complex therapies with high-risk medications.

Human factors further affect the potential for error. Nurses work in restricted, congested spaces with high traffic and frequent interruptions. They must master a growing number of new, complicated technologies, work longer hours and manage professional and personal distractions[1,2,5,6]. The combination of these demands can often exceed the ability of even highly experienced nurses to function without error.

Ensuring the safety of highly complex heparin administration requires a multidisciplinary approach. Unfortunately, literature on the nurse's perspective in safe heparin administration is limited; therefore, the following discussion is based on anecdotal reports and personal experience.

Challenges in heparin administration

The first challenge nurses face when administering heparin is look-alike labels. Until recently, vials containing 10,000 units/mL and those vials containing 10 units/mL had labels that closely resembled each other. Confusion between labels was one of factors leading to heparin errors in infants that resulted in mortality and morbidity.

Manufacturers have changed product labels to enhance visual differentiation between the two concentrations by nursing and pharmacy staff, but poorly labeled vials may still remain in hospital inventories. Therefore, hospitals must implement measures to ensure that vials of highly concentrated heparin are kept only in the hospital pharmacy and not stocked in patient care areas[7,8].

A second challenge is the complexity of calculating heparin infusion dose rates. Variable physician practices and lack of standardized protocols further increase the potential for error. A nurse might have two patients on heparin receiving different concentrations and/or different dosages based on weight-based or non-weight-based protocols. Within weight-based dosing protocols, practitioners may disagree on which weight to use in dosage calculations—current, admission or "dry" weight—further increasing nursing staff confusion. Nurses are inconsistently taught to double-check heparin dosages before administration and, even when correctly taught, inconsistently perform this practice because of time constraints. Many nurses are not highly skilled in dose calculations and find the complex calculations required for heparin dosage adjustments challenging[9].

A third challenge is obtaining and documenting a patient's weight[10]. Determining the patient's weight often is not consistently ordered or consistently performed. Staff may rely on patients to self-report their weight, which may be incorrect. Staff members do not always know the correct use and calibration of scales. Errors may occur in recording weights as pounds or kilograms. If these units of measures are confused, significant under or overdosing of heparin may occur and result in a serious adverse drug event.

A fourth challenge is posed by the implementation of new smart pump (computerized infusion) technology with dose-error-reduction software. Smart pumps assist nurses by providing dosage limits and warnings when doses are outside these limits. The nurse performs a series of entries to program the pump. If the dose programmed into the pump exceeds pre-established limits in the pump's database, the safety software generates an alert that must be addressed before infusion can proceed, thus helping to avert a potential error. When faced with competing priorities, a nurse has a perceived "need for speed" and may bypass the safety features offered by the pump[11]. Both Rothschild[12] and Keohane[13] found that the use of smart pump technology is beneficial in identifying errors but had no impact on the serious error rate in their facilities. Both authors concluded that this technology requires systematic implementation and continued follow-up to prevent clinicians from having to circumvent or bypass the safety system.

A fifth challenge is the lack of standardized heparin protocol. Most institutions allow a prescriber to individualize each order when prescribing heparin. This leads to variation in dosage (weight-based versus non-weight-based), titration schedules (every four hours, six hours and others) and monitoring protocols (timing and laboratory parameters). Because of shortages in nursing staffing, agency and floating nurses are often used. These nurses encounter variation both within and among facilities. Lack of standardization increases the likelihood of making incorrect assumptions or incorrect entries.

A sixth challenge is the recognition of heparin-related complications. The two primary complications of heparin therapy are over-anticoagulation and heparin-induced thrombocytopenia (HIT). A nurse is in the unique position of being the last step in the medication therapy process and the person who monitors the patient. Most nurses are well educated to monitor for over-anticoagulation but many are not educated to monitor for HIT. Detection of HIT can be challenging because of unpredictability and the use of heparin throughout acute care. Nurses caring for patients should be educated about these complications for all patients receiving either unfractionated heparin or low molecular weight heparin[14,15] to prepare them for both over-anticoagulation and HIT.

Conclusion

Nurses have a critical role in the safe use of heparin. The nurse must work as a full partner of a multidisciplinary team and advocate for a learning culture to prevent errors, for nurses' rights in heparin administration and, most importantly, for patient safety to be a priority for all practitioners. Other team members must respect nurses and listen to their concerns and observations. Without this partnership, consistently error-free heparin treatment cannot be realized.

References

1. Mayo AM, Duncan D. Nurse perceptions of medication errors: what we need to know for patient safety. *J Nurs Care Qual* 2004 Jul-Sep;19(3):209-17.
2. Tucker AL, Spear SJ. Operational failures and interruptions in hospital nursing. *Health Serv Res* 2006 Jun;41(3 Pt 1):643-62.
3. Pape TM. Applying airline safety practices to medication administration. *Medsurg Nurs* 2003 Apr;12(2):77-93; quiz 4.
4. Cook M. Nurses' six rights for safe medication administration. 2008 [cited 2008 February 23]; Available from: http://www.massnurses.org/nurse_practice/sixrights.htm
5. Hatcher I, Sullivan M, Hutchinson J, et al. An intravenous medication safety system: preventing high-risk medication errors at the point of care. *J Nurs Adm* 2004 Oct;34(10):437-9.
6. Schneider PJ. Applying human factors in improving medication-use safety. *Am J Health Syst Pharm* 2002 Jun 15;59(12):1155-9.
7. Institute for Safe Medication Practices. Another heparin error: Learning from mistakes so we don't repeat them. 2007 [cited 2008 February 23]; Available from: http://www.ismp.org/Newsletters/acutecare/articles/20071129.asp?ptr=y
8. Jennings J, Foster J. Medication safety: just a label away. *AORN J* 2007 Oct;86(4):618-25.
9. Matthew L. Injectable medication therapy: a patient safety challenge. *Nurs Stand* 2007 Apr 11-17;21(31):45-8.
10. Hilmer SN, Rangiah C, Bajorek BV, et al. Failure to weigh patients in hospital: a medication safety risk. *Intern Med J* 2007 Sep;37(9):647-50.
11. Fields M, Peterman J. Intravenous medication safety system averts high-risk medication errors and provides actionable data. *Nurs Adm Q* 2005 Jan-Mar;29(1):78-87.
12. Rothschild JM, Keohane CA, Cook EF, et al. A controlled trial of smart infusion pumps to improve medication safety in critically ill patients. *Crit Care Med* 2005 Mar;33(3):533-40.
13. Keohane CA, Hayes J, Saniuk C, et al.. Intravenous medication safety and smart infusion systems: lessons learned and future opportunities. *J Infus Nurs* 2005 Sep-Oct;28(5):321-8.
14. Cooney MF. Heparin-induced thrombocytopenia: advances in diagnosis and treatment. *Crit Care Nurse* 2006 Dec;26(6):30-6; quiz 7.
15. Valenstein PN, Walsh MK, Meier F. Heparin monitoring and patient safety: a College of American Pathologists Q-Probes study of 3431 patients at 140 institutions. *Arch Pathol Lab Med* 2004 Apr;128(4):397-402.

PROCEEDINGS

Using Heparin Safely: A Hospitalist Perspective

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Key points

- *An evidence-based heparin protocol can help to standardize and guide heparin dosage and adjustments.*
- *A venous thromboembolism (VTE) prevention protocol, which included order sets, real time patient identification and intervention increased the percent of patients with adequate VTE prophylaxis from 50% to 98% over a two-year period resulting in decreased rates of VTE and pulmonary embolism (PE).*
- *Active surveillance for adverse drug events (ADE) associated with heparin and other medications using rescue medication / pharmacist and laboratory triggers identifies far more events than relying on billing codes and voluntary reporting alone.*
- *Physician compliance with heparin safety measures can be improved by involving physicians when the anticoagulation management protocol is developed and ensuring the protocol is efficient and user-friendly.*

Need for protocol use

An evidence-based heparin protocol can be straightforward (Figure 1). So, why do physicians, especially interns and residents, not comply with it? One explanation is that physicians are overloaded because of distractions, interruptions and competing demands (Figure 2). A distracted physician can easily fail to adjust a heparin infusion, notice that a patient who is being treated with heparin has developed new thrombocytopenia or check renal function before choosing an anticoagulant. The highly complex clinical environment is a reality that must be addressed to improve heparin safety.

The aviation industry is recognized for low error rates and an excellent safety culture that promotes doing things right and speaking up if something is wrong. Each pilot is not expected to develop, or even recall, preflight safety checks before each take off; a checklist is already standard procedure. Similarly, physicians should not have to remember all of the details involved in decisions about the optimal monitoring, product, dose, frequency of administration and duration for each course of anticoagulation. Evidence-based information should be incorporated into a protocol that standardizes and guides heparin dosage and adjustments.

Aviation safety principles are based on the fact that pilots cannot evaluate information on an entire instrument panel to detect a minor abnormality. Pilots need warning lights. Physicians also need alerts, such as alerts for newly developing thrombocytopenia or for a history of heparin-induced thrombocytopenia (HIT), a condition which may occur with a normal platelet count or may be hidden in the past medical history, but not be listed as an allergy, and may therefore be easy to overlook.

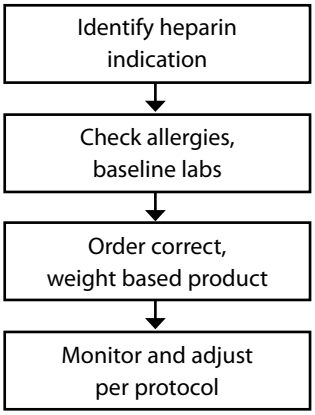
Improving VTE prophylaxis

At the University of California San Diego (UCSD), as at most medical centers, a large majority of inpatients are at risk for deep vein thrombosis (DVT) and pulmonary embolism (PE) and can benefit from subcutaneous heparin to reduce their risk. In January 2007, a baseline assessment showed that only 50% to 55% of patients received appropriate VTE prophylaxis; the VTE rate was 13.4/1000 patients. The baseline assessment highlighted the need for a hospital-wide VTE prophylaxis protocol.

A team of physicians, pharmacists, and programmers developed a VTE prophylaxis order set that employed a simple, three-tiered risk assessment tool. The first page of the computerized order set requires a physician to assess a patient as high, moderate, or low risk for VTE and included a link to a table of VTE risk factors. The second page prompted the prescriber to consider both absolute (e.g., active hemorrhage) and relative (e.g. cirrhosis) contraindications for prophylactic heparin therapy, as well as other conditions such as HIT or the presence of an epidural catheter.

Based on the patient's risk level and the

Figure 1. Physician's Brain on Protocol



presence or absence of contraindications, the protocol provided a suggested regimen on the third page. Most commonly, this included a subcutaneous heparin when not contraindicated, as well as intermittent compression devices for patients who were at high risk or unable to take pharmacologic prophylaxis. This screen also displays safety reminders, such as a warning that enoxaparin should not be used if there is renal insufficiency, and that dose reductions in unfractionated heparin (UFH) should be considered for small or elderly patients.

Compliance was ensured by mandating use of the protocol for all inpatient admissions and transfers. Implementation of the order set was followed by surveillance and real time alerts for patients who appeared to be untreated, but eligible for prophylaxis. These situations prompted notification of the treating physicians that VTE prophylaxis could be considered.

Results

During a two-year period, the percent of patients with adequate VTE prophylaxis increased from 50% to 98% (Figure 3). Preventable VTE decreased more than 80% and the total VTE rate was almost cut in half. The PE rate decreased from 4 to about 1.2 per 1,000 patients (Figure 4).

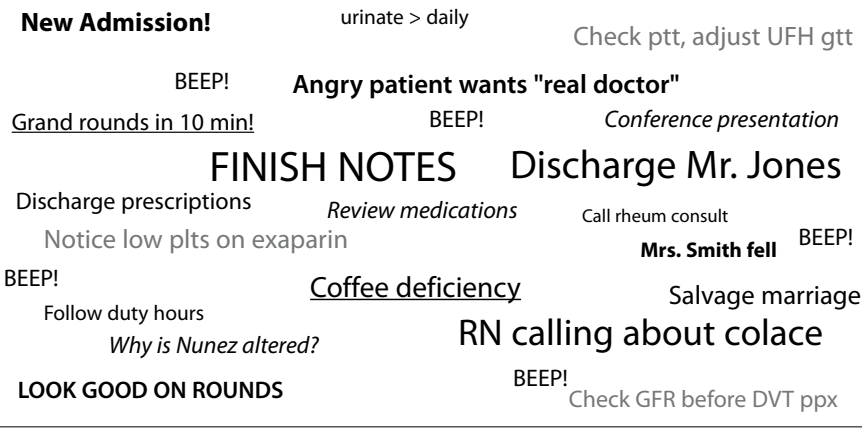
Investigators also sought to determine whether treatment had caused any harm. A retrospective review of service codes for secondary thrombocytopenia was conducted to determine the rate of HIT. A review of about 50,000 charts showed a relative risk of about 1.44, which was not significant.

Evaluating the risk of bleeding, a relatively rare event, led to another concern. Wein found that the relative risk of bleeding is about 1.5 for UFH and not significant for low molecular weight heparin [LMWH][1]. After implementing the order set, analysis of a sample population at UCSD found no bleeding events when reviewing anticoagulant-related adverse drug events (ADE). This observation raised the question of whether voluntary reporting and physician billing data provide trustworthy information on these events.

Improving ADE reporting

Intermountain Healthcare in Salt Lake City suggests that billing codes and voluntary reporting do not adequately reflect the real rate of ADEs. Their quality improvement team sought to determine how many ADEs could be detected with passive compared to active surveillance. During a period of time when a voluntary reporting system identified six ADEs (none serious), encouraging staff to report ADEs by making the system easy to use and protecting them from punishment identified 60 events. Lastly, a full-time pharmacist reviewed the use of antidotes, rescue medications and critical laboratory test results to identify patients whose charts should be reviewed to determine whether these events were the result of an ADE. For example, in the case of heparin-related complications, use of protamine or argatroban would suggest an adverse event. This active surveillance indentified 481 new ADEs[2]. When a passive search for ADEs is conducted, the result is often a false sense of security based on inaccurately low reported ADE rates—and opportunities to care for affected patients and prevent future complications are lost. In the case of the VTE prophylaxis protocol, an aggressive search for

Figure 2. Physician's Brain on Call

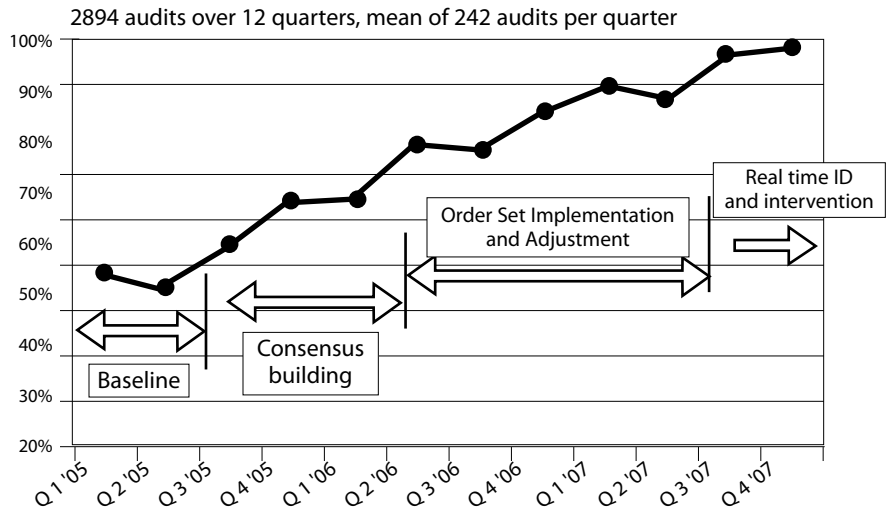


HIT complicating heparin therapy indentified more than 500 patients tested or treated for HIT, and preliminary analysis suggests that confirmed HIT was both exceedingly rare and not associated with use of the protocol, confirming its safety with regard to the development of HIT.

Heparin best practices

Despite a robust VTE prevention program, community and hospital acquired VTE still occurs, and usually results in a prolonged course of anticoagulation which can be complex and risky to administer. A UCSD evidence-based VTE protocol (Table 1) has been developed and is in the process of being implemented that incorporates evidence-based guidelines and standards from the Joint Commission on Hospital Accreditation. Selected components of this protocol include obtaining proper baseline laboratory tests, overlapping heparins with warfarin for at least five days (including two therapeutic INR measurements), patient education, timely laboratory and clinic follow-up, use of UFH when patients have a creatinine clearance less than 30, protocol-based UFH infusions and warfarin loading regimens, and long-term LMWH treatment for eligible patients with cancer. A grant-funded study will analyze the results of protocol implementation.

Figure 3. Percent of Randomly Sampled Inpatients with Adequate VTE Prophylaxis



As with the VTE prevention protocol, the ultimate goal is a user-friendly but thorough CPOE order set that makes it easier for physicians to make good decisions and more difficult to make mistakes. It may take six to eight months to develop CPOE order sets. While these are being developed, interim measures can be used such as paper versions of the protocol, staff education, and nursing protocols. Pharmacy collaboration is crucial, as it offers a chance to review orders before medication is delivered to the patient, ensuring that issues such as drug/warfarin interactions are addressed before patient harm can occur. One warning light already in place is the reporting of a calculated eGFR with every creatinine, which can alert doctors to the presence of renal failure when age or malnutrition blunts the elevation of creatinine levels.

Improving physician compliance

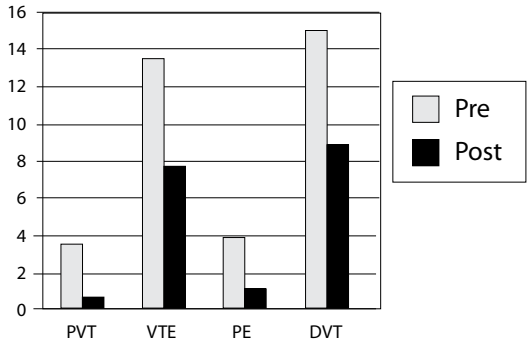
Physicians are trained to be self-reliant experts and leaders and to value their autonomy. They also tend to resist change. Soliciting their advice and involving them early when protocols are developed helps to increase physician compliance. If physicians are involved, they can use their experience to improve the protocol, are more motivated to make the protocol work, and feel less like they are being forced to do something. Late adopters may continue to resist using an order set from a VTE protocol because they do not believe their patients experience ADEs or they trust their own instincts over proven therapies. This reluctance may be addressed by publishing outcome data, presented the findings at educational sessions, such as grand rounds, seeing early adopters using the protocol and getting good results and ensuring the protocol makes their work simpler—and failure to use the protocol more difficult.

Table 1. UCSD VTE Heparin Goals

- Get proper baseline labs
- Give heparin 5+ days with INR > 2 for 2 days
- Give, document appropriate education
- Ensure timely lab / clinic follow up
- UFH, not LMWH, when CrCl > 30
- UFH infusions by protocol
- Offer chronic LMWH to CA patients

Figure 4. DVT Prophylaxis: Results

- "Preventative" VTE: 3.3 v 0.56*
  - RRR 83%; NNT 365
- VTE: 13.4 v 7.7*
  - RRR 43%; NNT 175
- PE: 3.95 v 1.22*
- DVT: 15 v 8.76*



All values per 1000 patients; p< .05; "hospital acquired only

Summary

The use of an evidence-based protocol can help standardize and guide heparin dosage and adjustments and reduce opportunities for error. Like airplane pilots, physicians need alerts and checklists to help ensure safety. Such a protocol should prompt a physician to consider both the use of standard care, and special situations in which deviation from standard care are appropriate for individual patients. For example, UCSD's heparin-based VTE prevention protocol encourages wide use of heparin unless contraindications are present, improving both VTE utilization and the rate of VTE. Tracking ADEs is important to identify possible adverse events from protocols, but requires active investigation to yield reliable results; real time investigation also offers opportunities to intervene in patients who either need therapy or have suffered an adverse event. Soliciting physician advice and involvement when the protocol is developed can help increase physician compliance—as well as identify clinical insights that improve the protocol.

References

1. Wein L, Wein S, Haas SJ, Shaw J, Krum H. Pharmacological venous thromboembolism prophylaxis in hospitalized medical patients: a meta-analysis of randomized controlled trials. *Arch Intern Med.* 2007;167(14):1476-86.
2. Data from LDS hospital, Salt Lake, presented by Brent James, MD, at the Intermountain Healthcare Advanced Training Program in Quality.

PROCEEDINGS

Heparin-induced Thrombocytopenia

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Key points

- *Compared with the more common, non-immune-mediated heparin-induced thrombocytopenia (HIT), immune-mediated HIT is associated with a greater reduction in platelet counts (50%) and increased incidence of thrombosis.*
- *Since HIT can occur in any setting where heparin therapy is used, it is important that platelet counts be monitored and professionals be educated about recognizing HIT.*
- *After HIT is suspected, it is important to consider treatment with another parenteral anticoagulant such as a direct thrombin inhibitor (DTI).*
- *Target aPTT ranges should be established based on the ratio to baseline aPTT.*
- *Since aPTT assays may respond differently to a DTI, sharing of dosing protocols may result in different infusion rates.*

There are two forms of thrombocytopenia caused by exposure to heparin. The more common, non-immune-mediated form occurs within the first few days after exposure to heparin when a slight decrease in the platelet count occurs. In this situation it is unclear whether heparin therapy needs to be stopped, because it has not been associated with thrombosis. In contrast, the less frequent, immune-mediated heparin-induced thrombocytopenia (HIT) is associated with a greater reduction in platelet counts (50% reduction). Lower platelet counts during the acute phase of HIT have been correlated with an increased incidence of thrombosis[1].

The development of HIT-associated thrombosis can occur up to 30 days out but may be most common during the first few days after onset of thrombocytopenia. Since HIT can occur in any setting where heparin therapy is used, it is important to monitor platelet counts and educate professionals about recognizing HIT.

Recognition of HIT

No laboratory test alone can reliably diagnose HIT. Currently diagnosis depends on assessment of associated heparin-exposure history, timing of the onset of thrombocytopenia, the magnitude of the drop in platelet count, presence of other causes of thrombocytopenia or a positive HIT-antibody test.

Three onset patterns have been observed after heparin exposure. The onset of HIT can be immediate if there has been a recent exposure to heparin. Onset more commonly occurs approximately four to ten days after heparin exposure. Delayed onset may even occur up to 40 days after discontinuing heparin.

Monitoring

To recognize and prevent HIT-related complications, the platelet count should be closely monitored to recognize decreasing values and the potential onset of the syndrome. Pre-test probability tools, such as the 4T's proposed by Warkentin, can assist clinicians in determining presence of HIT[2-3]. One way to do this is to incorporate platelet count monitoring into heparin order sets. The frequency of platelet count monitoring may depend on the situation, as suggested in the College of American Pathologists-proposed guidelines[4].

Management

The description and corresponding definition of HIT can depend on the clinical situation of the patient. Acute HIT may be defined as the period of time when the platelet count is low and thrombosis risk highest. During this period, it is important to consider treatment with another parenteral anticoagulant such as a direct thrombin inhibitor (DTI). This treatment may be followed by a period when the platelet count is recovering and alternative anticoagulation therapy is being administered.

Management considerations include transitioning to prolonged anticoagulant therapy for one month for isolated HIT (no associated thrombosis) or for at least three months for HIT thrombosis syndrome (HITTS). For patients with a history of HIT after platelet count has recovered and prolonged antico-

agulation has been discontinued, starting anticoagulant therapy for a separate indication may require an alternative approach.

After HIT is suspected, it is important to initiate an alternative management plan. This includes use of an alternative anticoagulant and an understanding of how its use should be initiated and monitored. It is important to have rapid access to an alternative agent and information available on its use, because bedside clinicians may have very limited clinical experience. In the case of the DTIs, the INR may also rise because of a crossover reaction with the assay resulting in values that do not reflect corresponding anticoagulation in the patient. Clinicians should be educated to recognize the potential for false assay results before automatically stopping the infusion if there is a high INR in warfarin-naïve patients.

DTI dosing approaches should also consider altered drug elimination in liver, renal of cardiac dysfunction, or ongoing procedures with increased risks for bleeding[5]. Target aPTT ranges should be established based on the ratio to baseline aPTT. The aPTT range established for heparin should not be used because the pharmacology of each agent and how it influences the aPTT differs. As with the aPTT and heparin, different aPTT assays may respond differently to a DTI[6]. Therefore it is important to keep in mind that any sharing of dosing protocols may result in different infusion rates.

Summary

Immune-mediated HIT is associated with an increased incidence of thrombosis and can occur in any patient for whom heparin is used. A means should be developed to monitor platelet counts, educate professionals about recognition and management of HIT, and provide rapid access to an alternative agent such as a DTI. Target aPTT ranges should be established based on the ratio to baseline aPTT to ensure accurate infusion rates.

References

1. Warkentin TE. Clinical presentation of heparin-induced thrombocytopenia. *Semin Hematol* 1998;35 (4 suppl 5):9-16; discussion 35-6.
2. Warkentin TE. Heparin-induced thrombocytopenia: pathogenesis and management. *Br J Haematol* 2003; 121:535-5.
3. Janatpour KA, Gosselin RC, Dager WE, et al. Usefulness of optical density values from heparin- platelet factor 4 antibody testing and probability scoring models to diagnose heparin induced thrombocytopenia. *Am J Clin Path* 2007;127:429-33.
4. Warkentin TE. Platelet count monitoring and laboratory testing for heparin-induced thrombocytopenia. *Arch Pathol Lab Med* 2002;126:1415-23.
5. Dager WE, Dougherty JA, Nguyen PH, et al. Heparin-Induced Thrombocytopenia: A Review of Treatment Options and Special Considerations. *Pharmacother* 2007; 27:564-87.
6. Gosselin RC, King JH, Janatpour KA, et al. Comparing direct thrombin inhibitors using aPTT, ecarin clotting time and thrombin inhibitor management testing. *Ann Pharmacother* 2004;38(9):1383-8.

CareFusion Center for Safety and Clinical Excellence Invited Conference

Improving Heparin Safety

March 13-14, 2008

Attendees

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Vice President and Chief Patient Safety Officer
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3. *Charlie Ham, PharmD*
4. *Richard Johannes, MD*
5. *Steve Lewis, MD*
6. *Natasha Nicol, PharmD*
7. *Carl Peterson, PharmD*
8. *Ray Stermer, RPh, MBA*
9. *Michael Yang, MD*

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