TRANSITIONS OF CARE FOR PATIENTS ON ANTICOAGULATION THERAPY

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Transition of Care for Patients on Anticoagulation Therapy

FINANCIAL DISCLOSURE:
Advisory Board/Consulting:
  Janssen Pharmaceuticals, Inc.
  Boehringer Ingelheim Pharmaceuticals, Inc.
Objective

- Discuss the role of the anticoagulation provider for improving transitions of care
  - Switching between anticoagulants
  - Moving between healthcare settings or home
transition
/tranˈziSHən,-ˈsiSHən/

noun
1. the process or a period of changing from one state or condition to another.
   "students in transition from one program to another"
synonyms: change, passage, move, transformation, conversion, metamorphosis, alteration, handover, changeover; More

verb
1. undergo or cause to undergo a process or period of transition.
   "the network ought to be built by the federal government and then transitioned into private industry"
Why are Care Transitions Important?

- Poor management of care transitions (among drug choices or care settings) can diminish health and increase costs

  inadequate transitions responsible for

  $25 - $45 billion

  in 2011

Health Affairs, Robert Wood Johnson Foundation, Health Policy Brief, Sept 13, 2012
What statement BEST describes your day-to-day practice in relation to oral anticoagulant therapy?

1. I administer anticoagulants as ordered but have little to do with anticoagulant drug management.
2. I prescribe and monitor warfarin and/or heparin.
3. I triage questions or provide instructions to patients on oral anticoagulants.
4. I prescribe and monitor warfarin, heparin and/or NOACs (dabigatran, rivaroxaban or apixaban).
5. I work full time in an anticoagulation clinic.
My knowledge and skills to effectively educate patients and families about all aspects of oral anticoagulants, including the NOACs (dabigatran, rivaroxaban and apixaban) are:

1. Limited to warfarin
2. Comprehensive and current with best practice
3. I need help
AB is a 38 yr old female s/p left knee arthroscopic surgery 2 weeks ago. She presents to the emergency room with spreading L leg pain with mild swelling. She was diagnosed with a L femoral vein DVT and started on IV heparin and admitted. On the next day, her pain and swelling begin to subside. How should she be transitioned from IV heparin to SQ LMWH?

1. Give SQ LMWH, then turn off IV heparin 1 hour later
2. Give SQ LMWH, then turn off IV heparin 4 hours later
3. Turn off IV heparin, give SQ LMWH dose at same time
4. Turn off IV heparin, give SQ LMWH dose 4 hours later
# Pharmacokinetics of Parenteral Anticoagulants

<table>
<thead>
<tr>
<th></th>
<th>IV Heparin</th>
<th>SQ Heparin</th>
<th>LMWH</th>
<th>Fondaparinux</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>T max</strong> (time to reach maximum concentration/effect)</td>
<td>~ 6 hours</td>
<td>~ 6 hours</td>
<td>3 – 5 hours</td>
<td>~ 3 hours</td>
</tr>
<tr>
<td><strong>T ½</strong> (time to fall to 50% of concentration/effect)</td>
<td>30–150 min (dose-dependent)</td>
<td>30–150 min (dose-dependent)</td>
<td>4 – 7 hours (longer in renal impairment)</td>
<td>17 – 21 hours (longer in renal impairment)</td>
</tr>
</tbody>
</table>
AB is ready for discharge to home. On the morning of hospital DAY 3, her INR is 2.2 after receiving 3 days of warfarin 5mg daily. How should she transition from parenteral anticoagulation to warfarin?

1. Stop LMWH at time of hospital discharge
2. Stop LMWH when INR ≥ 2, twice within 24 hours
3. Stop LMWH when INR ≥ 2, and after a minimum overlap of 5 days
4. Stop LMWH when INR ≥ 2, twice within 24 hours and after a minimum overlap of 5 days
2012 ACCP Recommendations for Treatment of VTE

- Initiate VKA on the same day as parenteral therapy (Grade 1B)
- Goal INR 2 – 3 (Grade 1B)
- Discontinue parenteral anticoagulant therapy after a **minimum of 5 days** **AND** when **INR ≥ 2** for at least 24 hours (Grade 1B)

Kearson C et al. Chest 2012; 141(2 suppl):e419s-e494s
Vit K-Dependent Clotting Factor
Elimination Half-life

- Factor II (prothrombin) 42 – 72 h
- Factor VII 4 – 6 h
- Factor IX 21 – 30 h
- Factor X 27 – 48 h
- Prot C 9 h
- Prot S 60 h

Early increase in PT/INR reflects reduction of Factor VII (has the shortest half life).
True anticoagulation is not achieved until Factor II synthesis is inhibited, ~ 5 days

- Warfarin 36 h
Hospital Discharge

35,079,000 hospital discharges in US (2010)

- Home
- Adult family home
- Assisted living facility
- Skilled nursing facility
- Rehabilitation center
- Transitional care hospital

 +/- home health services

National Hospital Discharge Survey 2010
www.cdc.gov/nchs/nhds.htm
Warfarin Dosing Tips

What experience tells us:

- 0.5 mg to 20+ mg daily to reach and sustain therapeutic INR range
- Influenced by patient sensitivity and host of other factors

Dose Initiation

- Obtain baseline values
- Avoid super large loading doses (>10mg)
- 4-5 mg orally daily (or 2-2.5 mg daily if very old, low body weight)
- Assess INR 3-4 days, adjust dose accordingly
- Frequent INR checks until stable INR response and weekly dose estimated
### Warfarin Dosing Tips

- First time slightly out of range, no dose change but check in 1 week
- Made dose adjustments by 10 – 20% of weekly mg total
- Distribute changes across 7 days
- Use boost or omit doses based on assessment
- Watch trends, fine tune accordingly

#### Maintenance Dosing

<table>
<thead>
<tr>
<th>Su</th>
<th>Mo</th>
<th>Tu</th>
<th>We</th>
<th>Th</th>
<th>Fr</th>
<th>Sa</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>2.5</td>
<td>5</td>
<td>2.5</td>
<td>5</td>
<td>2.5</td>
<td>5</td>
<td>27.5</td>
</tr>
<tr>
<td>5</td>
<td>2.5</td>
<td>5</td>
<td>5</td>
<td>2.5</td>
<td>5</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>2.5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>32.5</td>
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<tr>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>35</td>
</tr>
</tbody>
</table>
INR Monitoring

What experience tells us:

- Average interval between INR testing is 2.4 weeks
- Few patients achieve monthly INR testing on a consistent basis

Frequency of Monitoring:

- In setting of very high INR and doses held, check 1-2 days
- Weekly dose change, check 1-2 weeks
- Max interval: 4 weeks (can be exceptions) if INR and weekly dose stable
Almost 25% of medical errors in outpatient settings can be attributed to poor follow-up of abnormal test results.

How do you complete communication to patients on routine results? critical results?

- Technical and system solutions to manage and produce ‘work lists’
Maintenance: “INR” v. “Patient” Care

- “Checking an INR” and making a subsequent dose adjustment is NOT patient assessment.
- Dose decision making often requires additional patient-specific information not known by a number.
Pill Color and Mg Size

Medication safety errors (near misses) often associated with changes in pill sizes
Adverse Events after Hospital Discharge

CARE TRANSITION = TIME OF PATIENT VULNERABILITY

- Patients have an adverse event within 3 weeks of discharge
- Patients have a medication-related adverse event after transitioning from hospital to nursing home
- Patients have a medication-related adverse event while receiving home healthcare services after discharge

2 – Boockvar K et al. Arch Intern Med 2004; 164(5):545-50
Top Drugs Involved in ED Visits by Older Americans

Budnitz DS et al. NEJM 2011; 365:2002-12
Cost to Medicare for potentially preventable 30-day readmissions
Transition to Home

“Bundled” interventions to improve hospital D/C process and strengthen coordination of care

- Prevent adverse events after hospital discharge
- Reduce readmission rates

Focus on interventions to keep patients knowledgeable and safe
Care Transition Models

- Care Transition Model (E Coleman – U of Colorado)
  - Transition coaches teach patients
- Transitional Care Model (M Taylor – U of Penn)
  - Chronically ill, high-risk older adults
- Project RED (Re-Engineered Discharge) (BU Med Ctr)
  - Relies of 12 reinforcing components
- Guided Care (Lipitz Center at John Hopkins)
  - Patient-centered care for multiple, chronic conditions
- Project BOOST (Better Outcomes by Optimizing Safe Transitions) (Society of Hosp Medicine)
  - Multidisciplinary coach mentors
- CMS Community-based Care Transitions Program (CCTP) (Affordable Care Act)
  - High-risk Medicare beneficiaries
- Medical Homes
  - Primary care practices that operate as ‘medical homes’
Healthcare Resource Utilization after Hospital Discharge to Home

Successful Models for Improving Care Transitions (Medicare beneficiaries)

30-day All-Cause Rehospitalizations per 1000 beneficiaries per quarter, 2006-2010

Interventions

- Self-care activities
- Medication management & reconciliation
- Phone follow-up after hospital discharge (transitions between care settings)
- Follow-up on test results
  - Role of patient v. role of healthcare provider
- Electronic health records
What if AB needs surgery?

- Stop warfarin approx. 5 days before (Grade 1C)
- Resume 12 – 24 h after surgery and when adequate hemostasis (Grade 2C)

**High risk of thromboembolism (MHV, AF, VTE) → Bridging anticoagulation (Grade 2C)**

Douketis JD et al. Chest 2012; 141(2)(Suppl):e326s:e350s
Bridging: high risk period, requires careful communication of plan to entire team, including patient!

<table>
<thead>
<tr>
<th>Day -5</th>
<th>Day -3</th>
<th>Day -2</th>
<th>Day -1 Procedure</th>
<th>Day 0</th>
<th>Day +1</th>
<th>Day +2</th>
<th>Days 2 - 9</th>
<th>Day +10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin: Stop warfarin</td>
<td></td>
<td></td>
<td>If minor, may resume in eve</td>
<td>If major, resume if not already done on previous day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

INR:
- Check INR 1
- Overlap warfarin and heparin at least 5 days
- Monitor platelets

LMWH:
- Begin LMWH inj bid
- Cont LMWH inj bid
- AM dose ONLY
- Resume when adequate hemostasis
- D/C when INR ≥ 2 (x 2 in 24 hours) and minimum 5 days overlap

If less than 1.5, proceed with planned procedure
If 1.5 – 1.8, consider reversal with Vit K
If greater than 1.8, reversal with Vit K (1mg SC or 2.5 mg PO)
Timing of Hospital Readmission for DVT or PE

- Primary DVT or PE: 5.3% readmission
- Secondary DVT or PE: 14.3% readmission

Spyropoulos AC, Lin J. J Manag Care Pharm. 2007;13(6):475-86
Readmission Rate for DVT or PE as Primary or Secondary Diagnosis

Recurrent DVT event was associated with 21% greater cost compared to initial DVT event.

* Readmissions with hospital stay less than 3 days were excluded.

DVT=deep vein thrombosis; PE=pulmonary embolism; VTE=venous thromboembolism.

Spyropoulos AC, Lin J. J Manag Care Pharm. 2007;13(6):475-86
How to Avoid Re-admissions

During care transitions, patients likely:

- Receive little information on how to care for themselves
- Medication side effects to look out for
- Who to ask questions

Why are the causes:

- Poor care coordination
- Physicians often do not know when patients are discharged and care needs
- No incentives to do better with payment systems

IOM 2001 – Crossing the Chasm
AB is frustrated with the inconvenience and time associated with INR testing as well as persistent adjustment with her warfarin dose. Her insurance co-pay for rivaroxaban is affordable and she wants to switch. How should she be transitioned from warfarin to rivaroxaban?

1. Stop warfarin, start rivaroxaban when INR < 3
2. Stop warfarin, start rivaroxaban in 24 hours
3. Begin rivaroxaban, stop warfarin after 24 hour overlap
4. Begin rivaroxaban, stop warfarin after 72 hour overlap
### Pharmacokinetics of NOACs

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>T max</strong></td>
<td>1.25 – 3 hours</td>
<td>2 – 4 hours</td>
<td>1 – 3 hours</td>
</tr>
<tr>
<td><strong>T ½</strong></td>
<td>12 – 14 hours</td>
<td>5 – 9 hours</td>
<td>8 – 15 hours</td>
</tr>
<tr>
<td><strong>Dialyzable</strong></td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Renal excretion of unchanged drug</strong></td>
<td>80%</td>
<td>66%</td>
<td>25%</td>
</tr>
</tbody>
</table>

*NOACs = Novel Oral Anticoagulants (dabigatran, rivaroxaban, apixaban)*

Pradaxa PI. Boehringer-Ingelheim, April 2013
Xarelto PI. Janssen, Aug 2013
Eliquis PI. Bristol-Myers Squibb, Dec 2012
| DABIGATRAN  
Pradaxa® | RIVAROXABAN  
Xarelto® | APIXABAN  
Eliquis® |
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td><strong>NVAF</strong></td>
<td><strong>NVAF</strong></td>
<td><strong>NVAF</strong></td>
</tr>
</tbody>
</table>
| • 150mg twice daily  
• 75mg twice daily if CrCl 15-30 | • 20mg daily w/ meal  
• 15mg daily w/ meal if CrCl 15-50 | • 5mg twice daily  
• 2.5mg twice daily if 2 of: >70yrs, <61kg, or Cr>1.4 |
| **DVT Prophylaxis** | **VTE Treatment** | **Reduce VTE Recurrence** |
| • 10mg daily x35d hip, x12d knee  
• Use with caution if CrCl 30-50 | • 15mg twice daily x 21d, then 20mg daily w/ food  
• Use with caution if CrCl 30-50 | • 20mg daily w/ food  
• Use with caution if CrCl 30-50 |
Impact of Renal Impairment on Dabigatran Pharmacokinetics

<table>
<thead>
<tr>
<th>Renal Function</th>
<th>CrCl (mL/min)</th>
<th>Increase in AUC</th>
<th>Increase in $C_{\text{max}}$</th>
<th>$t_{1/2}$ (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>$\geq 80$</td>
<td>1x</td>
<td>1x</td>
<td>13</td>
</tr>
<tr>
<td>Mild</td>
<td>50-80</td>
<td>1.5x</td>
<td>1.1x</td>
<td>15</td>
</tr>
<tr>
<td>Moderate</td>
<td>30-50</td>
<td>3.2x</td>
<td>1.7x</td>
<td>18</td>
</tr>
<tr>
<td>Severe+</td>
<td>15-30</td>
<td>6.3x</td>
<td>2.1x</td>
<td>27</td>
</tr>
</tbody>
</table>

$^+$Patients with severe renal impairment were not studied in RE-LY

“Assess renal function during therapy as clinically indicated and adjust therapy accordingly.”

Pradaxa PI, April 2013
# Advantages of NOACs for Transitions

<table>
<thead>
<tr>
<th>Advantage</th>
<th>Clinical Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid onset of action</td>
<td>No need for bridging</td>
</tr>
<tr>
<td></td>
<td>BUT REQUIRES CAREFUL COORDINATION</td>
</tr>
<tr>
<td>Predictable anticoagulant effect (fixed doses)</td>
<td>No need for routine lab monitoring and associated dose adjustment</td>
</tr>
<tr>
<td></td>
<td>BUT STRONG RENAL FUNCTION IMPlications</td>
</tr>
<tr>
<td>Low potential for food interactions</td>
<td>No dietary precautions or worries</td>
</tr>
<tr>
<td>Lower potential for drug interactions</td>
<td>Fewer drug interactions/restrictions</td>
</tr>
<tr>
<td></td>
<td>BUT IMPORTANT Pgp or CYP INTERACTIONS</td>
</tr>
</tbody>
</table>
## Concerns about NOACs for Transitions

<table>
<thead>
<tr>
<th>Concerns</th>
<th>Clinical Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missed dose(s)</td>
<td>Determine compliance with medication taking (twice daily v. daily)</td>
</tr>
<tr>
<td>Frequency of assessing renal function</td>
<td>Dose adjustments or stop use</td>
</tr>
<tr>
<td>Initial recognition by all health care providers and first responders</td>
<td>Unaware of anticoagulant drug use</td>
</tr>
<tr>
<td>No reversal agent</td>
<td>Need for immediate reversal</td>
</tr>
<tr>
<td>No lab value to assess anticoagulant effect</td>
<td>Peak effect, urgent surgery</td>
</tr>
</tbody>
</table>
Care Transitions: Hospital to Home

- Direct communication of care plan to all parties
- Follow-up phone call to patient
- Follow-up appointment reminder
- What is patient’s understanding?
  - Confirmation of drug access and ability to pay

How is above accomplished?
“We suggest that health-care providers who manage oral anticoagulation therapy should do so in a systematic and coordinated fashion, incorporating patient education, systematic INR testing, tracking, follow-up, and good patient communication of results and dosing decisions.”

Holbrook A et al. Chest 2012; 141(suppl):e152s-e184s
Role of Anticoagulation Management Services to Improve Transitions of Care

- Patient Education
- Comprehensive INR & Dose Management
- Structured Follow-up Processes for Compliance
- Communications

Transitions in Care

Anticoagulation Management Services
www.excellence.acforum.org

• Useful resource library structured in 5 pillars of care:
  ➢ Drug Therapy
  ➢ Disease State Management
  ➢ Transition & Coordination of Care
  ➢ Service Operational Performance
  ➢ Patient & Family Education

• An online self-assessment that is a roadmap to what excellence looks like in anticoagulation and the chance for your practice to gain recognition
• Enhanced with member contributions
• Created by multidisciplinary team of AC Forum members
Antithrombosis Services in the Future

- Inpatient services to educate, aid in optimal drug selection and management, facilitate discharge process that is patient-centered
- Outpatient services expand beyond traditional INR/warfarin dose monitoring focus to incorporate NOACs and provide stewardship on antithrombotic services
  - Innovations in education, communications, patient involvement
Resources

- Are you at risk for a DVT - http://www.stoptheclot.org/
- OSG Call to Action, Sept 15, 2008 - http://www.surgeongeneral.gov/topics/deepvein/
- www.acforum.org Anticoagulation Forum
- http://excellence.acforum.org See Resource Center
- www.clotcare.com ClotCare Online Resource
- www.natfonline.org North American Thrombosis Forum