Anticoagulation at the End of Life

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OBJECTIVES

- Compare the Non Vitamin K Oral Antagonists (NOACs) with Warfarin, Low Molecular Weight Heparin (LMWH) and Unfractionated Heparin (UFH) for efficacy, safety, and cost
- Apply concepts of anti-coagulation risk assessment to hospice patients
- Depict the benefits of a pharmacist led anti-coagulation protocol in the hospice organization
- Implementing an Anticoagulation Protocol in your organization

Common Indications for Anticoagulation in Hospice

- A.Fib
- Cancer Related DVT/PE
Medications for Anticoagulation

- Lovenox
- Warfarin
- Non Vitamin K Oral Antagonists (NOACs)
  - Dabigatran (Pradaxa)
  - Rivaroxaban (Xarelto)
  - Apixaban (Eliquis)
### MOA

<table>
<thead>
<tr>
<th>MOA</th>
<th>Pradaxa (Dabigatran)</th>
<th>Xarelto (Rivaroxaban)</th>
<th>Eliquis (Apixaban)</th>
<th>Savaysa (Edoxaban)</th>
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</thead>
<tbody>
<tr>
<td>Direct Thrombin Inhibitor</td>
<td>Anti-Xa</td>
<td>Anti-Xa</td>
<td>Anti-Xa</td>
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### 4 INDICATIONS

1. **NVAF**
   - Yes | Yes | Yes | Yes |
2. **Acute VTE Treatment**
   - Yes | Yes | Yes | Yes |
3. **Secondary VTE Prevention**
   - Yes | Yes | Yes | No |
4. **Primary VTE Prophylaxis After Hip/Knee Replacement**
   - No | Yes | Yes | No |

### Dosing

**NVAF Dosing**

| CHADS2VASc ≥ 2 | 150mg BID | 30mg/min → 75mg BID | 5mg BID | 60mg daily |

**VTE TX Dosing**

| Dosing | 150mg BID after 5-10 days | 150mg BID x 21 days, then 20mg daily X 6mo | 10mg BID X 7 days, then 5mg daily X 6mo | 60mg daily with LMWH, then weight based |

**Secondary Prophylaxis Dosing**

| Dosing | 150mg BID | 20mg Daily after ≥ 4mo treatment X 6-12mo | 2.5mg BID after ≥ 4mo treatment X 6-12mo | D/C |

**Primary Prophylaxis Dosing**

| Dosing | NONE | 10mg Daily Hip X 35d Knee X 12d | 2.5mg BID Hip X 15d Knee X 12d | NONE |

### Drug Rotations

**TO WARFARIN**

| CrCl ≥ 50, start warfarin 3 days prior | CrCl 10-50, start warfarin 2 days prior | CrCl 3-19, start warfarin 1 day prior | CrCl < 19, none |

**SIDE EFFECTS**

| Dosing | Stop warfarin and LMWH when next dose due w/va, 65; LMWH when Hg <2 |

**TO ASPIRIN**

| Dosing | Stop Aspirin 2 days prior; do not restart aspirin 2 days after; do not restart aspirin 2 days after |

**CONTRAINDICATIONS**

| Dosing | Oral only option, parenteral option |

### Other Information

**Counseling**

| Dosing | Do not crush | May crush | May crush | CrCl < 95, can not use |

| Dosing | Take ASAP unless next dose due within 6hr | Take ASAP | Take ASA on same day, do not take 2 doses in one day |

| Dosing | Take ASAP on same day, do not take 2 doses in one day |

| Dosing | Take ASAP on same day, do not take 2 doses in one day |
NOACs and BLEEDING

- Intracranial bleeding is reduced 50%
- Outcome of intracranial bleeding is no worse than that of warfarin
- Fatal bleeding is less common
- GI bleeding is more common, mortality rates were lower with dabigatran over warfarin
- Reversal agents are under development.

Do NOT use NOACs if:

- Mechanical heart valves
- End stage renal disease
- Cancer related event – no studies

NOACS vs Warfarin

- Faster onset –> no bridging
- More predictable anticoagulant response –> no monitoring
- No dietary Vit K influence
- Fewer drug-drug interactions
- Less intracranial bleeding
- Shorter offset of action
- 1-2 times daily vs once daily
- Monitoring uncertain vs INR
- RENAL clearance vs non-Renal
- Reversal Agents
- Expensive
Atrial Fibrillation

- NVAF is the most common indication for the patients in our hospice organization so we will concentrate the risk assessment on this patient population

Atrial Fibrillation

- 5x higher stroke risk - Afib strokes are more fatal/disabling than non-Afib strokes
- Warfarin - reduces stroke risk by 64% and mortality by 25%
- NOACs reduce stroke risk by 19%
- NOACs vs warfarin - reduced all cause mortality by 10% and ICH by 52%
- 25% higher GI bleed (except apixaban) than warfarin
- ** NOACs are non-inferior for prevention of stroke and systemic embolism in AF patients, and are associated with less ICH and reduced all cause mortality

CASE PRESENTATION

Mr. Jones is a 96 yr old man admitted to hospice with Senile Degeneration of the Brain. He has secondary diagnoses including hypertension and atrial fibrillation.

Current medications:
- donepezil
- risperidone
- warfarin - 4mg daily except 6mg MWF
- lisinopril
- APAP
- metoprolol
- docusate
- bisacodyl
- famotidine

On admission, INR is 3.8
Atrial fibrillation increases stroke risk 5 fold. The risks of bleeding must be weighed for Mr. Jones. Warfarin decreases his stroke risk to about 2%, but he is now at an 8% risk of a GI hemorrhage. If he has 6 months or less of living, is this worth the risk?

The patient wants to continue the warfarin

Pharmacy recommendations:
Hold 2 doses and recheck INR

On recheck, the INR is now 2.9.

Pharmacy recommendations:
Restart warfarin at 4mg daily except 6mg on Mondays (reduced total weekly dose in the 10-20% range as recommended in the CHEST 2012 guidelines)
Recheck INR in 1 week.

1 week later INR is 4.3.

Questions asked to nurse/patient:
1. What dose is the patient taking?
2. Has the patient had alcohol intake recently?
3. Has Mr. Jones had any dietary changes?
4. Has Mr. Jones started any new medications in the past few days?

Mr. Jones developed a UTI 5 days ago and was started on Bactrim by his PCP.

Pharmacy Recommendations:
Hold warfarin for 2 doses. Recheck INR at this time and reassess.

After 2 held warfarin doses, INR is back in range at 2.7, and the antibiotic course is completed.

Pharmacy recommendations.
Restart warfarin at 4mg daily except 6mg on Mondays. Recheck INR in 1 week.

1 week later, INR is 2.8

Patient decides to discontinue warfarin.
CANCER AND THROMBOSIS
The American Society of Clinical Oncology (ASCO) Practice Guidelines in a nutshell:

- Most cancer patients in the hospital require thromboprophylaxis
- Very few ambulatory cancer patients require thromboprophylaxis
- Multiple Myeloma patients receiving chemo +/- dexamethasone should receive LMWH or low dose ASA
- Cancer patients having surgery require prophylaxis before surgery and 7-10 days after surgery, high risk patients up to 4 weeks
- LMWH is the recommended anticoagulant for treatment and secondary prophylaxis
- Non vitamin K oral anticoagulants (NOACs) are NOT recommended for patients with cancer and VTE
- Anticoagulation should not be used solely to extend survival
- Cancer patients should be periodically assessed for VTE risk
- Patients should be educated on the signs and symptoms of VTE

PRIMARY TREATMENT and SECONDARY PREVENTION

- LMWH RECOMMENDED
- UH with severe renal impairment (CrCl < 30ml/min)
- Long term therapy
  - LMWH preferred, but warfarin is an acceptable alternative
  - CrCl < 30 and anti-factor Xa monitoring unavailable, warfarin is recommended
- Duration 3-6 months - must weigh risk vs. benefit (clinical model to predict VTE risk in cancer patients not yet validated)
- Treatment >6 months has not been investigated

NOACs in Cancer-Associated Thrombosis

- Cancer patients not included in the NOAC trials for FDA approval
- More GI hemorrhage than warfarin
Pharmacist Led Anticoagulation Protocol

1. Detail INR targets for specific anticoagulation indications
   - Most target INRs are 2-3, however, mitral valve replacements are 2.5-3.5

2. Outline dose change regimens for sub-therapeutic and supra-therapeutic INRs
   - Warfarin doses should be increased/decreased by 10-20% of the current total weekly dose (TWD) according to sub and supra therapeutic levels.

3. Provide guidance on rotation between anticoagulants and bridging warfarin with LMWH
   - Recommendations for anti-coagulation rotation differ between different NOACs and warfarin, rotating to or from warfarin with a NOAC, and bridging with LMWH. Not all NOACs require LMWH bridging.

4. Provide guidelines on INR testing time frames referenced from the 2012 CHEST Guidelines
   - For STABLE patients, the CHEST guidelines recommend up to 12 weeks between INR testing.
   - Are hospice patients stable?

5. Ensures patient follow up and education on risks vs. benefits of anticoagulation
   - Patients will be educated on the risks and benefits at every nurse visit as the patient progresses in disease state and declines in overall health.
   - As the INR gets more difficult to regulate, this education becomes even more paramount to patient safety.

6. Pharmacists will take the burden of anticoagulation care off of the physician
   - Clinically trained pharmacists are experts in anticoagulation.
Implementing an Anticoagulation Protocol in your organization

- Decide who will be the implementer
  - In house pharmacist
  - Consulting pharmacist
  - Medical Director

- The pharmacist will write a protocol
  - The protocol will detail all possible anticoagulation treatments and parameters through evidence-based medicine
  - Specific nursing processes and education will be implemented to ensure patient safety

- The protocol will be reviewed by ..... and signed by ......

- The pharmacist will provide education on anticoagulation to all clinical staff introducing the anticoagulation protocol

- The nursing staff will be trained on point of care testing machines

- Nurses will be required to obtain INRs for all patients on warfarin within 24hr of admission, reporting to the pharmacist for further instruction

- All instruction from the pharmacist will be based on the written and approved Anticoagulation Protocol for the organization.
Sources/Questions?