Medication Safe Practice Review of Anticoagulant Therapy

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USA - QuarterWatch™ (2016 Annual Report) Part II: Oral Anticoagulants—The Nation’s Top Risk of Acute Injury from Drugs

Netherlands - Anticoagulants were involved in 8.3% of all reported medication errors reports. Dreijer A et al Int J Qual In Health Care June 2019
The clotting pathways

Extrinsic Pathway
- Damage to tissue outside the vessel
  - Tissue Thromboplastin
    - Inactive Factor X
      - Activated Factor X
        - Prothrombin
          - Fibrinogen
            - Fibrin
              - Factor XIII
                - Blood Clot

Intrinsic Pathway
- Damage to the blood vessel
  - Cascade of clotting factors
    - Activated Factor X
      - Prothrombin
        - Fibrinogen
          - Fibrin
            - Factor XIII
              - Blood Clot

Coumadin works here

Heparin works here

Intrinsic pathway Amplification
- XIIa
  - Xla
  - VIIIa
  - IXa

Extrinsic pathway Initiation
- VIIa
  - FT

PROPAGATION
- PARENTERAL
  - Fondaparinux
  - Low-molecular-weight heparin
  - Bivalirudin

ORAL
- Rivaroxaban
- Apixaban
- Edoxaban
- Dabigatran

THROMBUS FORMATION
- Fibrin
  - Thrombus
Death And Disability From Warfarin-Associated Intracranial And Extracranial Haemorrhages

• 13,559 adults with nonvalvular atrial fibrillation and identified patients hospitalized for warfarin-associated intracranial and major extracranial haemorrhage. Data on functional disability at discharge and 30-day mortality were obtained from a review of medical charts and state death certificates. The relative odds of 30-day mortality by haemorrhage type were calculated.

Results
• 72 intracranial and 98 major extracranial haemorrhages occurring in more than 15,300 person-years of warfarin exposure. At hospital discharge, 76% of patients with intracranial hemorrhage had severe disability or died, compared with only 3% of those with major extracranial haemorrhage.
• Of the 40 deaths from warfarin-associated haemorrhage that occurred within 30 days, 35 (88%) were from intracranial haemorrhage. Compared with extracranial haemorrhages, intracranial events were strongly associated with 30-day mortality (odds ratio 20.8 [95% confidence interval, 6.0-72]) even after adjusting for age, sex, anticoagulation intensity on admission, and other coexisting illnesses.

Conclusions
• Among anticoagulated patients with atrial fibrillation, intracranial haemorrhages caused approximately 90% of the deaths from warfarin-associated haemorrhage and the majority of disability among survivors. When considering anticoagulation, patients and clinicians need to weigh the risk of intracranial haemorrhage far more than the risk of all major haemorrhages.
# Types of Medication Errors With Anticoagulant Therapy

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Types of medication errors</th>
<th>Root causes</th>
</tr>
</thead>
</table>
| Warfarin            | • Wrong loading and maintenance doses prescribed  
                       • In-adequate INR/clinical monitoring  
                       • Wrong dose administered/error following complex dosing regimen  
                       • Clinical contra-indications  
                       • Drug-drug interaction  
                       • Drug-food interaction  
                       • Omitted medicine/ not reintroduced after surgery | • Poor communication especially at transition of care  
                                                                      • Inadequate protocols/procedures/prescribing forms or screens  
                                                                      • Inadequate training of health staff, carers and patients  
                                                                      • No clinical role for pharmacists dispensing the medicine  
                                                                      • Inadequate clinical audit |
| Unfractionated heparin | • Wrong dose prescribed  
                       • Wrong dose prepared and administered  
                       • Wrong rate of administration  
                       • Mix-ups between treatment and flushing doses and infusions  
                       • Mix-ups between heparin and other infusions  
                       • Clinical contra-indication  
                       • Omitted or delayed therapy | • Many of the above  
                                                                      • Mix-ups with wrong strength medicine vials  
                                                                      • Calculation errors  
                                                                      • Inadequate clinical audit |
### Types Of Medication Errors With Anticoagulant Therapy

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| Low molecular weight heparin | • Wrong dose errors – dose not adjusted for body weight and renal failure  
|                           | • Clinical contra-indications - especially in immobile, non-surgery patients after hospital stay  
|                           | • Drug-drug interaction  
|                           | • Omitted medicine                                                                                   | • Inadequate protocols/procedures/prescribing forms or screens  
|                           |                                                                                                       | • Inadequate training of health staff, carers and patients  
|                           |                                                                                                       | • No clinical role for pharmacists dispensing the medicine  
|                           |                                                                                                       | • Inadequate clinical audit                                                                            |
| NOACS                     | • Prescribing outside licensed indications  
|                           | • Dose errors, limited data on use in patients at the extremes of body weight and those with renal and hepatic impairment  
|                           | • the higher rates of gastrointestinal bleeding with dabigatran and rivaroxaban / clinical contraindications  
|                           | • Look alike errors – Plavix (clopidogrel 75mg, 300mg and Pradax (dabigatran 75mg,110mg,150mg)  
|                           | • Complex reversal procedures to treat bleeding  
|                           | • Drug – drug interactions  
|                           | • Omitted medicine/ not reintroduced after surgery                                                        | • NOACS are only proven and licensed for some of the clinical indications for more established anticoagulants  
|                           |                                                                                                       | • Inadequate protocols, procedures, prescribing forms or screens  
|                           |                                                                                                       | • Inadequate training of health staff, carers and patients  

## Licensed Indications For NOACS

<table>
<thead>
<tr>
<th>Clinical indication</th>
<th>Licensed use in the UK (NICE evaluation)</th>
</tr>
</thead>
</table>
| Prevention of stroke in adults with non-valvular atrial fibrillation | Apixaban TA275  
Dabigatran TA249  
Edoxaban TA355  
Rivaroxaban TA256 |
| Treatment and prophylaxis for recurrent DVT and PE       | Apixaban TA341  
Dabigatran TA327  
Edoxaban TA354  
Rivaroxaban TA287, TA261 |
| Prevention of venous thromboembolism after elective hip or knee surgery | Apixaban TA245  
Rivaroxaban TA170  
Dabigatran TA157 |
| Prevention of adverse outcomes after acute management of acute coronary syndrome | Rivaroxaban TA335 |
Oral Anticoagulants: A Review of Common Errors and Risk Reduction Strategies
Types of Safe Medication Practice Alerts
Guidance

Unfractionated heparin

- All patients should have a baseline aPTT performed before initiation of therapy.

- Platelet counts should also be measured just before therapy with UFH, and regular monitoring of platelet counts may be required if UFH is administered for longer than four days.

Low molecular weight heparin

- The weight of the patient is used to calculate the treatment dose required of LMWH. The medication chart (when in use) and clinical record should have the weight of the patient accurately recorded. At the beginning of therapy, patients should be weighed and, during treatment, where applicable.

- When prescribing treatment doses of LMWH, renal function should be taken into account.

- Dose calculation tools are available for different LMWH products, specific clinical indications and varying body weights.

- Rationalise LMWH products used within an organization.
• **Vitamin K antagonists (e.g. warfarin)**

• Prior to commencing anticoagulation, a risk assessment should be undertaken and documented, and repeated on an annual basis.

• Prescribers should discuss the risks, benefits and implications of long-term warfarin treatment with newly diagnosed patients.

• This discussion should be documented and decision aids used where possible.

• The baseline prothrombin time (or INR) should be determined.

• The appropriate (rapid or slow) induction should be used. This should reduce the likelihood of ineffective or excessive anticoagulation and some can also be used to predict the likely long-term daily doses of warfarin.

• INR should be measured regularly, particularly during the induction period.

• Computer dosing software could be used when available.

• Anticoagulant treatment booklets may be issued to all patients; these booklets could include
  • advice for patients on anticoagulant
  • treatment, an alert card to be carried by the patient at all times, and a section
  • for recording INR results and dosage information.

• There should be reliable follow-up systems in primary care to ensure that patients on warfarin are reviewed regularly and not lost to follow-up.
• **Newer oral anticoagulants /direct oral anticoagulants**
  • When prescribing a NOAC an in-depth knowledge of its pharmacology and clinical use is needed.
  • Prior to prescribing, conducting a risk–benefit assessment should be considered.
  • Careful patient selection and monitoring ensures the best outcomes.
  • Before prescribing a NOAC creatinine clearance should be calculated using ideal body weight and documented.
  • If renal function is impaired, excessive anticoagulation and drug accumulation can occur. Renal function should be monitored at least annually. Monitoring frequency may be increased to every three or six months due to declining renal function or dehydration, and amongst older persons.
  • These factors should be communicated through all transitions of care to ensure proper monitoring.
  • NOACs have fewer drug interactions than warfarin; however, many clinically significant interactions exist.
  • Individual patient bleeding risks should be considered and specialist advice could be sought, as these are often complex situations.
  • Counselling of patients and caregivers could include communicating the discharge information from hospital care, promoting regular and adequate follow-up and explaining how to recognize and respond to bleeding, and to seek medical attention immediately if bleeding is suspected.
Between December 2012 and May 2015, 42,962 medication errors were reported to the Central Medication incidents Registration reporting system in the Netherlands. They measured the total number of anticoagulant medication error reports per month, divided by the total number of medication error reports per month (comparing the pre- and post-guideline phase) and the total number of causes of 1000 anticoagulant medication errors before and after introduction of a national guideline on integrated antithrombotic.

Anticoagulants were involved in 8.3% of the medication error reports. A random selection of 1000 anticoagulant medication error reports revealed that low-molecular weight heparins were most often involved in the error reports (56.2%). Most reports concerned the prescribing phase of the medication process (37.1%) and human factors were the leading cause of medication errors mentioned in the reports (53.4%).

Publication of the national guideline on integrated antithrombotic care had no effect on the proportion of anticoagulant medication error reports. Human factors were the leading cause of medication errors before and after publication of the guideline.
Patient safety alert

Actions that can make anticoagulant therapy safer

Anticoagulants are one of the classes of medicines most frequently identified as causing preventable harm and admission to hospital. Managing the risks associated with anticoagulants can reduce the chance of patients being harmed in the future.

This patient safety alert has been developed in collaboration with the British Society for Haematology (BSH) and a broad range of other clinical organisations and individual clinicians, patients and patient groups.

Action for the NHS and the independent sector

The National Patient Safety Agency (NPSA) is recommending that NHS and independent sector organisations in England and Wales take the following steps:

1. Ensure all staff caring for patients on anticoagulant therapy have the necessary work competences. Any gaps in competence must be addressed through training to ensure that all staff may undertake their duties safely.

2. Review and, where necessary, update written procedures and clinical protocols for anticoagulant services to ensure they reflect safe practice, and that staff are trained in these procedures.

3. Audit anticoagulant services using BSH/NPSA safety indicators as part of the annual medicines management audit programme. The audit results should inform local actions to improve the safe use of anticoagulants, and should be communicated to clinical governance, and drugs and therapeutics committees (or equivalent). This information should be used by commissioners and external organisations as part of the commissioning and performance management process.

4. Ensure that patients prescribed anticoagulants receive appropriate verbal and written information at the start of therapy, at hospital discharge, on the first anticoagulant clinic appointment, and when necessary throughout the course of their treatment. The BSH and the NPSA have updated the patient-held information (yellow) booklet.

5. Promote safe practice with prescribers and pharmacists to check that patients' blood clotting (International Normalised Ratio, INR) is being monitored regularly and that the INR level is safe before issuing or dispensing repeat prescriptions for oral anticoagulants.

6. Promote safe practice for prescribers co-prescribing one or more clinically significant interacting medicines for patients already on oral anticoagulants, to make arrangements for additional INR blood tests, and to inform the anticoagulant service that an interacting medicine has been prescribed. Ensure that those dispensing clinically significant interacting medicines for these patients check that these additional safety precautions have been taken.

7. Ensure that dental practitioners manage patients on anticoagulants according to evidence-based therapeutic guidelines. In most cases, dental treatment should proceed as normal and oral anticoagulant treatment should not be stopped or the dosage decreased inappropriately.

8. Amend local policies to standardise the range of anticoagulant products used, incorporating characteristics identified by patients as promoting safer use.

9. Promote the use of written safe practice procedures for the administration of anticoagulants in social care settings. It is safe practice for all dose changes to be confirmed in writing by the prescriber. A risk assessment should be undertaken on the use of Monitored Dosage Systems for anticoagulants for individual patients. The general use of Monitored Dosage Systems for anticoagulants should be minimised as dosage changes using these systems are more difficult.

https://webarchive.nationalarchives.gov.uk/20171030125102/http://www.nrls.npsa.nhs.uk/resources/?entryid45=59814&q=0%c2%acanticoagulant%c2%ac
Safety Indicators For Oral Anticoagulants

Safety indicators for patients starting oral anticoagulant treatment

Different loading protocols are used depending upon the urgency to achieve a therapeutic level of anticoagulation, see section 4 of the 2005 update of guidelines on oral anticoagulation (Baglin et al, 2006).

1. Percentage of patients following a loading protocol appropriate to indication for anticoagulation.
2. Percentage of patients developing INR > 5·0 within first 2 months of therapy.
3. Percentage of patients in therapeutic range at discharge (for inpatients being transferred to outpatient care).
4. Percentage (incidence) of patients suffering a major bleed in first month of therapy and percentage suffering major bleed with INR above therapeutic range.
5. Percentage of new referrals to anticoagulant service (hospital or community-based) with incomplete information, e.g. diagnosis, target INR or inappropriate target with reference to BCSH guidelines, stop date for anticoagulant therapy, dose of warfarin on discharge, list of other drugs on discharge.
6. Percentage of patients that were not issued with patient held information and written dose instructions at start of therapy.
7. Percentage of patients that were discharged from hospital without an appointment for next INR measurement or for consultation with appropriate health care professional to review and discuss treatment plan, benefits, risks and patient education.
8. Percentage of patients with subtherapeutic INR when heparin stopped (fast loading patients only, e.g. treatment of acute VTE).

Safety indicators for patients established on oral anticoagulant treatment

1. Proportion of patient-time in range (if this is not measurable because of inadequate decision/support software then a secondary measure of percentage of INRs in range should be used).
2. Percentage of INRs > 5·0.
3. Percentage of INRs > 8·0.
4. Percentage of INRs > 10 INR unit below target (e.g. percentage of INRs < 1·5 for patients with target INR of 2·5).
5. Percentage of patients suffering adverse outcomes, categorised by type, e.g. major bleed.
6. Percentage of patients lost to follow up (and risk assessment of process for identifying patients lost to follow up).
7. Percentage of patients with unknown diagnosis, target INR or stop date.
8. Percentage of patients with inappropriate target INR for diagnosis, high and low.
9. Percentage of patients without written patient educational information.
10. Percentage of patients without appropriate written clinical information, e.g. diagnosis, target INR, last dosing record.
Important information for patients taking oral anticoagulants

Introduction
This booklet has been given to you because you are starting to take a medicine known as an anticoagulant. A healthcare professional will go through this book with you, explain what it all means and answer any questions you may have. They will be able to give you advice at the start of your anticoagulant therapy, when you leave hospital, on your first visit to the anticoagulant clinic, and at any other time you need it.

Things that can affect the control of anticoagulation

Diet
It is important to eat a well balanced diet.
Consult your doctor or practice nurse if you need to diet to lose weight.
Any major changes in your diet may affect how your body responds to your anticoagulant medication.

Other medicines
Many medicines can interact with anticoagulants.
If, during your course of anticoagulants, you are also starting or stopping another medication, the prescriber may advise that you should have a blood test within five to seven days of starting the new medication. This is to make sure that your INR remains within the desired range. Please contact your anticoagulant clinic for further advice.

Serious side effects
The most serious side effect of anticoagulants is bleeding. If you experience any of the following, seek medical attention and have an urgent INR test:
- prolonged nosebleeds (more than 10 minutes);
- blood in vomit;
- blood in sputum;
- passing blood in your urine or faeces;
- passing black faeces;
- severe or spontaneous bruising;
- unusual headaches;
- for women, heavy or increased bleeding during your period or any other vaginal bleeding.

If you cut yourself, apply firm pressure to the site for at least five minutes using a clean, dry dressing.

In the UK, the colours of warfarin tablets are:
- 0.5mg (500 micrograms) – white
- 1mg – brown
- 3mg – blue
- 5mg – pink

Do not confuse the dose in mg with the number of tablets that you take.
Patient Held Information 2

# Anticoagulant Treatment Record

<table>
<thead>
<tr>
<th>Date</th>
<th>INR</th>
<th>Daily dosage (mg)</th>
<th>Comments</th>
<th>Signature</th>
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## Implementing Patient Safety Alert 18: Anticoagulant Therapy Resource [UPDATE]

Published 4th August 2011, updated 19th July 2019 · Medicines Use and Safety

### 2SV
<table>
<thead>
<tr>
<th>Secondary Care</th>
<th>Description</th>
<th>Contact Information</th>
</tr>
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<tbody>
<tr>
<td>2S.1.1.V</td>
<td>Dartford and Gravesham NHS Trust</td>
<td>Comprehensive policy with FAQ document.</td>
</tr>
<tr>
<td>2S.1.2.V</td>
<td>Queen Victoria Hospital NHS Foundation Trust</td>
<td>Comprehensive policy: if interacting drugs are prescribed the doctor is responsible for checking INR &amp; in outpatient setting for telling patient to have INR checked in 4-7 days and informing their AC clinic of the interacting drug.</td>
</tr>
<tr>
<td>2S.1.3.V</td>
<td>Oxford University Hospitals NHS Foundation Trust</td>
<td>Anticoagulation protocol with guidance on dual antiplatelet therapy with vitamin K antagonists.</td>
</tr>
<tr>
<td>2S.1.4.V</td>
<td>Barts Health NHS Trust</td>
<td>Standards state systematically what clinical pharmacists need to do on a day to day basis for inpatients.</td>
</tr>
<tr>
<td>2S.1.5.V</td>
<td>Wirral University Teaching Hospital NHS Foundation Trust</td>
<td>Anticoagulation protocol with guidance on discharging patients</td>
</tr>
<tr>
<td>2S.1.6.V</td>
<td>King’s Thrombosis Centre</td>
<td>Comprehensive chart – includes a section for antiplatelets.</td>
</tr>
</tbody>
</table>

What Are Quality/Safety Improvement Collaboratives?

• Quality improvement methodology that “brings together groups of practitioners from different healthcare organisations to work in a structured way to improve one aspect of the quality of their service. It involves a series of meetings to learn about best practice in the area chosen, about quality methods and change ideas, and to share their experiences of making changes in their local settings”.

• It involves five essential features: there is a specified topic; clinical experts and experts in quality improvement provide ideas and support for improvement; multi-professional teams from multiple sites participate; there is a model for improvement (setting targets, collecting data and testing changes); and the collaborative process involves a series of structured activities.

• Components of collaborative model Selecting a topic for improvement Developing a consensus on standards of care Producing a “change package” (not what to do but how to do it ) Establishing an organisational structure to support buy- in and shared responsibility with key stakeholders Enrolling participants Key learning sessions with intervening action periods.
Questions for discussion

• Has your centre published any information concerning harms from anticoagulants?
• Do these materials only focus on high-lighting the risks to patient safety?
• Do they also include safer practice recommendations?
• How have these practice recommendations been developed?
• Have you included implementation support materials?
• Have you included metrics to measure improvement?
• Have you linked with quality/safety improvement collaboratives?
• Can the above processes and publications be further improved?
• Is there action that the International Medication Safety Network should take?