New Oral Anticoagulants: Practical Experience

Oral Anticoagulation Update Day
12th September 2012
University of Birmingham

ESC AF Guidelines 2012

Management of Atrial Fibrillation
Focus of 2012 Update

- Anticoagulation risk stratification
- Use of novel oral anticoagulants (NOACs)
- Left atrial appendage occlusion/excision
- Pharmacological cardioversion (vernakalant)
- Oral antiarrhythmic therapy (dronedarone, and short term therapy)
- Left atrial catheter ablation

Anticoagulation - General

Recommendations for prevention of thromboembolism in non-valvular AF - general

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
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<tr>
<td>Antiplatelet therapy to prevent thromboembolism is recommended for all patients with AF, except in those patients (both male and female) who are at low risk (age &gt;65 years and low AF), or with contraindications.</td>
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<td>The choice of antithrombotic therapy should be based on the absolute risks of stroke/thromboembolism and bleeding and the net clinical benefit for a given patient.</td>
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<td>The CHA2DS2-VASc score is recommended as a means of assessing stroke risk in non-valvular AF.</td>
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NICE vs. Local Guidance

NICE says no
- We say no

NICE says yes
- We say no

Introduction of NOACs

NOACs not a lifestyle drug
TTR should be used as criteria
Bleeding risks are the same or higher

Responding to NICE TAs

Some Opinions...

4.2 The Committee heard from the clinical specialists and patient experts that the current standard treatment for the prevention of stroke and systemic embolism in people with atrial fibrillation is warfarin, and that because of its lower efficacy, aspirin is used only in people for whom warfarin is unsuitable. The Committee also heard that warfarin, although an effective treatment, is associated with a number of problems. The main concerns for people with atrial fibrillation were fear of having a stroke and anxiety about the difficulty of keeping the INR within the satisfactory therapeutic range. The Committee heard from the patient experts that stroke is a major concern for people with atrial fibrillation and that stroke severity is usually greater in this group than in people who have strokes from other causes. The patient experts also highlighted that many people taking warfarin are outside their target therapeutic INR range at any one time and that warfarin, unlike dabigatran, is associated with a number of inconveniences that make adherence difficult. These include numerous food and drug interactions that can have an impact on people’s work, social and family life, and regular monitoring and dose adjustments that can cause disruption and inconvenience. The Committee accepted the limitations of warfarin therapy, and the considerable effort that it may have on the lives of the people who take it, and recognised the potential benefits of dabigatran for people with atrial fibrillation.

4.6 The Committee discussed the effectiveness of dabigatran compared with warfarin according to INR control. It noted the evidence presented by the ERG that people with good INR control with warfarin may not gain additional clinical benefit by taking dabigatran. However, the clinical specialists emphasised the importance of the significantly lower rates of intracranial haemorrhage and haemorrhagic stroke associated with both doses of dabigatran compared with warfarin in the RE-LY trial, and that this effect is maintained in people with good INR control. The Committee heard that haemorrhagic stroke and intracranial haemorrhage have devastating and life-threatening consequences and concluded that the lower rates associated with dabigatran represent an important advance in the treatment of atrial fibrillation alongside reduction in ischaemic stroke. It concluded that this applied to all patients with atrial fibrillation, including those with good INR control, and that there were also benefits of taking a treatment that didn’t need INR monitoring or dietary restriction.
The aim of this advice is to promote the safe and effective use of dabigatran within its licensed indication in BCUHB for the prevention of stroke and systemic embolism for patients with nonvalvular atrial fibrillation.

The advice:

1. Warfarin, with dose titrated to a target INR of 2 to 3, remains the anticoagulant of choice for stroke prevention in AF. The focus of AF management should be to identify patients with AF and undertake stroke risk assessment using the CHADS² risk assessment tool, or more recently introduced CHA²DS²-VASc risk assessment tool (see Appendix 1).

   Patients with a CHADS²/CHA²DS²-VASc score ≥ 2 should be initiated on warfarin in the first instance, unless contraindicated.

2. In warfarin naive patients, if there are compelling reasons (see below) not to initiate warfarin then dabigatran initiation should be undertaken only by Secondary Care clinicians specialising in stroke prevention in AF (e.g. Cardiology or the Stroke team). However in this group of patients continued prescribing by General Practitioners is appropriate i.e. dabigatran’s BRAG List designation for stroke prevention in AF is AMBER WITHOUT SHARED CARE. Compelling reasons include patients who are:

   - Unable to take warfarin due to allergy or contraindications (that is not otherwise a contraindication to anticoagulant therapy in general). Note that a bleeding risk that would lead to contraindication of warfarin would also contraindicate dabigatran.

3. For patients prescribed warfarin previously dabigatran will only be considered as an alternative to warfarin for stroke prevention in AF in patients who are:

   - Unable to achieve an INR within the target therapeutic range (TTR) for at least 50% of the time over a period of 6 months (excluding first month after initiation) on warfarin. The TTR can be calculated automatically with most INR monitoring software systems.

Cost-effectiveness: Hidden gain

- High risk but not anticoagulated
  - Professional reluctance
  - Patient reluctance
  - Patient difficulty warfarin
  - Continue on Warfarin

- High bleeding risk/event
  - New Agents

On Warfarin

Self Selection

- This is a first for me
- Patient driven almost entirely
- Patients are (scarily) well informed
  - Not the Daily Mail factor!
  - Extensive reading beforehand
  - Professional or expert articles & websites
  - Bring literature to help me (just in case...)
  - Nuanced & detailed questioning
  - Understand NICE recommendations & financial implications, drug differences and indications

Patient Selection

- My last 6 NOAC patients
  1. Warfarin not tolerated / controlled
     - 78yr male permanent AF on warfarin
     - Having vague SE blamed on warfarin
     - TTR 6 months 48%
  2. Previous problems warfarin & DCCV
     - 32yr male recurrent AF seen end of July
     - DCCV in May cancelled twice as INR control poor
     - Holiday → schedule NOAC 4/52 before DCCV
  3. Perceived risk of warfarin
     - 77yr lady new diagnosis AF, CHADS²-VASc=5
     - Husband recently admitted to nursing home with an ICH secondary to warfarin
4. Urgency & logistics for OAC
   - 58yr post-AVR and reduced LV July 2012
   - Went into AFL a month after; seen Aug 24th
   - Scheduled TOE guided DCCV Aug 28th (clot in LA!)

5. Traveller (leisure or business)
   - 84yr lady new diagnosis of AF
   - Travels alone extensively to remote destinations
   - Varied diet and enjoys her drink

6. Can’t do own medication / pillbox
   - 54yr male with learning difficulties
   - Innumerate beyond counting to 3

When don’t I start a NOAC?

- True high bleeding risk with warfarin
  - Matters of degree & type of risk
- Poor adherence to warfarin
  - Waste of time → expensive waste of time
- Soon after MI/PCI
  - Dual antiplatelet therapy?
- With prosthetic valves
  - At present

Selling last year’s model

- Customer comes in
- Sees the sales assistant (my AF nurses)
  - Explains why they need the product
  - 1hr pitch about how good the last years product is
  - Many buy into this
  - Others, unhappy & want to see the manager
- Manager (me)
  - Tries to sell them old stock again
  - Gives up and brings the new stuff from the back

Drug Usage Paradox

- ‘Simple’ defined population type
- Good clinical trial → Approval for use
- Select difficult patients (outside trial)
- Uncertain / poor outcomes
- Lack of confidence/ drug experience

Choice of OAC

- New or Old

Complex Choices

- Dabigatran vs. Rivaroxaban: not clear-cut
- Patients are very sophisticated
  - Well read
  - Appreciated differences
  - Compare relative benefits
- Key parameters seem to be
  - Convenience (od vs. bd)
  - Extent of protection vs. intra-cranial bleeding
  - Cost
  - Tolerance issues
Generally delighted
• ‘Seems far too easy’
• ‘what side-effects should I be expecting’
Self-selected & motivated group
Extensively counselled
1 patient switched NOAC
All rest still taking reliably
• keep asking for repeat prescriptions on time

Protect them against healthcare professionals!
Literature & information
• To take home
• To show doctors & pharmacists
Fact vs. Fiction
• Scare-mongering or mis-information
But these are still new drugs....
• ..and they are anticoagulants
Tesco is better than Boots!

Reversibility
• Is this really a big issue?
• Antidotes in development

Monitoring?
• Don’t do for most other anti-thrombotics
• Crude assessments possible

Clinical scenarios
• Cardioversion
• EP studies
• ACS & PCI – difficult area
• Confusion doses for other indications (e.g. VTE prophylaxis, DVT/PE Rx)

Cardioversion
• Monitor QRS duration after cardioversion
• Titrate to target heart rate

ESC - Bleeding & Cardioversion

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Where new might not be better

- Loss of income / service primary care?
- Will not eliminate anti-coagulation clinics (immediately)
- Other conditions needing warfarin
- True bleeding or high unacceptable risk
- Low risk patients
- Patients happy and stable on current Rx

Professional, Ethical & Legal Issues

- Duty of care to patient
- Informed consent
  - Laying out of all options – balanced & objective
  - Risk and benefits as applicable to patient
- Patient choice and partnership
- Legal status of NICE / AWMSG decision
- Cannot force warfarin on a patient
  - Can we deny any other treatment i.e. none?
  - Yet to be tested in court...

Conflicts of Interest...

- Advisory
- Entertainment
- Company & Products