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PUBLIC HEALTH

CHANGE OF HEART

Dabigatran is one of the new drugs that look set to shift how a major group of patients at risk of stroke – those with atrial fibrillation – are managed

Atrial fibrillation is the most common heart rhythm disorder and is responsible for approximately 22,500 strokes per year in the UK. Strokes caused by AF are generally more severe, with a higher risk of death or long term disability, and longer stays in hospital.

“One of the saddest things is when the patient presents for the first time with newly diagnosed atrial fibrillation in the context of a devastating stroke,” says Professor Gregory Lip, professor of cardiovascular medicine and adviser to the Stroke Association.

Stroke is the third leading cause of death in the UK behind heart disease and cancer. The cost of stroke management to the NHS is in the region of £3-4bn a year with the wider costs to society more than double this amount, not to mention the impact on families and carers. It's therefore little wonder that stroke is such a high priority for the NHS, as seen with the National Stroke Strategy and F.A.S.T. campaign.

Since AF-related strokes are more severe, these events are also more expensive to treat. It's estimated that the acute costs of treating an AF stroke are on average up to one third higher than a non-AF stroke. Costs associated with the ongoing long term consequences of AF stroke can average up to £26,000 per year. AF is more common in older people, so it will become an increasingly



important condition as the population ages.

However, on a positive note, preventative measures can be taken. AF can be diagnosed through opportunistic screening and patients with one or more stroke risk factors given an oral anticoagulant to help reduce

risk of strokes.

“Anticoagulation will prevent about 60 per cent of strokes,” says Professor Anthony Rudd, consultant stroke physician at Guy's and St Thomas' Hospital. But he adds: “The issue is that there are a large number of people who have AF which is not

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being effectively treated and as a result of that there are more strokes happening than need to.”

Secondary prevention is also suboptimal, with a considerable proportion of people who have had a stroke and been diagnosed with AF not receiving anticoagulation. Professor Rudd says: “A worry that the patients might be a bit too frail or they might fall [is] being used as an excuse not to give anticoagulation.”

In a survey of more than 1,000 GPs conducted for the Stroke Association by Ipsos MORI, 76 per cent acknowledged that stroke was a major consequence of AF but only 40 per cent said they would treat patients with warfarin. The drug is very effective but can be difficult to manage.

There's also some fear and dislike amongst the general public about taking warfarin, given the hassle around going for regular blood tests to monitor levels and modify the dosage.

Data from the National Institute for Health and Clinical Excellence suggests that only 54 per cent of patients who should be receiving anticoagulation currently do so. Care pathways for warfarin are inconsistent, which has led to under prescribing, poor patient compliance and many patients with incorrect drug levels.

For six decades warfarin has been the only viable anticoagulant for preventing stroke in patients with AF. But in March 2012, NICE published the technology appraisal guidance for dabigatran (see box) and this was followed in May by the NICE guidance for rivaroxaban. “Dabigatran is the first new development in anticoagulation in 60 years,” says Dr Mike Lavender, consultant in public health medicine at NHS County Durham.



Taking a blood sample. Warfarin levels have to be checked regularly

‘Much of the savings will be in stroke rehabilitation, often funded through social services budgets’

New oral anticoagulants including dabigatran do not require any routine coagulation monitoring. Patients take the same dose every day to get a consistent anticoagulant effect.

NICE has conducted a full critique of the clinical and economic data and concluded that the 150mg dosage is clinically more effective than warfarin in reducing the risk of stroke or systemic embolism, ischaemic stroke and vascular mortality. The 110mg dosage is non-inferior to warfarin. NICE also concluded that dabigatran is a cost-effective option for the NHS. While warfarin is cheaper than new oral anticoagulants such as dabigatran, NICE's cost-effectiveness evaluation looks at the bigger picture including the cost of mortality, hospitalisations and the need for regular monitoring with warfarin.

Treatment guidelines have been evolving in anticipation of

the new anticoagulants. The 2010 European Society of Cardiology guidelines for the management of AF recommend using the CHADS₂ stroke risk stratification scheme as an initial, rapid and easy to remember means of assessing stroke risk. It recommends giving oral anticoagulants to patients with a CHADS₂ score greater than 2. CHA₂DS₂-VASc is highlighted as an extension to CHADS₂; it includes additional stroke risk factors that may influence a decision on whether or not to anticoagulate.

The quality and outcomes framework (QOF) for GP reimbursement has changed this year. In previous years, GPs were paid for the proportion of patients receiving antithrombotic therapy, which could be either warfarin or antiplatelet therapy (aspirin). Many prescribers in primary care found it easier to give patients aspirin than struggle with the therapeutic management of warfarin. From this year, for AF patients identified with a CHADS₂ score greater than 1, payment will only be given for treatment with an anticoagulant and not aspirin.

The QOF change is progress, says Professor Lip, but needs further updating so that it includes CHA₂DS₂-VASc and is in line with the ESC guidelines.

In March 2012, the Royal College of Physicians of Edinburgh published a UK consensus document on the management of AF. Amongst the four key priorities were a call for opportunistic screening of over 65s, increased uptake of oral anticoagulant therapy, and discontinuing the use of aspirin for stroke prevention in AF.

“Up until now, people have thought ‘if we can’t anticoagulate we’ll put people onto aspirin instead,’” says Professor Rudd. “[The consensus statement is] quite

helpful because it does reinforce the need to anticoagulate.” Professor Lip adds: “If you have AF and [are] at risk of stroke, aspirin is not effective and can be potentially harmful.”

The new oral anticoagulants provide an opportunity to innovate and improve stroke prevention as outlined in the Department of Health's December 2011 *Innovation, Health and Wealth* report. Establishing effective anticoagulation services requires changes in culture and financial management. Investing in innovation to prevent disease will not produce a return on investment in year one and much of the savings will be in stroke rehabilitation, which is often funded through local authority social services budgets.

The implications of failing to embrace the new oral anticoagulants as an innovation in stroke prevention management are wide and deep. Whilst warfarin is an effective treatment for stroke prevention when it is well managed, it's well known that warfarin has significant inter and intra-patient variability which mean many patients struggle to be maintained within the recommended therapeutic range, or are unable to start/stay on warfarin at all. Historically, the stroke risk of patients with no viable alternative to warfarin has remained unacceptably high. Now that new oral anticoagulants are available and recommended by NICE, there is no reason why the vast majority of these patients should remain suboptimally treated. Failure to embrace this innovation could mean that thousands of strokes occur that could have been avoided, with the resultant health and financial implications. The increased cost of stroke has a huge impact on budgets across the whole care pathway, particularly stroke rehabilitation costs.

Not prescribing the new oral anticoagulants is a missed opportunity to streamline international normalised ratio monitoring services which are bursting at the seams in many areas. INR monitoring will always be needed, but nevertheless NHS services can benefit hugely from the release of capacity due to the arrival of the new oral anticoagulants, both in terms of finance and the quality of patient care. ●

NICE GUIDANCE FOR DABIGATRAN

Dabigatran etexilate is recommended as an option for the prevention of stroke and systemic embolism in people with nonvalvular atrial fibrillation with one or more of the following risk factors:

- previous stroke, transient ischaemic attack or systemic embolism
- left ventricular ejection fraction below 40 per cent

- symptomatic heart failure of New York Heart Association (NYHA) class 2 or above

- age 75 years or older
- age 65 years or older with one of the following: diabetes mellitus, coronary artery disease or hypertension.

Source: *Dabigatran etexilate for the prevention of stroke and systemic embolism in atrial fibrillation*, March 2012, NICE technology appraisal guidance 249, www.nice.org.uk/tg249

TACKLING THE 'MINDSET PROBLEM'

GPs and nurses nervous about the use of anticoagulants with frail people will need to be educated if the benefits are to be realised. Jennifer Taylor reports

The National Institute for Health and Clinical Excellence technology appraisal guidance for dabigatran was published in March 2012. It recommends dabigatran as an option for the prevention of stroke and systemic embolism for patients who meet certain criteria (see box, opposite).

Before starting dabigatran, patients should talk to a clinician about the risks and benefits of dabigatran, compared with warfarin. For patients already taking warfarin, the potential risks and benefits of switching to dabigatran should be considered in light of their level of international normalised ratio control.

The NICE clinical guideline for atrial fibrillation was published in 2006 and is currently under review. Clinical consensus has moved on since then, particularly regarding the risk stratification used to determine whether a patient should be anticoagulated and the role of aspirin. More recent clinical guidelines from the European Society of Cardiology, the American College of Chest Physicians and the Canadian Cardiovascular Society recommend that aspirin be marginalised and patients should instead be anticoagulated or, in some cases, left untreated. This is in contrast to the NICE clinical guideline which places greater emphasis on aspirin for patients at "low to moderate" risk of stroke. The quality and outcomes framework indicators for AF no longer provide equal incentives for the use of aspirin and anticoagulants, showing that the role of aspirin continues to diminish.

Once national guidance has been issued by NICE, it replaces local recommendations in order to promote equal access to treatment for all patients across England and Wales.



Heart monitoring. Atrial fibrillation is a heart rhythm disorder

'The risks of falls and bleeding are small compared to the risk of stroke in untreated patients'

"Technology appraisals are mandatory and that means that a PCT or its successor body is bound to implement it taking into account local needs and local circumstances," says Dr Charles Alessi, chairman of the National Association of Primary Care. "The population has a right to receive it and that is enshrined in the NHS

Constitution."

The NICE guidance for dabigatran was published on 15 March 2012 and from 15 June 2012 dabigatran must be made available on the NHS to any eligible patient in England and Wales for whom it has been deemed clinically appropriate.

Commissioners should consider expediting dabigatran's availability for patients with AF who are unstable on warfarin or warfarin intolerant, and patients at high risk of stroke considered unsuitable for warfarin, and currently treated with aspirin.

Warfarin takes a few days to reach effective levels and dabigatran is useful when rapid anticoagulation is needed. "If we need immediate anticoagulation, at the moment

we're having to put people onto a low molecular weight heparin treatment dose which means injections," says Professor Anthony Rudd, consultant stroke physician at Guy's and St Thomas' Hospital.

The drug will also be useful for patients who find regular blood tests for warfarin monitoring difficult, such as frail patients who cannot travel easily and patients with needle phobias.

NHS reforms are moving care out of hospital and implementing a primary care-led anticoagulation service and new oral anticoagulants such as dabigatran are a step in that direction. But many GPs and nurses are nervous about anticoagulation and education is needed. "The biggest problem that needs solving is a mindset problem around anticoagulating people who are potentially frail," says Professor Rudd. Clinicians worry about the risks of falls and bleeding but, in reality, these are small compared to the risk of stroke in untreated patients.

One concern about dabigatran is that patients must take two pills each day (unlike warfarin, which is once a day) and may forget the second one. But Dr Mike Lavender, consultant in public health medicine at NHS County Durham, says: "The balance of benefits against risks of bleeding ... [with] warfarin is relatively narrow ... so managing warfarin is far more difficult than simply taking a tablet twice a day."

"Compared with warfarin, there are advantages and some disadvantages but, for patients for whom warfarin is not suitable, dabigatran is a good option," says Dr Lavender. "This new drug has reminded us how important prevention of stroke is and this is an opportunity to do something about it." ●

CASE STUDY



Learning process:
educating patients
about the risk and
benefits of new
drugs will be vital

RISK AND REWARD

How one trust has transformed its pathway for patients at risk – and is offering education sessions to help their understanding of anticoagulants. By Jennifer Taylor

The new oral anticoagulants are being used for stroke prevention in patients with nonvalvular atrial fibrillation in Coventry and Warwickshire, where a pathway has been introduced.

An audit conducted in South Warwickshire, before the new oral anticoagulants such as dabigatran were introduced, revealed most patients who had a stroke with AF were on aspirin or nothing at all. Only about 20 per cent were on anticoagulation and, of these, just half were adequately anticoagulated. The findings are in line with international audit outcomes.

Under the pathway, new oral anticoagulants are considered for patients who have had a life-threatening bleed in the previous six months or a thrombotic event despite warfarin therapy; patients with poor or dangerous anticoagulant control (defined as two international normalised ratios greater than 8 in the previous six months or one INR greater than 12) and patients requiring domiciliary or ambulance transport to clinics, which is expensive. All patients have the appropriate stroke risk score, calculated using CHADS₂ or CHA₂DS₂-VASc.

The pathway is going to be extended to new patients presenting with nonvalvular AF,

‘Most AF patients die or end up in permanent residential care if they have a stroke’

who will be given the option of dabigatran or warfarin.

When dabigatran is deemed appropriate, patients attend a clinic – in South Warwickshire run by a specialist nurse – to go through criteria they need to meet and discuss the relative risks and benefits of the new drug. The importance of compliance is stressed as these drugs have a relatively short half life, unlike warfarin whose effect lasts several days.

Dabigatran is primarily excreted via the kidneys and patients’ renal function (calculated creatinine clearance) must be checked to ensure that the drug doesn’t accumulate and cause increased bleeding problems. Patients also need to know about the bleeding risks of anticoagulant therapy with warfarin and dabigatran. Dr Peter Rose, consultant haematologist at South Warwickshire Foundation Trust and University Hospitals Coventry and Warwickshire Trust,

says: “It’s probably going to be 1 to 2 per cent of patients per annum having a life threatening bleed, [but] it should be slightly less with the new oral anticoagulants.” At the end of the session patients sign a form to acknowledge that they have received the appropriate training and education and are comfortable with being started on an anticoagulant agent.

It has been recommended to the area prescribing committee that patients should be started on the new medication in a specialist service led by an anticoagulant lead in primary or secondary care. Regardless of the setting, an educational session should be held with the patient.

Patients should have an annual risk benefit assessment in primary care of the relative risks and benefits of continuing anticoagulation treatment, be it warfarin or a new oral anticoagulant.

The benefits of the new pathway will be assessed prospectively. Dr Rose hopes to see a significant reduction in AF patients having strokes and fewer life threatening bleeds with the new agents compared to warfarin. In the longer term, given the high cost of severe stroke to the NHS, he hopes the new pathway will be cost-effective.

“In order to make significant differences, it depends on affecting prescribing habits of colleagues, particularly in primary care,” says Dr Rose. GPs will need to identify patients with AF, stop using aspirin for stroke prevention in nonvalvular AF and ditch the misconception that oral anticoagulants are dangerous for elderly patients because they may have falls. Dr Rose says: “If they’ve got AF, [and are] elderly and at high risk of stroke then they’re much more likely to run into problems from that than from bleeding related to falls.”

There’s an incentive to change prescribing habits in the primary care quality and outcomes framework, which now pays GPs to identify AF patients at high risk of stroke (CHADS₂ greater than 1) and prescribe an anticoagulant. They won’t be paid for starting such patients on aspirin.

Spelling out the consequences of stroke in patients with AF is the best starting point for discussions with commissioners and clinicians in primary and secondary care about a new care pathway for anticoagulation.

Dr Rose says: “I don’t think it’s necessarily appreciated that most patients either die or end up in permanent residential care if they have a stroke and they’ve got AF.” ●