An update on management of stroke/TIA

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Stroke medicine is a rapidly evolving field. This commentary will summarise developments in the primary and secondary prevention of stroke in patients with atrial fibrillation, and the latest guidance on intravenous thrombolysis in acute ischaemic stroke.

The prevalence of atrial fibrillation (AF) increases with age[1] and is projected to double by 2050.[2] AF predisposes to stroke, with the risk increasing in those with predisposing factors (which frequently become more prevalent with age). Further, AF related strokes result in greater disability and higher mortality than those arising in non-AF patients.[3]

The European Society of Cardiology issued an update on the management of patients with AF. The CHA2DS2 VASc score has superseded the CHADS2 in risk assessment, due to its superiority in identifying those at truly low risk of stroke. The acronym is Congestive heart failure/left ventricular dysfunction, Hypertension, Age ≥75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74, and Sex category (female).[4] Those aged <65 years with no other risk factors (ie. lone AF) irrespective of gender do not need thromboprophylactic treatment as their risk is so low. Traditionally these patients were given antiplatelet therapy, however trial data such as that seen in the Japan AF Stroke Trial[5] demonstrated no overall benefit.

The ESC guidelines recommend those with a score of ≥1 be offered anticoagulant therapy preferable with a new oral anticoagulant agent (dabigatran, rivaroxaban) over warfarin. The RE-LY (Randomized Evaluation of Long-term anticoagulant therapY with dabigatran etexilate) trial demonstrated superiority of dabigatran 150mg BD over warfarin in stroke risk reduction in patients with AF and was associated with lower rates of intracranial haemorrhage.[6] The lower dose of 110mg BD (used in those ≥80 years, history of reflux or where bleeding is a concern) was associated with an equivalent stroke risk reduction as warfarin, but with significantly fewer intra and extra-cranial bleeds.

The ROCKET-AF trial comparing rivaroxaban versus warfarin found it to be non-inferior in stroke risk reduction with equivalent overall rates of haemorrhage. Sub-group analysis demonstrated lower rates of fatal and intracranial bleeds in the rivaroxaban group.[7]

The weaknesses with these agents include a non-significant increase in cardiac events with dabigatran. Also there is no available test of either agent to ensure concordance with therapy. Therefore should haemorrhage occur, there is no specific antidote. If the thrombin time, prothrombin time or activated partial thromboplastin time is elevated, this may suggest on-going anticoagulant effects; however these tests are not entirely reliable.

Bleeding risk is often cited as a concern when considering starting patients on oral anticoagulant therapy. The HAS-BLED score (Hypertension with systolic >160mmHg, Abnormal renal/liver function (1 point each), Stroke, Bleeding, Labile INRs, Elderly, and Drugs or alcohol (1 point each)) allows bleeding risk stratification, and identifies factors that should be corrected when possible prior to starting such treatment.[8] Whereas a score of ≥3 indicates high risk, ultimately the decision whether or not to start treatment hinges on the overall stroke risk and an informed discussion with the patient.

Elderly patients with AF have been consistently shown to be those at highest risk of stroke, yet there is an anxiety surrounding the use of oral anticoagulants in these patients. The Birmingham Atrial Fibrillation Study of the Aged (BAFTA) study was an randomised controlled trial comparing warfarin to aspirin in those aged ≥75 years.[9] The warfarin group had a significant reduction in stroke rates while the rates of haemorrhage were equivalent in the two groups. Cognitive impairment,

compliance issues, therapeutic monitoring and drug interactions are very real concerns in the elderly population. Such risk factors should be mitigated whenever possible. An advantage with the new oral anticoagulant agents in these patients is the removal of the need for monitoring, the significantly fewer drug interactions, the lower bleeding profile and the potential for their administration in a blister pack. As these drugs are largely excreted by the kidneys, care should be exercised in those with renal impairment. In acute illnesses associated with fluid losing states, renal function should be monitored, and in the event of deterioration such anticoagulants may need to be discontinued temporarily.

The recent National Clinical Guideline for Stroke (4th edition) has introduced radical changes to the management of patients with AF. Patients with AF having experienced a TIA should undergo brain imaging. Once haemorrhage has been excluded, anticoagulation should commence with an agent with a rapid onset such as low molecular weight heparin or one of the new oral anticoagulant agents.[10] Further, the decision on when to commence anticoagulation following a stroke depends on the size of the infarct, beginning within two weeks in those with smaller lesions.

Intravenous thrombolysis with recombinant tissue Plasminogen Activator (rt-PA) in ischaemic stroke remains the mainstay of treatment in the acute phase due to the strong evidence base and relatively few resources required for successful implementation of the service. While there is no mortality benefit with alteplase, significantly more patients treated will be independent. This has been demonstrated in all age groups when given within three hours of symptom onset.[11] Between 3–4.5 hours there is also benefit in disability reduction in those aged under 80 years as demonstrated in the ECASS III trial.[12] Between 4.5–6 hours post symptoms, thrombolysis is unlikely to be beneficial, but is unlikely to harm either. Treatment is associated with an early increase in symptomatic and fatal intracranial bleeds, but the mortality rates are equivalent over the longer term. The European License for rt-PA has been extended to 4.5 hours for acute ischaemic stroke. The take home message however, is the earlier rt-PA is administered, the better the outcome. Treatment within the first 90 minutes of onset increases the odds of a favourable outcome by 2.1 fold, within 91–180 minutes by 1.7 fold and within the 181–270 minute window by 1.3 fold.[13]

The healthcare burden from stroke is significant. It is the leading cause of disability in the UK. Reducing this relies on collaborative working between primary and secondary care and public education on the symptoms and signs of stroke. Identifying and addressing risk factors, early referral for specialist opinion where needed, making sure patients receive (and are taking) the right treatment for their needs and a reduction in stroke onset to needle times are crucial in this battle.

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