News from the 23rd European Stroke Conference

The European Stroke Conference meeting was held in Nice, France, from May 6th–9th 2014. It was a busy programme with over 1,500 abstracts presented, as well as educational programmes presented alongside the scientific and clinical content. Dr Paul Guyler, Consultant Stroke Physician, Southend University Hospital, NHS Trust reports on some of the highlights.

GTN in acute stroke

A number of major randomised controlled trials reported final results at the meeting, including the ENOS (Efficacy Of Nitric Oxide In Stroke) trial.

Nitric oxide (NO) has multiple actions and is a potential candidate for the treatment of acute stroke. Among the properties which may be beneficial are lowering blood pressure, cerebral vasodilation, and improvements in central and systemic haemodynamics. NO donors are effective in experimental stroke, and pilot studies in patients suggest that one, glyceryl trinitrate (GTN), can be delivered easily as a transdermal preparation. Around half of all patients admitted with acute stroke are taking antihypertensive therapy immediately prior to their stroke. No data exist as to whether it is beneficial or safe to stop or continue this treatment during the acute phase.

ENOS, organised by the University of Nottingham, was a prospective, international, multicentre, randomised, controlled, factorial trial designed to test two questions related to the management of blood pressure immediately post-stroke: the safety and efficacy of NO, given as transdermal GTN; and the safety and efficacy of stopping or continuing prior antihypertensive medication.

To answer the first question, the GTN arm in the study (inclusion systolic blood pressure of 140–220 mmHg) looked at the effect of blood pressure lowering by transdermal GTN on death and dependency at three months. This was found to be neutral: GTN was safe and lowered blood pressure by about 7 mmHg systolic/4 mmHg diastolic compared with control. The median time to enrolment was 26 hours.

In subgroup analysis, the group treated less than six hours from onset seemed to show a benefit in outcome, whereas later time periods did not. This comes on the heels of the recently published RIGHT study (The Rapid Intervention With glyceryl trinitrate in Hypertensive Stroke Trial)[1] which demonstrated clinical benefits of blood pressure lowering with transdermal GTN for stroke patients enrolled in the field in a time period of under four hours.

Antihypertensives in acute stroke

The second question addressed whether prior antihypertensive medication should be continued or temporarily stopped during the acute phase of stroke for seven days.

There were significant differences in blood pressure in the two arms throughout the study, which indicates that the two groups were being treated differently. Despite this, there was no evidence of significant benefit that pre-existing blood pressure lowering therapy must be continued in all patients immediately. In the majority of patients, there is no evidence of harm, although continuation of medication in the prevalence of dysphagia leads to pneumonia and a poor outcome. In the absence of other ongoing/planned trials it may be best to stabilise patients and obtain enteral access before continuing blood pressure therapy after a few days.

Nevertheless, hypertension is the single most important modifiable risk factor in the prevention of recurrent stroke and both ENOS and COSSACS (The Continue Or Stop post-Stroke Antihypertensives Collaborative Study)[2] demonstrate significantly lower blood pressure in the continue arm at seven days at a level that should provide long-term benefit.

Dr Paul Guyler (Southend University Hospital NHS Trust)

From a cardiological perspective, witholding beta blockers for one week in the control arm of stroke patients did not lead to any increase in myocardial events.

Getting to know NOACs

There was much information and debate during the meeting regarding atrial fibrillation, anticoagulation and the non-VKA oral anticoagulants (NOACs). The introduction of the NOACs represents a 'paradigm shift' in anticoagulation management. Despite the major advantage that routine coagulation monitoring is not necessary with NOACs, many aspects of their use currently remain restricted and unfamiliar to practising clinicians.

Despite the European Society of Cardiology guidelines for atrial fibrillation management,[3] in the UK most patients presenting with stroke and atrial fibrillation have not been anticoagulated prior to stroke.

Dr Benjamin Bray *et al.* (King's College, London) presented data extracted from the Sentinel Stroke Audit Programme and the national register of stroke care in England and Wales, which included all patients with acute

stroke aged ≥18 years admitted to 148 stroke units from January–September 2013.

Of 33,935 patients with acute stroke, the prevalence of atrial fibrillation was 20.1% (n=6,809). A minority (37.8%, n=2,538) had been treated with an oral anticoagulant prior to stroke and 30-day mortality was higher for patients not anticoagulated.

In another study looking at cardiometabolic stroke, pre-treatment with oral anticoagulation was a factor associated with less stroke severity and better outcomes. This was shown in three-year data comparing severity and functional outcomes of cardioembolic stroke according to anticoagulation levels on admission, presented by Dr I Illan-Gala *et al.* (IdiOAZ Health Research Institute, Hospital Universitano La Paz, Madrid, Spain).

Louise Ward *et al.* (East Kent Hospitals University Foundation Trust) presented results from a community staff survey of primary care professionals comparing their knowledge and views regarding the prescription and clinical management of NOAC therapy, pre- and post-education. It was evident from the results that the education session improved professional understanding, which will have a direct impact upon the NOAC pathway.

NOACs in secondary prevention

Experience of the use of NOACs on an acute stroke unit and stroke prevention (TIA) clinic was presented by Dr Suman Gill and colleagues (Watford General Hospital). They found NOACs were well tolerated and welcomed by patients. Their experience from introducing a proforma, which included not only CHA_2DS_2-VASc and HASBLED scoring but also rationale for choosing NOAC, blood results and confirmation of discussion with and consent from the patient, greatly helped allay the initial suspicions of general practitioners and also overcome a reluctance to prescribe.

Dr Sajid Alam *et al.* (Southend University Hospital NHS Foundation Trust) presented a retrospective study comparing two cohorts of patients in secondary prevention. NOACs have been used as an option as first line for secondary prevention of stroke in the setting of atrial fibrillation at Southend since 2013. Prior to this, the drug of choice for anticoagulation was warfarin.

They found the use of NOACs for secondary prevention has fewer adverse events when compared to warfarin. The rates of adverse events at six months were 6.3% with NOACs compared with 24% with warfarin. Stroke and major bleeding end points showed a risk of recurrent ischaemic stroke of 1.7% with NOACs versus 12% with warfarin (all warfarin events were due to sub-therapeutic anticoagulation). Risk of life-threatening bleeding on NOACs was 1.6% versus 8% with warfarin. They identified no issues with adherence or compliance.

In another study, Dr SA Al-AlShaikh *et al.* (University of Glasgow) looked at adherence to secondary prevention medications in the first 90 days after ischaemic stroke. They found this ranged between 68.9%–88.0% – anticoagulants had the best adherence compared to antiplatelets, lipid lowering and hypoglycaemic medication.

Patient involvement in anticoagulation

Patient perceptions and oral anticoagulant prescription practice after stroke, were the subjects of a presentation from Dr L Openshaw and co-workers (Royal Berkshire NHS Foundation Trust, Reading). Their study found that more effort is needed to improve patient involvement in the decision of starting anticoagulant medication, and more emphasis should also be placed on the explanation given of atrial fibrillation and the type of treatment advised. This has a significant improvement on patient understanding and knowledge.

Take-home messages on the NOACs are that more patients should be adequately risk stratified and treated appropriately with oral anticoagulation. Further education of primary care and patient information will be crucial in decision making and adherence. Used according to their licence, NOACs seem to have good tolerability and safety profiles when compared to warfarin. It is important that stroke physicians and cardiologists take a lead in this area, particularly with newly published NICE guidance on atrial fibrillation.[4]

New NICE atrial fibrillation guidelines encourage best practice

Since 2012 three NOACs have been approved by NICE. However, there is evidence that these drugs are not being as widely prescribed as they could.[5] The new generation of oral anticoagulants are potential lifesavers for some people with atrial fibrillation – particularly those who find it difficult to achieve optimal anticoagulation on warfarin or those who are intolerant to warfarin. They are also an option for people newly diagnosed with atrial fibrillation who have a higher risk of stroke and for those currently taking aspirin for stroke prevention.[5]

Call for involvement in cardiovascular datasets

An archive of stroke trial datasets was established around six years ago by Professor Kennedy Lees (Institute of Cardiovascular and Medical Sciences, University of Glasgow) and an international group of senior clinical trialists in stroke. This archive has grown into the Virtual International Stroke Trials Archive (VISTA), with over 49,600 patients' data, which has led to 60 peer-reviewed publications.

Applying the successful concepts of VISTA, Dr A Abdul-Rahim (on behalf of the VICCTA collaborators) reported the establishment of and progress with the Virtual International Cardiovascular and Cognitive Archive (VICCTA) that extends data access and resources to the wider cardiovascular and cognition fields.

Professor Kennedy Lees (University of Glasgow)

The VICCTA collaborators have developed specific eligibility criteria for entry of trial or registry data into six subsections of the new archive and are already populating the archive with trial datasets. Trialists are invited to lodge data on heart failure, ischaemic heart disease, atrial fibrillation, diabetes and metabolic disorders, thromboembolism and cognition.

VICCTA is a living archive of completed cardiovascular clinical trials and registries. It can extend the value of clinical research at low cost, without threatening commercial or intellectual property interests. VICCTA also has the potential to deliver valuable research output to inform the efficiency of future cardiovascular and cognition research.

VICCTA currently holds international trial datasets with approximately 198,114 patients' data. Data enrolment to all subsections continues but with extensive data already available, the archive is open to analysis proposals.

The first projects are expected to present results in late 2014. Examples of these include development and validation of various predictive models in heart failure population, and novel exploratory analysis.

Atrial tachyarrhythmias in stroke/TIA patients

In addition, VICCTA is being used as a collaborative platform to adding trials dealing with detection of atrial fibrillation post-stroke/transient ischaemic attack (TIA).

The clinical significance of atrial tachyarrhythmia of less than the conventional 30 seconds cut-off for post-stroke/TIA patients is uncertain, particularly as the frequency of these 'short' bursts could also vary. The aim is to combine available data from completed atrial fibrillation detection trials to facilitate exploratory and epidemiological analyses of stroke recurrence risk and predictors associated with short atrial tachyarrhythmia post-stroke. Investigators are invited to join a pooling group to amalgamate the datasets from the individual trials with an aim to translate this into better secondary prevention after stroke, with an evidence-based, stratified approach to treatment.

The contribution of further data to VICCTA is welcomed and researchers are invited to collaborate as contributors or users (via www.viccta.org or email VICCTA@glasgow.ac.uk)

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