# Abstracts

## Oral anticoagulant and antiplatelet therapy and peripheral arterial disease

A recent article in the *New England Journal of Medicine* shows that adding oral anticoagulant therapy to antiplatelet therapy in patients with peripheral vascular disease was no more effective in preventing major cardiovascular events than antiplatelet therapy alone and increased the incidence of life-threatening bleeding.

Atherosclerotic peripheral vascular disease is associated with an increased risk of myocardial infarction, stroke and death from cardiovascular causes. It is known that antiplatelet drugs reduce this risk. These authors set out to look at the possible role of including anticoagulant drugs.

They randomly assigned 2 161 patients to combination therapy with an antiplatelet agent and an anticoagulant, or to an antiplatelet agent alone and followed them up for a mean of 35 months. Myocardial infarction, stroke, or death from cardiovascular causes occurred in 132 of 1 080 patients receiving combination therapy (12.2%) and in 144 of 1 081 patients receiving antiplatelet therapy alone (13.3%). Myocardial infarction, stroke, severe ischaemia, or death from cardiovascular causes occurred in 172 patients receiving combination therapy (15.9%) compared with 188 patients receiving antiplatelet therapy alone (17.4%). Life-threatening bleeding occurred in 43 patients receiving combination therapy (4.0%) compared with 13 patients receiving antiplatelet therapy alone (1.2%).

The conclusion was that the combination of therapy had no benefit and increased the risk of life-threatening bleeding.

The Warfarin Antiplatelet Vascular Evaluation Trial Investigators. *NEJM* 2007; 357: 217-227.

## Hypertension: two drugs better than one

The combination of aliskiren and valsartan at maximum recommended doses is more effective at reducing blood pressure than either agent alone. This recent study in the *Lancet* suggests that using aliskiren and valsartan at maximum recommended doses is more effective at reducing blood pressure than using either agent alone.

As the authors point out, the renin system is a key target for antihypertensive therapy. All major clinical trials to date have shown that angiotensin enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are successful in reducing cardiovascular, renal and metabolic events in a broad range of patients. But, the few studies that have focused on the combination of the maximum therapeutic doses of an ACE inhibitor and an ARB have given equivocal results on blood pressure in studies that were designed to look at renal outcomes.

Aliskiren is the first in a new class of orally active direct renin inhibitors approved for the treatment of hypertension, and blocks the renin system at its point of activation by directly inhibiting plasma renin activity. Two studies have provided preliminary indications that the combination of aliskiren and the ARB valsartan provides greater reductions in blood pressure than does monotherapy and effectively suppresses plasma renin activity despite the synergistic increase in plasma renin concentration.

This study was designed to assess the blood pressure-lowering effects of dual renin system intervention with the combination of aliskiren and valsartan at their maximum approved therapeutic doses.

In this double-blinded study, 1 797 patients with hypertension were randomly assigned to receive once-daily aliskiren 150 mg, valsartan 160 mg, a combination of aliskiren 150 mg and valsartan 160 mg or placebo for 4 weeks. This was followed by titration to the maximum recommended dose for another 4 weeks. The primary endpoint was a change in mean diastolic blood pressure from baseline to week 8.

During the study 196 patients dropped out, mainly because of lack of therapeutic effect. At the end of the study (week 8), the combination of aliskiren 300 mg and valsartan 320 mg lowered diastolic blood pressure from baseline by 12.2 mmHg, which was significantly more than either monotherapy or placebo. Rates of adverse events and laboratory abnormalities were similar in all groups.

The conclusion was that the combination of aliskiren and valsartan at maximum recommended doses provided significantly greater reductions in blood pressure than monotherapy with either agent in patients with hypertension and the tolerability profile is acceptable.

Oparil S, *et al. Lancet* 2007; 370: 221-229.

## Self-monitoring blood glucose: is it useful?

Conventional wisdom says that diabetics who monitor their own blood glucose should maintain tighter control, but the evidence is not convincing. This recent paper in the *British Medical Journal* overturns the idea that diabetics who self-monitor their blood glucose maintain better diabetes control.

As the authors of this paper point out, the number of type 2 diabetics is rising around the world, and with it comes an increasing challenge to monitor and manage the disease successfully. Self-monitoring of blood glucose by people with type 2 diabetes has been thought to improve glycaemic control and is recommended. But this study of 453 patients with type 2 diabetes, incorporating 48 general practices in Oxfordshire and South Yorkshire, did not provide convincing evidence that self-monitoring blood glucose improved glycaemic control.

Researchers split the participants into two groups – training one group in the use of self-monitoring devices and advising them to regularly contact their doctors with the results and another group who were trained to interpret their results and act on them. A control group consisted of patients who had standardised care, with glycosylated haemoglobin measurements every 3 months. At 12 months, the differences in glycosylated haemoglobin between the three groups was not significant, suggesting that self-monitoring is not as effective as previously supposed – and is

no better than normal care.

Farmer A, *et al. Br Med J* 2007; 335: 493.

## *Visual inspection screens for cervical cancer in developing countries*

Visual screening of the cervix, using acetic acid, is an effective way of preventing cervical cancer in developing countries. This, according to a study from Tamil Nadu, India, published in the *Lancet* recently.

Cervical cancer is still a common cancer among women in developing countries – in 2005 developing countries accounted for 85% of the estimated 493 000 new cases and 273 000 deaths that occurred worldwide. In the developed world, regular cervical cancer screening programmes have substantially reduced the burden of disease among women. But such programmes are not available in the countries that carry the highest burden of disease – namely sub-Saharan Africa, south and south-east Asia, Oceania, Central and South America and the Caribbean.

As a result, visual inspection (VIA) with 3 - 5% acetic acid has been proposed as an alternative screening method. Several studies have shown VIA to have an acceptable sensitivity in detecting cervical intraepithelial neoplasia (CIN). Modelling has suggested that, in resource-poor countries, single-round VIA screening once a lifetime is a cost-effective method to reduce disease burden, but whether or not it can achieve a significant reduction in cervical cancer incidence and mortality in real programme settings is not clear. The Christian Fellowship Community Health Centre, India, and the International Agency for Research on Cancer (IARC) of WHO, France, jointly did a cluster randomised trial to assess the efficacy of VIA screening to reduce cervical cancer incidence and mortality in a high-risk population in India.

This study shows that single-round VIA screening can substantially reduce the incidence of cervical cancer and mortality from the disease. Of the 114 study clusters in Dindigul district, India, 57 were randomised to one round of VIA by trained nurses, and 57 to a control group. Healthy women aged 30 - 59 years were eligible for the study. Screen-positive women had colposcopy, directed biopsies and, where appropriate, cryotherapy by nurses during the screening visit. Those with larger precancerous lesions or invasive cancers were referred for appropriate investigations and treatment. Of the 49 311 eligible women in the intervention group, 31 343 (63.6%) were screened during 2000-2003; 30 958 control women received the standard care. Of the 3 088 (9.9%) screened positive, 3 052 had colposcopy, and 2 539 directed biopsy. Of the 1 874 women with precancerous lesions in the intervention group, 72% received treatment. In the intervention group, 274 430 person years, 167 cervical cancer cases, and 83 cervical cancer deaths were accrued compared with 178 781 person-years, 158 cases, and 92 deaths and in the control group during 2000 - 2006.

Sankaranarayanan R, *et al. Lancet* 2007; 370: 398-406.

**BRIDGET FARHAM**

## *Single Suture*

### *Gene therapy for Alzheimer's*

A team from Harvard Medical School have used gene therapy to boost levels of the enzyme neprilysin in mice with the equivalent of Alzheimer's disease. Neprilysin is already known to degrade the amyloid protein found in the brains of people with the disease and its levels are also reduced in Alzheimer's patients. The team took fibroblast cells from the skin of the mice and engineered them to contain the gene for neprilysin. When they injected these cells into the hippocampus, nearby plaques disappeared. And plaques further away also appeared to be affected, diminishing in density. The gene had been altered to create a form of neprilysin that can travel through the body instead of remaining bound to cell membranes – so it can travel to the point of plaque accumulation rather than just staying on the cell. The ultimate goal would be to incorporate the cells into a small implant that could be placed anywhere under the skin.

*New Scientist* 2007; 1 September: 21.