

# Developments in cardiology presented

New findings of importance for the treatment of heart disease were presented at an international conference recently. **Mojgan Sani** reports

## Euroaction study sets preventive care standards

The final results of the Euroaction study were presented by David Wood's multi-disciplinary team from Imperial College London. The study addressed the cardiovascular health of over 10,000 coronary patients (acute coronary syndromes and stable angina patients) and high risk patients, through patient education.

The programme, based in 12 hospitals and 12 general practice centres, involved a team of nurses, dietitians, physiotherapists and physical activity specialists, GPs and cardiologists, who had undergone specialist five-day training. Participants were randomised to either the Euroaction arm or to receive usual care. Professor Wood said that:

- 72 per cent of coronary patients taking part in the Euroaction arm achieved recommended fruit and vegetable consumption, compared with 35 per cent in the usual care arm
- 55 per cent of Euroaction arm patients reduced consumption of saturated fat to <10 per cent of total energy compared with 40 per cent of the usual care arm
- 17 per cent of the Euroaction arm patients met their weekly intake of oily fish (>3 times a week) compared with 8 per cent of usual care arm



**Fruit and vegetable consumption rose in the intervention arm**

The World Congress of Cardiology, organised by the European Society of Cardiology and the World Heart Federation, took place in Barcelona, Spain, from 2 to 6 September

- 58 per cent of coronary patients who were smokers at the time of their cardiovascular event stopped smoking and remained non-smokers at one year compared with 47 per cent receiving usual care
- 54 per cent of Euroaction arm patients achieved physical activity targets of 30 to 45 minutes of exercise four or five times a week compared with 20 per cent of usual care patients
- Central obesity (a waist circumference of more than 94cm in men and 80cm in women) was reduced and an ideal waist circumference was achieved in 35 per cent of coronary patients compared with 22 per cent of usual care patients
- A total cholesterol of <5mmol/L was achieved by 78 per cent of Euroaction arm patients compared with 71 per cent of the usual care patients

Professor Wood said: "With current treatment failing too many cardiovascular patients across Europe, Euroaction has stepped up to the professional challenge of translating scientific evidence into effective care." He stressed that guidelines were difficult to implement, but that the Euroaction approach sets a new standard for preventive care in Europe, which all hospitals and general practices can achieve.

## Benefits of intensive lipid lowering therapy

Studies have shown that many patients with lipid-lowering therapy do not reach the low-density lipoprotein-cholesterol target goals recommended in guidelines. This was confirmed in the Reality study (presented by Alberto Corsini, of Milan, Italy). It demonstrated that 60 per cent of patients did not achieve the goal. He added that the goal is less likely to be achieved in high-risk patients with CHD than in those with risk factors for CHD. Reasons include poor compliance with statin therapy, time and upward titration of the dose, diet and lipoprotein metabolism.

Dr Corsini, said that failure of statin monotherapy was attributable to the "rule of six", which stated that every doubling of the dose contributes only an additional 6 per cent in LDL-reduction. The efficacy of inhibiting both absorption and production was demonstrated in the EASE trial, where ezetimibe co-administered with a statin produced significant additional improvements in LDL-cholesterol levels and goal attainments.

## Telemedicine techniques for patients at home

A new telemedicine approach allow heart failure patients to be safely cared for at home. A European study presented by Andrea Mortara, of Milan, Italy, demonstrated that the system could monitor patients' risk factors, respiration and vital signs without the need for hospital appointments.

All patients received the usual care and those randomised to telemonitoring were given a special telephone line, digital scales and automatic blood pressure monitor. Three telemonitoring strategies were studied. The first

was simple voice contact by telephone, the second included the intermittent monitoring of vital signs in addition, and the third added periodic 24-hour continuous monitoring of electrocardiogram, respiration and physical activity using a self-positioning recorder.

Dr Mortara concluded that "home telemonitoring is feasible in heart failure patients". He added: "The system does not just collect information, but encourages patients to change their behaviour. It pushes patients to control their blood pressure and weight."

## Alzheimer's: the impact of vascular disease

John Kastelein, from Amsterdam, the Netherlands, presented clinical data suggesting that many patients with vascular disease will also develop Alzheimer's disease. Alzheimer's disease is a degenerative disease and early symptoms may be more difficult to recognize. The onset of dementia is gradual with cognitive decline and short-term mem-

ory deficits typically the earliest indications. He explained: "There was an emphasis on the role of cardiologists in terms of identifying such patients. It was suggested that initial warning signs are likely to manifest in several ways such as missed appointments, repetitive questions, or a tendency to look at a relative or partner when asked a question."

## Critically important role of HDL-cholesterol in management of dyslipidaemia

The role of high-density lipoprotein cholesterol (HDL-C) in managing dyslipidaemia is becoming critically important. The evidence that HDL-C protects against the development of atherosclerosis is now compelling, said Philip Barter, of Sydney, Australia. He explained that HDL-C promotes the efflux of cholesterol from macrophages in the artery wall. It also seems to inhibit the oxidative modification of LDL-C, is anti-inflammatory and antithrombotic. The importance of targeting HDL-C as a therapeutic strategy is

further highlighted by the fact that there is an alarming and escalating world-wide epidemic of low HDL states, such as type 2 diabetes and metabolic syndrome.

He added that "statins have significant effects on LDL-C and complex effects on HDL metabolism but in general they have little effect on HDL-C levels, producing on average about 5–6 per cent increase. Data on HDL-C raising compounds, such as nicotinic acid, are less extensive but trials on such therapeutic agents and new classes are ongoing."

## Beta-blockers in chronic heart failure: new positive findings from the CIBIS III trial

Renal dysfunction is a frequent comorbidity in chronic heart failure (CHF). Cardiologists have recently recognised the so-called "cardio-renal syndrome", and nephroprotection is becoming an accepted therapeutic target in CHF. Piotr Ponikowski, of Wroclaw, Poland described the findings of CIBIS (Cardiac Insufficiency Bisoprolol Study) III clinical trials. In CIBIS III, initial monotherapy with either bisoprolol or enalapril for six months, followed by their combination for six to 24 months similarly influenced mortality and morbidity in patients over 65 years old with stable, mild-to-moderate systolic CHF. The design of the trial offers a unique opportunity to compare potential nephroprotective

effects of bisoprolol-first and enalapril-first regimens (including monotherapy with bisoprolol or enalapril).

Dr Ponikowski described the findings of the trial as novel: "Both treatment regimens are equally effective irrespective of the presence or absence of renal dysfunction at baseline and they similarly affect renal function. However, despite optimal pharmacological treatment with a combination of acetylcholinesterase inhibitor and beta-blocker, renal function progressively deteriorates during the natural course of CHF. CIBIS III is now suggesting that initiation of beta-blockers could even begin ahead of ACE-inhibitors in selected CHF patients."

## Expectations of antiplatelet agents in ACS

Coronary atherosclerosis is the primary cause of heart disease as a chronic inflammatory process that can be converted into an acute clinical event by plaque rupture and arterial thrombosis (ACS), resulting in acute coronary syndrom. ACS consists of two groups: unstable angina and non-Q wave myocardial infarction, and ST segment elevation MI (STEMI). The excessive mortality rate of ACS is primarily due to rupture and thrombosis of the atherosclerotic plaque. Inflammation has a critical role in plaque destabilisation. Thienopyridines such as clopidogrel play a significant role in reducing mortality. The effectiveness of thienopyridine therapy has had a major impact on the clinical outcome of patients undergoing percutaneous coronary intervention.

Franz-Josef Neumann, of Bad Krozingen, Germany, described the factors affecting the effectiveness of thienopyridine therapy. He said that "in the Excelsior study, baseline platelet aggregation before administration of clopidogrel accounted for 30 per cent of the variability in platelet aggregation at the time

of intervention after loading with 600mg clopidogrel. Adequate time from clopidogrel loading is crucial for achieving optimal effect. In the Credo trial, preloading with clopidogrel 300mg was no more effective than preloading with placebo during the first 15 hours after the loading dose. On the other hand studies have shown that loading with clopidogrel 600mg can achieve a near maximal effect on platelet aggregation within two hours. There was also a suggestion that the effectiveness of the maintenance therapy at 75mg per day may also be suboptimal for platelet inhibition and future trials may give a more precise answer on whether to double the dose to 150mg per day."

He added that "it is recognised that a number of patients fail to respond adequately to standard doses, a phenomenon known as 'clopidogrel resistance'. A third-generation thienopyridine (prasugrel) is in development in order to achieve a faster onset of action, higher potency and greater inhibition of adenosine diphosphate-induced platelet aggregation compared with clopidogrel."

## Targets for smoking cessation treatments

Emerging pharmacological therapies showing promise in the area of smoking cessation are the  $\alpha 4\beta 2$ -nicotinic acetylcholine receptor agonist varenicline and vaccines, including those that form nicotine-specific antibodies that bind nicotine in the serum.

Ivan Berlin, of Paris, France, explained that varenicline provides relief from nicotine withdrawal and craving through its agonist properties, and blocks the satisfying effects of tobacco. Because of its high affinity for the receptor sites, tobacco cannot stimulate these receptors and produce its effect".

He added that nicotine vaccines currently being researched work by the formation of a large nicotine-antibody complex that cannot cross the blood-brain barrier. Thus nicotine from tobacco cannot be metabolised, creating a lower need for nicotine intake. "Endocannabinoids act in the central nervous system on cannabinoid (CB1) receptors. Rimonabant, a selective CB1 antagonist, inhibits nicotine-induced dopamine release and nicotine self-administration. In studies it antagonised weight increase related to smoking cessation." Further clinical trials are ongoing.

## Walnuts reduce risk of heart disease

A study from Pennsylvania State University shows that walnuts can significantly reduce C-reactive protein (CRP) and harmful plaque adhesion molecules, two significant markers of inflammation. Furthermore, walnuts reduce cell adhesion molecules associated with atherosclerosis aiding in prevention of heart disease. Penny Kris-Etherton, primary investigator, said: "The important new finding with our research is that a diet high in walnuts beneficially affects multiple risk factors for coronary heart disease, which can have a greater impact on decreasing cardiovascular risk than just targeting single risk factors."

A study in patients with type 2 diabetes showed that a whole food diet with walnuts can reduce LDL cholesterol by as much as 10 per cent. Primary investigator Linda Tapsell, of Wollongong, Australia, said: "Walnuts are an easy and convenient way of getting polyunsaturated omega-3 fatty acids into the diet. They are particularly important for people with diabetes because they are a simple snack food, which is an integral part of the management of diabetes." These findings are significant. According to the Australian Diabetes Association, more than 65 per cent of people with diabetes die from heart disease or stroke. The World Health Organization reports that at least 171 million people worldwide have diabetes and this will likely double by 2030.