ACE inhibitor reduces cardiovascular events by 22%

Susan Mayor *Barcelona*

Adding an angiotensin converting enzyme (ACE) inhibitor to standard care in patients at high risk of cardiovascular events reduces the risk of cardiovascular death, non-fatal myocardial infarction, and stroke by nearly one quarter. This is the finding of a major study presented at last week's annual meeting of the European Society of Cardiology, held in Barcelona.

In contrast, negative results in a trial with an oral platelet glycoprotein IIb-IIIa antagonist (showing no difference in survival in patients with unstable angina or myocardial infarction when compared with aspirin) seemed to signal the end of the line for these agents, after similar findings in two previous trials.

The first study—the heart outcomes prevention evaluation (HOPE)—showed that patients randomised to the ACE inhibitor ramipril (10 mg/day) gained a 22% reduction in the combined end point of cardiovascular death, non-fatal myocardial infarction, and stroke. The relative risk was 0.78 (95% confidence interval 0.70 to 0.86). The rate after four and a half years was 14% compared with 18% in those given placebo.

There were highly significant reductions in a whole range of end points, including revascularisation, hospital admission, development of diabetic complications, and, intriguingly, the onset of new diabetes.

The multicentre study included a total of 9541 patients at high risk of cardiovascular events: any evidence of vascular disease (coronary heart disease, stroke, or peripheral vascular disease) or diabetes plus one other coronary risk factor.

The study, which was jointly funded by the Medical Research Council of Canada, Hoechst Marion Roussel (makers of ramipril) and the manufacturers of a natural Vitamin E supplement, was stopped early by the independent data monitoring committee, after a mean follow up of 4.4 years, when it saw the major reduction in cardiovascular end points.

The lead investigator, Salim Yusuf, professor of medicine at McMaster University, Hamilton, Canada, reported: "The survival curves for the groups treated with ACE inhibitor and placebo separated early, and carried on diverging over time." The benefits of treatment with ACE inhibitors were similar in patients with normal blood pressure to those in patients with hypertension.

Professor Peter Sleight, joint chairman of the HOPE study and emeritus professor of cardiovascular medicine at the University of Oxford, commented: "The findings suggest that the large reduction in cardiovascular events is due to something other than the blood pressure lowering effect of ACE inhibitors."

Professor Victor Dzau, professor of medicine and chairman of Harvard Medical School and Brigham Women's Hospital, Boston, commented: "The benefit is due to a direct mechanism of action within the blood vessel wall. Reducing angiotensin II—raised levels of which activate proinflammatory molecules and make plaques more prone to rupture—breaks the vicious cycle of atherosclerosis. What is exciting for me is that this is proof of concept, translating molecular research all the way through to patient care."

"We should now think of the renin-angiotensin system as an independent risk factor for vascular disease," suggested Professor Yusuf. This indicates that the benefits seen in the HOPE study may be achieved with all ACE inhibitors in a wide range of patients.

A second study examined whether sibrafiban or aspirin yields the maximum protection from ischaemic heart events after acute coronary syndromes (SYMPHONY I). The results showed no difference in the risk of death, myocardial infarction, or severe, recurrent ischaemia between the oral glycoprotein IIb-IIIa antagonist sibrafiban (10% at 90 days for high dose treatment) and aspirin (9.8%) in a total of 9233 patients with post-acute coronary syndrome (unstable angina or myocardial). □

Susan Mayor's trip to Barcelona was paid for by Parke-Davis Medical, which does not manufacture either ramipril or sibrafiban.

Project makes emergency pill more available

Bryan Christie *Edinburgh*

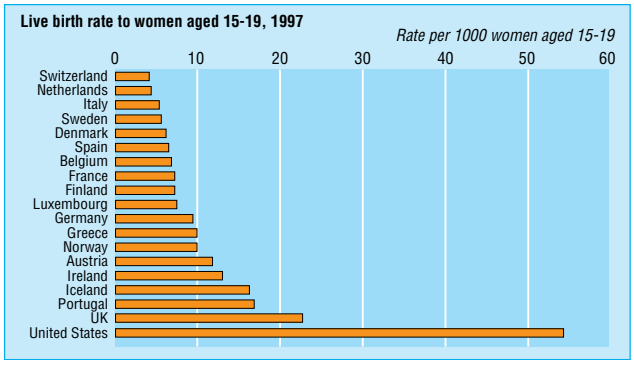
Restrictions on the way emergency contraception is prescribed in Great Britain are being lifted for 85 000 women in Scotland who are to be offered supplies of the pills to keep at home.

More than 100 general practices in Lothian, Scotland, have agreed to take part in the two year research project which is designed to see if improving the availability of emergency contraception will reduce unplanned pregnancies and lower the abortion rate. General practitioners will offer all suitable women aged between 16 and 29 years up to five packs of the pills for use in the event of unprotected intercourse.

Until now women have had to seek an urgent appointment with their general practitioner to be prescribed emergency contraception within 72 hours after unprotected intercourse. In many cases intercourse will have taken place at the weekend and it may be difficult to get an appointment on a Monday. Doctors in Lothian say that the difficulties and embarrassment faced by women in the past in obtaining emergency contraception have resulted in it being underused.

At the end of two years, the change in the abortion and unplanned pregnancy rate of women attending the 100 general practices will be compared with any change in rates at all the other practices in the region.

Both the BMA and the Royal College of Obstetricians and Gynaecologists have supported moves to make emergency contraception available over the counter in pharmacies, as now happens in France. This has always been strongly resisted in Britain by antiabortion groups and the Catholic church.



The United Kingdom has the highest teenage birth rate in western Europe

Anna Glasier, director of the Lothian Family Planning Service, said she believes that emergency contraception will eventually be made available in Britain through pharmacies but until then other methods have to be examined to overcome the limitations on access.

A pilot study carried out in Lothian among 530 women who were given the pills to keep at home showed that they used them safely and responsibly. They did not abandon more reliable methods of contraception nor were they more likely to use the emergency method repeatedly.

Dr Glasier said that despite the widespread availability of free contraception, about 1800 abortions were performed every year in Lothian in women under 30. It is hoped that the project will reduce the number by about 15%. "That would be a public health success," she said. □