KEEPS: reassurance on heart effects of HRT

Four years of hormone-replacement therapy (HRT) started soon after the onset of the menopause improved depression and anxiety in healthy women without promoting or worsening cardiovascular disease, the results of the KEEPS study show.

The study, presented at the North American Menopause Society 2012 Annual Meeting held in Orlando, Florida, US, involved 700 women who took either oral conjugated equine oestrogens (Premarin®) 0.45 mg/day (lower than the 0.625 mg/day used in the Women's Health Initiative [WHI] study), transdermal oestradiol (Climara®) 50 micrograms/day, or placebo. Women taking the active oestrogens received 200 mg of micronised progesterone for 12 days each month.

As expected, both types of hormone therapy relieved menopausal symptoms, such as hot flushes and night sweats and had favourable effects on bone mineral density compared with placebo.

WHI results hinted that the timing of therapy may be important. In general, the women in WHI started hormone therapy at an older age (mean age 63 years) than in most previous studies. In KEEPS, however, all the women were within three years of menopause when they entered the study (mean age 52) and had no evidence of cardiovascular disease.

In KEEPS, oestrogen therapy did not increase blood pressure levels. Oral oestrogen had small but favourable effects on high-density lipoprotein and low-density lipoprotein but increased triglycerides and C-reactive protein. Transdermal oestrogen had no effect on biomarkers but improved glucose levels and insulin sensitivity. Carotid ultrasound showed no differences in the progression of arterial wall thickness among the three treatment groups. There was a non-significant trend toward less progression of coronary artery calcium in the hormone therapy groups.

New diabetes guidelines stress individual patient needs

The European Association for the Study of Diabetes (EASD) and the American Diabetes Association (ADA) have published new guidelines on the treatment of type 2 diabetes, which are less prescriptive than previous guidelines. They advocate more patient involvement and give guidance on the rational approach to the choice of therapy.

While general recommendations regarding the intensiveness of glycaemic therapy focused in the past on a HbA1c target below 7%, the new statement emphasises that goals must be individualised, with the precise target taking into account patient's attitude and expected treatment efforts, the risk

associated with glycaemia and other adverse effects, disease duration, life expectancy, other co-morbidities, established vascular complications, and the patient's own resources and support system.

It notes, for example, some patients may feel that the weight gain associated with a particular diabetes therapy is unacceptable, whereas others may consider risk of hypoglycaemia as the primary factor in selecting treatment. And patients who are older with multiple co-morbidities will have different issues compared with a younger newly-diagnosed person that is otherwise healthy.

EASD president, Professor Andrew Boulton (University of Manchester) said: "The overarching goal should be to reduce blood glucose concentrations safely to a range that will substantially minimise long-term complications, but always keeping in mind the potential adversities with treatment burden, particularly in the elderly".

Other key points from the guidelines include:

- Diet, exercise and education to remain the foundation of any type 2 diabetes treatment programme
- Unless there are prevalent contraindications, metformin is the optimal first-line drug
- After metformin, there are limited data to guide treatment. Combination therapy with an additional one or two oral or injectable agents is reasonable, aiming to minimise side effects where possible
- Ultimately, many patients will require insulin therapy alone or in combination with other agents to maintain glucose control.

More on diabetes risk with statins

Another study has found a slight increase in fasting glucose levels in patients at increased risk of type 2 diabetes taking statins. The study (published in *BMJ* online 13th September 2012) was conducted by a Finnish group who concluded that their findings suggest statin use "might have unfavourable effects on glucose metabolism and hamper beneficial effects of lifestyle intervention in people at high risk of type 2 diabetes".

While the researchers say that that the benefits of statin therapy for the prevention of cardiovascular disease in people with an increased risk of type 2 diabetes are still unequivocal, they suggest that such patients on statins need to focus even more on intensive lifestyle intervention, with a healthy diet, non-smoking, and physical activity.

In the study, 2,798 patients at high risk of diabetes were followed for one year. Patients were given counselling on lifestyle interventions; fasting blood glucose was measured at baseline and one year. Results showed that 484 individuals (17.3%) used statins at baseline. Of these patients, 7.5% developed type 2 diabetes during follow-up compared with 6.5% of those not taking statins, a non-significant difference. However, fasting glucose increased significantly by 0.08 mmol/L in statin users but remained unchanged in non-users.