British Heart Foundation

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HORMONE REPLACEMENT THERAPY: AN UPDATE

For many years there has been consensus that hormone replacement therapy, HRT, is an effective means of controlling and/or relieving the vasomotor and urogenital symptoms associated with the menopause. Though these symptoms are often referred to as short term some women experience problems, particularly with urogenital symptoms, for five or more years. Duration of use of HRT is increasing, not only to treat menopausal symptoms but also as a means of delaying the onset or progression of osteoporosis. Longer term use of HRT requires careful consideration of the balance of potential risks and benefits.

HRT and cardiovascular disease

Observational studies report that the risk of ischaemic heart disease may be reduced by up to 40% in women who use HRT, either oestrogen alone or combined oestrogen and progestogen. However, cause and effect has not been established and HRT users generally are healthier than non-users so that the results could be explained by selection bias (Factfile 12/96). Two long term randomised controlled primary prevention trials, one in the US and one international (Womens International Study of long-Duration Oestrogen after Menopause) with a major UK component (part funded by BHF), are underway to establish whether HRT does reduce the risk of ischaemic heart disease.

Two recent US trials suggest that HRT does not have a role in secondary prevention of heart disease. The Heart and Estrogen/progestin Replacement Study, HERS, in women with existing heart disease found no effect of combined oestrogen and progestogen on myocardial infarction or coronary death after treatment for 4.1 years[1]. This trial initiated great debate because it reported that the overall null effect comprised what appeared to be an early adverse effect followed by a trend towards benefit, though neither effect was statistically significant. The Estrogen Replacement and Atherosclerosis (ERA) trial looking at angiographic progression of existing disease found no effect of oestrogen alone or combined oestrogen and progestogen[2].

The investigators on the US primary prevention trial have also reported a very small increase in the number of myocardial infarctions, strokes and thromboembolism, which did not reach statistical significance, in women taking HRT compared with those taking placebo after two and three years treatment. Full data have not been released so the findings are difficult to interpret though it is noteworthy that the trial is continuing.

HRT and stroke

HRT does not appear to reduce the risk of strokes. Results from observational studies on primary prevention have been inconsistent but overall indicate no benefit. The US Women's Estrogen for Stroke Trial (WEST) in postmenopausal women who had already had one stroke showed that after three years treatment the combined rate of non-fatal and fatal stroke was similar in the oestrogen and placebo groups. Furthermore randomised control studies show that, on average, HRT does not increase blood pressure.

HRT and breast cancer

A reanalysis, published in 1997, of almost all the data then known on HRT and breast cancer indicated that HRT increased the risk of breast cancer in current and recent users, that the risk increased with duration of use but returned to the level of non-users about five years after use was discontinued. In current or recent users the risk appeared to increase by 2.3% per year of use, an increase similar to that of delaying the onset of the menopause by one year. Most of the data came from women using oestrogen alone but similar effects were seen in the smaller number of users of combined oestrogen and progestogen[3]. Subsequent publications have largely endorsed this.

HRT, dementia and cognitive decline

A recent systematic review and meta-analysis of twenty-nine studies suggests that HRT users may have a lower risk of dementia but stresses that, particularly in view of the methodological limitations of the studies, confirmation is required from randomised trials[4]. The same review reported that, in women with menopausal symptoms but not in asymptomatic women, HRT may have a beneficial effect on verbal memory, vigilance, reasoning and motor speed. Evidence of the effects of HRT on cognitive decline awaits the results of the ongoing long-term randomised trials.

14 Fitzhardinge Street, London W1H 6DH
Telephone 020 7935 0185 Website www.bhf.org.uk

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Conclusion

Advising patients about the long-term use of HRT is not an easy task. General practitioners need to explain that there is uncertainty about the balance of long-term risks and benefits that will not be resolved until the results of the primary prevention trials are known.

Women should be told about these potential benefits and risks and that it is not known whether HRT will be beneficial for the heart. HRT should not be prescribed solely to prevent heart disease in healthy women and in those with a history of arterial disease HRT should not be used for secondary prevention.

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