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Looking at HRT in perspective

Helping women make informed choices

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With average life expectancy in developed countries now exceeding 80, many women will live around a third of their lives after the menopause and may experience related problematic symptoms for several years. This can have a detrimental effect on quality of life, including personal relationships and working life.[1 2]

More than 75% of those experiencing the menopause report symptoms, and over 25% describe their symptoms as severe. Average duration of symptoms is seven years, and a third of women have symptoms for longer. The menopause can also have a detrimental effect on bone and cardiovascular health.[3]

For those seeking help, the National Institute of Health and Care Excellence (NICE) and others[1 2 4] recommend an individualised and comprehensive approach that includes advice on exercise, optimising weight, stopping smoking, and reducing alcohol consumption as well as management options such as hormone replacement therapy (HRT). The latest evidence for women considering HRT is reassuring, including for all-cause mortality. Assessing the effect on all-cause mortality is particularly relevant as it looks at death as the endpoint for both the benefits and risks.

The main indication for HRT remains control of problematic menopausal symptoms and improving quality of life. Evidence from randomised trials shows clear benefits in this context,[5] and no arbitrary limits should be placed on duration of use.[1 2 4] HRT may help relieve short term cognitive symptoms related to the menopause, but this should be clearly differentiated from dementia prevention. Evidence does not support use of HRT to reduce the risk of dementia.[1 2 4 6 7]

The risk of breast cancer associated with HRT remains a concern for many women. Current evidence suggests that oestrogen only formulations are associated with little or no change in the risk of breast cancer, while combined HRT (oestrogen plus a progestogen) can be associated with an increased risk. This appears duration dependent and may vary with the type of progestogen used.[1 8-10] However, the risk is low (absolute excess risk of breast cancer over 10 years is 3-7/1000 women taking combined HRT for up to 5 years),[10] particularly compared with risks associated with other modifiable risk factors such as obesity and alcohol intake.

Benefits

Risk of breast cancer should be placed in the context of the overall benefits from HRT. For most women with problematic symptoms the benefits are likely to outweigh the risks.[1 2 4 8-10] NICE's review of trials and cohort studies shows that HRT significantly protects against fragility fractures related to osteoporosis and helps prevent osteoporosis in both spine and hip.[1 2 4]

Furthermore, evidence from a Cochrane review of randomised trials and from large observational studies in symptomatic menopausal women suggests that HRT (with or without progestogen) started before the age of 60 or within 10 years of the menopause may protect against cardiovascular disease. Timing of commencement is critical to this effect, often referred to as the cardiovascular timing hypothesis.[1 2 4 11-13]

In an analysis of placebo controlled trials in a total of 8311 women, the Cochrane review noted a significant reduction in coronary heart disease, including cardiovascular mortality, among women who started HRT before the age of 60 (10/1000 *v* 18/1000 with placebo; relative risk 0.52, 95% CI 0.29 to 0.96). An additional analysis in 9088 women found a significant reduction in all-cause mortality (16/1000 *v* 22/1000 with placebo; 0.70, 0.52 to 0.95).[11]

This protective effect was not seen among women who started HRT more than 10 years after the menopause in either the long term follow-up of the Women's Health Initiative trials (WHI) or the Cochrane analysis. Notably, there was no increase in risk of cardiovascular events, cardiovascular mortality, or all-cause mortality.[11]

A pooled analysis of the WHI trials found a significant reduction in all-cause mortality during the intervention phase among women aged 50 to 59 years who took HRT for an average of 5.6 years (combined HRT) or 7.2 years (oestrogen only) compared with placebo in a study with a median of 18 years' follow-up (hazard ratio 0.69, 95% CI 0.51 to 0.94).[14]

An analysis of long term follow-up data of 9939 women aged 50-79 from WHI also reported a significant reduction in all-cause mortality among 1129 women aged 50-59 who took oestrogen-only HRT after bilateral salpingo-oophorectomy compared with those who received placebo (hazard ratio 0.68, 0.48 to 0.96).[13]

A systematic review and meta-analysis of observational studies and randomised trials noted a significant reduction in all-cause mortality in women who started HRT before the age of 60 within the observational studies. However, no significant reduction was noted in the subgroup analysis of randomised trials.[15]

Finally, a systematic review and meta-regression analysis of 31 randomised trials found that women who started HRT under the age of 60 had lower odds of coronary heart disease (odds ratio 0.61, 0.37 to

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1.00), cardiovascular mortality (0.61, 0.37 to 1.00), and all-cause mortality (0.72, 0.57 to 0.91) compared with controls or those not taking HRT.[16]

The balance of benefits and risks, however, does not support use of HRT for primary or secondary prevention of disease, and international guidance recommends against use of HRT without a clear indication.[2 4]

Access to accurate information about the menopause, and to help and support from reliable sources, makes women better placed to manage the menopause transition and improve their quality of life. Healthcare providers should take an individualised approach to assessment and empower women to make informed decisions based on unbiased, evidence based information applied effectively. Nobody should be suffering in silence or feel that the effect of the menopause is not adequately recognised.

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