CONSENSUS STATEMENT ON HORMONE REPLACEMENT THERAPY*

INTRODUCTION

Hormone replacement therapy (HRT) is the administration of oestrogen (with progestogen in women with uteruses). It is currently licensed to treat symptoms resulting from oestrogen deficiency and to prevent bone loss. Different preparations and routes of administration may have different safety profiles. The term HRT includes tibolone, which combines oestrogenic and progestogenic activity with weak androgenic activity.

Recently, large randomised controlled trials have improved understanding of benefit but have raised concerns about the risks of therapy.

WHAT IS THE ROLE OF OESTROGEN IN THE MANAGEMENT OF CARDIOVASCULAR DISEASE?

Cardiovascular disease (CVD) is the commonest cause of morbidity and mortality in postmenopausal women. Recent studies suggest that the risk of stroke is, and that of myocardial infarction may be, increased in women over 50 starting HRT. There is no evidence to justify using HRT for either primary or secondary prevention of coronary artery disease or stroke. A woman requiring HRT for menopausal symptoms should have her coronary heart disease risk assessed. If this is increased, she should be offered appropriate evidence-based therapy and lifestyle advice, especially on smoking cessation, before commencing HRT. Women already on HRT who have no increased cardiovascular risk or disease have no need to stop HRT. This needs to be reconsidered if a cardiovascular event occurs.

Oral oestrogen increases the risk of venous thromboembolism (VTE). If women wishing to use HRT have risk factors for VTE it may be prudent to use a transdermal formulation.

WHAT IS THE ROLE OF OESTROGEN IN THE PREVENTION AND MANAGEMENT OF CENTRAL NERVOUS SYSTEM DISORDERS?

Observational studies suggest that the risk of Alzheimer's disease (AD) is reduced, or onset delayed, in women on HRT. However, the Women's Health Initiative (WHI) trial demonstrated no reduction in the risk and an increase in all-cause dementia in women using HRT. Other interventional studies have reported no beneficial effects of HRT on cognition, mood or functional outcomes in AD. Thus there is no role for HRT in the prevention or treatment of AD.

Women undergoing the climacteric often complain of mood change but it is unclear if the menopause is associated with depression. There is insufficient evidence for HRT use in the treatment of endogenous depression. However, HRT may improve well-being by reducing night sweats and insomnia.

Hormone replacement therapy can induce premenstrual syndrome (PMS) in some women. This results from the progestogen and may be helped by modifying its administration, e.g. intra-uterine delivery.

Although not strictly a central nervous system disorder, loss of libido is common in post-menopausal women. The cause is multifactorial and the individual's psychosocial status and situation should always be considered. Psychosexual therapy may be useful.

Oestrogen therapy alone does not restore libido but, for a few women, it may be effective in combination with androgens. Tibolone may also be effective.

WHAT IS THE ROLE OF OESTROGEN IN THE PREVENTION/MANAGEMENT OF OSTEOPOROSIS?

The WHI study demonstrated a decrease in fracture risk in women currently using HRT but the benefit of fracture prevention for most women is outweighed by the overall risks of HRT. Therefore HRT cannot be recommended as a first-line therapy for the prevention and treatment of osteoporosis except for women requiring treatment for menopausal symptoms.

Anti-osteoporosis therapy should be based upon increased absolute fracture risk determined by factors including age, previous fracture history and bone mineral density. As bisphosphonates reduce fracture risk and do not have adverse effects on the breast and cardiovascular system, they should be the first-line treatment.

For women intolerant of bisphosphonates, or where there is evidence of failure of response, treatment options include HRT.

*The Consensus Conference on Hormone Replacement Therapy was held on 7 and 8 October 2003 at the Royal College of Physicians of Edinburgh.

WHAT IS THE RELATIONSHIP BETWEEN OESTROGEN AND BREAST CANCER?

Most observational studies, and the largest trials, have demonstrated an increased risk of breast cancer associated with HRT, the relative risk increasing with duration of use. Recent observational studies suggest the increased risk is greater with combined HRT than with oestrogen alone or with tibolone.

Hormone replacement therapy increases mammographic density which reduces the sensitivity and specificity of screening and may delay the diagnosis of breast cancer. The effect is greatest with preparations containing progestogen and does not appear to occur with tibolone.

Although women diagnosed with breast cancer while on HRT are more often node-positive at first diagnosis, the effect on mortality is not yet clear.

There is no evidence that HRT use is associated with an increased risk of recurrence among breast cancer survivors. Troublesome symptoms of oestrogen deficiency are common in women receiving treatment for breast cancer. Hormone replacement therapy has been given with tamoxifen but should be avoided in women taking aromatase inhibitors. Further research is necessary.

Women are likely to have been alarmed by recent reports of HRT risks. The reality is that the absolute breast cancer risk is small. It equates to an extra two to six cases of breast cancer per 1,000 women treated with HRT for five years, depending on patient age and preparation used.

HOW SHOULD HRT BE DEPLOYED IN CLINICAL PRACTICE?

Eighty percent of women experience menopausal symptoms and 45% of them find the symptoms distressing. Although usually self-limiting (two to five years), some women experience symptoms for many years.

Hormone replacement therapy is highly effective in the relief of vasomotor symptoms and alleviates hormone-related mood change and insomnia. Systemic or vaginal oestrogen is effective for urogenital symptoms. The benefit of symptom relief has to be offset against the small increase in absolute risk of breast cancer, CVD and stroke. In view of this, individualised advice is needed. Absolute risks and benefits need to be explained to each woman considering HRT. Alternative therapies, including lifestyle changes should be discussed. Written information should be provided.

Treatment should aim to use the lowest effective dose and should be reviewed annually in light of new knowledge and changes in the woman's risk factors. Women who choose to take HRT for more than five years should be counselled about the long-term risks. When HRT is stopped, symptoms may return and some women may wish to restart HRT after reassessment and counselling.

Women with a premature menopause (natural or surgical) have traditionally been encouraged to take HRT until age 50. Although evidence is lacking, it is reasonable for this practice to continue. Hormone replacement therapy use in women with premature menopause probably increases the risk of breast cancer to that of women who do not have a premature menopause.

The use of HRT remains controversial. Evidence shows it has an important role in the relief of menopausal symptoms. Women need advice on the balance of risks and benefits as well as support to make a choice that is right for them.