Magazine: Back-Issue Article

HRT - What's the latest?

Many women remain confused and worried about the use of HRT for menopausal symptoms. Dr Heather Currie examines the latest findings about this treatment and discusses the pros and cons to help you make an informed choice.

Hormone replacement therapy continues to be surrounded by confusion and controversy with newspaper headlines about HRT appearing on a regular basis. Over the last decade it has changed from being used by millions of women, often long term and seen as being good for flushes, good for bones and good for heart, in fact good for almost anything, to being used only for "severe" symptoms at the lowest effective dose for the shortest possible time. The correct path probably lies somewhere in between these two extremes.

So what has caused this dramatic turn around? The publication of results of large trials and studies, particularly the Womens' Health Initiative trial and the Million Women study, with the associated media interest has led to many women and health professionals losing confidence in HRT, yet menopausal symptoms have not gone away and as yet, no other treatment has been shown to be as effective as HRT in controlling menopausal symptoms. It is unfortunate that sensational headlines are what are most remembered, even though the reports have often provided a balanced view, keeping risks in perspective. It is also unfortunate that initial results of risks of HRT from the WHI trial received so much publicity whereas further analysis of the results which has shown a much more reassuring picture, received little media attention. Further, the Million Women study has been hugely criticised in relation to the study design and many experts feel that it is difficult to draw accurate conclusions from the results, yet it is often quoted as showing definite associations of increased risks of cancer with HRT.

So what are the actual risks?

Venous thromboembolism

Venous thromboembolism (VTE) is the development of a blood clot, usually in a vein in the leg, which can occasionally pass through the circulation to the heart and the lungs (pulmonary embolus). From the WHI trial, VTE occurred in 1.7 per 1000 women aged over the age of 50, not taking HRT and this was doubled in those taking HRT, the risk still being small. Reassuringly, for women aged 50-59 who were of normal weight, the incidence of VTE in the HRT group was the same as in those on an inactive tablet (placebo). The greatest risk is within the first year of use and is most relevant to women who have other risk factors, including previous or family history of blood clot, obesity, immobility or underlying blood clotting problem. It is very likely that transdermal estrogen (patch or gel) and lower doses of oral estrogen may not carry the same risk.

Breast Cancer

Long term HRT use (>5 years after the age of 50) is thought to associated with a small increased risk of breast cancer. From both the WHI trial and Million Women study, estrogen only HRT carries less risk than estrogen combined with progestogen, the WHI trial demonstrating **no** increased risk with estrogen only taken for up to 7 years, in fact a decreased risk was shown. From the WHI trial, overall, combined HRT probably accounted for 3-4 extra cases of breast cancer per 1000 women who took combined HRT from the age of 50 for 5 years, but the increased risk in the combined HRT group in fact only occurred in the women who had taken HRT before the trial and then taken it for the duration of the trial. By 5 years after stopping HRT, the risk returns to baseline. It is possible that women who develop breast cancer while taking HRT may have a lower mortality rate than those who develop breast cancer when not taking HRT. To keep this concern about breast cancer in perspective, postmenopausal obesity or 2 units of alcohol per day confer a greater increased risk of breast cancer than 5 years of HRT but understandably, breast cancer risk is one of the commonest concerns.

Endometrial Cancer

Endometrial cancer is cancer of the lining of the womb (uterus). Estrogen only given to women with an intact uterus increases the risk of endometrial cancer. Estrogen combined with cyclical progestogen (sequential HRT) reduces this risk and estrogen combined with continuous progestogen (continuous combined or period free therapy) practically eliminates this risk.

Stroke

Both estrogen only and combined HRT were associated with a small increased risk of stroke in the WHI trial. In women aged 50 to 59 not taking HRT, stroke occurred in 3 per 1000 women over 5 years. 5 years of HRT was associated with 1 additional case. A later study reported from Sweden of almost 17,000 women aged 45 to 73 years, showed no significant association between hormone use and risk of stroke. Of the HRT users who did have a stroke, the risk was associated with advancing age, smoking, obesity and hypertension. Therefore in the absence of other risk factors, the risk of stroke from HRT is extremely small and in fact there is some evidence that lower doses of estrogen than were used in the WHI trial can reduce the risk of stroke compared to placebo.

Risk or benefit?

Heart disease

For many years, HRT was thought to reduce risk of coronary artery disease. However, the WHI trial showed early, small increased risks in cardiovascular events, but this increase was only significant in the women who were 20 or more years post menopause. Women who were less than 10 years postmenopausal when starting combined HRT, and women taking estrogen only, showed **no** increased risk with a likelihood of reduced risk. The dose, type and route of HRT used are important in cardiovascular effect, as is the timing of commencement of therapy; HRT started early in the menopause has no harmful effects on the risk of heart disease but once disease of the arteries has developed, commencing HRT may promote further damage. It is therefore very unlikely that HRT used for women in the early menopause for control of menopausal symptoms will be harmful for the heart and may still yet be shown to be beneficial if started early enough.

Alzheimer's disease

Some studies show a reduction in risk in HRT users but the WHI showed an increased risk, though only in the older women. Later analysis from the Women's Health Initiative Memory Study in fact showed for women who took HRT before the age of 65, there was a reduced risk of all-cause dementia of 46% and a reduced risk of Alzheimer's disease of 64%.

A major difference between trials such as the WHI trial and the studies which have often shown a reduced risk of both heart disease and dementia with HRT, is that in the WHI trial, women commenced HRT some time after the menopause, (only 10% were in the early menopausal years and on average, the women were 12 years post menopause with the age range being 50 to 79 years), whereas in observational studies, HRT has generally been commenced early in the menopausal years to control menopausal symptoms. It has been proposed that there is a "window of opportunity" whereby, if HRT is commenced early enough, it may be beneficial not only for control of symptoms and prevention of osteoporosis, but also for prevention of heart disease and dementia; the debate continues!

Benefits of HRT

Symptom Control

The main reason for using HRT continues to be for control of menopausal symptoms for which it has been shown to be effective in placebo controlled trials. Symptoms are likely to affect about 70% of menopausal women and for many, no other currently available products, either prescribed or "over the counter" will be as effective.

Prevention and treatment of Osteoporosis

HRT is beneficial for preventing osteoporosis by its effect on bone resorption, bowel calcium absorption and renal calcium re-absorption. Although it is not currently recommended as first line treatment of osteoporosis, it still has an important role for women with premature menopause and those with risk factors for osteoporosis who also have menopausal symptoms.

Heart disease

It seems likely that when used within the first 10 years of the menopause, HRT is beneficial for the cardiovascular system but currently it should not be used with this as the primary indication; further trial results are awaited.

Other possible benefits include reduced risk of colon cancer, reduced risk of type 2 diabetes, improved dentition, improved skin healing and reduced wrinkles, reduced macular degeneration and reduced cataract formation but these are all controversial.

Premature menopause

It is currently recommended that women who experience a premature menopause (menopause before the age of 40), should be offered HRT and should be encouraged to continue HRT at least until the average age of the menopause (51-52 years in the UK). HRT in this situation is not only controlling menopausal symptoms, but is also providing prevention of osteoporosis and heart disease, both of which are known to be increased in women who have an untreated premature menopause.

The benefits and risks of HRT are influenced by age, duration of therapy, medical history, family history and severity of symptoms. These factors vary between women, and even for each woman will change with time and with development of other medical problems. Treatment has to be individualised and has to be reviewed annually.

Generally, for women with menopause age <50 years, the benefits of HRT for both symptom control and long term health, far outweigh the risks. For women aged between 50 and 60 years who are troubled by menopausal symptoms, the benefits of HRT outweigh the risks. For women aged 60 to 70 years, the benefits roughly equal risks and management should be individualised, and for women aged >70 years, the risks are likely to outweigh the benefits. Even with the older women, if symptoms are significant and unresponsive to other therapies, HRT can still be considered as long as an informed choice is made.

Overall, HRT still has an important role in menopause management and when used appropriately and reviewed, the benefits outweigh the risks for by far the majority of users.