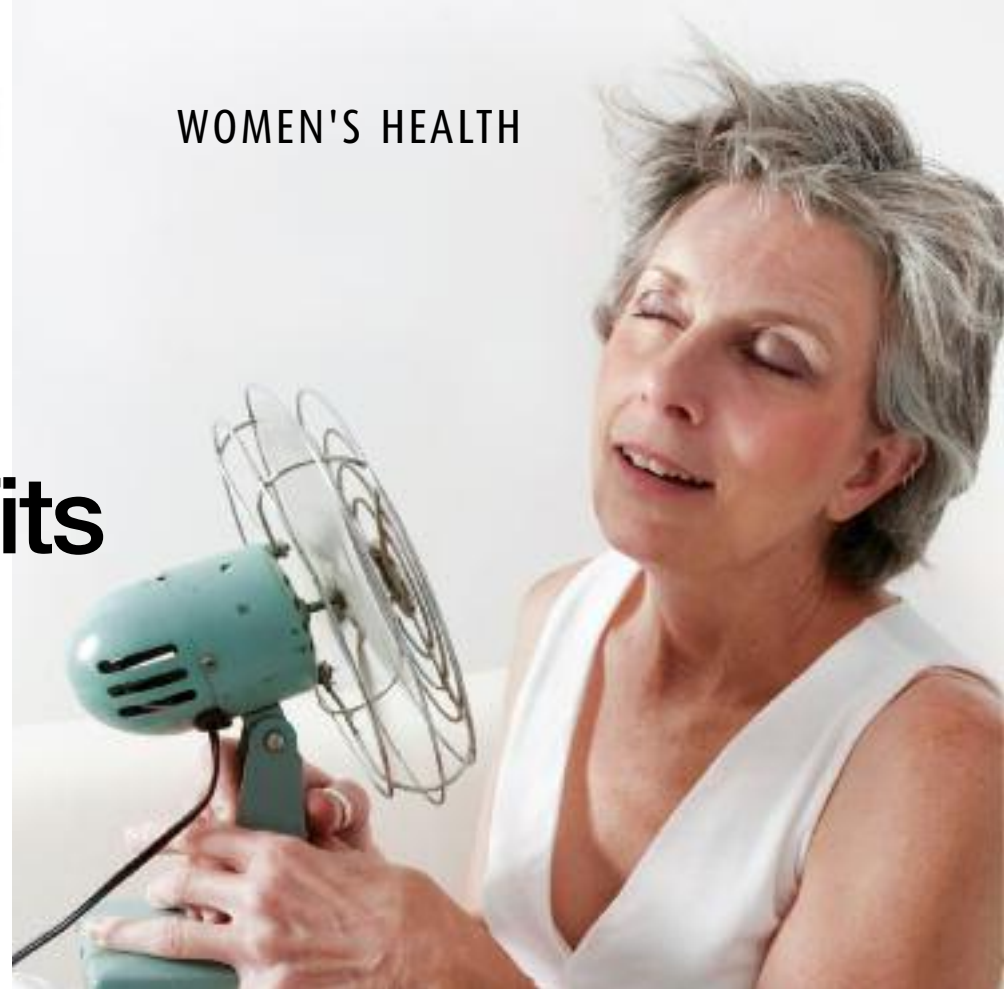
What are the benefits and risks of HRT?



ELIZABETH FARRELL AM, FRANZCOG, FRCOG

Opinions concerning the benefits and risks of HRT have varied over the past decade. Maintaining and regularly updating one's knowledge about HRT is paramount so accurate information can be given to patients.

MedicineToday 2012; 13(4): 59-61

Dr Farrell is Head of the Menopause Unit, Monash Medical Centre, Southern Health, Melbourne, Vic, and Past President of the Australasian Menopause Society.

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Hormone replacement therapy (HRT) is the most effective treatment for menopause symptoms in peri- and postmenopausal women, in particular for the vasomotor symptoms of hot flushes and sweats and symptoms relating to the atrophic changes in the urogenital tract. Over-the-counter alternative products have no better effect than placebo. About 20% of women will have moderate to severe symptoms that interfere with quality of life, and longitudinal studies have shown that significant symptoms may last up to a mean of eight years, with about 10% of women affected having symptoms for 10 years or more.

Opinions concerning the benefits and risks of HRT have varied over the past decade. This article aims to summarise the current position, as given in the most recent recommendations of the International Menopause Society.[1]

All menopausal women should be advised to develop a healthy lifestyle program in addition to possibly taking HRT. This lifestyle plan should include healthy eating, cessation of smoking, limiting alcohol intake, being a healthy weight and undertaking regular exercise, and will depend on the age of the woman at the time of her menopause.

INDICATIONS FOR HRT

The indications for prescribing HRT are:

- the presence of moderate to severe menopausal symptoms impacting on a woman's ability to function normally, and
- as a first line therapy in young women with osteoporosis.

Some of the menopause symptoms women experience are listed in the box on page 60.

MONITORING OF PATIENTS ON HRT

A woman who is prescribed HRT should be reviewed after two to three months, have her regimen tailored over further visits and then be seen at least yearly after her regimen is effective in improving her symptoms and quality of life. Regular screening is recommended, with a yearly risk–benefit analysis being made.

The duration of therapy should not be fixed but reassessed yearly. HRT can be ceased every four to five years to see

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MENOPAUSE SYMPTOMS[1]

- Hot flushes
  - in 80% women
  - significant in 20% of affected women
  - last longer than five years in 25% of affected women
- Night sweats
- Muscle/joint pains
- Formications
- Anxiety, irritability
- Sleep disturbances
- Lessened memory, concentration
- Vaginal dryness, low libido
- Fatigue
- Overall diminished wellbeing

if symptoms recur; it may be required for five to 10 years, or perhaps longer.

PREMATURE AND EARLY MENOPAUSE

Women experiencing a premature menopause (before the age of 40 years) or an early menopause (before the age of 45 years) are at greater health risks of early onset of osteoporosis, cardiovascular disease and perhaps also an increase in mood disorders and dementia. It is usually advised that these women take HRT at least until they are 50 years of age.

These younger women often require high dose therapy, either HRT or the oral contraceptive pill, for effective symptom control and to preserve bone density.

HRT PRESCRIBING

The HRT products available include tablets, patches and gels. Recently there has been a reduction in the number of products available for women because pharmaceutical companies have withdrawn various products for financial reasons (not because of any safety issues).

The dose of HRT prescribed should be the lowest effective dose that reduces symptoms and improves quality of life, but should always be individualised, sometimes requiring up to six months to determine the appropriate combination of hormones.

Combined therapy of oestrogen and a progestogen (E+P) should be prescribed in women with a uterus, and oestrogen alone (oestrogen replacement therapy; ERT) in women who have had hysterectomies. Cyclical progestogens (E+P) are used in perimenopausal cycling women and continuous progestogen (E+P) after menopause. Tibolone is another option for postmenopausal women. Urogenital symptoms can be treated appropriately with vaginal oestrogen therapy either alone or in combination with HRT.

So-called 'bioidentical' or 'natural' HRT products, which are formulated from imported hormones by local compounding pharmacies, are untested for long-term safety and efficacy and avoid the safeguards of TGA registration. They are a potential medicolegal hazard for prescribers and should not be advocated.

Most studies in women using HRT have been in western industrialised countries with mainly Caucasian populations. The research literature needs to be interpreted accordingly, and may not necessarily be applicable to all community groups. The incidences of menopause symptoms and of various medical conditions, such as breast cancer, will also vary within our population, depending on a woman's country of origin and the length of time she has lived in Australia.

NEW MESSAGE ABOUT HRT NEAR MENOPAUSE

In 2007, the Women's Health Initiative (WHI) investigators reanalysed their data about coronary heart disease (CHD) that had lead to scare headlines in 2002.[2] They found there was an 'absence of excess risk of CHD and the suggestion of reduced total mortality in younger women'. This offered reassurance to those women initiating HRT under the age of age 60 years for symptom control. No morbidity was significantly increased in this group, which is the group normally treated with HRT. Meta-analysis of other studies supports this conclusion.

A recent follow-up study of the WHI showed a reduced risk of breast cancer in the women who took oestrogen alone for seven years. This is also reassuring for these women.[3]

BENEFITS AND RISKS OF HRT

Benefits

HRT has the following beneficial effects:

- relieves vasomotor symptoms of hot flushes and sweats
- reverses urogenital atrophic symptoms, such as vaginal dryness, loss of lubrication
- prevents bone loss due to oestrogen deficiency associated with menopause
- decreases osteoporosis fractures in the spine and hip
- reduces risk of diabetes
- improves connective tissues in skin, joints, arteries and intervertebral discs.

If HRT is commenced in healthy women around the time of the final menstrual period, there may be a reduction in cardiovascular risk and a reduction of Alzheimer's dementia.

HRT may have beneficial effects on the following menopause symptoms:

- aches and pains in joints and muscles
- insomnia or sleep problems
- loss of libido
- mood disturbance
- quality of life.

HRT may also improve sexual function, and the specific HRT conjugated equine oestrogens plus medroxyprogesterone acetate when used for more than four years may reduce the risk of colon cancer.

Risks

Most studies on the risks of HRT focus on the risks of cancer associated with its use. Risks of specific cancers and of other conditions are summarised below.

Breast cancer

The WHI study has shown no increase in

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the risk of breast cancer in first-time E+P HRT users five years after treatment initiation. It has shown a small increase four to five years after treatment initiation in those with prior use (less than 0.1% per year or fewer than one per 1000 women per year of use).

The WHI and the Nurses' Health Study have shown there was no increase in risk of breast cancer after seven to 15 years of use of ERT.

Little information is available on different doses, routes of administration of oestrogen, progesterone, progestogens and androgens. Cessation of HRT leads to a lowering of risk and after five years the risk is the same as the general population of the same age. Mammographic breast density is increased with HRT, and this may decrease the ability to interpret mammograms accurately.

Endometrial cancer

The risk of endometrial cancer is increased in women with an intact uterus taking unopposed oestrogen therapy. The risk will increase with increasingly higher doses of oestrogen and will remain for many years even after the oestrogen has been stopped. Therefore, women should always be given a progestogen to protect the endometrium against the proliferative effect of oestrogen. An adequate progestogen dose will reduce the risk of endometrial hyperplasia and cancer.

Tibolone use is not associated with an increase in the risk of hyperplasia or endometrial cancer.

Ovarian cancer

There is no evidence showing an increased risk of ovarian cancer in women taking combined HRT. A very small increase in risk has been shown with long-term oestrogen-only therapy.

Lung cancer

A statistically significant small increase in the risk of non-small cell lung cancer has been shown in older women taking HRT for five years but there was no increased risk in women in the 50- to 59-year-old group.

Coronary artery disease

Increasing age at time of initiation of HRT has been shown to lead to increased risk of coronary events, especially in older women with pre-existing coronary disease. The events are increased in the first year of therapy. No increased risk of coronary events was shown when HRT was initiated near the menopause, and there may even be possible protection.

Stroke

The age of the woman, her cardiovascular risks (such as hypertension) and the route of administration of E+P or ERT are all factors that influence the risk of stroke. The WHI and the Nurses' Health Study both showed an increase in risk in women taking oral E+P or ERT of one additional stroke per 1000 person years. In an observational study, transdermal oestradiol at doses of 50 μg or less showed no increase in risk of stroke.

Tibolone is associated with a small increase in risk of stroke in older women.

Venous thromboembolism

Venous thromboembolism (VTE) is the major risk associated with the taking of oral oestrogens. The risk also increases with increasing age, obesity and thrombophilias, and may vary according to the type of progestogen being taken. Transdermal oestrogens seem to have a lower risk of VTE, related to the avoidance of the first-pass pathway of metabolism.

Tibolone is not associated with an increased risk of VTE.

Alzheimer's dementia

There is an increase in dementia in older women commenced on E+P/ERT. In the 65 to 79 years age group, ERT leads to an excess risk of 1.2 per 1000 person years and E+P to an excess risk of 2.3 per 1000 person years.

Gall bladder disease

The risk of gall bladder disease (and cholecystectomy) is increased with E+P.

CONCLUSION

HRT remains the most effective treatment for menopause symptoms, particularly the vasomotor symptoms and the atrophic changes. Maintaining and regularly updating one's knowledge about the menopause and HRT is paramount for each professional to be able to give information accurately. Each woman should be counselled about the benefits and risks of HRT in a manner that allows her to make an informed decision. Written or website information will also help her to confirm her decision. MT

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FURTHER READING

A list of further reading is included in the pdf version of this article available at www.medicinetoday.com.au.

COMPETING INTERESTS: Dr Farrell has been on advisory committees and received educational and research grants from various pharmaceutical companies over the past 10 years but does not think these associations have influenced the content of this article.

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