An update on hormone therapy for menopause

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Menopausal hormone therapy (MHT) is an effective treatment that can be offered to most women with menopausal symptoms, following an appropriate assessment and using a shared decision-making process. Recent guidelines from the International Menopause Society recommend there is no need for a mandatory limit to the duration of MHT.

Menopausal hormone therapy (MHT) is the most effective treatment for menopausal symptoms.[1,2] However, women and their doctors have been confronted with conflicting information about the risks of MHT rather than being provided with information about its benefits. In the wake of a new understanding of the risks and benefits, doctors can now confidently prescribe MHT to symptomatic women who have no contraindications.[3] The timing of initiation and the type and route of administration are important in optimising benefits and minimising potential risks of MHT.

The menopause consultation

Women often present to their GP at menopause with a range of symptoms, including hot flushes and night sweats, joint and muscle pains, mood changes and genitourinary symptoms, usually with some change in the menstrual cycle. The consultation with a perimenopausal or menopausal woman should include exploring the woman's concerns and reviewing her general medical history, with particular attention to cardiovascular disease and risk factors, cancer, osteoporosis and venous thromboembolism (VTE).[4]

This consultation is also a good opportunity to check that the woman is up to date with cervical screening tests and mammography, and to discuss healthy lifestyle choices. Measuring the level of follicle-stimulating hormone is not necessary if the woman has menstrual disturbance and is at the usual age of menopause (45 to 55 years). Blood tests are warranted in women younger than 45 years to confirm ovarian insufficiency and to rule out other causes of the symptoms and menstrual disturbance.

The decision to prescribe MHT should be a shared process, with the GP providing evidence to assist the woman to make a decision based on her personal circumstances and preferences. However, women with an early menopause (younger than 45 years) or a premature menopause (younger than 40 years) require especially careful assessment and support. MHT is recommended in these women until at least 51 years of age, in the absence of contraindications (Box 1).[5-7] Following this, the decision about whether to continue with MHT should be made on the same basis as it is for other women of this age.

Remember that MHT is not a contraceptive. Contraception is recommended for two years after the final menstrual period in women under 50 years and for one year in those over 50 years.[8]

Benefits and risks of menopausal hormone therapy

Our understanding of the benefits and risks of MHT has evolved since the findings of the Women's Health Initiative (WHI) trial were first published more than a decade ago.[9] This trial reported increased risks of cardiovascular events, breast cancer and VTE in participants using MHT.

It is now largely agreed that not only were the claims of harm exaggerated, but that the findings have limited relevance to the typical perimenopausal or menopausal woman who is considering using MHT.[2] The recently published long-term follow up

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1. CONTRAINDICATIONS TO MENOPAUSAL HORMONE THERAPY[6]

- Contraindications to menopausal hormone therapy include:
  - breast, endometrial and other hormone-dependent cancers
  - undiagnosed vaginal bleeding.
- Conditions that may require modification of mode of delivery include:
  - established cardiovascular disease (treated hypertension is not a contraindication)
  - venous thromboembolism (VTE; depending on the context, transdermal oestrogen may be prescribed for some women with a history of VTE)[7]
  - active liver disease (may be better with transdermal therapy).

Nonhormonal treatment options can also be considered for the treatment of vasomotor symptoms in women with contraindications.

of WHI participants found no difference in the rate of all-cause mortality between women randomised to MHT or placebo. Moreover, for women aged 50 to 59 years who were randomised to MHT, the hazard ratio for all-cause mortality during the intervention phase of the study was 0.69 (95% confidence interval [CI], 0.51 to 0.94).[10] The International Menopause Society advises that MHT carries few risks when prescribed for symptomatic women without contraindications if initiated in women aged under 60 years or within 10 years of menopause.[5]

Despite the evident benefits of MHT in resolving menopausal symptoms and improving quality of life, women are often focused on the potential risks. These concerns should be addressed in a proactive fashion.

- Breast cancer. This is usually the foremost concern, especially since the results of the WHI study. In that study, oestrogen alone was associated with a decrease, rather than an increase, in breast cancer compared with placebo. The increase in breast cancer identified in the combined oestrogen–progestogen study equates in absolute terms to less than 1.0 case per 1000 women per year of use.[5] Epidemiological data suggest that the risk is lower with progestogens other than medroxyprogesterone acetate.[11]
- Cardiovascular risk. If MHT is initiated within 10 years since the last menstrual period (LMP) or before the age of 60 years, coronary heart disease (death from cardiovascular causes and nonfatal myocardial infarction) is reduced by 48% (relative risk [RR], 0.52; 95% CI, 0.29 to 0.96; absolute difference, 7 per 1000 women). There is no clear evidence of an association with stroke in younger women.[12]
- Venous thromboembolism. The risk of VTE is heightened by obesity, smoking, increasing age and use of oral, but not transdermal, MHT (Box 2, Case 1).[13]

How to prescribe MHT

Women who have had a hysterectomy do not need a progestogen and should be prescribed oestrogen alone in either a transdermal or oral preparation.

Women with an intact uterus require a progestogen in addition to oestrogen to prevent endometrial hyperplasia. For women whose LMP was less than 12 months ago, the progestogen should be cyclical. Use of continuous combined oestrogen and progestogen too soon after the LMP can result in unpredictable breakthrough bleeding. For women whose LMP was more than 12 months ago, continuous combined oestrogen plus progestogen therapy can be used. Approved pharmaceutical preparations with combinations of oestrogen and progestogen have been shown in clinical trials to provide symptom relief and endometrial protection.[1,14]

Options other than oral or transdermal oestrogen–progestogen fixed combinations may be suitable for some women. They include the following.

- The intrauterine system containing the progestogen levonorgestrel is an option for providing endometrial protection for perimenopausal or postmenopausal women. It may be combined with either oral or transdermal oestrogen. It has the added benefits of providing contraception and managing heavy menstrual bleeding.
- A tissue-selective oestrogen complex (TSEC) is the combination of oestrogen and a selective oestrogen receptor modulator. The latter confers endometrial protection without the use of a progestogen. A TSEC combining conjugated oestrogens and bazedoxifene is now available in Australia. It can be used for women who are more than 12 months past their LMP and may be useful in those with troublesome mastalgia.[15] It is available on private prescription.
- A micronised preparation of MHT containing a natural progesterone is available in Australia. It is not available in a combination with oestrogen, which needs to be prescribed separately. Micronised progesterone can be prescribed in a continuous regimen (100 mg/day) or in a cyclical regimen (200 mg/day for 12 days of the calendar month). It can have a mildly sedative effect, which can be beneficial for some women, and it is recommended that it be taken at night. Some data suggest superior safety in terms of breast cancer risk compared with synthetic progestins.[11] Micronised progesterone is available on private prescription.
- Tibolone is a progestin that is metabolised to steroids with oestrogenic, progestogenic and androgenic effects. It may be used for women who are more than 12 months past their LMP. It may have deleterious effects on HDL cholesterol levels.[16] Tibolone is available on private prescription.

Compounded 'bioidentical hormone therapy' lacks safety and efficacy data and is not recommended.[17]

Recent guidelines published by the International Menopause Society recommend that, contrary to the advice quoted on MHT product information, there should be no mandatory limit to the duration of MHT.

The Australasian Menopause Society (www.menopause.org.au/hp/management) provides a guide to MHT preparations available in Australia, along with information on other aspects of menopause management.

Treatment of vulvovaginal and urinary symptoms

Vaginal dryness and urinary urgency and frequency are common in perimenopausal and postmenopausal women. In contrast with vasomotor symptoms, which may settle over time, genitourinary symptoms generally do not improve. It is important to ask patients about these symptoms because women will often not volunteer them. In addition to nonhormonal options such as lubricants, oestrogen is helpful in treating vaginal dryness and may also assist in preventing urinary frequency and urinary tract infections. Many women with systemic symptoms who take MHT will have improvement in their symptoms, but some women will require the addition of topical oestrogen. For women who have only genitourinary symptoms, topical oestrogen can be prescribed.

Duration of treatment

Women who are prescribed MHT should be reviewed to check on its efficacy and side effects, with treatment tailored accordingly. All patients should be followed up at least annually to update their history. There is no need for an arbitrary maximum duration for MHT. Recent guidelines published by the International Menopause Society recommend that, contrary to the advice quoted on MHT product information, there should be no mandatory limit to the duration of MHT.[5] It should be used in the dose required to address the treatment goals and for as long as there is a need. Of course, the mode of delivery and the type of MHT should be adjusted according to age and circumstance. Moreover, in a study from Finland, women who stopped had an increased risk of cardiac or stroke death compared with those who continued.[18] In the absence of emerging contraindications, women can continue MHT as long as it is addressing therapeutic goals, either symptoms, quality of life or long-term health such as preservation of bone density (Box 2, Case 2).

Conclusion

Menopause is an ideal time to assess a woman's health and promote a healthy lifestyle. Most women who have bothersome menopausal symptoms can be offered MHT, following an appropriate assessment and discussion of the relevant evidence using a shared decision-making process. MT

2. CASE SCENARIOS

Case 1: A 49-year-old woman with a history of deep vein thrombosis

Linh, aged 49 years, presented to her GP to discuss whether she could take menopausal hormone therapy (MHT) for her vasomotor symptoms. Her last menstrual period was at age 47 years. Linh's medical history included a deep vein thrombosis (DVT) when she was 29 years. Her leg had been immobilised after a knee reconstruction. At that time, she had been on the combined oral contraceptive pill and she received anticoagulation for three months. Linh had no further DVTs and subsequently had two children, followed by a hysterectomy for heavy menstrual bleeding. There was no family history of venous thromboembolism (VTE) and Linh was a nonsmoker with a normal body mass index. She had results normal on thrombophilia screening. Linh's DVT was provoked by immobilisation and the use of the oral contraceptive pill. Transdermal oestrogen is not associated with an increase in VTE or recurrence of VTE, so Linh could be prescribed an estradiol patch 50 mcg per 24 hours, twice weekly for her menopausal symptoms.

Case 2: Continuing MHT use after the age of 60 years

Helen presented to her GP at age 52 years with hot flushes, night sweats and insomnia. Her last menstrual period was five months previously. She was keen to try MHT and had no contraindications. She commenced oral MHT with estradiol 1 mg/day and dydrogesterone 10 mg/day (for 14 days of the month). With this regimen, she had good control of her symptoms and a light withdrawal bleed each month.

After 12 months she changed to the continuous combined form of the preparation (estradiol 1 mg/day and dydrogesterone 5 mg/day). She had some irregular bleeding for the first two months but then experienced amenorrhoea. She had a yearly review with her GP. She returned to her GP when she was 61 years because her friends had told her it was dangerous to continue MHT after the age of 60 years. She had tried stopping but her symptoms returned.

About 40% of women will experience vasomotor symptoms into their 60s, and for some women these symptoms will continue indefinitely. Helen's GP explained that if MHT was still meeting her needs, she could continue to take it for as long as she wished to, providing she attended for regular follow ups.

References

A list of references is included in the online version of this article (www.medicinetoday.com.au).

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