Combined Menopausal Hormone Therapy (MHT)

KEY POINTS

- MHT is the most effective treatment for hot flushes and night sweats.
- Only women with an intact uterus need the addition of a progestogen.
- The risks are small in most women within 10 years of their final menstrual period.
- Non-oral routes of administration have fewer risks than oral preparations.
- See AMS information sheet Guide to Equivalent HRT/MHT Doses for a list of products available in Australia and New Zealand.

The menopause is the final menstrual period and usually happens between the ages of 45 and 55 years. Around this time, women may experience symptoms such as hot flushes, sweating, vaginal dryness, loss of libido, irritability, sleep disturbance and muscle/joint pains. Oestrogen therapy is the most effective means of treating these symptoms. It will also prevent bone loss.

In a woman with an intact uterus, unopposed oestrogen therapy increases the risk of endometrial hyperplasia and cancer (1). Therefore, women who have not had a hysterectomy should take a progestogen as well, to provide endometrial protection. Note that there is no therapeutic advantage of prescribing progestogen (either a progestin or natural progesterone) to women who have had a hysterectomy, (with the possible exception of women with symptomatic residual intra-peritoneal endometriosis) (2). In fact, there is a distinct disadvantage in terms of increased breast cancer and thrombotic risk and adverse changes in cardiovascular risk factors (3) (see information sheet on Benefits and Risks).

Combined menopausal hormone therapy may be given as "cyclical", where the oestrogen is given daily and the progestogen is given for 10-14 days of the month, or "continuous" where both oestrogen and progestogen are given daily. "Cyclical" produces withdrawal vaginal bleeds whereas "continuous" should not.

As a general rule, cyclical hormone therapy is used for a woman who is in the menopausal transition and is having some irregular spontaneous menses or is very recently postmenopausal, but it can be continued longer if preferred. Continuous hormone therapy is a convenience often preferred by older women. Early introduction of continuous MHT close to the menopausal transition may lead to irregular, unscheduled breakthrough bleeding. Breakthrough bleeding may occur in the first six months of any MHT regimen but any unscheduled bleeding after that should be investigated.

Combination packs of either cyclical or continuous preparations are available. These improve medication compliance and ensure reliable endometrial exposure to progestogen. If, for reasons of intolerance to either the formulation or the mode of delivery, it is thought necessary to "mix and match" oestrogen and progestogen preparations, it is important to emphasise to the patient that reliable endometrial protection depends upon sufficient progestogen exposure (4).

Types of oestrogens

- Oestrogens are available as tablets, skin patches, and gels.
- Patches or gels may be better for those with gut absorption problems.
- Patches or gels are also better for those who have high triglyceride concentrations or who are at risk of venous thromboembolic disease (5). This includes those who are overweight and smokers.
- Vaginal oestrogen in creams, pessaries or tablets is available for vaginal dryness or dyspareunia.

Types of progestogens

- The term "progestogen" encompasses both natural progesterone and synthetic preparations which act on the progesterone receptor. The term "progestin" is used purely for the synthetic preparations. Progestins may be derived from progesterone or other steroids (such as testosterone) and most have other biological effects, such as on either the androgen receptor, the glucocorticoid receptor or the mineralocorticoid receptor, in addition to their progestogenic effects (6).
- Progestogens are mostly taken orally. The only progestogen which is reliably absorbed through the skin is norethisterone, used in the combined MHT patches. Progesterone creams are not reliably absorbed and do **not** confer adequate endometrial protection.
- Micronised progesterone capsules, a form of natural progesterone, are available in New Zealand but not yet in Australia.
- An alternative method is to deliver the progestogen directly to the endometrium using the levonorgestrel containing intrauterine system (Mirena).
- There is no evidence that either progesterone troches or progesterone cream confer adequate endometrial protection (7).

Other MHT

- Tibolone is a synthetic progestogenic hormone which, once metabolized, acts like oestrogen, progestogen and testosterone (see AMS information sheet on Tibolone for Post -Menopausal women).
- Testosterone – is sometimes added to MHT and may improve libido and energy in some women (see AMS information sheet on Low Libido and Testosterone Therapy).

Before prescribing

- A full history and clinical examination should be done, exploring possible contraindications or relative contraindications to MHT or to specific formulae.
- Mammograms, breast checks and cervical screening should be up to date in all women over 50 years whether they are taking MHT or not.
- Any unexplained vaginal bleeding should be investigated.
- Ensure the patient understands benefits and risks (see Information sheet on Benefits and Risks).

Choice and adjustment of therapeutic regimens

- The choice of oestrogen dose depends upon how a woman's symptoms respond and on her well-being, not on measurement of blood levels.
- Transdermal preparations are preferred for women with malabsorption, risk or past history of DVT, migraine, untreated hypertension and significant liver disease.
- Most problems with intolerance are related to the progestogen. These include mood changes, bloating, headache, and mastalgia. These symptoms may benefit from a change to a different progestogen formulation or mode of delivery.
- Progestogens should be taken cyclically for 10-14 days each month, aiming for a predictable monthly bleeding pattern, or continuously, which is designed to give no bleeding. However irregular bleeding is common with all regimens, particularly during the first three to six months of use. After this time, investigation with ultrasound +/- hysteroscopy and endometrial sampling is indicated. An adjustment of the progestogen to oestrogen dose ratio may fix the problem.
- For women who cannot tolerate progestogen tablets, an alternative is to try the levonorgestrel intrauterine system (Mirena), although some systemic absorption occurs with this device.

The benefits of MHT

- MHT is the most effective treatment for hot flushes and night sweats.
- MHT also effectively treats vaginal dryness.
- Reducing menopausal symptoms with MHT may improve quality of life.
- MHT reduces the risk of postmenopausal bone fracture, including hip fracture (3).
- MHT use is not associated with weight gain (8).

Managing the risk

- Regular breast checks and screening mammograms should be performed in women over 50 years whether they are taking MHT or not.
- MHT should be reviewed annually by the woman in consultation with her doctor. Personal benefits versus risk should be discussed.
- If a woman using MHT develops symptoms suggesting DVT or stroke she should stop the MHT and seek medical attention (see AMS information sheet on Menopausal Treatments and the Risk of Blood Clots).
- Oral MHT increases the risk of venous thromboembolism. In women less than 60 years the risk is low. The risk increases with age and other risk factors such as obesity, previous thromboembolism, smoking and immobility. The risk is less with the use of transdermal preparations and also with the use of oestrogen alone (5).

Continuation or cessation of combined MHT

- The dose and duration of MHT should be consistent with treatment goals, such as symptom relief, and should be individualized (9).
- Women who go through menopause before 45 years are advised to take MHT until the average age of menopause, i.e. around 50 years. The discussion and decision to continue MHT is then the same as it is for women are experiencing menopause at the usual age and considering starting MHT (See AMS information sheet on Premature Ovarian Insufficiency).
- The risk of breast cancer is primarily associated with combined oestrogen/progestogen therapy and related to the duration of use. The risk of breast cancer attributable to combined MHT is small and decreases after treatment is stopped. Oestrogen alone has not been shown to increase breast cancer risk in high quality randomized controlled trials.
- Oral MHT increases the risk of stroke and the risk increases with age. Stroke risk is not significantly altered in women younger than 60 years with normal blood pressure. The risk may be less with the use of oestrogen gel or skin patches.
- Cessation of MHT is associated with increased cardiovascular and cerebrovascular events and increased risk of fracture (10, 11).

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