Menopause and its Management

As women move towards the menopause menstruation becomes erratic and eventually stops. There are a number of secondary effects described as 'menopausal symptoms' - see 'Presentation' section, below.

The climacteric, menopausal transition stage, or perimenopause, is the period of change leading up to the last period. The menopause itself is a retrospective diagnosis of the time when menstruation permanently ceases. It can only be defined with certainty after twelve months' spontaneous amenorrhoea.

Premature ovarian insufficiency (POI) occurs in around 1% of women under the age of 40 years and is a syndrome consisting of amenorrhoea, elevated gonadotrophins and oestrogen deficiency. The term early menopause is used for those women who go through their menopause between 40-45 years.

Epidemiology

Population studies identify smoking and low socio-economic factors as being associated with premature menopause. Other factors which can affect the age at which women have their final period include age at menarche, parity, previous oral contraceptive history, BMI, ethnicity and family history[1].

Many women do not seek medical advice for menopausal symptoms. Variations in consultation patterns for menopause depend on many factors, including cultural and educational differences as well as psychosocial difficulties.

Aetiology

The menopause is a natural phenomenon which occurs in all women when their finite number of ovarian follicles becomes depleted. As a result, oestrogen and progesterone hormone levels fall, and luteinising hormone (LH) and follicle-stimulating hormone (FSH) increase in response.

The menopause can be 'induced' by surgical removal of the ovaries or by iatrogenic ablation of ovarian function by chemotherapy, radiotherapy or by treatment with gonadotrophin-releasing hormone (GnRH) analogues.

Presentation

Menopausal symptoms are attributed to tissue sensitivity for lower oestrogen levels. This primarily affects the oestrogen receptors in the brain. The experience of women varies widely; some are debilitated and others are unaffected by their symptoms. Some women experience symptoms while still menstruating and others not until a year or more after their last period.

The menopausal transition stage usually begins when women are in their mid-to-late 40s. The final menstrual period (FMP) usually occurs between the ages of 45 and 55. The average age of the menopause in women in the UK is 51 years.

Around 80% of women going through their menopause experience symptoms and around a quarter have severe symptoms, but only a small proportion of menopausal women take hormone replacement therapy (HRT)[2]. Symptoms of the menopause last far longer than most women anticipate; frequent menopausal vasomotor symptoms, including night sweats and hot flushes, persist in more than half of women for more than seven years[3].

Menstrual irregularity

- The majority of women notice irregularities to the menstrual cycle, which may last for up to four years.
- The cycle may lengthen to many months or shorten to 2-3 weeks.
- An increase in the amount of menstrual blood loss is common.
- Approximately 10% of women have an abrupt cessation of periods.

Hot flushes and sweats

- These are hallmark symptoms.
- Hot flushes commonly affect the face, head, neck and chest and last for a few minutes.
- They are caused by a loss of homeostasis by the central thermoregulatory centre.

Urinary and vaginal symptoms

- Urogenital symptoms arise directly from loss of the trophic effect of oestrogen.
- These may include dyspareunia, vaginal discomfort and dryness, recurrent lower urinary tract infection and urinary incontinence.
- Urinary symptoms may not manifest until 5-10 years after the menopause.
Sleep disturbance

- This is a common symptom reported by women.
- Symptoms may be secondary to vasomotor symptoms, are affected by psychosocial factors and may contribute to depression, irritability and poor concentration\(^4\).

Mood changes

- These may include anxiety, nervousness, irritability, memory loss and difficulty concentrating.
- Perimenopause is accompanied by an increased risk of new and recurrent depression\(^5\).
- There is some evidence that those women who have a history of premenstrual and postnatal depression have a higher risk of depression during their menopause\(^6\). These women are typically well during pregnancy.

Loss of libido

- This can be caused by a number of hormonal factors; oestrogen, progesterone and testosterone have all been implicated.
- Vaginal dryness, loss of self-image and other psychosocial factors also play a part.

Other changes

These may include brittle nails, thinning of the skin, hair loss and generalised aches and pains. These are due to falling oestrogen levels.

Differential diagnosis

The diagnosis will usually be obvious from the clinical picture but may be harder to make in younger women in the early stages of the menopause.

Other causes of secondary amenorrhoea, such as pregnancy and hypogonadotrophic hypogonadism, may need to be considered.

Investigations\(^7\)

The diagnosis of the menopause in the majority of women is a clinical one and investigations are usually not recommended.

Laboratory tests are not required in the following otherwise healthy women aged over 45 years with menopausal symptoms:

- Perimenopause based on vasomotor symptoms and irregular periods.
- Menopause in women who have not had a period for at least 12 months and are not using hormonal contraception.
- Menopause based on symptoms in women without a uterus.

FSH levels may be useful to diagnose the menopause in women using hormonal contraception. Two levels are required, 2 or 6 weeks apart.

Tests which may be undertaken in some women

- **FSH levels**:
  - There is no need for the FSH level to be tested in most women.
  - A raised FSH is not diagnostic for the menopause. A high level will just indicate a lack of ovarian response at a point in time.
  - FSH testing could be considered to diagnose menopause in women aged 40-45 years with menopausal symptoms, including a change in their menstrual cycle.
  - FSH testing should be undertaken in women aged under 40 years in whom POI is suspected.

- **TFT** - to differentiate thyroid disease symptoms from menopausal symptoms.
- **Blood glucose** - may be considered in some women, as diabetes can cause similar symptoms.
- **Blood cholesterol and triglycerides** - consider if the woman has any cardiovascular risk factors.
- **Cervical screening and mammograms** - ensure the woman is up to date with her cervical screening and also mammograms (if appropriate).
- **A pelvic scan** - may be considered for those women with atypical symptoms.

Tests which are usually unhelpful

- LH
- Estradiol
- Progesterone

The following tests **should not be used** to diagnose perimenopause or menopause in women aged over 45 years:

- Anti-Müllerian hormone
- Inhibin A or B
- Estradiol
- Antral follicle count
- Ovarian volume
Associated diseases

The relationship between the menopause and the development of associated conditions is sometimes difficult to differentiate from age-related morbidity but is easiest to demonstrate in cases of premature primary and secondary ovarian failure.

- **Cardiovascular disease**: including coronary artery disease, stroke and peripheral arterial disease. These all increase significantly after the menopause.
- **Osteoporosis**: the link between osteoporosis and oestrogen deficiency is well documented. Menopause and the accompanying loss of ovarian oestrogens is associated with declines in bone mineral density (BMD)\(^8\). Low oestrogen levels are associated with an increased risk of both hip and vertebral fractures in older women. This association is actually independent of age and body weight.
- **Redistribution of body fat**: fat tends to be redistributed around the abdomen with age. This is recognised as being an independent risk factor for cardiovascular disease and diabetes.
- **Alzheimer's disease**: women have a higher incidence of Alzheimer's disease than men, indicating that the declining oestrogen levels during menopause may influence its pathogenesis. One study has shown that HRT initiated during the perimenopausal period could delay or preferably prevent future development of neurodegenerative diseases like mild cognitive impairment and Alzheimer's disease\(^8\).

Management

An individualised approach should be undertaken at all stages of diagnosis, investigation and management of menopause\(^7\). Women should receive adequate information about the symptoms and treatment of the menopause, including benefits and risks of treatment. In addition, women who are likely to go through the menopause as a result of surgical or medical treatment should be given information about menopause and fertility before their treatment.

Healthy lifestyle

Encourage a healthy lifestyle. Stopping smoking, losing weight and limiting alcohol are all beneficial to a woman going through the menopause. Women should also be encouraged to take regular aerobic exercise and to ensure they have adequate calcium intake (around 700 mg/day). Avoidance or reduction of caffeine may help.

HRT

HRT is the most effective treatment to relieve the symptoms caused by the menopause completely, although it may not be suitable for everyone. HRT is particularly effective in treating:

- Vasomotor symptoms (hot flushes/night sweats).
- Mood swings.
- Vaginal and bladder symptoms.

Vasomotor symptoms are usually improved within four weeks of starting treatment and maximal benefits will be gained by three months. Vasomotor symptoms may persist for many years (the average is just over seven years) and therefore treatment may need to be continued. Regular assessment of the benefits versus the risks of ongoing treatment should be undertaken at least annually.

Vaginal symptoms tend to be slower to respond to treatment and to recur if treatment is stopped. There is good evidence for the efficacy of topical HRT in the short-term treatment of menopausal atrophic vaginitis\(^10\). Vaginal symptoms are improved, vaginal atrophy and pH decrease and there is improved epithelial maturation with topical oestrogen preparations compared to placebo or non-hormonal gels. However, vaginal lubricants can be effective to use as non-hormonal alternatives, especially if the main symptoms are pain on intercourse due to dryness.

HRT also prevents and reverses bone loss.

Psychological symptoms\(^7\)

- HRT can often help to alleviate low mood which arises as a result of the menopause.
- Cognitive behavioural therapy (CBT) can also be beneficial.
- There is no good evidence that antidepressants improve the low mood that is associated with the menopause.

See also separate Hormone Replacement Therapy (including Benefits and Risks) article.

Alternatives to HRT

Alternatives to HRT are available and may be useful for women with contra-indications to hormonal treatment (such as hormone-dependent tumours) or for those who perceive the risks of HRT to be too great.

There is no good evidence that alternative treatments are effective. The efficacy and safety of unregulated compounded bio-identical hormones are unknown\(^11\).

The quality, purity and constituents of complementary treatments may be unknown\(^7\).
Selective serotonin reuptake inhibitors (SSRIs) are effective for vasomotor symptoms in some women but their effect is often short-acting[12]. Venlafaxine is also effective in some women[13]. The National Institute for Health and Care Excellence (NICE) recommends that they are not routinely prescribed as first-line management of vasomotor symptoms.

Herbal or complementary treatments

- Phyto-oestrogens are naturally occurring compounds found in plant sources, that are structurally related to oestradiol.
- They appear to have both oestrogenic and anti-oestrogenic effects on human oestrogen receptors.
- The main types of phyto-oestrogen are isoflavones, including genistein, daidzein and glycitein, lignans and coumestans.
- Foods such as soy beans, as well as nuts, wholegrain cereals and oilseeds, are the foods most rich in phyto-oestrogens.
- Phyto-oestrogens can be taken in the form of tablets containing concentrated isoflavones, such as red clover.
- The efficacy of phyto-oestrogens has not been proven in randomised clinical trials[14]. However, one meta-analysis has shown that the use of phyto-oestrogens is associated with a reduction in frequency of hot flushes and that their side-effects are similar to those with placebo[15].
- There is a wide array of botanical medicines (such as black cohosh, sage, ginkgo biloba) available to take as an alternative approach to HRT for menopause. However, data documenting efficacy and safety are limited. None of the available botanicals is as effective as hormone therapy in the management of vasomotor symptoms[16].
- Many women choose to try these products, as they believe them to be safer and more ‘natural’ than prescribed medication. However, most herbal products available in the UK are not subject to the same regulatory requirements as licensed medications and, as such, are not subject to the same degree of standardisation. There may be variability between products or a lack of clarity as to what ingredients a particular product contains. Botanical medicines may interact with other medicines.

In addition, there is currently insufficient evidence to suggest that they are safe to be taken by women with oestrogen-dependent cancer - eg. breast cancer. There are no safety data available in relation to their risk of venous thromboembolism (VTE).

Early menopause management

Early menopause is defined as a menopause between the ages of 40 and 45 years. This occurs in up to 20% of women.

All women with an early menopause have an increased risk of osteoporosis, cardiovascular disease and dementia if they are not given HRT appropriately.

In essence, the principles of oestrogen replacement are the same as for women experiencing menopausal symptoms and problems at any age. However, the symptoms may be more severe in premature menopause, particularly after surgical menopause, often requiring higher doses of oestrogen than those needed following spontaneous menopause at a later age. In addition, the aetiology of the premature or early menopause needs to be considered, as this may change the treatment offered (eg, if it were following surgery for an oestrogen-sensitive cancer).

Women with an early menopause should be offered HRT unless contra-indicated. It is normally continued until they reach at least 51 years. There is no evidence that there is any increased risk of breast cancer compared with normally menstruating women of the same age. They may need larger doses of HRT to control vasomotor symptoms[17].

Refer to the Premature Ovarian Insufficiency article for more detailed information about that condition.

Further reading & references

- Menopause; NICE Quality Standard, February 2017


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