

Managing menopausal symptoms

Many women experience devastating menopausal symptoms to the extent their quality of life is reduced and daily tasks start to become a burden. Other women suffer only minor, well manageable symptoms that allow them to lead their life as they always have. While the variety of symptoms seems endless, there are few pathways of treatment. **Drs Etienne Horner and Nicholas Panay** review the management options.

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In the light of the controversy since the publication of the results of the Women's Health Initiative¹ and the Million Women Study², managing menopausal women has become a very difficult task for patients, doctors and other healthcare professionals. The British Menopause Society has therefore an 'integrated healthcare pathway for the menopausal woman' updated and published³. The ovaries are the only endocrine glands (except thymus and placenta) that cease to function before the end of life. The median age of the menopause in Western countries occurs at about 52–54 years. The coming to an end of ovulation and ovarian endocrine function in the ageing woman represents a meaningful transition. Menopause being a normal developmental process, there is a psychological adjustment as well as physical and anatomical change. Women in transition to menopause need to be well informed about all their current treatment options, and the doctor/healthcare professional relationship is of utmost importance as an atmosphere of confidence and trust is mandatory to achieve satisfying results.

Definitions

The definitions given follow the formulations of the World Health Organisation (WHO) and the International Menopause Society (IMS):

> Menopause: a permanent cessation of menstruation resulting from the loss of ovarian follicular activity. A natural menopause is recognised to have occurred after

12 consecutive months of amenorrhea.

There is no adequate marker for this event.

> Pre-menopause: the beginning of the climacteric transition, which starts a few years (two to five) before menopause.

- > Premature menopause: ideally, premature menopause should be defined as menopause that occurs at an age more than two standard deviations below the mean estimate for the reference population. The age of 40 years is usually used as an arbitrary cut-off.
- > Premature ovarian failure: a condition of ovarian defect with primary or secondary amenorrhoea before the age of 40 years.

The Women's Health Initiative (WHI)¹ and the Million Women Study² have caused considerable alarm by reporting that venous thromboembolism, strokes, heart attacks and breast cancer are more common in women with hormone replacement therapy (HRT). Unfortunately, both studies were the focus of press conferences before they were discussed by the scientific community⁴. The newspaper headlines are now fixed in the public memory regardless of any final scientific revision. It will be up to the doctor to reassure women on HRT about their treatment with in-depth discussions about risks and side effects; for those who are about to start with HRT it should be with the understanding that the treatment is for specific symptoms and low bone density — and is not a lifestyle drug. Recent smaller studies, such as the WHISP study of John Stevenson⁵, will potentially produce a new message regarding the risks and benefits of HRT.

The climacteric syndrome

The withdrawal of oestradiol and progesterone leads to adaptory changes of the hormonal regulatory system. The autonomous nervous system is imbalanced and causes typical early symptoms of hormonal deficit. These climacteric changes are mostly superimposed by symptoms of ageing, which is very distressing for women going through menopausal transition. There are a great variety of symptoms and, together with personal character and cultural background, this can complicate the assessment and differential diagnosis. Vasomotor symptoms such as hot flushes, night sweats and vaginal dryness are the most current menopausal symptoms. However, hot flushes are the earliest and most prominent symptoms of oestrogen deficiency. The prevalence of hot flushes increases from the premenopause; it is maximal two to three years after the menopause and decreases thereafter⁶. In Asian countries, hot flushes occur less frequently, possibly due to the higher consumption of soy oestrogens. Vaginal dryness is seen as a cardinal symptom of menopause^{7,8} and is present in approximately 50

per cent of menopausal women. Further menopausal symptoms include dysfunctional heart disorders (palpitations, rapid and irregular heart beats), sleep disorders, mood changes, irritability, anxiety, tiredness, lack of energy, memory loss, urogynaecological symptoms (dysuria, pollakisuria, stress/urge incontinence, recurrent cystitis), bone loss and lack of libido. This is not a complete list of symptoms but the above mentioned seem to be the most frequent.

The Melbourne Women's Midlife Project⁹ — at a duration of nine years — is the longest study of women through the menopausal transition and examined 33 symptoms. Vasomotor symptoms, insomnia, vaginal dryness and breast tenderness changed significantly during early and late menopausal transition.

Lack of libido

The female androgen deficiency syndrome (FADS) is characterised by loss of energy, loss of libido, depression, loss of self confidence and headaches. These are also frequent complaints in women who have had a hysterectomy and oophorectomy. Twenty to 40 per cent of women suffer from female sexual dysfunction (FSD)¹⁰. For many women it is physically disconcerting, emotionally distressing and socially disruptive¹¹. FSD is classified in four different disorders: sexual desire, sexual arousal, orgasmic and sexual pain disorders. This definition of different FSD may be helpful for the clinician in correctly approaching the complaints and therapy possibilities.

Bone loss

Osteoporosis is a metabolic bone disease characterised by a low bone mass and microarchitectural deterioration of bone tissue followed by enhanced bone tissue¹². In menopausal women, bone loss occurs as a result of the increase in the level of bone resorption as compared to the level of bone formation. This is induced by oestrogen deficiency together with age. In the first five years after the menopause bone loss is accelerated to about one to five per cent per year. Afterwards, the bone loss stabilises at about 0.5 per cent per year¹³. With declining levels of bone mass the fracture risk becomes gradiently higher.

Cardiovascular disease

Cardiovascular disease is one of the main causes of

death in women in the twenty-first century. Menopause is associated with an increased risk of cardiovascular disease and outnumbers other classical causes of death in women, such as breast, cervical and ovarian cancer. Premenopausal women seem to be protected from cardiovascular disease compared with men in the same age range. The increased risk after menopause may be explained by oestrogen deficiency, responsible for the rapid acceleration of the cardiovascular risk, and by changes in abdominal fat content and worsening of blood lipid content¹⁴.

Depression

Depression is more common in women than in men¹⁵. The challenge is to determine whether the increase in depression is environmental or due to hormonal changes. The peaks of depression occur at times of hormonal fluctuation such as in the premenstrual, the postpartum and the perimenopausal phases. Women around the time of their menopause can suffer from increased depression two to three years before their periods stop. One of the first placebo-controlled studies against hot flushes, night sweats and vaginal dryness also had a mood elevating effect¹⁶. This study defined the menopausal syndrome and confirmed that oestrogens improved not only vasomotor symptoms, but also alleviated mood.

Urogenital atrophy

Oestrogen deficiency in menopause causes atrophic changes within the urogenital tract and therefore is associated with symptoms of frequency, urgency, nocturia, incontinence and finally recurrent infections¹⁷. To these symptoms more symptoms of vaginal atrophy can be added such as dyspareunia, burning, itching and dryness. It has been estimated that 10–40 per cent of all menopausal women are symptomatic¹⁸.

Treatment options

Treatment options fall under three headings: lifestyle changes; alternative and complementary therapies; and HRT.

Lifestyle changes: Before commencing any medical treatment it is very important to ensure that lifestyle has been optimised. There is some evidence that women who are more active tend to suffer less from menopausal symptoms¹⁹. Unfortunately, not all types of activity improve menopausal symptoms. The best activities are regular exercises, such as running and swimming. Menopausal symptoms can also be

aggravated by social and environmental factors and therefore reduction of stress can be helpful in ameliorating these symptoms. Limiting the intake of caffeine and alcohol can also reduce the severity and frequency of vasomotor symptoms²⁰.

Alternative and complementary therapies: There is poor evidence from randomised trials that alternative and complementary therapies improve menopausal symptoms, or even have the same benefits as non-oestrogen based treatments or HRT. Women often perceive complementary therapies to be a safe alternative to traditional hormone therapies. But there is concern these therapies may interact with other treatments with potentially fatal consequences. Some preparations may contain oestrogenic compounds and this could be a problem for women with oestrogen positive breast cancer. Phyto-oestrogens (soy, red clover, chick peas) are plant substances with similar effects to those of oestrogens. Japanese women appear to have lower rates of menopausal vasomotor symptoms, cardiovascular disease and osteoporosis as well as breast, colon, endometrial and ovarian cancers²¹. Herbal remedies — including black cohosh, evening primrose oil, dong quai, ginseng and wild yam cream — are widely used by menopausal women. With all alternative preparations the efficacy is maximally 50–60 per cent. We also should not forget some alternatives have their own adverse effects and risks — warnings have already been issued by regulatory bodies for some products.

HRT: Even though menopause is not life-threatening, for most women it interferes with quality of life. It seems the dilemma of balancing the benefits and risks of available therapies is probably greater for doctors than for patients²². Oestrogen-based treatments still play a major role in the treatment of menopausal symptoms. Treatment choice should be based on up-to-date information and targeted to an individual woman's need. HRT still offers the potential for the benefit to outweigh the harm, providing the appropriate regimen has been instigated in terms of dose, route and combination²³.

The success of HRT depends primarily on a good patient/doctor relationship and on compliance from both sides. The fears, doubts, expectations and wishes of the patient should be thoroughly discussed prior to start in order to create an atmosphere of trust between patient and doctor. HRT consists of an oestrogen combined with a progestogen in non-hysterectomised women. Different routes of systemic administration — such as oral, transdermal,

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Key points

- Hot flushes can have detrimental effect on work life and also a damaging effect on the sex life.
- HRT can help prevent osteopenia and osteoporosis.
- The choice of taking HRT or not will depend on the extent of symptoms together with health and personal wishes.
- Treatment will always be a personal, very individual decision by every woman going through the menopause and no one treatment is mandatory.
- Women benefit greatly from an integrated approach involving a continuing relationship with sensitive and well-informed clinicians.

subcutaneous and intranasal — are employed. Essentially oestrogen is given for the treatment of climacteric symptoms and for the improvement of low bone density.

There is good evidence from randomised controlled trials that oestrogen is effective to treat vasomotor symptoms and improvement is usually noted within four weeks²⁴. This is also the most common indication for HRT. Urogenital symptoms respond very well to oestrogens too, but improvement may take several months and long-term treatment is often required²⁵. Oestrogens also reduce the risk of spine and hip as well as other osteoporotic fractures. There used to be a dose of 2mg oestradiol daily as a bone conserving dose, but it is now evident that half of the dose conserves bones similarly²⁶.

Low libido may be improved with oestrogen therapy, but often adding testosterone leads to better results. Testosterone is indicated for women who present with the classical clinical symptoms of sexual dysfunction and/or lack of energy. Currently in the UK, testosterone for women is only licensed as an implant. Testosterone as a patch has been investigated over the last few years; the results are very promising in terms of efficacy and safety as well as increased frequency of satisfying sexual activity, and it is well tolerated in menopausal women²⁷.

Conclusion

HRT during menopause is an attempt to prolong a euhormonal state and to maintain an endocrine autonomous balance. The treatment is very effective, well tolerated and, if properly indicated and

administered, it is a low-risk procedure. Advice from most regulatory authorities following the Women's Health Initiative Study and Million Women Study have recommended that HRT should be continued for the shortest possible time in the lowest dose²⁸. It has been suggested five years should be the time for cessation of therapy, as an apparent increase of breast cancer occurs after this time²⁹. In the long term, substantive bone loss and cardiovascular disease can be prevented if they are due to oestrogen deficiency and have started with menopause. Androgen supplementation is likely to become standard practice in menopausal women as large randomised controlled trials have shown a psychological and physical benefit of adding testosterone to oestrogen/progestogen therapies^{30,31}.

Conflict of interest: Drs Horner and Panay have both acted in an advisory capacity and lectured for a number of pharmaceutical companies that manufacture HRT-related products.