Management of premature menopause

British Menopause Society Council Consensus Statement

Summary

The British Menopause Society Council aims to aid health professionals to inform and advise women about the menopause. There has been some confusion amongst women and health professionals since publication of the Women’s Health Initiative and Million Women studies about the management of premature ovarian failure (POF). Both studies were undertaken in women aged 50 and over and cannot be extrapolated to their younger counterparts who would normally be producing their endogenous oestrogen. Oestrogen-based replacement therapy is the mainstay of treatment for women with POF and is recommended at least until the average age of natural menopause (52 years in the UK). This view is endorsed by regulatory bodies such as the Committee on Safety of Medicines in the UK. No evidence shows that oestrogen replacement increases the risk of breast cancer to a level greater than that found in normally menstruating women, and women with POF do not need to start mammographic screening early.

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Introduction

Premature menopause is defined as menopause that occurs at an age more than two standard deviations below the mean estimated for the reference population. In the absence of reliable estimates of age of natural menopause in developing countries, the age of 40 years is used frequently as an arbitrary limit below which the menopause is said to be premature. In the developed world, however, the age of 45 years should be taken as the cut-off point. The condition is not uncommon. Overall, premature ovarian failure (POF) is responsible for 4-18% of cases of secondary amenorrhoea and 10-28% of primary amenorrhoea. It is estimated to affect 1% of women younger than 40 years and 0.1% of those under 30 years. The causes of POF are detailed below but in most cases none can be found.

Causes of premature ovarian failure

Primary

Chromosome abnormalities

Follicle stimulating hormone receptor gene polymorphism and inhibin B mutation

Enzyme deficiencies

Autoimmune disease
Secondary

Chemotherapy and radiotherapy

Bilateral oophorectomy or surgical menopause

Hysterectomy without oophorectomy

Infection

Consequences of oestrogen deficiency

Women with untreated premature menopause are at increased risk of developing osteoporosis and cardiovascular disease but at lower risk of breast malignancy.

1-4 Mean life expectancy in women with menopause before the age of 40 years is 2.0 years shorter than that in women with menopause after the age of 55 years. 3 Premature menopause can lead to reduced peak bone mass (if the woman is younger than 25 years) or early bone loss thereafter. The increased risk of coronary heart disease has been noted especially in smokers.

Management

1. Counselling

Patients must be provided with adequate information. 5 Women may find it a difficult diagnosis to accept, especially if they wish to have children. National self-support groups for POF exist, such as the Daisy Network in the UK (http://www.daisynetwork.org.uk/), and these provide helpful psychological support for many women. Women need to be aware that ovulation may occur again, often intermittently, and cyclical menstrual bleeding or even pregnancy can result. 6

2. Hormone replacement therapy.

Oestrogen replacement therapy is the mainstay of treatment for women with POF and is recommended until the average age of natural menopause (52 years in the UK). This view is endorsed by regulatory bodies such as the Committee on Safety of Medicines in the UK. 7 No evidence shows that oestrogen replacement increases the risk of breast cancer to a level greater than that found in normally menstruating women, and women with POF do not need to start mammographic screening early. 8 Hormone replacement therapy (HRT) or the combined oestrogen and progestogen contraceptive pill may be used. No clinical trial evidence attests the efficacy or safety of the use of non-oestrogen based treatments, such as bisphosphonates, strontium ranelate or raloxifene, in these women.

A commonly adopted form of treatment is the combined oral contraceptive pill. The latter has the psychological benefit of being a treatment used by many of the patient’s peer group. There is a paucity of controlled trial data on how to base treatment decisions. Women with POF who take HRT may need a higher dose of oestrogen to control vasomotor symptoms than women in their fifties.

Some patients report persistent tiredness, lack of energy, reduced libido or sexual function despite apparently adequate doses of oestrogen replacement. This may be more common in oophorectomized women, and consideration should be given to additional treatment with testosterone. Testosterone implants may be provided along with oestrogen. 9
3. Fertility issues

The lifetime chance of spontaneous conception in women with karyotypically normal POF has been estimated at 5-15%, with the age of the patient at the time of diagnosis being an important determinant. Donor oocyte in vitro fertilization (IVF) is the treatment of choice for women with primary and secondary POF. Women with spontaneous, karyotypically normal POF have similar success rates to women who undergo conventional IVF.

Very few options are available for preventative therapy before radiotherapy and chemotherapy. Mature oocytes and ovarian tissue cannot be cryopreserved easily; however, successful pregnancies have been achieved. Cryopreservation of embryos may be possible before treatment - if time allows and fertility drugs are not contraindicated.

Summary practice points

- Women with a premature menopause should normally be offered HRT until the average age of the menopause (52)
- Hormone replacement therapy (HRT) or the combined oestrogen and progestogen contraceptive pill may be used
- Women with POF who take HRT may need a higher dose of oestrogen to control vasomotor symptoms than women in their fifties
- Consideration should be given to additional treatment with testosterone especially in oophorectomised women
- Women with karyotypically normal POF may conceive naturally
References

Leaflet Courtesy:

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