The specialist authority for menopause & post reproductive health

Induced menopause in women with endometriosis

Endometriosis and menopausal symptoms

Endometriosis is a common condition affecting women of reproductive age and can be very painful and debilitating. Women with endometriosis may be treated medically, surgically or with lifestyle changes to help control the symptoms and severity of the disease. Some of the treatment offered can induce a menopause-like state, leading to a variety of symptoms ranging in severity. There is evidence to suggest that providing women with information of what to expect can reduce their psychological and physical morbidity (NICE Quality Standards[1]).

Why does inducing a menopause help the symptoms of endometriosis?

Endometriosis can develop when deposits of endometrium exist outside the uterine cavity which can then be stimulated and bleed with every cycle. By suppressing the menstrual cycle, the symptoms may resolve. Inducing menopause will stop ovarian cyclical activity and hence cyclical stimulation of endometriotic deposits.

The methods of inducing menopause are:

- Gonadotrophin releasing hormone agonists: These downregulate the pituitary gland and lower estrogen levels to within the menopausal range. They induce amenorrhoea and often menopausal symptoms.
- Surgery involving bilateral oophorectomy. This may be with or without a hysterectomy but will permanently induce menopause. The loss of libido is often more marked with a surgically induced menopause.

Why is Hormone replacement therapy (HRT) important in managing women with an induced menopause?

- Women with an induced or surgical menopause due to endometriosis are usually younger women, below the age of natural menopause. The loss of estrogen can predispose them to osteoporosis and cardiovascular disease. HRT has been shown to be protective for both of these factors[2].
- Distressing symptoms such as vasomotor, cognitive and vaginal can be alleviated by adequate HRT.
- Lack of libido is caused by the low estrogen state and loss of testosterone particularly in women with a surgical menopause.

What are the key points of managing women with endometriosis who have induced menopause?

- Offer HRT to all women unless there is a specific contra-indication e.g. hormone sensitive Breast Cancer, and continue it until at least the age of natural menopause[3].
- Women with induced menopause or surgical menopause are often younger than the natural age of menopause and may be relatively uninformed about what to expect from menopause and therefore education is important.
- Recognise that sudden onset of menopausal symptoms can be very distressing and difficult to cope with.
- Giving add-back HRT for those women with pharmacologically induced menopause is important for bone and cardiovascular protection and should improve patient compliance[2].
- Younger women often need higher doses of estrogen to relieve their symptoms

- HRT is not a contraceptive and adequate contraception is still required. HRT can be provided with the combined oral contraceptive pill.
- Continuous combined estrogen/progesterone HRT regimes should be used for women with a uterus and this can include estrogen in conjunction with a Mirena IUS.
- For hysterectomised women with endometriosis it is advised that continuous combined HRT is started for at least the first few years after surgery and until the age of natural menopause. There is some evidence that oestrogen only HRT may increase the risk of recurrence of pain over time and also a very small risk of malignant transformation so for these reasons it may be safer to maintain patients on a continuous combined regime[3,5]. This may be changed later to estrogen alone due to a possible better safety profile in women over the age of natural menopause but this needs to be balanced with the theoretical risk of reactivation and malignant transformation of any residual endometriosis, which can occur many years later. A pragmatic approach assessing the degree of extra uterine disease at the time of hysterectomy may be used to guide practice.

What are the common symptoms women can experience in induced menopause?

The symptoms women experience are wide ranging but may include:

- Vasomotor symptoms including hot flushes and night sweats
- Musculoskeletal symptoms including joint and muscle pains
- Low or changed mood and loss of libido
- Memory loss and anxiety
- Urogenital symptoms including vaginal dryness and recurrent urinary tract infections
- Hair loss

What are the non-pharmacological options for management of symptoms of the menopause for women with induced menopause?

- Regular exercise
- Weight management
- Cognitive Behavioural Therapy

What are the pharmacological options for management of menopausal symptoms for women with induced menopause?

- HRT is the first line treatment for both women after surgical menopause and as add-back therapy for those women receiving medical therapy which induces menopause.
- The evidence is uncertain about how soon to start HRT after induced menopause. For those on GnRH analogues, clinicians are recommended to commence add-back HRT with the start of GnRH agonist therapy to prevent bone loss and hypo-estrogenic symptoms[3]. For those with a surgical menopause there is no clear consensus on the ideal interval to start hormonal therapy post surgery. A decision should be made after discussion with the patient regarding the risk of reactivation of the endometriosis versus the sudden onset of menopausal symptoms.
- Continuous Combined Estrogen/Progesterone HRT or Tibolone can be used for women regardless of whether they have had surgery to remove their womb or not[4].
- For women with low libido, Tibolone may be helpful as it provides estrogen, progestogen and some androgenic activity. An alternative may be to prescribe testosterone gel alongside continuous combined HRT.
- Women with vaginal symptoms such as dryness and dyspareunia may benefit from vaginal estrogen in the form of vaginal tablets or cream and these can be safely prescribed with or without concurrent systemic HRT. Vaginal DHEA can be used as an alternative in women in whom oestrogen is not optimally effective.
- Women may benefit from concurrent management of underlying depression or anxiety.
- Discuss with women that over the counter medications can help menopausal symptoms but safety is uncertain, and they can interact with other medications. They are unlikely to offer bone or cardiovascular protection[4].

Is there a risk of worsening endometriosis on add-back Hormone Replacement therapy?

The estrogen threshold theory suggests that add-back HRT therapy or HRT after removal of the ovaries contains a low enough dose of estrogen for maintenance of bone density and relief of hypoestrogenic and vasomotor symptoms but not enough to reactivate endometriosis.

Is there a risk of reactivating endometriosis after oophorectomy on HRT and is there a risk of reactivated endometriosis transforming into cancer?

There is little high-quality data to answer these questions so the absolute risk of disease reactivation and malignant transformation cannot be quantified[5] but it has occurred in the literature. However, a recent study reassuringly found no increased risk in malignant transformation after 6 years follow up between oestrogen only and combined HRT regimes.[8] Consensus opinion is that for women after oophorectomy with little or no residual disease, treatment with HRT brings no or little extra risk of endometriosis recurrence or ovarian cancer. For women with significant residual disease, benefits of HRT may outweigh the risks if the woman is less than 45 years old at the age of menopause or if symptoms are severe.[6]

Therefore, for women who still have their uterus continuous combined HRT or Tibolone should be prescribed. For hysterectomised women with very little or no residual disease, estrogen-only HRT could be considered after initial therapy with continuous combined HRT as it may have a better safety profile in women over the age of natural menopause but this decision must be made on a case by case basis.

If recurrence does occur these women should be referred to a specialist with an interest in menopause and investigated for malignant change if symptoms persist.

References

1. National Institute for Health and Care Excellence (NICE). Menopause Quality Standard [QS143].2017. Available from: https://www.nice.org.uk/guidance/qs143/chapter/Quality-statement-5-Information-for-women-having-treatment-likely-to-cause-menopause.
2. National Institute for Health and Care Excellence (NICE). Menopause. NG23. November 2015. Available from: https://www.nice.org.uk/guidance/ng23/chapter/Recommendations.
3. European Society of Human Reproduction and Embryology. Management of women with Endometriosis.2022. *Endometriosis guideline* (eshre.eu)
4. Moen M.H.; Rees M.; Brincat M.; Erel T.; Gambacciani M.; Lambrinoudaki I.; et al. EMAS position statement: Managing the menopause in women with a past history of endometriosis. *Maturitas*. Sep 2010; 67(1):94-97
5. Gemmell, L C; Webster, K E; Kirtley, S; Vincent, K; Zondervan, K T; Becker, C M. The management of menopause in women with a history of endometriosis: a systematic review. *Human reproduction update*. Jul 2017; 23(4):481-500
6. Rozenberg, S; Antoine, C; Vandromme, J; Fastrez, M. Should we abstain from treating women with endometriosis using menopausal hormone therapy, for fear of an increased ovarian cancer risk? *Climacteric*. 2015; 18(4);448-452
7. Simpson, P D; McLaren JS; Rymer, J; Morris, E P. Minimising menopausal side effects whilst treating endometriosis and fibroids. *Post Reproductive Health*. 2015; Volume:21 issue:1
8. Tanmahasamut P, M Rattanachaiyanont 1, K Techatraisak 1, S Indhavivadhana 1, T Wongwananuruk 1, P Chantrapanichkul. Menopausal hormonal therapy in surgically menopausal women with underlying endometriosis. *Climacteric*. 2022. 25(4):388-394

Authors: Rosamund Malhas and Lynne Robinson in collaboration with the medical advisory council of the British Menopause Society.

REVIEWED: AUGUST 2022
NEXT REVIEW DATE: AUGUST 2025

Q1P2223

www.womens-health-concern.org
Reg Charity No: 279651
Company Reg No: 1432023

www.thebms.org.uk
Reg Charity No: 1015144
Company Reg No: 02759439