

Menopausal symptoms in breast cancer survivors:

management update

Clinical Questions

What are the causes of menopausal symptoms after treatment for breast cancer?

What are the evidence-based options (hormonal and non-hormonal) for the management of menopausal symptoms in breast cancer survivors?

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MENOPAUSE IN BREAST CANCER SURVIVORS

The increasing incidence of breast cancer combined with improving survival means that women live with the effects of cancer and its treatment for many years. Menopausal symptoms are a significant issue in breast cancer survivors for several reasons. Women taking hormone replacement therapy (HRT) at the time of diagnosis are advised to cease treatment. The majority of breast cancers are oestrogen receptor (ER)-positive, so treatments to block the effects of oestrogen (such as oral endocrine therapy and ovarian suppression/ablation treatments) form an important part of management. In addition, premenopausal women frequently experience an early menopause as a result of chemotherapy.

Menopausal symptoms in this setting are similar in nature to those experienced at natural menopause, and can include; hot flushes, night sweats, vaginal symptoms, emotional upset, musculoskeletal symptoms, and sexual dysfunction. However, they may be more abrupt in onset and more persistent. Aromatase inhibitors have the additional side effects of osteoporosis and arthralgia, and a switch to tamoxifen may produce better tolerance. Genetic predispositions to severe symptoms are a focus of current research. As well as affecting quality of life, these issues can compromise adherence to endocrine therapies, thus putting patients whose side effects are poorly managed at increased risk of recurrence. Menopausal symptoms can adversely impact on self-esteem, body image, and sexual function.¹ Anxiety and depression can contribute to these issues and should be managed as in other women.

HORMONE REPLACEMENT THERAPY IN BREAST CANCER SURVIVORS

Two large trials (HABITS and Stockholm) reported inconsistent findings related to the

use of systemic HRT after breast cancer. The HABITS trial reported a threefold increase in the risk of new primary or recurrent breast cancers, while the Stockholm trial found no increased recurrence risk after 4 years of therapy.^{2–4} Debate exists over whether the difference in outcome was due to the different therapy regimens used, or chance. Regardless, the use of systemic oestrogen is not recommended in breast cancer survivors.^{2–4} The LIBERATE trial studied the use of tibolone to manage menopausal symptoms and showed an increased risk of recurrence within the intervention group. However, the study lacked the power to assess tibolone alone (without aromatase inhibitors) on risk of breast cancer recurrence.⁵ Other hormonal preparations such as progestins and androgens may play a role in managing menopausal symptoms, but require further investigation.^{6,7}

Local vaginal hormonal therapy for vaginal symptoms may be suitable in some situations. If simple moisturising/lubricating products are not providing relief, then oestriol vaginal cream Ovestin® (Organon) can be considered. Ovestin does not increase circulating oestradiol and therefore may be preferable to an oestradiol vaginal pessary Vagifem® (Novo Nordisk) in women with ER-positive cancer taking aromatase inhibitors, as increased levels of circulating oestradiol may theoretically interfere with their action.^{6,8}

NON-HORMONAL THERAPIES

Lifestyle can impact not only on menopausal symptoms, but also risk of cancer recurrence, general health, all cause mortality, and wellbeing. Maintaining a healthy body mass index (BMI), ceasing smoking, limiting alcohol intake, and exercising regularly can moderate flushes, may reduce the risk of osteoporosis, can provide relief from arthralgia, and may also directly reduce the risk of breast cancer recurrence.^{1,6,8–10}

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Box 1. Summary points

- Breast cancer survivors have many reasons for experiencing menopausal symptoms.
- Conventional menopausal therapies are often contraindicated following a diagnosis of breast cancer.
- A variety of options are available to manage symptoms of menopause in breast cancer survivors.
- Managing menopausal symptoms may improve quality of life and cancer therapy adherence and decrease the risk of tumour recurrence.

Many symptoms will improve in time, without intervention. Hot flushes tend to improve over time in post-menopausal women not taking endocrine therapy and many clinical trials have demonstrated a large placebo effect (up to 70%) with interventions for menopausal symptoms.⁸ Symptoms related to endocrine therapy tend to stabilise after 3 months of therapy so women experiencing menopausal symptoms after starting endocrine therapy should be encouraged to persevere with therapy, perhaps with a short treatment holiday.¹¹

Selective serotonin reuptake inhibitors (SSRIs) and selective noradrenaline reuptake inhibitors (SNRIs) may reduce the severity and frequency of hot flushes, but side effects of dry mouth, headache, nausea, and insomnia may be experienced.⁶ Some SSRIs interfere with tamoxifen therapy, and therefore venlafaxine and desvenlafaxine are preferred options for these women.¹²

Gabapentin and clonidine have been shown to reduce menopausal hot flushes in breast cancer patients, although both have potential side effects.⁸

Cognitive impairment is a common symptom experienced by the survivors of breast cancer treated with adjuvant therapies (particularly chemotherapy) and this effect may be exaggerated during treatment induced menopause.⁶ One study has shown that modafinil (an antiepileptic) improved cognitive performance in survivors of breast cancer.³

COMPLEMENTARY THERAPIES

Evidence is lacking to support the use of alternative therapies to manage

menopausal symptoms in women with a history of breast cancer. However, paced respiration, hypnotherapy, and acupuncture have demonstrated some beneficial effects.^{1,8} Black cohosh is believed to produce significant reduction in hot flushes, yet evidence is lacking and concerns exist following reports of liver failure.¹ To support bone mineral density (BMD), supplementation of vitamin D (which may also reduce bone pain) and calcium are important; Tai Chi and vibration exercises have also been shown to increase BMD.¹³ Group cognitive behavioural therapy may also have a role.¹⁴

CONCLUSION

Menopausal symptoms are common in women after breast cancer treatment and these can significantly impact on quality of life and compliance with therapy. In most cases, HRT is not recommended, however a range of other management options is available to improve menopausal symptoms in breast cancer survivors (see Box 1).

Provenance

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