Menopause management after breast cancer

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Increasing breast cancer incidence and decreasing mortality have highlighted the importance of survivorship issues related to breast cancer. Management of menopause in breast cancer survivors is complex and menopausal symptoms should be treated to enhance quality of life and long-term health.

Breast cancer is the most common cancer affecting women in Australia. It was estimated that 20,640 women would be diagnosed with breast cancer in 2022.[1] Despite the high incidence of breast cancer, survivorship is high. The most recent statistics show that the five-year relative survival rate for women diagnosed with breast cancer in in 2013 to 2017 was 92%.[2]

As the number of breast cancer survivors increases, menopause has become an increasingly important issue for women who have had a breast cancer diagnosis. Most women diagnosed with breast cancer are postmenopausal, as are most survivors.[3] Further, premenopausal women diagnosed with breast cancer often experience early menopause because of breast cancer treatments.[4]

Management of menopause in women after breast cancer is complex, and menopausal symptoms can negatively affect quality of life and have potential long-term health impacts. Menopause symptoms are often more severe after breast cancer treatment – especially in women who become postmenopausal as a result of their treatment – and due to a paucity of effective treatment options, since menopausal hormone therapy (MHT; formerly known as hormone replacement therapy or HRT) is usually contraindicated. Common problematic symptoms of menopause are broadly classified as vasomotor, genitourinary and sexual dysfunction, and mood symptoms. Osteoporosis and cardiovascular disease are potential longer-term consequences related to menopause.

A multidisciplinary approach including breast cancer specialists, and possibly a menopause specialist, with the GP overseeing – if they are comfortable treating the menopausal symptoms – is recommended for treating menopause in women after a breast cancer diagnosis.[5]

Causes of menopausal symptoms

In women who have had a past diagnosis of breast cancer, bothersome menopausal symptoms may be associated with:

- natural menopause occurring concurrently with a breast cancer diagnosis
- recurrence of menopausal symptoms after cessation of MHT when breast cancer is diagnosed
- chemotherapy
- endocrine adjuvant therapy with tamoxifen or aromatase inhibitors (AIs)
- ovarian suppression secondary to gonadotrophin-releasing hormone (GnRH) agonists in premenopausal women
- risk-reducing bilateral oophorectomy.

Most breast cancers are estrogen receptor (ER) positive and the use of endocrine adjuvant therapy, by inducing oestrogen deprivation, improves disease-free survival. Tamoxifen acts as an ER antagonist in breast tissue with partial agonist effects on the endometrium, bone and vagina. AIs inhibit conversion of androgens to oestrogens, thereby reducing serum estradiol levels

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to below those seen in healthy postmenopausal women (<20 pmol/L). Among premenopausal women on chemotherapy for breast cancer, amenorrhoea leading to menopause is induced in up to 80% and increased risk of permanent amenorrhoea is observed with older age, longer duration of treatment, type of chemotherapy regimen and tamoxifen use.

Symptoms

Multiple factors influence menopause symptomatology, including age, type of menopause, lifestyle, comorbidities, demographic characteristics and psychosocial factors. Thus, the individual menopause experience may vary widely.

Vasomotor symptoms are reported by up to 95% of breast cancer survivors and are more severe compared with those reported by women without cancer.[6] Genitourinary symptoms such as vaginal dryness occur commonly in women with breast cancer, with 50 to 75% of breast cancer survivors reporting one or more symptoms.[7] Sexual dysfunction is common in women with breast cancer, affecting up to 70% of breast cancer survivors.

Menopausal symptoms are more frequent and severe in younger women with treatment-induced menopause compared with older women with breast cancer.[6] However, it can be difficult to distinguish between the effects of breast cancer treatments (joint aches and muscle pains are common symptoms in women taking AIs), menopause and ageing.

Cardiovascular disease and osteoporosis risk

Cardiovascular disease (CVD) and breast cancer share risk factors such as obesity and inactivity, as well as increased incidence in women aged over 50 years.[3] Hypertension is the most common comorbidity across all age groups of breast cancer survivors, and affects up to 50% of those aged over 65 years. CVD is the third most common comorbidity across all age groups.[3]

Bone loss and fractures in women who have had a diagnosis of breast cancer may result from:

- direct or systemic effects of the tumour[5]
- oestrogen deprivation leading to induced early menopause secondary to breast cancer therapies (i.e. chemotherapy, ovarian ablation or AIs)
- natural menopause and/or other secondary causes of bone loss such as corticosteroids.

The highest rates of bone loss (7 to 8% per year at the lumbar spine) are observed in premenopausal women treated with chemotherapy or GnRH suppression plus AIs.[8]

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Case scenario

Maria is a 45-year-old premenopausal woman with no family history of breast cancer. She presents to her GP for her breast check and cervical screen and a left breast lump is found on examination, which she was unaware of.

A mammogram and ultrasound show a suspicious 1 cm lesion in the left breast. Biopsy specimens show an intraductal carcinoma that is ER positive, progesterone receptor positive and HER2 negative.

Maria undergoes wide local excision of her breast cancer. One sentinel node is removed, which is negative.

She is advised to undergo radiotherapy and then to take tamoxifen orally. After starting tamoxifen, her periods become irregular and she experiences hot flushes and sweats, which impact on her quality of life. She is tired, has aches and pains, loss of libido and dyspareunia. She feels anxious and depressed and is worried about a cancer recurrence.

Management approach

Evaluation of menopausal symptoms

A very clear history of the symptoms and their impact on Maria's quality of life is needed, including the type, frequency, severity and impact of symptoms, and she should be asked to prioritise which symptoms have the most impact on her quality of life. Likely causes and triggers of symptoms should be identified, as well as what Maria hopes for from the treatment intervention. Vasomotor, genitourinary and sexual dysfunction symptoms and mood symptoms such as anxiety, depression and fear of recurrence are treated individually (see management strategies for specific menopausal symptoms below). Maria can be further supported with psychological support and education and referral to websites that have evidence-based information.

Lifestyle modification

Lifestyle modifications that may improve symptoms can be recommended. As relevant, Maria should be encouraged to stop smoking, maintain a healthy weight, limit alcohol intake, eat healthily and undertake daily physical activity.

CVD risk assessment

Cardiac risk factors need to be identified, including smoking, family history, depression, physical inactivity, body mass index (BMI) and blood pressure. Diabetes and lipid status also need to be determined.

Osteoporosis risk assessment

It is important to also identify osteoporosis risk factors, including age, BMI of less than 20 kg/m^2, family history of hip fracture, personal history of fragility fracture, smoking or use of corticosteroids for more than six months. Adequate calcium and vitamin D levels should be ensured. If the woman has risk factors for osteoporosis, consider referring her for bone density scanning (dual-energy x-ray absorptiometry) to help in the decision-making process. (This will have

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already been performed if she is being treated with an aromatase inhibitor.)

Management strategies for specific menopausal symptoms

Vasomotor symptoms

Managing hot flushes and night sweats through lifestyle modification can be recommended. Dressing in layers and using fans and water sprays may help these symptoms.

Medication options include use of a selective serotonin reuptake inhibitor (SSRI; e.g. escitalopram) or a serotonin and noradrenaline reuptake inhibitor (SNRI; e.g. venlafaxine), gabapentin, clonidine or oxybutynin, all of which are used 'off label'. Review the patient after four to six weeks and if there is no effect or she cannot tolerate the medication, then change to another nonhormonal agent. If there is still intolerance or no effect then discuss changing or suspending adjuvant therapy with the oncology team.

Note that some nonhormonal treatments with some SSRIs (fluoxetine and sertraline, but particularly paroxetine) should not be used with tamoxifen. It is possible to use a combination of an antidepressant and gabapentin if necessary for control of symptoms. These therapies usually provide a symptom response within four weeks. Nonpharmacological interventions such as cognitive behavioural therapy and hypnotherapy can also be considered. Current safety data do not support the use of MHT in breast cancer survivors. Only after all other options have failed, and after counselling and discussion with the woman's breast treatment team, a trial of MHT might be considered.

Genitourinary symptoms

Genitourinary symptoms can include vaginal dryness, loss of lubrication during sex, pain with sex, urinary urgency, urge incontinence and recurrent urinary infections. Lifestyle changes can be encouraged, including stopping smoking, addressing perineal hygiene and, if sexually active, regular sex. Regular use of vaginal moisturiser should be recommended.

If genitourinary symptoms persist, then consider a trial of vaginal estriol or estradiol preparation, or changing adjuvant therapy after consultation with the breast cancer team. Any dermatological problem or infection should be excluded and regular use of lubricant with vaginal intercourse encouraged.[9] Vaginal laser treatment has been promoted for vaginal dryness, but the studies at present are only short term and not placebo controlled.

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Sexual dysfunction

If Maria's sexual function is impaired, the pelvic floor should be examined for pain and tenderness. Consider referral to a pelvic floor physiotherapist for dyspareunia and overactive pelvic floor, and use of a vaginal dilator. Medications that are having a negative impact on sexual function need to be identified and changed. If necessary, refer Maria for psychosocial intervention, including couple counselling, sexual counselling, cognitive behavioural therapy and education from evidence-based websites.

Mood symptoms

Adjusting to the diagnosis of breast cancer as well as experiencing all of the treatments is often traumatic. When menopause occurs as a consequence of the treatments, dealing with menopause symptoms can be overwhelming and may lead to anxiety, mood swings and depression. Referral to a psychologist or counsellor may be helpful.

Conclusion

Increasing breast cancer incidence and decreasing mortality have highlighted the importance of survivorship issues related to breast cancer. Management of menopause in breast cancer survivors is complex and a multidisciplinary approach is considered the best approach for the successful management of vasomotor, genitourinary and sexual dysfunction symptoms, and prevention of osteoporosis and cardiovascular disease. Management of menopausal symptoms involves evaluation, individualised treatment of specific symptoms, psychological support and education. Lifestyle modification may help both symptoms and the longer-term consequences of menopause. MT

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