Does a Multidisciplinary Menopausal Symptoms after Cancer Clinic Reduce Symptoms?

Jade Hollingworth (jade.hollingworth@health.wa.gov.au)
King Edward Memorial Hospital
Lucy Walsh
King Edward Memorial Hospital
Stephanie Tran
University of Western Australia Medical School
Lesley Ramage
King Edward Memorial Hospital
Shavita Patel-Brown
King Edward Memorial Hospital
Manju Ambekar
King Edward Memorial Hospital
Jane Weeks
King Edward Memorial Hospital
Lucy Williams
King Edward Memorial Hospital
Paul A. Cohen
Saint John of God Hospital Subiaco

Research Article

Keywords: menopausal symptoms after cancer, cancer survivors, multidisciplinary care

Posted Date: June 21st, 2021

DOI: https://doi.org/10.21203/rs.3.rs-552369/v1

Abstract

Purpose

This study aimed to measure the prevalence of menopausal symptoms in patients attending a multidisciplinary model of care clinic at their initial clinic visit and their subsequent follow-up consultation using a validated patient reported outcome measure to assess whether menopausal symptoms after cancer had improved.

Methods

A retrospective review was conducted of patients attending the clinic in a 12-month period in 2017 (n=189). Recorded variables included patient demographics, details of index cancer, previous treatments and menopausal symptom management strategies. Severity of menopausal symptoms was evaluated using the Greene Climacteric Scale. The extent to which patients were bothered by symptoms were combined into two categories and dichotomized (present/absent). Differences in symptom prevalence between the initial consultation and first follow-up visit were examined using McNemar's Test.

Results

The majority of patients attending the clinic had a history of breast cancer (72%). 55% of patients were prescribed a non-hormonal therapy at their initial visit, most commonly gabapentin. Significantly fewer patients reported being bothered by hot flushes, fatigue, sleep difficulties and loss of interest in sex, anxiety or troubles concentrating at the first follow-up visit compared to their initial consultation ($p < 0.01$).

Conclusion

In this study there was an improvement in self-reported menopausal symptoms in a significant proportion of cancer survivors attending a multidisciplinary menopause clinic between their initial and first subsequent follow-up consultations.

Introduction

Menopause is marked by irregular menstrual cycles, hormonal changes and is often accompanied by vasomotor symptoms, sleep and mood disturbances, and changes in sexual desire and function. In Australia, almost a third of women will consult a doctor regarding symptoms of menopause [1]. Although not all women are bothered by symptoms of menopause, those with severe symptoms report significant impacts on their quality of life [2]. The symptoms of menopause in patients with a history of cancer are often more severe, owing to the nature and sudden onset of menopause, the need to abruptly cease menopausal hormone therapy (MHT) or the need for ongoing endocrine therapy if indicated. In a study of more than 500 women with a history of breast cancer, more than 60% of survivors had moderate to severe menopausal symptoms affecting both their and their partner's quality of life. The same study

showed that quality of sleep and decreased libido were also problematic in more than 50% of women [3]. Symptom severity can also contribute to poor compliance with prescribed endocrine treatment used to prevent cancer recurrence [4, 5].

Breast cancer is the most common cancer in women worldwide with more than 2 million new diagnoses annually [6]. In Australia, it is estimated that 19,807 women were diagnosed with breast cancer in 2020 [7] and 20–30% are pre-menopausal. Standard treatment (including chemotherapy, radiotherapy, concomitant oophorectomy and/or anti estrogenic endocrine treatment) often results in either early menopause or the exacerbation of pre-existing or previously controlled menopausal symptoms. The Australian Menopause Society states that hormone replacement therapy should be avoided in patients with a history of breast cancer due to the associated risk of new or recurrent cancer [8]. This recommendation is primarily based upon the results of a large randomized control trial that was stopped early in 2003, when an interim safety analysis demonstrated an increased risk of breast cancer recurrence in the MHT arm compared to placebo [9]. With advances in diagnosis and treatment resulting in improved 5-year survival, the number of breast cancer survivors is increasing, translating to a significant quality of life issue for many women [7].

The mainstay of management of menopausal symptoms in women with a history of breast cancer, and other estrogen-sensitive malignancies including endometrioid and low grade serous ovarian carcinomas, advanced endometrial adenocarcinomas and leimyosarcomas, includes lifestyle changes, cognitive behavioral therapy (CBT) and non-hormonal medications such as selective serotonin reuptake inhibitors (SSRI), selective noradrenaline reuptake inhibitors (SNRI), clonidine and gabapentin. A unique multidisciplinary model of care clinic - the Menopause Symptoms After Cancer (MSAC) Clinic - was developed at a tertiary women's hospital in Western Australia in 2003, and has been replicated throughout Australia and internationally [3]. Women attending the MSAC Clinic receive evidence-based information regarding non-pharmacological and non-hormonal treatments. However, there is limited evidence that such multidisciplinary care improves symptoms, patient satisfaction and quality of life [10]. The aim of the current study was to measure the prevalence of menopausal symptoms at patients' initial clinic visit and their subsequent follow-up consultation using a validated patient reported outcome measure, the Greene Climacteric Scale, to assess whether menopausal symptoms had improved.

Methods

A retrospective review was conducted of patients attending the MSAC Clinic at King Edward Memorial Hospital, Perth, Western Australia, between 1 January 2017 to 31 December 2017. Inclusion criteria were patients referred with menopausal symptoms and a history of malignancy. Patients that had attended the MSAC Clinic for an initial consultation prior to 1 January 2017 were excluded. Cases were ascertained from clinic appointment lists in the patient administration system WebPAS, and data were extracted from individual patient medical records and entered into a Microsoft Excel database for analysis.

The MSAC Clinic

The MSAC Clinic at this stand-alone tertiary women's hospital, which was started as the first of its kind in 2003, now seeing almost 200 new patients per year. There is a diverse range of patients with regards to the index cancer responsible for each patient's referral, with the most common being breast cancer patients which represent just over 70% of the clinic's population.

Patients at their initial consultation are seen by either a gynecologist or specialist Family Practitioner (FP) as well as a clinical nurse specialist. Patients are asked to fill in the Greene Climacteric Scale individually at each clinic visit which provides crucial guidance for areas in need of immediate management. Follow-up visits are based upon what management strategies have been implemented at the visit and the expected time for a change in symptoms to be evident, as well as severity of symptoms as experienced by the patient. Any patient who is commenced on a new medication is contacted via phone by the clinical nurse specialist within 2–4 weeks of this initial review.

In line with the multidisciplinary model of the clinic, there is involvement in patient care by a range of health care professionals including women's health physiotherapists, dieticians, clinical psychologists and sexual counselors. Care can also be coordinated between the clinic team and their colleagues in genetic counseling and endocrinology. The multidisciplinary team meet on a monthly basis to discuss specific cases and management plans, often for those patients with severe and/or refractory symptoms.

Variables

Variables recorded included patient age, cause of menopause (natural menopause prior to cancer diagnosis, surgical, chemotherapy or radiation induced menopause), referral source, details of index cancer, prior use of MHT, time since cancer diagnosis, time since referral to the clinic and initial consultation, current medication including endocrine therapy, management prior to referral and management instituted at the initial clinic visit. The Greene Climacteric Scale was used to evaluate climacteric symptoms and is composed of 21 items that evaluate vasomotor symptoms (two items), anxiety (six items), depression (five items), somatic symptoms (seven items) and sexuality (one item). For vasomotor symptoms the two questions were 'to what extent are you bothered by hot flushes?' and 'to what extend are you bothered by night sweats?' All items have four options that range from not at all (0), a little (1), quite a bit (2), to extremely (3) [11].

Statistical Analysis

Data were analysed using SPSS version 26 (IBM Corp., Armonk, N.Y., USA) with an alpha of .01 considered statistically significant. Categorical variables were described using frequency and percent, with missing data noted. Continuous scale variables were described using mean, median and standard deviation. The extent to which patients were bothered by symptoms 'quite a bit' and 'extremely' were combined into one category and dichotomized (present/absent). Differences in symptom prevalence between the initial MSAC consultation and first follow-up visit were examined using McNemar's Test.

Results

General

Between 1 January and 31 December 2017, 189 patients were seen for their initial consultation at the MSAC Clinic. The majority of patients (n = 136, 72%) had a history of breast cancer. Other cancers included; uterine, cervical, ovarian, haematological and colorectal, as detailed in Table 1.

Patient characteristics including age, marital and employment status and geographical location are demonstrated in Table 1. The mean age was 50 years (range, 24–81 years). Most new referrals came from gynecological oncologists (26.5%), oncology nurses (23.8%) and medical oncologists (16.9%) with FPs responsible for 10% of the referrals. Most patients (69.3%) were seen between 2 and 6 months from the time their referral was received, with only 2.6% of patients waiting more than 6 months for their initial consultation.

Menopause and Pre-existing Symptoms

Two-thirds of patients were postmenopausal at the time of their cancer diagnosis. The distribution between natural onset, chemotherapy-induced and surgically-induced was similar amongst the 3 groups (30.7%, 25.9%, 29.6% respectively). Most patients attended the clinic for the first time within 1 year of the cancer diagnosis (72.5%) with only 2.1% of patients being distant from their diagnosis by more 10 years. The majority of patients (75.1%) had never used MHT before, with a small proportion of patients (6.9%) reporting ongoing use of MHT. The remainder had ceased MHT prior to review, reporting ‘past use’. Over half (51.2%) of patients were taking an aromatase inhibitor (most commonly letrozole), whilst 8.5% were taking Tamoxifen.

The five most troublesome symptoms reported by women who completed the Greene Climacteric Scale were hot flushes, fatigue, difficulty sleeping, night sweats and loss of interest in sex (Table 2). More than 50% of patients were bothered by these symptoms ‘quite a bit’ or ‘extremely’. These symptoms were all present in more than 50% of patients (range 51.3 to 68.3%). Vaginal dryness was reported as ‘quite a bit’ or ‘extremely’ bothersome in 45.8% of patients, with cognitive and mood symptoms such as anxiety, irritability and difficulty concentrating having the same ratings in more than 30% of patients.

Symptom Management and Multidisciplinary Care

28% of patients were either already taking or had previously tried a systemic non-hormonal therapy (NHT) such as gabapentin, venlafaxine or clonidine and 55% of patients were commenced on a NHT at the initial visit, most commonly gabapentin (24.3%) followed by venlafaxine (13.2%). Non-hormonal vaginal moisturiser was recommended three times more often than topical vaginal estrogen, which was prescribed in 5.8% of patients (See Table 3).

Information regarding lifestyle modifications that may contribute to improved quality of life was provided to almost one third of patients (n = 56, 30.6%). This included advice regarding dietary changes, referral to an exercise program or information on the utility of CBT, mindfulness or acupuncture. 32% of patients

were referred to an allied health professional, mostly commonly a clinical psychologist (14.8%) or women's health physiotherapist (13.2%).

Complete data were available for 124 patients detailing severity of symptoms, as per the Greene Climacteric Scale, who attended both an initial consultation and a first follow-up visit. Fewer patients reported being bothered by hot flushes, fatigue, sleep difficulties and loss of interest in sex, anxiety or troubles concentrating at the first follow-up visit compared to their initial consultation ($p < 0.01$) (Table 4). Incomplete data was most often attributed to a failure of the patient to attend a face-to-face follow-up visit (n = 60, 92.3%). 31 of these followed up via telephone consult with the remaining 29 were not reviewed after their initial consultation. 3 patients had not completed the questionnaire at the initial consult and so no data was available for comparison, and only 2 patients who attended a face-to-face appointment who had filled in the questionnaire at their first visit, did not complete it at the first follow-up visit.

Discussion

Menopausal symptoms after cancer can have a significant impact on quality of life and may be more severe than after natural menopause [2, 5]. With the increasing incidence of cancer and improved survival rates, women in this situation represent an important population where the approach to symptoms needs to be coordinated, holistic and provided by an informed practitioner due to the need for avoidance of MHT in patients with estrogen sensitive cancers, and because of the multifaceted causes of such symptoms.

Symptom Management

Non-hormonal pharmacological and non-pharmacological therapies, in combination with lifestyle changes, are the mainstay of management in women with troublesome menopausal symptoms where MHT is contraindicated. Several studies have demonstrated that SSRIs and venlafaxine are effective in reducing the severity of hot flushes in this population [12, 13]. Purpose-designed CBT, hypnotherapy and acupuncture all show promising improvement in a range of symptoms including the severity and impact of hot flushes, quality of sleep and even sexual function [14, 15, 16].

Current clinical guidelines suggest the following for the management of vasomotor symptoms and sleep disturbance; SSRIs, SNRIs, gabapentin in combination with CBT, acupuncture and hypnotherapy. The basis of these recommendations is the suggestion of benefit, without increasing the risk of new or recurrent malignancy [7]. Gabapentin was the most commonly prescribed non-hormonal pharmacological therapy (prescribed to 24% of patients), followed by venlafaxine which was prescribed in 13% of patients. Guidelines advise against the use of both vitamin E and isoflavones for sleep disturbance due to the lack of evidence of any benefit [8]. In keeping with this the recommendation of vitamin E supplementation is uncommon, occurring in only 1.6% of patients.

Symptom Improvement

Not all patients who attended the initial consultation attended for a follow-up visit, however there was complete data available for 124 patients who attended and completed the Greene Climacteric Scale on both occasions. Unsurprisingly, the most commonly troublesome complaints were vasomotor symptoms including hot flushes and night sweats. This subset of patients demonstrated a clear and statistically significant improvement in the top 4 most bothersome symptoms when their self-assessment was compared ($p < 0.01$). Approximately 17% of patients reported improvement of hot flushes, sleeping difficulties and fatigue from ‘quite a bit’ and ‘extremely’ to ‘not at all’ or ‘a little’ (Table 4). Both anxiety and difficulty concentrating were also significantly improved at first follow-up visit. Although it did not reach statistical significance, improvement was also demonstrated in many other menopausal symptoms including irritability, muscle and joint pains and sexual function (loss of interest in sex and vaginal dryness).

Limitations

The study has important limitations that should be acknowledged including its retrospective design which has inherent selection bias. Data collection is limited by the quality and accuracy of record keeping. The study design prohibited the ability to control for confounding factors that may be have been associated with menopausal symptoms. A number of patients were lost to follow up, and missing data for these patients could not be included in the analysis, which may have biased the study’s findings. Data collectors were not blinded to the aims of this study and so presents another opportunity for bias to affect results. Further, the small sample size and heterogeneous patient population limits generalizability to larger patient populations in alternate settings.

Conclusion

In this study there was an improvement in self-reported menopausal symptoms in a significant proportion of cancer survivors attending a multidisciplinary menopause clinic between their initial and first subsequent follow-up consultations. Further research to investigate symptom prevalence beyond the first follow-up visit and assessment of specific non-hormonal pharmacological and non-pharmacological therapies, and their combinations, is warranted.

Declarations

Funding:

None

Conflicts of interest/Competing interests:

None

Availability of data and material:

Available on request

Code availability:

NA

Authors contributions:

Jade Hollingworth; substantial contribution to the conception and design, acquisition of data, drafted the work and approved the version to be published

Lucy Walsh, Stephanie Tran; substantial contribution to the acquisition of data, revised the work critically and approved the version to be published

Lesley Ramage, Manju Ambekar, Jane Weeks, Lucy Williams; substantial contribution to the conception of the work, revised the work critically and approved the version to be published

Shavita Patel-Brown; substantial contribution to the acquisition of data, revised the work critically and approved the version to be published

Paul Cohen; substantial contribution to the conception and design, interpretation of data, revised the work critically and approved the version to be published

Ethics approval:

Ethical approval for the study was granted by the Womens and Newborns Health Service Ethics Committee (Reference 27240, approved 6 June 2019).

Consent to participate:

The study was deemed low risk to participants and a waiver of consent was granted in accordance with the Australian National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018; accessed 19 October 2020).

Consent to publish:

Yes

References

1. Guthrie JR, Dennerstien L, Taffe JR, Donnelly V (2003) Health care-seeking for menopausal problems. Climacteric 6(2):112–117
2. Whiteley J, daCosta DiBonaventura M, Wagner J, Jose Alvir BS, Shah S (2013) The Impact of Menopausal Symptoms on Quality of Life, Productivity and Economic Outcomes. J Womens Health. https://doi.org/10.1089/jwh.2012.3719
3. Hickey M, Emery LI, Gregson J, Doherty DA, Saunders CM (2010) The multidisciplinary management of menopausal symptoms after breast cancer: a unique model. Menopause. https://doi.org/10.1097/gme.0b013e3181d672f6
4. Kligman L, Younus J (2010) Management of hot flashes in women with breast cancer. Curr Oncol. https://doi.org/10.3747/co.v17i1.473
5. Gupta P, Sturdee W, Palin SL et al (2006) Menopausal symptoms in women treated for breast cancer: the prevalence and severity of symptoms and their perceived effects on quality of life. Climacteric 9:49–58
6. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A (2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. https://doi/10.3322/caac.21492
7. Cancer Australia (2020) Breast cancer in Australia statistics. Australian Government. https://www.canceraustralia.gov.au/affected-cancer/cancer-types/breast-cancer/breast-cancer-australia-statistics. Accessed 12 December 2020
8. Cancer Australia (2016) Management of menopausal symptoms in women with a history of breast cancer. Australian Government. https://www.canceraustralia.gov.au/publications-and-resources/clinical-practice-guidelines/menopausal-guidelines/clinical-practice-recommendations-and-practice-points#_RECPP_31. Accessed 10 January 2021
9. Holmberg L, Anderson H (2004) HABITS (hormonal replacement therapy after breast cancer – is it safe?), a randomised comparison: trial stopped. Lancet. https://doi.org/10.1016/S0140-6736(04)15493-7
10. Fleissig A, Jenkins V, Catt S, Fallowfield L (2006) Multidisciplinary teams in cancer care: are they effective in the UK? Lancet. https://doi.org/10.1016/S1470-2045(06)70940-8
11. Greene J (1998) Constructing a standard climacteric scale. Maturitas. https://doi.org/10.1016/s0378-5122(98)00025-5
12. Shams T, Firwana B, Habib F et al (2014) SSRIs for hot flashes: a systematic review and meta-analysis of randomized trials. J Gen Inter Med. https://doi.org/ 10.1007/s11606-013-2535-9
13. Guthrie KA, La Croix AZ, Ensrud KE et al (2015) Pooled analysis of six pharmacologic and nonpharmacologic interventions for vasomotor symptoms. Obstet Gynecol. https://doi.org/ 10.1097/AOG.0000000000000927

14. Mann E, Smith MJ, Hellier J et al (2012) Cognitive behavioural treatment for women who have menopausal symptoms after breast cancer treatment (MENOS 1): a randomised controlled trial. Lancet Oncol. https://doi.org/ 10.1016/S1470-2045(11)70364-3
15. Hervik J, Mjaland O (2009) Acupuncture for the treatment of hot flashes in breast cancer patients, a randomized, controlled trial. Breast Cancer Res Treat. https://doi.org/ 10.1007/s10549-008-0210-3
16. Elkins G, Marcus J, Stearns V et al (2008) Randomized trial of a hypnosis intervention for treatment of hot flashes among breast cancer survivors. J Clin Oncol. https://doi.org/ 10.1200/JCO.2008.16.6389

Tables

Table 1

Patient characteristics (n = 189)

	N	%
Age (years)		
Mean	50.05	
Median	49	
Range	24-81	
Menopause status at time of cancer diagnosis		
Premenopausal	26	13.8
Perimenopausal	36	19.0
Postmenopausal	126	66.7
Missing data	1	0.5
Cause of menopause		
Natural menopause	58	30.7
Surgical menopause	56	29.6
Chemotherapy induced	49	25.9
Radiation induced	4	2.1
Other treatments	9	4.8
Unknown	7	3.7
Pre-menopausal	6	3.2
Referral source		
Gynecological Oncologist	50	26.5
Oncology Nurse	45	23.8
Medical Oncologist	32	16.9
Family Practitioner	19	10.1
Surgeon	18	9.5
Radiation Oncologist	10	5.3
Other	15	7.9
Index malignancy		
Breast	136	72.0
Endometrium/uterus	15	7.9
Uterine cervix	13	6.9

Ovary	8	4.2
Other gynecological	1	0.5
Haematological	7	3.7
Colorectal	6	3.2
Other	3	1.6
MHT* use		
Never use	142	75.1
Prior use	34	18.0
Current use	13	6.9
Time since cancer treatment		
<1 year	137	72.5
1 - <2 years	21	11.1
2 - <5 years	21	11.1
5 - <10 years	6	3.2
>10 years	4	2.1
Endocrine therapy		
None	59	31.2
Aromatase inhibitor	97	51.2
Tamoxifen	16	8.5
Bilateral oophorectomy	9	4.8
Goserelin	8	4.2
Time from referral to initial MSAC consultation**		
< 2 months	53	28.0
2 – 6 months	131	69.3
> 6 months	5	2.6
*MHT = Menopausal hormone therapy, **MSAC = Menopause symptoms after cancer		

Table 2

Ten most frequently reported symptoms (the extent to which patients were bothered ‘quite a bit’ and ‘extremely’ combined) at initial MSAC consultation (n = 179)

Symptom	N	%
Hot flushes	129	72.1
Fatigue	115	64.2
Difficulty sleeping	112	62.6
Sweating at night	110	61.5
Loss of interest in sex	97	54.2
Muscle and joint pains	93	52.0
Vaginal dryness	82	45.8
Anxiety	66	36.9
Difficulty concentrating	65	36.3
Irritability	61	34.1

Table 3

Management at initial MSAC consultation (n = 189)

	N	%
Prescribed non-hormonal therapies		
Gabapentin	46	24.3
Venlafaxine	25	13.2
SSRIs*	19	10.0
Clonidine	9	4.8
Vitamin E	3	1.6
Melatonin	2	1.0
Topical vaginal moisturiser	36	19.0
Prescribed MHT**		
Systemic estrogen	27	14.3
Topical vaginal estrogen	11	5.8
Information		
Osteoporosis & bone health	60	31.7
Diet	48	25.4
Mindfulness Meditation	16	8.5
Avoidance of bioidenticals	17	9
CBT	9	4.8
Acupuncture	5	2.6
Referrals		
Exercise program	47	24.9
Clinical psychologist	28	14.8
Physiotherapist	25	13.2
Sexual counselor	15	7.9
Dietitian	9	4.8
Urogynecologist	7	3.7
Endocrinologist	4	2.1
Psychiatrist	4	2.1

*SSRIs = Selective serotonin reuptake inhibitors, **MHT = Menopausal hormone therapy

Table 4

Ten most frequently reported symptoms (the extent to which patients were bothered ‘quite a bit’ and ‘extremely’ combined) in 124 patients for whom complete data were available and who attended both an initial MSAC consultation and first follow-up visit (n = 124)

Symptom	Initial consult N (%)	First follow-up N (%)	Δ symptoms N (%)	P value*
Hot flushes	90 (72.6)	69 (55.6)	21 (17.0)	**0.001**
Fatigue	83 (66.9)	61 (49.2)	22 (17.7)	**0.001**
Difficulty sleeping	78 (62.9)	58 (46.8)	20 (16.1)	**0.002**
Sweating at night	78 (62.9)	62 (50.0)	16 (12.9)	**0.009**
Loss of interest in sex	66 (53.2)	57 (46.0)	9 (7.2)	0.108
Muscle and joint pains	67 (54.0)	60 (48.4)	7 (5.6)	0.311
Vaginal dryness	55 (44.4)	44 (35.5)	11 (8.9)	0.035
Anxiety	44 (35.5)	27 (21.8)	17 (13.7)	**0.002**
Difficulty concentrating	50 (40.3)	33 (26.6)	17 (13.7)	**0.005**
Irritability	41 (33.1)	28 (22.6)	13 (10.5)	0.041
*McNemar Test, significance set at $p < 0.01$				