Cognitive behavioral therapy (CBT) and physical exercise (PE) for climacteric symptoms in breast cancer patients experiencing treatment-induced menopause: a multicenter randomized trial (EVA project).

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23475

Source
Nationaal Trial Register

Brief title
EVA Project

Health condition

1. Menopausal symptoms;

2. vasomotor symptoms;

3. urinary symptoms;

4. quality of life;

5. sexuality;

6. body- and self image;

7. psychological distress.

(NLD: menopauzale symptomen, vasomotorische symptomen, urinaire symptomen, kwaliteit van leven, seksualiteit, lichaams- en zelfbeeld, psychische klachten).

Sponsors and support

Primary sponsor: KWF Kanker Bestrijding
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Intervention

Outcome measures

Primary outcome

1. Menopausal symptoms;

2. vasomotor symptoms.

Secondary outcome

1. Urinary symptoms;

2. Sexuality;

3. Body- and self image;

4. Quality of life;

5. Psychological distress.

Study description

Background summary

Background:

Breast cancer is the most common form of cancer among women in the Netherlands. Approximately 11,000 women are diagnosed with breast cancer annually, of whom about 30% are below 50 years of age. Premenopausal women with breast cancer treated with chemotherapy or hormonal therapy may experience a premature onset of the menopause. Estrogen deficiency following adjuvant treatments leads to primary endocrine symptoms, including vasomotor and urogenital problems. Secondary symptoms include insomnia due to night sweats, dyspareunia due to vaginal dryness, weight gain, and psychological distress. The symptoms resulting from accelerated estrogen withdrawal can be pronounced and severe, and may adversely affect women's sexual functioning, body image, and overall HRQL. Healthy women who enter natural menopause are often prescribed hormone replacement therapy (HRT) to alleviate vasomotor and sexual symptoms. However, due to possible tumor-promoting effects, HRT is contraindicated for patients with a history of breast cancer. For these women, non-hormonal medications are frequently prescribed to treat vasomotor symptoms. Although these medications have been shown to yield moderate symptom relief, they also have a number of bothersome side effects. To alleviate urogenital symptoms, local vaginal moisturizing or estrogen cream is often prescribed. There is growing evidence that cognitive behavioral therapy (CBT) including relaxation techniques, and physical exercise may effectively reduce vasomotor symptoms in naturally occurring menopause. CBT and relaxation techniques are aimed primarily at the modification of precipitants of hot flushes and at stress management. Physical exercise on a regular basis affects neurotransmitters, which regulate central thermoregulation.

Purpose:

The proposed study will evaluate the efficacy of a supportive intervention program in alleviating menopausal symptoms, improving sexual functioning and enhancing the quality of life of younger women (< 50 years) with breast cancer who have become prematurely menopausal as a result of their treatment. Specifically, the study will evaluate CBT including relaxation (A), physical exercise (B), and a combination of A and B.

Plan of investigation:

This multicenter study will employ a prospective, full-factorial design. In total, 325 consenting women will be randomized to group A, group B, group AB or a usual care, 'waiting list' control

group (N = 81-81 per group). Upon completion of the study, the patients assigned to the control group will be given the opportunity to undergo either the A or B intervention program. The program will begin with a structured assessment of the target symptoms: hot flushes, night sweating and vaginal dryness. The overriding goal of the intervention is to provide symptomatic women with information skills and support to manage their symptoms more effectively. For group A, the intervention will consist of 6 weekly group CBT sessions of 1.5 hours, of 15 minutes of daily homework and a booster session at 3 months. The CBT will focus on understanding and self-control of menopausal symptoms. Relaxation techniques (paced respiration and muscle relaxation) will focus on the reduction of sympathetic nervous system activity, and are expected to have a positive impact on the frequency and intensity of hot flushes. For group B, the intervention will be an individually tailored, 12 week home-based physical exercise program of 2.5-3 hours per week, with instructions provided in-clinic on 2 occasions, and telephone support on 2 additional, interim occasions. The physical exercise program is intended to enhance fitness levels, in general, and to improve thermoregulation specifically related to hot flushes. Group AB will receive both the CBT and exercise program elements. Women allocated to the intervention groups will be asked to complete a battery of questionnaires assessing menopausal symptoms (the primary outcome), sexuality, body- and self-image, psychological distress and generic HRQL prior to the start of the program (baseline, T0), at 12 weeks (T1) and at 6 months follow-up (T2). Women allocated to the control group will complete the same questionnaire battery at parallel points in time.

Results/ relevance:

If demonstrated to be effective, the availability of a structured supportive intervention program (modules A, B or AB) will be a welcome addition to regular medical care offered to breast cancer patients with treatment-induced menopause. It is anticipated that such a program will have direct benefit in terms of symptoms relief and the improvement of patients' HRQL.

Study objective

1. Women in the CBT group, the PE group or the combined CBT-PE group (groups A, B and AB) will report significantly greater reduction from baseline to 3 and 6 month follow-up in overall levels of menopausal symptoms than patients in a usual care, waiting list control group, as assessed by the FACT-ES Scale and the Hot Flush Rating Scale;

2. Women participating in the combined intervention (Group AB) will report significantly greater reduction in overall levels of menopausal symptoms from baseline to 3 and 6 month follow-up than those participating in the CBT only or in the PE only groups. Due to different mechanisms of action, we expect that the combined modalities will be more effective than either modality alone. CBT is expected to lead to significant reductions in menopausal symptoms via cognitive restructuring and stress management, while PE is expected to impact primarily on metabolism of neurotransmitters responsible for thermoregulation;

3. Women exposed to the interventions (groups A, B and AB) will report significantly more improvement in sexual functioning, body- and self-image, psychological distress, and generic HRQL than those in the control group. We also hypothesize that women undergoing the PE program, including pelvic floor exercises (groups B and AB) will report greater improvement in urinary control from baseline to 3 and 6 month follow-up than women receiving CBT only or patients in the control group. However, given the low prevalence of urinary incontinence in this relatively young population, the study will not have sufficient power to demonstrate statistical significance. Nevertheless, we feel that is appropriate to provide pelvic floor exercises to women with urinary symptoms.

Study design

T0;

T1 at 12 weeks follow-up;

T2 at 6 months follow-up.

Intervention

Group A: CBT and relaxation. The CBT and relaxation training will consist of 6 weekly group sessions (with 8-10 participants per group) of approximately 1.5 hours duration. It will also include ¡®homework¡¯ assignments (e.g., keeping a daily diary to monitor symptoms and their precipitants). The CBT program is based on the work of Hunter & Liao. 41 It comprises the following elements: (1) information and advice about symptoms (e.g., hot flushes, night sweats and sexual functioning); (2) monitoring and modifying precipitants; (3) relaxation and stress reduction; (4) cognitive restructuring of unhelpful thoughts, elicited by group discussion; and (5) encouraging helpful behavioral strategies (e.g., pacing activities). The primary focus of the CBT will be on hot flushes and night sweats, but other symptoms (e.g., vaginal dryness), sexuality, body- and self-image, and mood disturbance will also be addressed. Relaxation will be demonstrated and practiced during each session and a tape will be provided for practicing at home. A ¡°booster¡± session will be held at 3 months. The CBT will be delivered by a social worker (intake; sessions 1-6), a nurse practitioner (part of session 1), and a psychologist/sexologist (part of sessions 5 and 6). Training of the health care providers will be provided on-site by Dr. Hunter.

Group B: Physical exercise program. The physical exercise program will include 4 individual contacts with a physiotherapist (one in-clinic intake of 30-45 minutes, two 15-minute telephone contacts, and a final 30-minute in-clinic session). Its core will be an individually tailored, home-based and self-directed physical exercise program 2.5-3 hours per week for 12 weeks and, where indicated, daily pelvic floor exercises. During the first, supervised intake session, training heart zones of the participant will be estimated. The exercise program will be individually designed, taking into consideration lifestyle, past and current levels of

activity, preferences for types of activities (e.g., walking, cycling, gym exercises, etc.), and any disabilities, Each woman will be given a heart-rate monitor, and will be instructed in its use to achieve a target heart rate (80% Karvonen). Women with urinary incontinence will be given pelvic floor exercises. In weeks 4 and 8, women will have a brief telephone contact with the physical therapist to discuss their experiences with the program and to make modifications, if necessary. Additionally, each week a telephone consultation hour will be scheduled during which women can call the physiotherapist to discuss their exercise program, if desired. At the end of the program (week 12) women will visit the clinic for a final session, during which advice will be given on how best to maintain the level of physical activity (as used in the program) following completion of the program. At this time the data from the heart monitor will be downloaded onto computer.

Group AB: Combined CBT and exercise program. Women assigned to Group AB will undergo the CBT and exercise elements of the program concurrently. To as great an extent as possible, the on-site CBT and in-clinic exercise training sessions will be scheduled on the same day.

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Eligibility criteria

Inclusion criteria

Women can be included if they are younger than 50 years of age, with histologically confirmed primary breast cancer (stages: T1 ¨C T4, N0 ¨C N1 and M0). All women will have been premenopausal at the time of diagnosis, have completed adjuvant chemotherapy (with the exception of herceptin, which can continue to receive) a minimum of 4 months and a maximum of 5 years prior to study entry. Women may currently be receiving adjuvant hormonal therapy. All women should be disease-free at time of study entry. Potentially eligible women will be screened for the presence of at least one of the following 3 menopausal symptoms during the previous 2-month period: hot flushes, sweating and/or vaginal dryness.

Exclusion criteria

Women will be excluded from the study if they lack basic proficiency in Dutch, if they have serious cognitive or psychiatric problems, or serious physical comorbidity that would preclude them from participating in a physical exercise program. Since physical exercise may be contraindicated as a treatment for hot flushes in obese women, 49 patients with a BMI ¡Ý 30 will be excluded from the study. Patients participating in concurrent studies or rehabilitation programs containing psychosocial interventions will also be excluded.

Study design

Design

Study type:	Interventional
Intervention model:	Factorial
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2008
Enrollment:	325
Type:	Anticipated

Ethics review

Positive opinion

Date:	17-12-2007
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL1130
NTR-old	NTR1165
Other	NKI : NKI 2006-3470
ISRCTN	ISRCTN wordt niet meer aangevraagd

Study results

Summary results
N/A