Original Article

Effects of pre-defined homoeopathic medicines to mitigate adverse dermatological effects of radiotherapy and vomiting of chemotherapy in breast carcinoma: A randomised, double-blind, placebo-controlled, pilot trial in the context of usual care

Purnima Shukla[1]*, Chaturbhuja Nayak[1], Mirza Qaiser Baig[2], Purak Misra[3]

[1]Department of Homoeopathic Materia Medica, Homoeopathy University, Jaipur, Rajasthan, [2]Department of Radiotherapy, BRD Medical College, Gorakhpur, Uttar Pradesh, [3]Department of Minimal Access and General Surgery, ESIC Hospital, Okhla, New Delhi, India

Abstract

Background: Radiotherapy and chemotherapy are used in breast cancer, but they cause an array of adverse effects including dermatological changes and vomiting. **Objective:** The objective of the study was to examine whether Usual Care (UC) plus pre-defined homoeopathic remedies can produce different effect beyond UC plus placebo in dermatological adverse effects of radiotherapy and vomiting of chemotherapy in breast carcinoma. **Methods:** In this double-blind, randomised, placebo-controlled, parallel-arm trial, 88 females suffering from dermatological adverse effects due to radiotherapy ($n = 41$) or vomiting due to chemotherapy ($n = 47$) were randomised to receive either UC + Homoeopathy (verum; $n = 44$) or UC + Placebo (control; $n = 44$). The outcome measures were the number of responders showing any reduction of grades of Acute Radiation Morbidity Scoring Criteria (ARMSC) of the Radiation Therapy Oncology Group and Common Toxicity Criteria (CTC) for vomiting, measured at baseline and after 7 and 14 days. Relative Risk (RR) with 95% Confidence Intervals (CIs) was assessed; Chi-square tests were run to report P values. **Results:** A protocol-compliant sample ($n = 80$; 8 dropped out, verum: 4, control: 4) was analysed. The number of responders as per the ARMSC score after 7 days (11/18 vs. 1/19, RR = 3.3, 95% CI = 1.7–6.3, $P = 0.001$) and 14 days (16/18 vs. 1/19, RR = 9.4, 95% CI = 2.5–35.2, $P < 0.001$) was statistically significant, favouring verum over control. Similar results were obtained according to the CTC scoring after 7 days (15/22 vs. 2/21, RR = 3.3, 95% CI = 1.7–6.3, $P < 0.001$) and 14 days (21/22 vs. 4/21, RR = 15.1, 95% CI = 2.2–102.4, $P < 0.001$). **Conclusion:** Pre-identified homoeopathic medicines appeared superior to placebo, warranting further evaluation.

Keywords: Breast carcinoma, Chemotherapy, Homoeopathy, Radiotherapy, Randomised controlled trial, Skin

Introduction

Breast cancer is the most common cancer in women both in the developed and less developed world, constituting about 22% of all female cancers. It is estimated that worldwide over 508,000 women died in 2011 due to breast cancer. Almost 50% of breast cancer cases and 58% of deaths occur in less developed countries. The incidence rates vary greatly worldwide from 19.3/100,000 women in eastern Africa to 89.7/100,000 women in western Europe. The lowest incidence rates are found in most African countries, but incidence rates are increasing in India also.[1] The incidence of breast cancer in India varies from as low as 5/100,000 females per year in rural areas to 30/100,000 females per year in urban areas. There is

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***Address for correspondence:** Dr. Purnima Shukla, Department of Homoeopathic Materia Medica, Homoeopathy University, Saipura, Sanganer, Jaipur, Rajasthan, India.
E-mail: drpurnimashukla2019@gmail.com

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an impression of higher incidence of breast cancer in younger women in India as most hospital-based series report the median age of breast cancer patients to be a decade younger than that of Western series. However, this may be due to a combination of the population structure and inherent bias against referral, treatment and ascertainment of breast cancer in the elderly in India rather than a true reflection. The incidence of breast cancer increases with age, and this is true in India like rest of the world.[2] Standard breast cancer management strategies include surgery, radiotherapy, chemotherapy and biological and hormonal therapies. Surgery is the first line of treatment in all the cases, barring few inoperable advanced stage cases. It may be followed by chemotherapy or radiation therapy or both. Hormone receptor-positive cancers are often treated with hormone-blocking therapy; similarly monoclonal antibodies, or immune-modulating treatments, may be administered in certain cases of metastatic and other advanced stages of breast cancer.

The results of several studies indicated that conventional treatment based on surgery, radiotherapy and chemotherapy is often associated with adverse side effects.[3] The adverse effects of chemotherapy include bone marrow suppression, xerostomia, hair loss and thinning, infertility, skin and nail changes, nausea and vomiting, menopausal syndrome and cognitive impairment or dysfunction. The adverse effects of radiotherapy include radiodermatitis, telangiectasia, brachial plexopathy, nausea and fatigue.

Available literature reveals that in spite of the rapid strides in the field of oncology, a cost-effective, perfect and safe treatment to check the mortality rate is still a goal to be achieved. Many patients with cancer use complementary therapies, usually alongside orthodox treatments and Homoeopathy was in the top five most commonly used complementary therapies by cancer patients in seven out of 14 European countries by patients with cancer.[4,5] A systematic review of 26 surveys from 13 countries reported that up to 64% of patients with cancer (average 31.4%) used complementary therapy at some stage of their illness. Recent studies suggest that additive homoeopathic medicines to standard therapies might be used to enhance survival[6] and improve the quality of life in cancer patients.[7] Homoeopathic literature also suggests a list of remedies to counter the adverse effects of chemotherapy and radiotherapy.[8,9] Published researches provided promising evidences in favour of Homoeopathy to treat the adverse effects of conventional treatment in breast carcinoma.[10,11] Some potential homoeopathic remedies for radiation exposure are *Radium bromatum*, *X-ray*, *Uranium nitricum*, *Strontium carbonicum*, *Calendula officinalis*, *Cadmium sulphuratum*, *Cadmium iodatum* and *Ceanothus americanus*. It is highly recommended to prescribe the remedies in proper dosage under skilled professional homoeopathic care.[12] In an open, randomised controlled trial (RCT), a homoeopathic complex was experimented against placebo to treat chemotherapy-induced nausea and vomiting in 55 patients, but no significant difference between the groups was elicited.[13] In a double-blind, RCT, non-individualised, standardised remedy comprising *Cobaltum* and *Causticum* was experimented against placebo in 82 patients for protection against radiation. Patients rated symptom severity score as 4.7 in *Cobaltum* patients, 5.4 in *Causticum* patients and 8.5 in placebo patients.[14] In a double-blind, RCT, a homoeopathic complex Traumeel S® was tested against placebo in 32 children suffering from cancer, undergoing stem cell transplantation, and chemotherapy-induced stomatitis. Patients' rated symptom severity was significantly less in the Homoeopathy group than that in the placebo patients, thus favouring the use of Traumeel S®.[15] However, in an international, multicentric, double-blind, randomised trial comparing Traumeel with placebo in patients aged 3–25 years undergoing myeloproliferative haematopoietic stem cell transfer, there was no statistically significant difference in mucositis in the Traumeel group compared with that of placebo group ($P = 0.13$). Although there was a trend towards less narcotic usage in the Traumeel patients, no beneficial effect from Traumeel was demonstrated for mucositis.[16] In another randomised trial, *Calendula* was compared against trolamine for the prevention of acute dermatitis during irradiation for breast cancer in 254 patients. The occurrence of acute dermatitis of Grade 2 or higher was statistically significantly lower (41% vs. 63%; $P < 0.001$) with the use of *Calendula* than with trolamine. Moreover, patients receiving *Calendula* had less frequent interruption of radiotherapy and significantly reduced radiation-induced pain. Thus, *Calendula* was found to be highly effective for the prevention of acute dermatitis of Grade 2 or higher and was recommended for patients undergoing post-operative irradiation for breast cancer.[10] In another double-blind, RCT, non-individualised, standardised remedy comprising *Belladonna* C7 and *X-ray* C15 was compared against placebo in 66 patients suffering from skin reactions after chemotherapy, but no significant differences were reported.[17] Daub *et al.* studied homoeopathic medicines for preventing adverse effect of venous cannulations in patients receiving chemotherapy.[13] Bourgois studied the role of homoeopathic medicines to protect venous function in women undergoing intravenous chemotherapy with no statistical significant difference.[18]

Thus, the overall scenario remains quite inconclusive about the effects of Homoeopathy in comparison with placebo in mitigating the dermatological adverse effects of radiotherapy and vomiting of chemotherapy in breast carcinoma. Hence, the investigators intended to examine whether usual care (UC) plus pre-defined homoeopathic medicines can produce significantly different treatment effect beyond UC plus placebo (UC + Pl) in the said conditions – both the conditions being very frequently encountered in the author's practice.

Methods

Trial design

This prospective, double-blind, randomised, placebo-controlled, parallel-arm trial was conducted at the Department of Radiation Oncology, B. R. D. Medical College, Gorakhpur,

Uttar Pradesh - 273013, India. The study protocol (unpublished) was submitted as a PhD synopsis of the corresponding author to the Homoeopathy University, Jaipur, Rajasthan, India, and was approved by the Institutional Ethics Committee of the University (Letter No. HU/2014/853/A; dated 20 September 2014) prior to initiation and enrolment; however, the trial was not registered in any trial registry due to some unavoidable circumstances. The proposed plan of work adhered to the ethical guidelines of the Declaration of Helsinki.[19]

Study duration

The trial started in February 2015 and was ended by January 2016.

Participants

Inclusion criteria were females suffering from the dermatological adverse effects of radiotherapy or vomiting due to chemotherapy of Grade I to III of both Acute Radiation Morbidity Scoring Criteria (ARMSC) and CTC scorings, respectively, age of 21–70 years and providing written consent to participate. Exclusion criteria were patients undergoing both radiotherapy and chemotherapy, ARMSC and CTC Grades IV; those unwilling to participate or having inability to comply with the trial requirements; those declined to provide informed consent; those with other uncontrolled systemic diseases and/or pathologies, psychiatric illness; those with ongoing use of homoeopathic medicines for any chronic diseases and those with drug or substance abuse and/or dependence.

Intervention

Experimental arm (verum)

The patients randomised to this arm received UC plus homoeopathic medicines from a list of nine pre-identified remedies (UC + Homoeopathy; verum: $n = 44$) – *Apis mellifica*, *Arsenicum album*, *Belladonna*, *Cadmium sulphuricum*, *Carcinosinum*, *Ipecacuanha*, *Phosphorus*, *Radium bromide* and *X-ray* [Table 1]. The shortlisting of the homoeopathic medicines was based on severity of symptoms in different grades and author's previous clinical experience (unpublished), better supported by the homoeopathic literature, Murphy's *Materia Medica*[8] and *Synthesis Repertory*.[9] The author's personal experience suggested that ARMSC Grades 1–3 can successfully be treated with *Arsenicum album*, *Belladonna* and *Radium bromide,* respectively, as the 1st-line remedies and, if failed, with *Carcinosinum*, *Apis mellifica* and *X-ray* and *Carcinosinum* subsequently. Similarly, CTC Grades 1–3 can be treated successfully with *Ipecacuanha*, *Arsenicum album* and *Cadmium sulphuricum* as the 1st-line remedies, respectively and, if failed, with *Cadmium sulphuricum* and P*hosphorus,* respectively. The medicines were prescribed in homoeopathic centesimal potencies (30c and 200c) to the patients experiencing side effects. Each dose consisted of four cane sugar globules medicated with a single drop of the indicated medicines. Repetition was 24, 12 or 8 hourly or even oftener, depending on the individual requirement of the case. Each dose was instructed to be taken orally on a clean tongue with an empty stomach. Duration of the therapy was 2 weeks. The homoeopathic medicines were obtained from Good Manufacturing Practice-certified pharmaceuticals. A single homoeopathic medicine from the list of pre-defined remedies was prescribed on each occasion taking into account the clinical presentation and consensus between two physicians. The individualised dose was based on physicians' judgement of susceptibility and consensus of two homoeopaths. As per usual homoeopathic prescribing procedures, if the first remedy was not helpful, the patient's symptoms were reassessed and a new remedy was prescribed. Each of the two prescribers in the study possessed master degree in Homoeopathy with more than 30 years of experience of practicing classical Homoeopathy. UC was administered and monitored all through by a conventionally trained and experienced radiotherapist as per the latest available guidelines for post-mastectomy radiotherapy[20] and chemotherapy[21] in personalised dosage catered to the patients' needs.

Control arm

Patients randomised to this arm received UC as above plus placebo (UC + Pl; control: $n = 44$). The placebo was indistinguishable from verum by appearance, smell and taste. Each placebo dose consisted of four cane sugar globules no. 30 moistened with a single drop of dispensing alcohol, instructed to be taken thrice a day orally on a clean tongue in an empty stomach. The duration of therapy was 2 weeks. Participants in the control arm were assessed similarly by the same two experienced homoeopaths as was done in the experimental arm. The 'placebo prescription' was similar to that for patients receiving actual medicines.

Usual care

It consisted of five types of chemotherapy drug regimens prescribed as per the personalised need of the enrolled patients – CMF, FAC followed by CMF, CMF alternated with EV, CMFVP and FEC (C = cyclophosphamide,

Table 1: Medicines used in different stages

Treatment strategies	ARMSC Grade 1	ARMSC Grade 2	ARMSC Grade 3
1st line of medicines	*Arsenicum album*	*Belladonna*	*Radium bromatum*
2nd line of medicines	*Carcinosinum*	*Apis mellifica*	*X-ray, Carcinosinum*
	CTC Grade 1	**CTC Grade 2**	**CTC Grade 3**
1st line of medicines	*Ipecacuanha*	*Arsenicum album*	*Cadmium sulphuratum*
2nd line of medicines	*Cadmium sulphuratum*	*Phosphorus*	*Phosphorus*

ARMSC: Acute Radiation Morbidity Scoring Criteria, CTC: Common Toxicity Criteria

M = methotrexate, F = 5-fluorouracil, A = adriamycin, E = epirubicin, V = vincristine and P = prednisone).

Outcomes

The outcome measure was the proportion of patients improved (i.e., n/N) as per the ARMSC and the Common Toxicity Criteria (CTC) version 3.0 for vomiting;[22-24] the assessment timeline was 7 days and 14 days. The ARMSC and CTC were created by the Radiation Therapy Oncology Group (RTOG) in 1985 and the US National Cancer Institute (NCI) in 1983 for the grading of radiotherapy- and chemotherapy-related effects, respectively. These scales are unpublished, yet widely used in clinical trials.[25] Assessment, both pre- and post-medication, was done by a conventionally trained and blinded radiotherapist. Responders were defined *a priori* as those patients showing any reduction of grades in the ARMSC or CTC scores over the defined time points. The ARMSC grading system was developed by the RTOG to classify radiotherapy effects. It identifies five grades – 0 (no reaction), 1 (faint erythema, dry desquamation, epilation and diminished sweating), 2 (moderate, brisk erythema, exudative dermatitis in plaques and moderate oedema), 3 (exudative dermatitis, besides cutaneous folds and intense oedema) and 4 (ulceration, haemorrhage and necrosis). However, only the dermatological component of this scale was used. The RTOG score has been widely employed for >25 years and is accepted and acknowledged by medical and nursing communities. The CTC scoring for vomiting was as follows – 0 (none), 1 (one episode in 24 h, intravenous fluids indicated <24 h), 2 (2–5 episodes in 24 h), 3 (more than 6 episodes in 24 h, intravenous fluids or total parenteral nutrition indicated >24 h) and 4 (life-threatening consequences).

Sample size

There has been no published placebo-controlled trial of similar design in the said condition. This precluded the formal calculation of standardised difference (effect size) and sample size. We assumed a medium effect size (w) of 0.3. Now keeping $\alpha = 0.05$, minimum power $(1 - \beta)$ recommendation = 0.80 and allocation ratio 1:1, to detect a significant difference between the two proportions of responder samples by goodness-of-fit Chi-square test through a 2 × 2 contingency table, the calculated sample size came to be 88.

Randomisation

SPSS software Statistical Package for the Social Sciences, version 20.0 (IBM Corp., IBM SPSS Statistics for Windows, Armonk, NY: USA)-generated random numbers were used to generate the random sequence in strict confidentiality by third parties, who were not allowed to influence the study in any way. The list was generated using restricted eight different blocks of size 10 and a single block of size 8 to maintain equal distribution between the groups and 1:1 ratio (8 × 10 = 80; 80 + 8 = 88; verum: 44, control: 44). The randomisation chart with allocated codes was available to the pharmacist for dispensing from coded vials.

Blinding

The participants, the investigators and the pharmacists were blinded to the allocated codes. Blinding was carried out by a third party in strict confidentiality to generate two sets of alike vials filled with either medicated or non-medicated (placebo) globules (moistened with either medicine or dispensing alcohol), and they were not allowed to influence the study in any ways. The prescriptions were sent to the pharmacist who was responsible for dispensing as per the random number chart from either of the two sets of vials of identical appearance – one containing genuine homoeopathic preparation prepared in the standard manner, or placebo, indistinguishable from each other, along with a set of vials containing known 'non-medicated' cane sugar globules no. 30 (placebo). Randomisation codes '1' and '2' were labelled on the vials in strict confidentiality. The codes were broken at the end of the trial after the data set was frozen. Blinding was checked for all patients early in the trial by an independent third party, before the treatment was expected to take effect by asking the patients in which group they believed they were in; otherwise, any positive effect would break the code, especially when chances of diffusion of treatment could not be removed.

Statistical methods

All the collected data in the standardised format were subjected to data extraction in a specially designed Microsoft Office Excel® Spreadsheet v. 2007(Redmond, Washington, United States of America) and underwent statistical analysis – both descriptive and inferential. The protocol-compliant sample was analysed in the end. Given the objective of classifying the patients as 'responders' and 'non-responders' in the two groups over 2 weeks and thereby comparing the two proportions, the authors were of the opinion that a 'per-protocol' analysis was permissible, and seemed to be preferable over an 'intention-to-treat' analysis. Descriptive statistics were presented in terms of absolute values, percentages, means and standard deviations, as appropriate. The groups were checked for comparability of sociodemographic characteristics and outcome measures at baseline using independent *t*-test (for continuous data) or Chi-square test (for categorical data). The number of responders was assessed as per the ARMSC and CTC scoring after 7 and 14 days. Relative risks (RRs) with 95% confidence intervals (CIs) were reported. Chi-square tests were performed to report *P* values which were set at <0.05 (two tailed) as statistically significant. SPSS® IBM® version 20 software was used for the analysis of the data. Graphs were generated in Microsoft Office Word® v. 2007. Reporting adhered to the CONSORT[26] and ReDHoT guidelines[27] for reporting trials.

Ethical issues

Prior to enrolment, each patient was provided with a patient information sheet in local vernacular Hindi, detailing the study aims and objectives, methods, risks and benefits of participating and confidentiality issues. Subsequent to this, a written informed consent was obtained. Ethical clearance was obtained prior to initiation. Thus, the study conformed to the ethical standards.

Results

Participant flow

A total of 144 patients with breast cancer suffering from the adverse effects of radiotherapy or chemotherapy were screened preliminarily; 36 were screened out. The rest of the majority of 108 patients fitted the symptoms of the pre-identified medicines, with the reason being that the therapeutic approach of using the pre-identified medicines is 'clinical' (based on 'common' symptoms) instead of 'individualised' (i.e., based on 'uncommon, peculiar, characteristics symptoms'). These 108 patients underwent detailed screening as per the specified eligibility criteria; twenty were excluded for varying reasons. As the considered symptomatology pertained to the common symptoms, none were excluded on the basis of symptom dissimilarity. A total of 88 patients were enrolled in the study and randomised to either verum (UC + Homoeopathy) or control (UC + Pl) in 1:1 ratio. A total of eighty patients completed the follow-up; eight patients dropped out – four in each group. The protocol-compliant sample ($n = 80$) was analysed in the end [Figure 1].

Baseline data

The two groups were comparable as per baseline features that is, no statistically significant differences existed between the groups in terms of age ($\chi^2 = 0.732$, $P = 0.947$), residence ($\chi^2 = 0.853$, $P = 0.356$), education ($\chi^2 = 0.524$, $P = 0.769$), employment ($\chi^2 = 0.321$, $P = 0.852$), socioeconomic status ($\chi^2 = 0.970$, $P = 0.616$), duration of illness ($\chi^2 = 0.643$, $P = 0.996$), breast cancer types confirmed through biopsy ($\chi^2 = 0.182$, $P = 0.999$), therapies instituted ($\chi^2 = 0.050$, $P = 0.823$), lymph node involvement status ($\chi^2 = 0.667$, $P = 0.414$), number of chemotherapy cycles instituted ($\chi^2 = 0.193$, $P = 0.661$) and chemotherapy regimens ($\chi^2 = 0.683$, $P = 0.953$) and ARMSC ($\chi^2 = 0.260$, $P = 0.878$) and CTC grades ($\chi^2 = 0.712$, $P = 0.701$). Lymph node involvement was found in six cases only; three in either groups [Table 2].

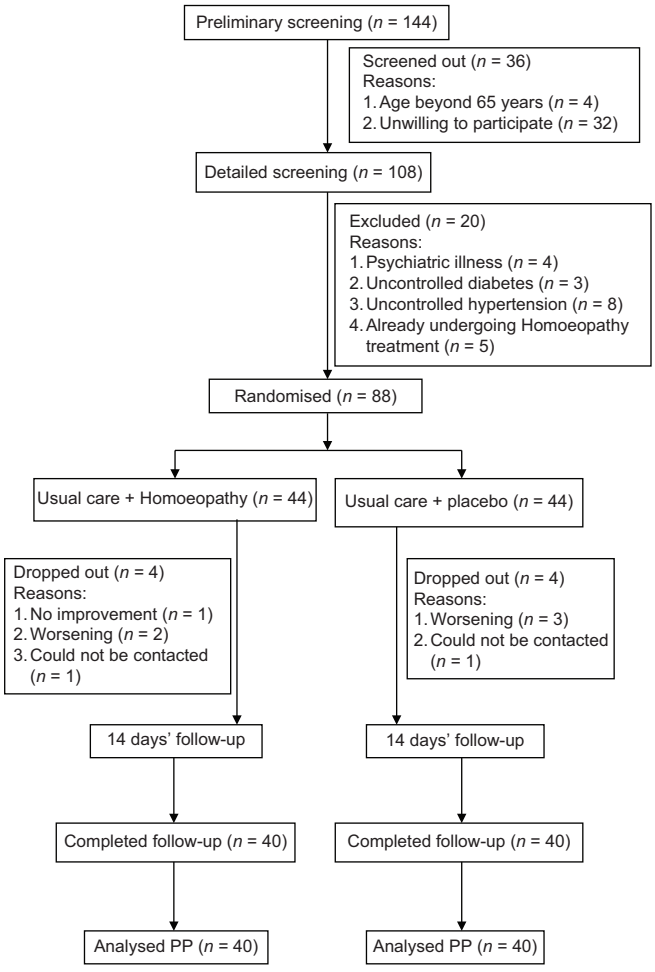

Figure 1: Study flow diagram. PP: Per protocol

Numbers analysed

After 14 days, four patients dropped out in each group that is, 80 patients were protocol compliant that entered into the final analysis.

Outcomes and estimation

The numbers of responders versus non-responders as per ARMSC score after 7 days (11/18 vs. 1/19 [61.1% vs. 5.3%], RR = 3.3, 95% CI = 1.7–6.3, $\chi^2 = 10.7$, $P = 0.001$) and 14 days (16/18 vs. 1/19 [88.9% vs. 5.3%], RR = 9.4, 95% CI = 2.5–35.2, $\chi^2 = 22.8$, $P < 0.001$) was statistically significant favouring verum over control. Similar results were obtained also according to CTC scoring after 7 days (15/22 vs. 2/21 [68.2% vs. 9.5%], RR = 3.3, 95% CI = 1.7–6.3, $\chi^2 = 13.1$, $P < 0.001$) and 14 days (21/22 vs. 4/21 [95.5% vs. 19%], RR = 15.1, 95% CI = 2.2–102.4, $\chi^2 = 22.7$, $P < 0.001$) [Figures 2 and 3].

Harms

No harms and adverse or unintended effects were reported from either group during the trial. Temporary worsening of the existing complaints followed by rapid improvement (probably 'homoeopathic aggravation') was observed in 18 out of 40 cases (45%) in the verum arm only.

Medicines used

Patients presenting with ARMSC Grade I (follicular, faint or dull erythema epilation; dry desquamation or decrease in

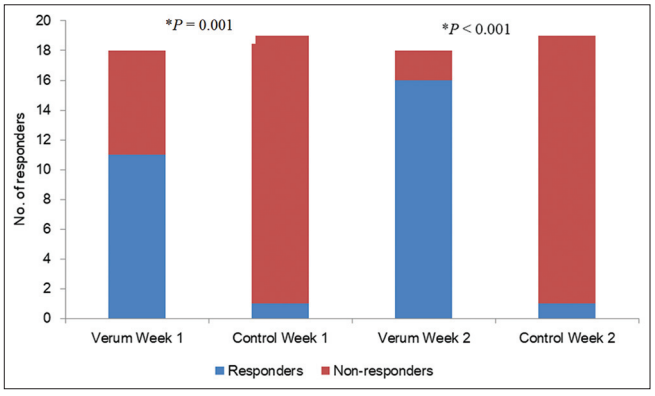

Figure 2: Stacked column diagram showing the overall distribution of treatment outcomes in the two groups as per Acute Radiation Morbidity Scoring Criteria scoring ($n = 37$); *Chi-square test applied; $P < 0.05$ (two tailed) considered statistically significant

Table 2: Comparison of baseline features between the two groups (*n*=80)

Characteristics	Verum (*n*=40)	Control (*n*=40)	*P*
Age groups (years)			
21-30 (*n*=3)	2 (5.0)	1 (2.5)	0.947
31-40 (*n*=18)	8 (20.0)	10 (25.0)	
41-50 (*n*=34)	18 (45.0)	16 (40.0)	
51-60 (*n*=17)	8 (20.0)	9 (22.5)	
61-70 (*n*=8)	4 (10.0)	4 (10.0)	
Residence			0.356
Rural	27 (67.5)	23 (57.5)	
Urban	13 (32.5)	17 (42.5)	
Education			
8th standard or less	14 (35.0)	11 (27.5)	0.769
9th-12th standard	18 (45.0)	20 (50.0)	
Graduate or above	8 (20.0)	9 (22.5)	
Employment			
Service	11 (27.5)	10 (25.0)	0.852
Business	7 (17.5)	9 (22.5)	
Household work	22 (55.0)	21 (52.5)	
Socioeconomic status			
Low	19 (47.5)	18 (45.0)	0.616
Middle	17 (42.5)	15 (37.5)	
Affluent	4 (10.0)	7 (17.5)	
Duration of illness			
12 months or less (*n*=14)	8 (20.0)	6 (15.0)	0.996
13-24 months (*n*=35)	17 (42.5)	18 (45.0)	
25-36 months (*n*=14)	7 (17.5)	7 (17.5)	
37-48 months (*n*=2)	1 (2.5)	1 (2.5)	
49-60 months (*n*=5)	2 (5.0)	3 (7.5)	
61-72 months (*n*=3)	2 (5.0)	1 (2.5)	
>72 months (*n*=7)	3 (7.5)	4 (10.0)	
Breast cancer types confirmed through biopsy			
Infiltrating duct carcinoma (*n*=64)	31 (77.5)	33 (82.5)	0.999
Infiltrating duct carcinoma with hepatomegaly with multiple hypoechoic areas (*n*=5)	3 (7.5)	2 (5.0)	
Infiltrating duct carcinoma with bilateral ovarian cyst (*n*=1)	1 (2.5)	0 (0)	
Infiltrating duct carcinoma with metastasis to lymph nodes (*n*=6)	3 (7.5)	3 (7.5)	
Infiltrating duct carcinoma with metastasis to bone (*n*=1)	0 (0)	1 (2.5)	
Infiltrating duct carcinoma with metastasis to opposite breast and chest wall (*n*=1)	0 (0)	1 (2.5)	
Intracystic papillary carcinoma (*n*=1)	1 (2.5)	0 (0)	
Carcinoma breast with carcinoma thyroid with right-sided pleural effusion with secondaries in the lung (*n*=1)	1 (2.5)	0 (0)	
Therapies			
Mastectomy plus radiotherapy (*n*=37)	18 (45.0)	19 (47.5)	0.823
Mastectomy plus chemotherapy (*n*=43)	22 (55.0)	21 (52.5)	
Loco-regional radiotherapy–lymph node involvement status (*n*=6)	*n*=3	*n*=3	0.414
1-3 positive (*n*=3)	2 (66.7)	1 (33.3)	
≥4 positive (*n*=3)	1 (33.3)	2 (66.7)	
Number of chemotherapy cycles undergone (*n*=43)	*n*=22	*n*=21	0.661
1-3 (*n*=32)	17	15	
≥4 (*n*=11)	5	6	
Chemotherapy regimens (*n*=43)	*n*=22	*n*=21	
CMF (*n*=14)	6 (27.3)	8 (38.1)	0.953
FAC followed by CMF (*n*=13)	7 (31.8)	6 (28.6)	
CMF alternating with EV (*n*=7)	4 (18.2)	3 (14.3)	
CMFVP (*n*=5)	3 (13.6)	2 (9.5)	
FEC (*n*=4)	2 (9.1)	2 (9.5)	

Contd...

Table 2: Contd...

Characteristics	Verum (*n*=40)	Control (*n*=40)	*P*
ARMSC grades for dermatological conditions			
I (*n*=11)	6 (15.0)	5 (12.5)	0.878
II (*n*=19)	9 (22.5)	10 (25.0)	
III (*n*=7)	3 (7.5)	4 (10.0)	
CTC grades for vomiting			
I (*n*=29)	16 (40.0)	13 (32.5)	0.701
II (*n*=11)	5 (12.5)	6 (15.0)	
III (*n*=3)	1 (2.5)	2 (5.0)	

Values presented as absolute *n* (%); Chi-square test; $P<0.05$ (two tailed) considered statistically significant. C: Cyclophosphamide, M: Methotrexate, F: 5-Fluorouracil, A: Adriamycin, E: Epirubicin, V: Vincristine, P: Prednisone, CTC: Common toxicity criteria, ARMSC: Acute Radiation Morbidity Scoring Criteria

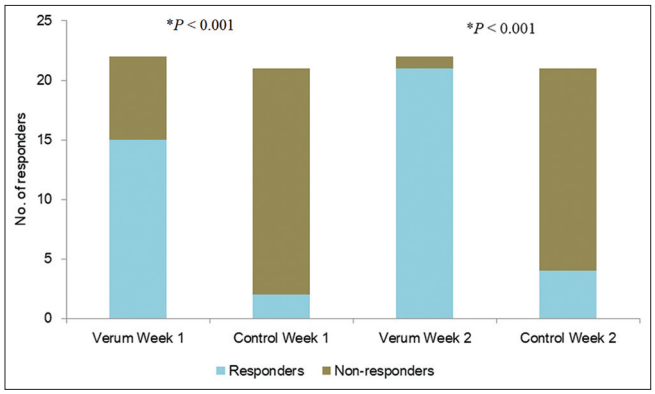

Figure 3: Stacked column diagram showing the overall distribution of treatment outcomes in the two groups as per Common Toxicity Criteria scoring ($n = 43$); *Chi-square test applied; $P < 0.05$ (two tailed) considered statistically significant

sweating), Grade II (tender, bright erythema; patchy, moist desquamation or moderate oedema) and Grade III (confluent, moist desquamation other than skin folds; pitting oedema) were given *Arsenicum album* 30C, *Belladonna* 30C and *Radium bromide* 30C, respectively. In non-responding cases, after due re-assessment of the cases, *Carcinosinum* 200C, *Apis mellifica* 30C and *X-ray* 30C were prescribed. Patients presenting with CTC Grades I, II and III were prescribed with *Ipecacuanha* 30C, *Arsenicum album* 30C and *Cadmium sulphuricum* 30C, respectively. The non-responders were reassessed and were prescribed *Cadmium sulphuricum* 30C and *Phosphorus* 30C. Doses were administered as per individual requirements as decided appropriate to the case and condition. Any reduction in grades was marked as 'responded' [Tables 3-6].

Discussion

Our study found that UC + Homoeopathy produced significant treatment benefit in comparison to UC + Pl by reducing ARMSC and CTC scores, thus mitigating the dermatological adverse effects of radiotherapy and vomiting of chemotherapy in women suffering from breast carcinoma.

The study design was 'gold standard' (i.e., RCT) to examine the efficacy of any intervention; here UC + Homoeopathy. We used 'double-blind' technique in order to minimise bias to the maximum possible extent. Two pre-validated scoring systems – ARMSC and CTC – were used, thus substantiating the validity of the study findings. Instead of complexes or standardised medicines, we opted for pre-defined, homoeopathic medicines, of which, a few (e.g., *Radium bromide*, *Cadmium sulphuratum*, *Belladonna* and *X-ray*) were experimented in trials previously,[12,17] but on individualistic approach only. Frass *et al*., 2015[7] studied the efficacy of additive individualised Homoeopathy to standard anti-cancer care in an open, pragmatic RCT design on 373 patients, revealing significant improvement in global health status and subjective well-being. We used pre-defined remedies in the place of individualised ones using more robust double-blind, placebo-controlled design, but on a relatively less number of patients. In a single-blind RCT on 254 patients by Pommier *et al*. in 2004,[10] *Calendula* ointment was found to be better than trolamine ointment in preventing post-radiation dermatitis. Unlike this study, we did not use external applications in our trial, and ours was a double-blind trial. The RCT by Daub *et al*., 2000,[13] was placebo controlled, but open labelled and compared two complexes – *Vomitusheel S* suppository and *Gastricumeel* tablets – against placebo in 44 patients, but found no difference with placebo. Like ours, Kulkarni *et al*., 1988,[14] compared two predetermined remedies – *Cobaltum* and *Causticum* – with placebo using double-blind design in 82 patients with radiotherapy and found significant symptom relief in the verum group than control group. In another study of similar design with ours, Balzarini *et al*., 2000,[17] elicited a non-significant trend favouring two predetermined remedies – *Belladonna* 7 CH and *X-ray* 15 CH – over placebo. In another double-blind, placebo-controlled trial, Oberbaum *et al*.,[15] found promising effects of a complex *Traumeel S* in comparison with placebo in thirty children suffering from radiation-induced stomatitis. Contrarily, in another double-blind, placebo-controlled trial on 190 patients, Sencer *et al*., 2012, could not find any beneficial effect of *Traumeel S* against placebo. Thus, overall, RCTs testing complex remedies have remained contradictory in outcomes, whereas the trials with predetermined

Table 3: Adopted treatment algorithm and outcomes for dermatological adverse events of radiotherapy – used medicines in verum

	ARMSC Grade 1 (*n*=6)	ARMSC Grade 2 (*n*=9)	ARMSC Grade 3 (*n*=3)
Treatment	*Arsenicum album* 30C	*Belladonna* 30C	*Radium bromatum* 30C
Follow-up 1st week	4/6 responded	6/9 responded	1/3 responded
Revised treatment	Reassessment of non-responders; *Carcinosinum* 200C prescribed	Reassessment of non-responders; *Apis mellifica* 30C prescribed	Reassessment of non-responders; *X-ray* 30C prescribed
Follow-up 2nd week	6/6 responded	9/9 responded	1/3 responders, *Carcinosinum* 200C prescribed to non-responders

ARMSC: Acute Radiation Morbidity Scoring Criteria

Table 4: Outcomes in placebo group for adverse events of radiotherapy

	ARMSC Grade 1 (*n*=6)	ARMSC Grade 2 (*n*=10)	ARMSC Grade 3 (*n*=3)
Treatment	Placebo	Placebo	Placebo
Follow-up 1st week	1/6 responded	No responders; 0/10	No responders; 0/3
Treatment	Placebo	Placebo	Placebo
Follow-up 2nd weeks	1/6 responders	No responders; 0/10	No responders; 0/3

ARMSC: Acute Radiation Morbidity Scoring Criteria

Table 5: Adopted treatment algorithm and outcomes for vomiting of chemotherapy – used medicines in verum

	CTC Grade 1 (*n*=13)	CTC Grade 2 (*n*=8)	CTC Grade 3 (*n*=1)
Treatment	*Ipecacuanha* 30C	*Arsenicum album* 30C	*Cadmium sulphuratum* 30C
Follow-up 1st week	9/13 responded	6/8 responded	Non-responders
Revised treatment	Reassessment of non-responders; *Cadmium sulphuratum* 30C prescribed	Reassessment of non-responders; *Phosphorus* 30C prescribed	Reassessment of non-responder; *Phosphorus* 30C prescribed
Follow-up 2nd weeks	All responders	All responders	Non-responders

CTC: Common Toxicity Criteria

Table 6: Outcomes in placebo group for adverse events of chemotherapy

	CTC Grade 1 (*n*=12)	CTC Grade 2 (*n*=8)	CTC Grade 3 (*n*=1)
Treatment	Placebo	Placebo	Placebo
Follow-up 1st week	2/12 responded	No responders	Non-responders
Treatment	Placebo	Placebo	Placebo
Follow-up 2nd weeks	3/12 responded	1/8 responded	Non-responders

CTC: Common Toxicity Criteria

remedies generated promising results. We planned UC to continue uninterruptedly and mutually in the two study arms because of ethical concerns. The drop out rate was 10% in the study; thus provision should be made for such attrition during sample size calculation in future trials. The study was conducted at a single centre. As Homoeopathy prescriptions largely depend on the skill of the prescribers, the study outcomes may vary in different settings and with different prescribers. Our study was underpowered because we actually ran subgroup analyses on a relatively smaller sample than recruited to account for two different groups of patients receiving either radiotherapy or chemotherapy, hence the efficacy of Homoeopathy cannot be established or claimed. Hence, an adequately powered trial is warranted with patient-rated, validated, quality-of-life outcomes. The basis of treatment was pre-identified homoeopathic medicines, thus presenting a form of contemporary Homoeopathy practice. However, one important limitation was that we restricted our analysis to protocol-compliant sample only. Using an intention-to-treat approach would have been more appropriate than this. Having used only centesimal potencies in this trial for the purpose of convenience in dispensing and intake of dosage, pragmatic trials comparing the effectiveness of centesimal and 50 millesimal potencies or Homoeopathy versus UC might also be promising endeavours. We also restricted the choice of the remedy from a list of pre-defined medicines. If we had not opted for this identified list prior to the identification of the medicines, the option would have been there for a long array of medicines to choose from, and that might have blurred the scenario by introducing further bias in this relatively less explored condition. We also limited our assessment to dermatological adverse effects of radiotherapy and vomiting of chemotherapy, the conditions frequently reported in the

author's practice. Treatment effects in other adverse events also need to be explored in future trials by engaging a number of specialists of the concerned fields.

The results of our study warrant cautious interpretation and sincere consideration of Homoeopathy as an adjunctive and complementary aid to standard care in mitigating radiotherapy- or chemotherapy-induced adverse effects, especially dermatological conditions and vomiting. Studies those assessed the efficacy of the same remedy or complex formulations, being prescribed to all the participants in a trial, were inherently contradictory with the principles of Homoeopathy itself. Hence, adherence to the basic doctrines of Homoeopathy is suggested for any future trials aiming to assess the efficacy or effectiveness of Homoeopathy.

Conclusion

Our study found significant treatment benefit of pre-defined homoeopathic medicines against placebo in reducing ARMSC and CTC scores in the mutual context of UC. Through the integration of Homoeopathy into conventional care, an integrative medicine approach may facilitate mitigating the dermatological adverse effects of radiotherapy and vomiting of chemotherapy in an effective manner. We propose independent replications and further research evaluating both cost and clinical effectiveness in a multicentre approach on a larger sample size.

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Conflicts of interest

None declared.

References

1. WHO. The Global Burden of Disease: 2004 Update. Geneva: WHO; 2008. Available from: https://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf?ua=1. [Last acessed on 2018 Jan 23].
2. Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. Eur J Cancer 2001;37 Suppl 8:S4-66.
3. Goi T, Nakazawa T, Kimura Y, Sawai K, Morikawa M, Katayama K, *et al*. Retrospective analysis of chemotherapy-induced nausea and vomiting (CINV) in colorectal cancer patients treated with antiemetics. J Palliative Care Med 2012;S1:006.
4. Coleman MP, Quaresma M, Berrino F, Lutz JM, De Angelis R, Capocaccia R, *et al*. Cancer survival in five continents: A worldwide population-based study (CONCORD). Lancet Oncol 2008;9:730-56.
5. Molassiotis A, Fernández-Ortega P, Pud D, Ozden G, Scott JA, Panteli V, *et al*. Use of complementary and alternative medicine in cancer patients: A European survey. Ann Oncol 2005;16:655-63.
6. Gaertner K, Müllner M, Friehs H, Schuster E, Marosi C, Muchitsch I, *et al*. Additive homeopathy in cancer patients: Retrospective survival data from a homeopathic outpatient unit at the Medical University of Vienna. Complement Ther Med 2014;22:320-32.
7. Frass M, Friehs H, Thallinger C, Sohal NK, Marosi C, Muchitsch I, *et al*. Influence of adjunctive classical homeopathy on global health status and subjective wellbeing in cancer patients – A pragmatic randomized controlled trial. Complement Ther Med 2015;23:309-17.
8. Murphy R. Homoeopathic Medical Repertory. 2nd ed. New Delhi: B. Jain Publishers (P) Ltd.; 2002.
9. Schroyens F. Synthesis. Repertorium Homoeopathicum Syntheticum. 9.1 ed. London: Homeopathic Book Publishers; 2013.
10. Pommier P, Gomez F, Sunyach MP, D'Hombres A, Carrie C, Montbarbon X. Phase III randomized trial of *Calendula officinalis* compared with *Trolamine* for the prevention of acute dermatitis during irradiation for breast cancer. J Clin Oncol 2004;22:1447-53.
11. Schlappack O. Homeopathic treatment of radiation-induced itching in breast cancer patients. A prospective observational study. Homeopathy 2004;93:210-5.
12. Milazzo S, Russell N, Ernst E. Efficacy of homeopathic therapy in cancer treatment. Eur J Cancer 2006;42:282-9.
13. Daub EA, Gerhard I, Bastert G. Homeopathic antiemetics in chemotherapy: A prospective, randomized study. Obstetrics Gynecology. 2000;60 Suppl 1:s157.
14. Kulkarni A, Nagarkar BM, Burde GS. Radiation protection by use of homoeopathic medicines. Hahnemann Hom Sand 1988;12:20-3.
15. Oberbaum M, Yaniv I, Ben-Gal Y, Stein J, Ben-Zvi N, Freedman LS, *et al*. A randomized, controlled clinical trial of the homeopathic medication TRAUMEEL S in the treatment of chemotherapy-induced stomatitis in children undergoing stem cell transplantation. Cancer 2001;92:684-90.
16. Sencer SF, Zhou T, Freedman LS, Ives JA, Chen Z, Wall D, *et al*. Traumeel S in preventing and treating mucositis in young patients undergoing SCT: A report of the Children's Oncology Group. Bone Marrow Transplant 2012;47:1409-14.
17. Balzarini A, Felisi E, Martini A, De Conno F. Efficacy of homeopathic treatment of skin reactions during radiotherapy for breast cancer: A randomised, double-blind clinical trial. Br Homeopath J 2000;89:8-12.
18. Bourgois JC. Protection of the Venous Capital at the perfuse with a long course in breast cancer. Double blind clinical trial: Arnica with a placebo control. Paris: Université Paris Nord XIII, Faculté de Médecine; 1984.
19. World Medical Association. WMA Declaration of Helsinki – Ethical principles for medical research involving human subjects. JAMA 2013;310:2191-4.
20. Truong PT, Olivotto IA, Whelan TJ, Levine M, Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. Clinical practice guidelines for the care and treatment of breast cancer: 16. Locoregional post-mastectomy radiotherapy. CMAJ 2004;170:1263-73.
21. Shenkier T, Weir L, Levine M, Olivotto I, Whelan T, Reyno L, *et al*. Clinical practice guidelines for the care and treatment of breast cancer: 15. Treatment for women with stage III or locally advanced breast cancer. CMAJ 2004;170:983-94.
22. National Cancer Institute. Common Terminology Criteria for Adverse Events v. 3.0. Bethesda: National Cancer Institute; 2003. Available from: https://ctep.cancer.gov/protocolDevelopment/electronic_applications/docs/ctcaev3.pdf. [Last accessed on 2019 Jan 23].
23. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys 1995;31:1341-6.
24. Franklin HR, Simonetti GP, Dubbelman AC, ten Bokkel Huinink WW, Taal BG, Wigbout G, *et al*. Toxicity grading systems. A comparison between the WHO scoring system and the Common Toxicity Criteria when used for nausea and vomiting. Ann Oncol 1994;5:113-7.
25. Trotti A. The evolution and application of toxicity criteria. Semin Radiat Oncol 2002;12:1-3.
26. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: Updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c332.
27. Dean ME, Coulter MK, Fisher P, Jobst K, Walach H. Reporting data on homeopathic treatments (RedHot): A supplement to CONSORT. Homeopathy 2007;96:42-5.

ब्रेस्ट कार्सिनोमा में रेडियोथेरैपी और कीमोथेरैपी के प्रतिकूल प्रभाव को कम करने के लिए पूर्व–परिभाषित होम्योपैथिक औषधियाँः सामान्य देखभाल के संदर्भ में एक रैंडोमाइज्ड, डबल–ब्लाइंड, मार्गदर्शी परीक्षण

पृष्ठभूमिः रेडियोथेरैपी और कीमोथेरैपी का उपयोग ब्रेस्ट कैंसर में किया जाता है, परन्तु इसके दुष्प्रभाव दिखाई पड़ते हैं। **उद्देश्यः** यह परीक्षण करना कि क्या सामान्य देखभाल (यूसी) और पूर्व–निर्धारित होम्योपैथिक औषधियाँ ब्रेस्ट कार्सिनोमा में रेडियोथेरैपी और कीमोथेरैपी के प्रतिकूल प्रभाव को कम करने में यूसी के साथ प्लैसिबो (पीएल) से अतिरिक्त प्रभाव उत्पन्न कर सकती हैं। **पद्धतिः** इस प्रत्याशित, डबल ब्लाइंड, रैंडोमाइज्ड, प्लैसिबो–नियंत्रित, समानांतर आर्म परीक्षण में, रेडियोथेरैपी (एन=41) और कीमोथेरैपी (एन=47) के दुष्प्रभावों से पीड़ित 88 महिलाओं को यूसी+होम्योपैथी (वेरम; एन=44) या यूसी+पीएल (कंट्रोल; एन=44) ग्रहण करने के लिए रैंडोमाइज्ड,किया गया। प्रमाणित मापदंडो को एक्यूट रेडिएशन मॉर्बिडिटी स्कोरिंग क्राइटेरिया (एआरएमएससी) और कॉमन टॉक्जिसिटी क्राइटेरिया (सीटीसी) के माध्यम से निर्धारित परिणामों का आंकलन आधाररेखा पर और 7 दिनों और 14 दिनों के उपरांत किया गया। अन्य जांचों में पी मूल्यों को सूचित करने के लिए 95 प्रतिशत कॉन्फिडेंस इंटरवेल्स (सीआई) के साथ, रिलेटिव रिस्क (आरआर) और चि स्क्वायर जांचों को भी सम्मिलित किया गया। **परिणामः** आठ रोगियों को छोड़ दिया गया (वेरमः 4, कंट्रोलः 4)। प्रोटोकॉल कंप्लाएंट नमूने (एन=80) का विश्लेषण किया गया। दो परीक्षण भुजाएँ आधाररेखा पर तुलनीय थी। एआरएमएससी के अनुसार, प्रतिक्रियादाताओं (रेस्पॉन्डर्स) की संख्या 7 दिनों के पश्चात (11/18 वर्सेस 1/19, आरआर=3.3, 95 प्रतिशत सीएल 1.7 से 6.3 तक, पी=0.001) और 14 दिनों के पश्चात् (21/22 वर्सेस 4/21, आरआर=15.1, 95 प्रतिशत सीएल 2.2 से 102.4 तक, पी0.001) जो वेरम ओवर कंट्रोल के संदर्भ में सांख्यिकीय रूप से महत्त्वपूर्ण थी। **निष्कर्षः** ब्रेस्ट कार्सिनोमा में रेडियोथेरैपी और कीमोथेरैपी के पश्चात् प्रतिकूल प्रभावों को कम करने में पूर्व निर्धारित होम्योपैथिक औषधियाँ प्लैसिबो से अधिक बेहतर प्रतीत हुई। सुदृढ़ डिजाईन और स्वतंत्र प्रतिकृतियों का प्रयोग करते हुए आगे का मूल्यांकन अधिपत्रित है।

Médicaments homéopathiques prédéfinis pour atténuer les effets indésirables de la radiothérapie et de la chimiothérapie dans le carcinome du sein: essai pilote randomisé, en double aveugle, contrôlé par placebo dans le cadre des soins habituels

Contexte: La radiothérapie et la chimiothérapie sont utilisées dans le cancer du sein, mais entraînent des effets indésirables. **Objectif:** d'Examiner si les soins habituels (SU) associés à des médicaments homéopathiques pré-identifiés peuvent produire un effet au-delà de la SU plus un placebo (Pl) pour atténuer les effets indésirables de la radiothérapie et de la chimiothérapie dans le carcinome du sein. **Méthodes:** Dans cette étude prospective, en double aveugle, randomisée, contrôlée par placebo, à bras parallèle, 88 femmes souffrant d'effets indésirables de la radiothérapie (n = 41) et de la chimiothérapie (n = 47) ont été randomisées pour recevoir soit une SU + homéopathie (verum ; n = 44) ou UC + Pl (contrôle; n = 44). Les résultats, évalués au moyen d'échelles validées, les critères de notation de la morbidité aiguë des radiations (ARMSC) et les critères communs de toxicité (CTC), ont été mesurés à la base de référence et après 7 et 14 jours. D'autres tests comprenaient le risque relatif (RR) avec des intervalles de confiance (IC) à 95% et des tests du chi carré pour rapporter les valeurs p. **Résultats:** Huit patients ont abandonné (verum: 4, contrôle: 4). Un échantillon conforme au protocole (n = 80) a été analysé. Les deux bras d'essai étaient comparables à la base de référence. Nombre de répondeurs selon le score ARMSC après 7 jours [11/18 vs 1/19, RR = 3,3, IC à 95% 1,7 à 6,3, P = 0,001] et 14 jours [16/18 vs 1/19, RR = 9,4, IC à 95% 2,5 à 35,2, p <0,001] étaient statistiquement significatifs, favorisant le verum par rapport au contrôle. Des résultats similaires ont été obtenus dans la notation CTC après 7 jours [15/22 vs 2/21, RR = 3,3, IC à 95% 1,7 à 6,3, p <0,001] et 14 jours [21/22 vs 4/21, RR = 15,1, IC à 95% 2,2 à 102,4, p <0,001]. **Conclusion:** Les médicaments homéopathiques pré-identifiés semblaient supérieurs au placebo pour atténuer les effets indésirables après radiothérapie et chimiothérapie dans le carcinome du sein. Une évaluation plus poussée utilisant des conceptions robustes et des réplications indépendantes est justifiée.

Medicamentos homoeopáticos predefinidos para mitigar los efectos adversos de la radioterapia y la quimioterapia en el carcinoma mamario: Un ensayo piloto aleatorizado, doble ciego, controlado con placebo en el contexto de la atención habitual

Fondo: La radioterapia y la quimioterapia se utilizan en el cáncer de mama, pero causa efectos adversos. **Objetivo:** Examinar si la atención habitual (UC) más los medicamentos homoeopáticos preidentificados pueden producir efecto más allá de la UC más placebo (Pl) en la mitigación de los efectos adversos de la radioterapia y la quimioterapia en el carcinoma mamario. **Métodos:** En este ensayo prospectivo, doble ciego, aleatorizado, controlado con placebo, en brazo paralelo, 88 mujeres que sufrían efectos adversos de la radioterapia (n=41) y quimioterapia (n=47) fueron aleatorizadas para recibir UC homoeopatía (verum; n =44) o UC+Pl (control; n=44). Resultados evaluados a través de escalas validadas, los Criterios de Puntuación de Morbilidad por Radiación Aguda (ARMSC) y los Criterios Comunes de Toxicidad (CTC), se midieron al inicio, y después de 7 y 14 días. Otras pruebas incluyeron riesgo relativo (RR) con intervalos de confianza del 95% (CI) y pruebas cuadradas de chi para reportar valores p. **Resultados:** Ocho pacientes abandonaron (verum: 4, control: 4). Se analizó la muestra compatible con el protocolo (n =80). Los dos brazos de prueba fueron comparables en la línea de base. Número de respondedores según la puntuación de ARMSC después de 7 días [11/18 vs.1/19, RR =3,3, IC del 95% 1,7 a 6,3, P=0.001] y 14 días [16/18 vs. 1/19, RR=9.4, 95% CI 2.5 para 35.2, p<0.001] estadísticamente significativas, favoreciendo el verum sobre el control. Resultados similares se obtuvieron en la puntuación CTC después de 7 días [15/22 vs.2/21, RR-3,3, IC del 95% 1,7 a 6,3, P<0,011] y 14 días [21/22 frente a.4/21, RR-15.1, 95% CI 2.2 a 102.4, P<0.001]. **Conclusión:** Los medicamentos homoeopáticos preidentificados parecían superiores al placebo en la mitigación de los efectos adversos después de la radioterapia y la quimioterapia en el carcinoma mamario.Se garantiza una evaluación adicional mediante diseños robustos y replicaciones independientes.

Vordefinierte homöopathische Arzneimittel zur Milderung der Nebenwirkungen von Strahlentherapie und Chemotherapie bei Brustkarzinom: Eine randomisierte, doppelblinde, Placebo-kontrollierte Pilotstudie im Rahmen der üblichen Pflege

Hintergrund: Strahlentherapie und Chemotherapie wird bei Brustkrebs angewendet, verursacht aber Nebenwirkungen. **Ziel:** Es sollte untersucht werden, ob die übliche Pflege (UC) plus voridentifizierte homöopathische Arzneimittel eine Wirkung jenseits von UC plus Placebo (Pl) bei der Milderung der Nebenwirkungen von Strahlentherapie und Chemotherapie bei Brustkarzinom entfalten können. **Methoden:** In dieser prospektiven, doppelblinden, randomisierten, placebokontrollierten, parallelenarmstudie wurden 88 Frauen mit nebenwirkungender Strahlentherapie (n=41) und Chemotherapie (n=47) randomisiert, um entweder UC Homöopathie zu erhalten. verum; n=44) oder UC Pl (Steuerung; n=44). Ergebnisse, bewertet durch validierte Skalen Akutstrahlung Morbidität Bewertungskriterien (ARMSC) und Gemeinsame Toxizitätskriterien (CTC),wurden zu Beginn und nach 7 und 14 Tagen gemessen.Andere Tests umfassten relatives Risiko (RR) mit 95% Konfidenzintervallen (CI) und Chi-Quadrat-Tests, um p-Werte zu melden. **Ergebnisse:** Acht Patienten fielen aus (Verum: 4, Kontrolle: 4). Protokollkonforme Probe (n=80) wurde analysiert.Die beiden Versuchswaffen waren zu Beginn vergleichbar. Anzahl der Responder nach ARMSC-Score nach 7 Tagen [11/18 vs. 1/19, RR=3.3, 95% CI 1.7 zu 6.3, P=0.001] und 14 Tage [16/18 vs. 1/19, RR=9.4, 95% CI 2.5 to 35.2, p<0.001] statistisch signifikant waren, was verum über die Kontrolle begünstigte.Ähnliche Ergebnisse wurden bei der CTC-Bewertung nach 7 Tagen erzielt [15/22 vs. 2/21, RR=3.3, 95% CI 1.7 to 6.3, P<0.001] und 14 Tage [21/22 vs. 4/21, RR=15.1, 95% CI 2.2 zu102.4, P<0.001]. **Schlussfolgerung:** Voridentifizierte homöopathische Medikamente schienen Placebo bei der Milderung von Nebenwirkungen nach Einer Strahlentherapie und Chemotherapie bei Brustkarzinom überlegen zu sein.Eine weitere Auswertung mit robusten Designs und unabhängigen Replikationen ist gerechtfertigt.

预定义的同源药物，以减轻放疗和化疗对乳腺癌的不利影响：在常规护理背景下的随机、双盲、安慰剂对照的试验

背景: 放射治疗和化疗用于乳腺癌，但造成不良反应。目的：检查常规护理 （UC） 加上预先识别的同性病药物是否可以产生超出 UC 加安慰剂 （Pl） 的效果，以减轻放疗和化疗对乳腺癌的不利影响。方法：在这个前瞻性、双盲、随机、安慰剂对照、平行手臂试验中，88名患有放射治疗（n=41）和化疗（n=47）不良反应的女性被随机接受UC+同源病（茴香; n=44）或UC+Pl（控制;n=44）。结果，通过经过验证的尺度评估急性辐射发病率评分标准（ARMSC）和常见毒性标准（CTC），在基线测量，并在7和14天后。其他测试包括具有 95% 置信区间 （CI） 的相对风险 （RR） 和卡方检验以报告 p 值。[：8名患者辍学（茴：4，控制：4）。 结果: 八名病人辍学(茴香: 4, 控制: 4). 分析了符合协议的样本（n=80）。两种试验武器在基线上是可比的。7 天后根据 ARMSC 分数计算响应者数 [11/18 与. 1/19, RR=3.3, 95% CI 1.7 to 6.3, P=0.001] 和14天 [16/18 vs. 1/19, RR=9.4, 95% CI 2.5 to 35.2, p<0.001] 具有统计学意义，赞成对控制。 7天后在CTC评分中获得了相似的结果 [15/22 vs. 2/21, RR=3.3, 95% CI 1.7 至 6.3, P<0.001] 和14天 [21/22 vs. 4/21, RR=15.1, 95% CI 2.2 to 102.4, P<0.001]. 结论: 预识别的同源药物似乎优于安慰剂在缓解乳腺癌放疗和化疗后的不利影响。需要使用可靠的设计和独立复制进行进一步评估。