The Breast 41 (2018) 127–132

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Efficacy of scalp cooling in reducing alopecia in early breast cancer patients receiving contemporary chemotherapy regimens

Arlene Chan [a, *], Astrid Bauwens [b], Sally Pontre [c], Sally Jackson [c], Frances McGlone [c], Tracie Ernenwein [c], Jun Chih [d], Christopher Reid [d]

[a] Breast Cancer Research Centre-WA and Curtin University, Perth, WA, Australia
[b] Ramsay Health, Perth, WA, Australia
[c] Breast Cancer Research Centre-WA, Nedlands, WA, Australia
[d] Schools of Public Health & Preventative Medicine, Curtin University & Monash University, Australia

ARTICLE INFO

Article history:
Received 10 June 2018
Received in revised form
15 July 2018
Accepted 16 July 2018
Available online 18 July 2018

Keywords:
Scalp cooling
Contemporary chemotherapy
Early breast cancer

ABSTRACT

Introduction: Hair loss as a result of chemotherapy for early breast cancer (EBC) is a frequent and distressing side effect. Minimising hair loss may improve mood and body image. Our aim was to determine scalp cooling (SC) efficacy in EBC patients receiving contemporary chemotherapy regimen, to inform future patients choice to use SC or not.

Methods and Results: Prospective cohort study of 60 stage 1–3 EBC patients recommended to receive taxane or anthracycline-taxane chemotherapy regimens. The primary outcome was incidence of minimal hair-loss (MHL - defined as 60% Dean grade 1 or 2). Patients were categorised by chemotherapy (3 groups) and randomised 1:1 within each group to two scalp cooling temperature settings using the Dignitana Dignicap machine (secondary endpoint). Patients reported degree of hair loss using the Dean score on day 1 of each cycle and following the last chemotherapy.

Results: On an intention-to-treat basis, 33% of patients reported MHL, thus our primary endpoint was not achieved. Patients receiving taxane-only chemotherapy had the highest rate of MHL (45%). No other factors (including hair type, age, body weight, temperature setting) predicted for MHL. Patient-reported anxiety reduced significantly in all patients, but no difference was observed for depression or body image irrespective of degree of hair loss. SC-related adverse events were uniformly of low grade and all resolved.

We would recommend the use of SC for all patients receiving taxane-based chemotherapy, with its use for those patients recommended for anthracycline-taxane regimens being made on an individual basis. Trial Registration ***anztr.org.au ACTRN12615001106527***.

1. Introduction

Chemotherapy-induced alopecia (CIA) is one of the most commonly occurring and distressing side effect of breast cancer treatment. Studies indicate that even with the knowledge of temporary hair loss, more than half of respondents describe this symptom as being burdensome, as well as an outward sign of cancer associated with negative self-image and feelings of depression and anxiety [1–5].

Although CIA is almost always reversible after chemotherapy, current options to prevent CIA from occurring are limited [1,3]. Scalp cooling (SC) to reduce the degree of CIA has been utilised for over 40 years and is currently the most effective technique in reducing CIA when compared with no scalp cooling [3,6–8].

Despite consensus in the literature that scalp cooling is effective, several variables have been suggested to influence its success. These include hair thickness, type and dose of chemotherapy treatment, scalp temperature and cap fitting technique [9]. Scalp cooling in patients receiving taxane-based regimens has been shown to be more effective than those receiving anthracycline with or without taxanes [1,6]. It has been suggested that lowering the scalp subcutaneous tissue to 22 °C is necessary to prevent alopecia, with pre-clinical studies, suggesting that temperatures of

* Corresponding author. Breast Cancer Research Centre-WA, 101 Monash Ave, Nedlands, Perth, WA 6009, Australia.
E-mail address: arlenechan@me.com (A. Chan).

https://doi.org/10.1016/j.breast.2018.07.006
0960-9776/

14 °C–18 °C may be even more effective [9,10].

This study was initiated in an effort to address the comparative efficacy of SC in women receiving different contemporary chemotherapy regimens, in an effort to inform future patients in their decision-making as to whether to use SC or not. Further we explored the impact of the degree of CIA on mood and body image, whether lowering the SC temperature beyond the usual setting of 5 °C could lead to greater efficacy and plan long-term follow-up to observe for the incidence of scalp metastases.

2. Materials and methods

2.1. Study design

Consecutive patients with stage I to III breast cancer treated in a single institution were invited to participate in this study. The key inclusion criteria included women aged over 18 years who were recommended to receive one of the following chemotherapy regimens docetaxel cyclophosphamide (TC), docetaxel, cyclophosphamide and trastuzumab (TCH), docetaxel, doxorubicin, cyclophosphamide (TAC), doxorubicin, cyclophosphamide (AC), doxorubicin, cyclophosphamide – paclitaxel (AC-P) (2 or 3 weekly), fluorouracil, epirubicin and cyclophosphamide – docetaxel (FEC-D) in the neoadjuvant or adjuvant setting; conversant in English; provided signed consent and agreed to undergo follow-up for 10 years. Patients were ineligible if chemotherapy was given on a weekly schedule; had a history of cold sensitivity, cold agglutinin disease, cryoglobulinemia, cryofibrinogenemia or cold traumatic dystrophy; had existing alopecia of any grade as assessed by the clinician and were known to have hypersensitivity to silicon.

Consenting patients were categorised according to their recommended treatment regimen as determined by the treating oncologist: Cohort 1 taxane-based regimens - TC or TCH; Cohort 2 concurrent anthracycline and taxane - TAC and Cohort 3 anthracycline with or without sequential taxane – AC, AC-P, FEC-D (Fig. 1).

Cohort 1 underwent treatment TC (docetaxel 75 mg/m^2, cyclophosphamide 600 mg/m^2); TCH (docetaxel 75 mg/m^2, carboplatin AUC 6, trastuzumab 8 mg/kg loading and 6 mg/kg every 21 days for 52 weeks), Cohort 2 underwent treatment TAC (docetaxel 75 mg/m^2, doxorubicin 60 mg/m^2, cyclophosphamide 600 mg/m^2), Cohort 3 underwent treatment FEC-D (fluorouracil 500 mg/m^2, epirubicin 100 mg/m^2, cyclophosphamide 500 mg/m^2, docetaxel 100mg/m^2, AC-P (doxorubicin 60 mg/m^2, cyclophosphamide 600 mg/m^2, paclitaxel 175 mg/m^2).

Patients within each cohort were randomised on a 1:1 ratio to the SC system set at 5 °C or 3 °C for the duration of their chemotherapy treatment. This was done by a member of staff uninvolved in the trial conduct and using a sequentially numbered card system. The treating clinician were blinded to the temperature assignment.

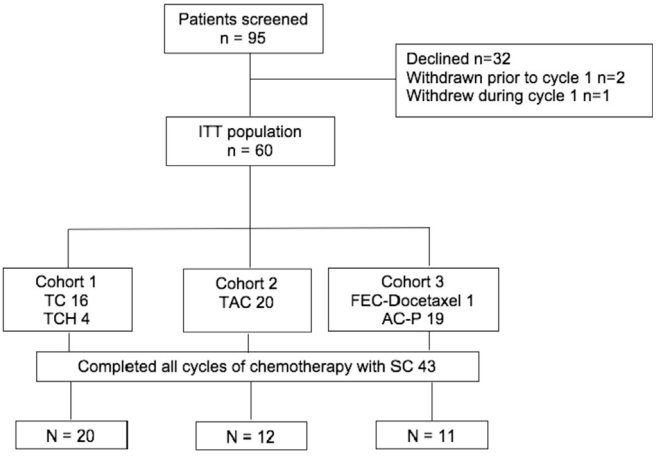

Fig. 1. CONSORT diagram.

The primary outcome measure was to assess the proportion of patients who self-reported Dean score grade 1 or 2 (<25% and 25%–50% hair loss, respectively and defined as minimal hair loss) at two to four weeks after completion of chemotherapy compared to baseline. Secondary outcome measures included association of hair loss to anxiety, depression and body image; an exploratory evaluation of the efficacy between temperature setting of 3 °C as compared to 5 °C. The default temperature setting of 5 °C is considered to be equivalent to a scalp temperature of 22 °C. We hypothesized lowering the temperature setting on this system to 3 °C would simulate a scalp temperature below 22 °C. All SC-related adverse events were reported from commencement of chemotherapy until up to 28 days following the last cycle. The study received ethics approval from the institutional human ethics and research committee and was conducted in accordance with the Helsinki Declaration.

2.2. Treatment

The Dignitana Dignicap is a TGA approved refrigerated cooling system – the details of machine schematics are well documented. Prior to the first cycle of chemotherapy, the appropriate sized cap for each patient was determined by the study nurse. At the start of each treatment, the patient's cap was fitted by the study nurse in accordance with the product information recommendations and the temperature was set according to assigned randomisation. SC was initiated 30 min prior to the start of chemotherapy with the cooling cap worn throughout chemotherapy treatment and for a further 90 min following chemotherapy completion.

2.3. Study assessments

Patients reported degree of hair loss using the 5-point Dean's scale [11], as did the treating clinician, on day one from cycle two onwards (comparing this to the cycle immediately preceding) and then at 14–28 days after the last cycle of (comparing this to baseline). All other study assessments were done at this same time point throughout the study. Patient mood was assessed by the Patient Health Questionnaire-9 (PHQ-9) [12] and Generalised Anxiety Disorder (GAD-7) [13], whilst the patient's body image was assessed with the Body Image Scale (BIS) [14] questionnaires. Information on the use of any head covering was also collected. An optional consent was signed by patients who were agreeable for a pre- and post-chemotherapy photograph of their hair. Patients who utilised the SC for all cycles of chemotherapy were asked at the end of chemotherapy treatment if they considered the device worthwhile and whether they would use SC again, if needed in the future. Adverse events were recorded throughout the study and assessed by the investigator as to a causality relationship to the SC device.

2.4. Statistical analyses

For the primary outcome, we anticipated that the incidence of patients reporting minimal hair loss (i.e. Dean score of 1 or 2) after completion of planned cycles of chemotherapy would be 60% in the population overall, as compared to the 5% or lower incidence traditionally seen in this clinical setting without the use of SC. To detect this difference with 80% power at a one-sided significant level of 0.025 (lower from 0.05 as Bonferroni correction applied to enable multiple groups comparisons), stratifying for treatment cohorts, a final sample of 10 per group was required. Assuming a