SA Journal of Oncology
ISSN: (Online) 2523-0646, (Print) 2518-8704

Does hair curl variation influence the efficacy of scalp cooling in the prevention of chemotherapy-induced alopecia in breast cancer patients? A randomised pilot trial

Authors:
Odirile Obuseng[1]
Nonhlanhla Khumalo[2]
Thurandrie Naiker[1]
Tselane Thebe[1]

Affiliations:
[1]Department of Radiation Oncology, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

[2]Division of Dermatology, Department of Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

Research Project Registration:
Project Number: 892/2016

Corresponding author:
Odirile Obuseng,
odiobu@gmail.com

Dates:
Received: 14 Apr. 2021
Accepted: 07 May 2021
Published: 24 June 2021

How to cite this article:
Obuseng O, Khumalo N, Naiker T, Thebe T. Does hair curl variation influence the efficacy of scalp cooling in the prevention of chemotherapy-induced alopecia in breast cancer patients? A randomised pilot trial. S. Afr. j. oncol. 2021;5(0), a181. https://doi.org/10.4102/sajo.v5i0.181

Background: Scalp cooling is reported to reduce Chemotherapy-induced alopecia (CIA).

Aim: To compare the efficacy of scalp cooling for straight versus curly hair in a pilot trail.

Setting: A radiation oncology breast cancel clinic.

Methods: This 20-month randomised controlled trial recruited females (18–65 years) to receive chemotherapy (Adriamycin or Epirubicin and Cyclophosphamide followed by Paclitaxel) with or without scalp cooling. Outcomes were percentage alopecia (*Severity ALopecia Tool)* by hair curvature and treatment retention.

Results: Forty eight patients (24 per group) were randomised; four in each group withdrew before first study visit and photographs of three in the cooling group could not be found for assessment. Thus 77% constituted the intention-to-treat population (17 cooling vs. 20 control). Agreement on alopecia severity was good overall (intra-class correlation coefficient [ICC] = 0.94; 95% confidence interval [CI]: 0.85–0.97) and at six of seven time points. Overall, cooling significantly reduced CIA, relative to no-cooling (58.15 ± 28.46 vs. 37.29 ± 20.52; $p = 0.0167$); however, percentage alopecia was cosmetically significant. There was no difference in CIA between cooling participants with straight ($n = 8$) versus curly hair ($n = 9$), ($p = 0.0740$).

The number of patients completing the various cycles of chemotherapy declined from 77.1% at cycle 1 to 18.8% at cycle 7 for the whole study, and from 100% each to 17.6% and 30.0% for cooling and control groups, respectively ($p = 0.451$).

Conclusion: This study suggests that hair curvature has no significant impact on the efficacy of scalp cooling to reduce CIA, however, this requires confirmation.

Keywords: alopecia; breast cancer; chemotherapy; chemotherapy-induced alopecia; efficacy; hair curvature; scalp cooling.

Introduction

Breast cancer is the most diagnosed malignancy and the leading cause of cancer death amongst women worldwide. In 2018, the number of newly diagnosed cases was estimated to be 2.1 million, accounting for almost 25% of all cancers in women.[1] Chemotherapy (neoadjuvant or adjuvant) is often administered in the curative setting as it has been shown to reduce the 10-year relative risk of death from breast cancer by approximately 35%[2] as well as the risk of recurrence by treating micrometastatic disease.[3] This treatment, although effective against cancer cells, is associated with unintended effects on other normal cells such as hair follicles, which may result in alopecia.[2]

Chemotherapy-induced alopecia (CIA), although reversible, has been described as one of the most common and distressing side effects of cancer therapy, affecting approximately 65% of all patients and influencing treatment decisions in some women who want to avoid hair loss.[4] Hair loss has also been associated with lower overall quality of life (QOL)[5] and was found to contribute to depression, a condition associated with poor adherence to chemotherapy and risks of cancer progression.[6] In the first study of its kind, Lemieux et al.[5] compared mortality amongst women with non-metastatic breast cancer treated with chemotherapy who used scalp cooling to reduce CIA compared to similar women who did not. They found no negative impact on survival for women who used scalp cooling with their chemotherapy.

Scalp cooling has been proven effective in reducing CIA.[7] In a recent review of three studies as well as two prospective trials, in which patients were randomised to chemotherapy either with or without scalp cooling, minimal or no hair loss was seen in patients who received scalp cooling in contrast to almost 100% alopecia for patients in the control groups. The effectiveness of this intervention is reported to depend on many factors including hair curvature, with improved outcomes suggested in patients with a 'Caucasian' type of hair.[4] This claim has never been validated in a randomised prospective trial and prior outcomes are derived mainly from patients with straight hair; therefore, it remains unclear whether these results can be generalised to patients with curlier hair curvature.

In a randomised prospective clinical study, the Scalp Cooling Alopecia Prevention (SCALP) trial, the cooling system was significantly more likely to cause less hair loss. In this trial, although no multivariate analysis by hair type is stipulated, demographic information shows that only 12% of the study population was black or African American.[3] In another prospective study, the use of scalp cooling was associated with less hair loss after chemotherapy. In this study, as with previous trials, black women constituted a minority of the study population with only 10.4% representation.[8]

Objectives

The objectives of the study were as follows:

- To determine whether scalp cooling is less effective in patients with curly hair compared to those with straight hair and to verify findings from previous research indicating that the severity of CIA is less in participants receiving scalp cooling versus those that are not.
- To assess feasibility of conducting a definitive trial in terms of recruitment and retention.

Methods

Trial design

The trial was a pilot monocentric, prospective, investigator initiated, randomised (patient) controlled single blind (three independent dermatologists) study of scalp cooling versus no cooling in breast cancer patients receiving neoadjuvant or adjuvant chemotherapy in a 21-day cycle. Equal randomisation (1:1) was employed to provide the greatest power for testing effectiveness in a future definitive randomised controlled trail (RCT).

After obtaining institutional approval to conduct the study, the trial inclusion criteria were amended to include patients receiving neoadjuvant chemotherapy. This was in keeping with a recent update to the Groote Schuur Hospital (GSH) departmental breast cancer clinical protocol.

The study was conducted in cooperation between the Department of Radiation Oncology Breast Clinic and the Division of Dermatology at GSH.

Sample size

Using an online sample size calculator, ClinCalc.com (https://clincalc.com), it was estimated that 46 participants would be a large enough sample to provide a measure of the impact of hair curl variation on scalp cooling. This was based on the following assumptions: mean hair loss of 95% and 50% within the non-cooling and cooling groups, respectively; 0.05 probability of a type 1 error and powered at 95% to detect a difference between the two groups. A target of 52 patients was set to account for attrition.

Participants

According to the inclusion criteria, participants should: (1) belong to female gender; (2) belong to the age group 18–65 years; (3) have had breast cancer surgery – mastectomy or breast conserving methods, with or without lymph node removal, < 12 weeks before inclusion or planned surgery after neoadjuvant chemotherapy; (4) have had planned antineoplastic therapy with chemotherapy, Adriamycin or Epirubicin and Cyclophosphamide followed by Paclitaxel (AC/EC -P), including written consent. Participants were excluded if they had: (1) evidence of alopecia at baseline, (2) planned radiation therapy of the skull before or during the study, (3) antineoplastic therapy within 6 months prior to baseline, (4) inadequately treated hypo or hyperthyroidism, (5) known cold sensitivity, cold agglutinin disease, cryoglobulinemia and cryofibrinogenemia, (6) enrolled in another study at the time of recruitment, (7) refused to participate in the study or withdrawn consent before the first post-treatment assessment.

At the end of each week, the investigator collected and scanned the files of all patients seen in the breast clinic within that week to determine eligibility. Potential participants were then called by the investigator to schedule a screening appointment prior to commencement of chemotherapy. Once eligibility was confirmed, informed written consent was obtained followed by a thorough scalp examination to exclude baseline alopecia. Pictures and hair samples were then taken and sent to the University of Cape Town Hair and Skin Research (HAS) Lab for analysis and geometric classification. Using objective measures of curliness, such as a curve diameter meter, curl meter and wave crest assessment, hair was assigned to eight groups (I–VIII), with I–IV and V–VIII being classified as straight and curly, respectively.

Randomisation

Prior to commencement of recruitment, sequence generation was done using the online programme 'Research Randomizer' (https://www.randomizer.org). The total number of participants were divided into two groups of 26 each, curly and straight hair. For each of these groups, this number was input into the programme with resultant generation of a randomised sequence of the letters A and B, in a 1:1 ratio. It was already decided before randomisation that A would represent allocation to the cooling arm and B the control arm. After recruitment and hair type testing, patients were

allocated to either the straight or curly group and assigned to either undergo cooling or not, based on the corresponding letter (A or B) alongside their sequential listing within the relevant group.

Interventions

At the first chemotherapy treatment visit, participants were notified of their study group allocation. For participants randomised to receive scalp cooling, the appropriately sized cooling cap was selected ensuring good contact with the scalp. The scalp was then pre-cooled for 30 min prior to commencement of treatment. Scalp cooling was continued throughout the administration of chemotherapy and for 90 min afterwards. Patients randomised to the control group received chemotherapy only.

At all subsequent visits, patients were asked to complete a hair loss questionnaire. This was followed by obtaining standardised clinical photographs and hair sampling.

Analytical methods

The research statistician encoded the data in Microsoft Excel. Stata MP version 14 software was used for data processing and analysis.

Efficacy of scalp cooling, including in patients with curly versus straight hair, was determined by objective comparative percentage hair loss analysis between the groups: three dermatologists not involved in (and blinded) the trial were chosen to grade photographs using the *Severity ALopecia Tool* (SALT) and a mean score between the dermatologists was used to allocate severity.

A one-way analysis of variance (ANOVA) was performed to compare the mean change in CIA severity between participants with curly and straight hair whilst an independent *t*-test was used to make a similar comparison between the cooling and non-cooling groups. Significant ANOVA results were further analysed using Tukey honest significant difference (HSD) (one way). Intra-class correlation coefficient (ICC) was used to assess agreement between the three dermatologists.

Recruitment and retention were assessed by the ability to enrol the pre-set number of participants and the number of patients retained through each subsequent cycle of chemotherapy, respectively. A chi-square test was performed to assess the dropout rate between the cooling and non-cooling groups. $p \leq 0.05$ was considered statistically significant.

Results

Recruitment

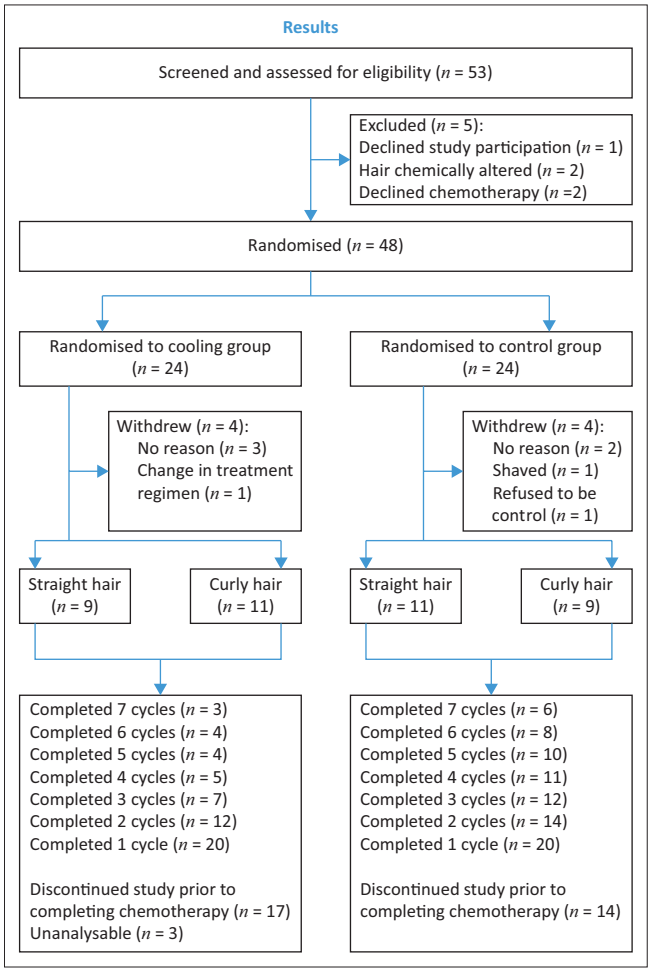
Fifty-three eligible female patients with breast cancer were enrolled from the (location masked for blind review) specialist breast clinic between May 2017 and November 2018. Study recruitment closed once the intended sample size had been reached.

Participant flow

Out of the 53 eligible patients screened, 48 (90.6%) fulfilled the randomisation criteria and agreed to participate in the study. Study retention figures through the chemotherapy cycles are reflected in Figure 1[9]. Thirty-seven (77.1%) of the randomised patients completed at least one cycle of chemotherapy, with analysable pictures, and were included in the final intention-to-treat (ITT) analysis, including: 17 (45.9%) and 20 (54.1%) in the scalp cooling and control arms, respectively, of which 18 (48.6%) and 19 (51.4%) had curly and straight hair, respectively. The reasons provided for participant withdrawal through the various cycles of chemotherapy are outlined in Table 1.

Baseline data

Participants in the two groups, cooling and non-cooling, were similar in terms of age, mean number of chemotherapy cycles completed, hair relaxer or colour use, smoking history, breast cancer subtype and prescribed treatment regimen. However, a higher proportion of patients in the cooling group were given adjuvant chemotherapy compared to the



Source: Adapted from Eldridge SM, Chan CL, Campbell MJ, et al. CONSORT 2010 statement: Extension to randomised pilot and feasibility trials. BMJ. 2016;355:i5239. https://doi.org/10.1136/bmj.i5239

FIGURE 1: Flow diagram of progress through phases of pilot trial.

non-cooling group (53% vs. 20%) and conversely, a higher proportion of patients in the non-cooling group were given neo-adjuvant chemotherapy compared to the cooling group (80% vs. 40%); see Tables 2 and 3.

Outcomes and estimation

Photographs of alopecia severity were blindly, individually, assessed for each participant and time point by three dermatologists using the SALT score.

TABLE 1: Reasons for withdrawal.

Reason	Total	Cooling	No cooling
Shaved hair	6	2	4
Scalp cooling side effects	7	7	0
Defaulted chemotherapy	4	1	3
Chemotherapy stopped	1	1	0
No reason provided	13	6	7
Total	**31**	**17**	**14**

TABLE 2: Baseline characteristics by treatment group.

Characteristics	Categories	Cooling (n = 17)		No cooling (n = 20)		p
		Frequency	Percentage	Frequency	Percentage	
Hair type	Straight	8	47	11	55	0.630
	Curly	9	53	9	45	
Hair relaxer or colour use	Yes	7	41	10	50	0.591
	No	10	59	10	50	
Smoker	Yes	3	18	3	15	0.811
	No	12	71	12	60	
	Ex-smoker	1	6	3	15	
	Unknown	1	6	2	10	
Adjuvant chemo	Yes	9	53	4	20	0.036*
	No	8	47	16	80	
Neo-adjuvant chemo	Yes	8	47	16	80	0.036*
	No	9	53	4	20	
IDC†	Yes	17	100	18	90	0.489
	No	0		2	10	
Chemotherapy regimen	EC-P	9	53	7	35	0.331
	AC-P	8	47	13	65	

IDC, invasive ductal carcinoma, EC-P, Epirubicin followed by Paclitaxel; AC-P, Adriamycin and Cyclophosphamide followed by Paclitaxel.

*, Statistically significant $p < 0.05$.

†, The most common type of breast cancer.

TABLE 3: Further baseline characteristics by treatment group.

Characteristics	Cooling (n = 17) Mean ± s.d.	No cooling (n = 20) Mean ± s.d.	p
Age (years)	47.76 ± 10.28	49.35 ± 7.56	0.5930
Number of cycles completed	2.94 ± 2.36	4.05 ± 2.58	0.1846

s.d., standard deviation.

When the mean overall change in alopecia severity post-chemotherapy was compared in the ITT population, no statistically significant difference in CIA severity was found between participants with curly (n = 9) and straight (n = 8) hair (36.11 ± 18.33 in the curly-cooling group; 50.89 ± 37.04 in the curly no-cooling group; 38.63 ± 23.98 in the straight-cooling group; 64.09 ± 18.84 in the straight no-cooling group; p = 0.0740). However further analysis, using Tukey HSD, showed that the mean change in alopecia severity at cycles 2 and 3 were significantly higher in participants with curly hair randomised to the control group compared to those with curly hair that underwent scalp cooling. p-values were 0.0138 and 0.0347, respectively (Table 4).

The mean change in alopecia severity post-chemotherapy (overall) was significantly higher in the non-cooling group compared to the cooling group, 58.15 ± 28.46 and 37.29 ± 20.52, respectively, with p = 0.0167. This result supports previously reported evidence for the efficacy of scalp cooling to reduce the severity of CIA. When results were analysed by cycle (Table 5), statistically significant differences were also found at cycles 2, 3 and 5, 80.79 ± 17.63 versus 42.90 ± 34.26; 89.25 ± 13.66 versus 57.43 ± 11.43; and 79.50 ± 27.21 versus 44.25 ± 26.42; with p values of 0.0018, 0.0055 and 0.0477, respectively.

The overall ICC value for the observation of the three assessors was estimated to be 0.94 (95% confidence interval [CI]: 0.85–0.97). Further, agreement on alopecia severity was good in six of seven time points (Table 6).

TABLE 5: Comparative chemotherapy-induced alopecia through each cycle of treatment in the cooling versus non-cooling groups.

Cycle	Cooling		No cooling		p
	n	Mean ± s.d.	n	Mean ± s.d.	
Overall post-chemo	17	37.29 ± 20.52	20	58.15 ± 28.46	0.0167*
Cycle 1	17	25.18 ± 20.28	20	33.40 ± 30.97	0.3555
Cycle 2	10	42.90 ± 34.26	14	80.79 ± 17.63	0.0018*
Cycle 3	7	57.43 ± 11.43	12	89.25 ± 13.66	0.0055*
Cycle 4	5	66.40 ± 18.73	11	82.45 ± 18.08	0.1255
Cycle 5	4	44.25 ± 26.42	10	79.50 ± 27.21	0.0477*
Cycle 6	4	26.75 ± 30.25	8	62.63 ± 37.85	0.1322
Cycle 7	3	29 ± 17.47	6	51.33 ± 39.07	0.4188

s.d., standard deviation.

*, Statistically significant $p < 0.05$.

TABLE 4: Comparative chemotherapy-induced alopecia through each cycle of treatment across the following groups: curly hair-cooling, curly hair-no cooling, straight hair-cooling, straight hair-no cooling.

Cycle	Curly-cooling		Curly-no cooling		Straight-cooling		Straight-no cooling		p
	n	Mean ± s.d	n	Mean ± s.d	n	Mean ± s.d	n	Mean ± s.d.	
Overall post-chemo	9	36.11 ± 18.33	9	50.89 ± 37.04	8	38.63 ± 23.98	11	64.09 ± 18.84	0.0740
Cycle 1	9	19.11 ± 17.03	9	32.11 ± 36.06	8	32 ± 22.53	11	34.45 ± 27.92	0.6084
Cycle 2	6	39 ± 37.02	5	90.40 ± 12.28	4	48.75 ± 34.07	9	75.44 ± 18.43	0.0138*
Cycle 3	6	54.17 ± 31.76	4	95.25 ± 6.95	1	77 ± 0	8	86.25 ± 15.54	0.0347*
Cycle 4	5	66.40 ± 18.73	4	85.50 ± 13.20	0	-	7	80.71 ± 21.16	0.2981
Cycle 5	4	44.25 ± 26.42	4	86.75 ± 18.86	0	-	6	74.67 ± 32.39	0.1229
Cycle 6	4	26.75 ± 30.25	4	70.50 ± 24.96	0	-	4	54.75 ± 50.54	0.2867
Cycle 7	3	-	3	-	0	-	3	-	0.5172

s.d., standard deviation.

*, Statistically significant $p < 0.05$.

Interpretation: based on the 95% CI of the ICC estimate, values less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90 are indicative of poor, moderate, good and excellent reliability, respectively.

The overall CIA risk ratio (RR), as well as after each cycle of chemotherapy, was calculated, and is shown in Table 7.

Ancillary analyses

There was insufficient evidence to suggest a difference in the severity of alopecia caused by the two chemotherapy regimens, Adriamycin or Epirubicin plus Cyclophosphamide and Paclitaxel, 68.64 ± 15.90 versus 52.24 ± 38.02 and 58.25 ± 22.66 versus 70.60 ± 29.55; with *p*-values of 0.1581 and 0.3005 for AC versus P and EC versus P, respectively.

Harms

The study dropout rate was similar in the cooling versus control groups (17 vs. 14), *p*-value of 0.451. A comparison of the attrition rate between the two groups found a non-significant difference after all cycles except cycle 5 where there was a significantly higher dropout rate in the cooling group relative to the no-cooling group (80% vs. 50%, $p = 0.047$). Three participants from the cooling group were accidentally deleted from the study camera further reducing analysable data.

Discussion

Overview

Overall, the mean change in CIA severity was not significant between participants with straight and curly hair. However, within the curly group, significantly higher CIA severity was found in the control group, relative to those receiving scalp cooling, at two time points: post cycles 2 and 3. Furthermore, the mean change in alopecia severity post-chemotherapy (overall) was significantly higher in the non-cooling group compared to the cooling group.

TABLE 6: Intra-class correlation coefficient values through the chemotherapy cycles.

Cycle	ICC	95% CI
Overall	0.94	0.85–0.97
Baseline	0.94	0.89–0.97
Cycle 1	0.94	0.89–0.97
Cycle 2	0.91	0.80–0.96

ICC, intra-class correlation coefficient; CI, confidence interval.

TABLE 7: Chemotherapy-induced alopecia risk ratio: curly versus straight hair.

Cycle	Number	Risk ratio (RR)	95% CI
Overall post-chemo	37	0.99	0.85–1.16
Post cycle 1	37	0.94	0.77–1.14
Post cycle 2	24	1.08	0.93–1.27
Post cycle 3	19	1.00	1.00
Post cycle 4	16	1.00	1.00
Post cycle 5	14	1.00	1.00
Post cycle 6	12	1.00	1.00
Post cycle 7	9	1.00	1.00

CI, confidence interval.

Interpretation

Although no previous trials defined comparative CIA outcomes by hair curvature as a study objective, in one of the trials a multivariate analysis failed to show that hair type had a statistically significant impact.[10] This analysis seems to be in keeping with our findings of no statistically significant difference in CIA between curly versus straight hair. Although the mean change in alopecia severity at cycles 2 and 3 were significantly higher in participants with curly hair randomised to the control group, compared to those that underwent scalp cooling, these are to be interpreted with caution as the overall risk reduction was not statistically significant, with a RR of 1.08 (95% CI: 0.93–1.27) and 1 (95% CI: 1), respectively, as demonstrated in Table 7.

Findings from this study (Table 6) seem to be in keeping with previous findings demonstrating a significant reduction in alopecia in patients who used scalp cooling whilst receiving chemotherapy regimens that normally cause severe CIA, relative to those that did not use scalp cooling during treatment. Despite this benefit, some patients reported that the percentage, as well as pattern and distribution, hair loss was still large and made it cosmetically difficult to conceal, with some opting to rather shave their heads instead.

The ICC value for the three observers was indicative of good to excellent reliability (Table 4).

The variable timing of chemotherapy administration between the cooling and non-cooling groups, as demonstrated in Tables 2 and 3, is not expected to affect outcomes as the chemotherapy regimens are similar and the timing of administration of chemotherapy is not known to influence susceptibility to CIA.

An unexpected finding in this study was 7 (41.18%) out of 17 patients in the scalp cooling arm withdrawing from the study because of device-related side effects (previous studies have reported rates of between 2.8% and 6.18%). Of these, six (35.29%) cited headaches as the main reason for withdrawal whilst two (11.76%) withdrew as a result of feeling cold and one (5.88%) because of scalp tenderness.

The results of this trial support the feasibility of conducting a larger definitive randomised trial involving breast cancer patients as a result of receiving chemotherapy (neo-adjuvant or adjuvant) as part of their radical treatment. Despite the inability to meet all predetermined criteria and timelines we believe this trial still demonstrates feasibility albeit with a need for protocol and resourcing amendments to improve recruitment and retention rates. With regard to recruitment, we believe we were probably too confident when targeting a 2-month recruitment period, however with faster hair classification turnaround times an improvement can be made on the 18-month timeline attained. To address both the shortfall in recruitment and retention in a future trial, we believe the solution is an improvement in human resourcing as well as securing more scalp coolers.

One of the goals of this pilot study was to investigate the feasibility of a future definitive trial based on study recruitment and retention. It was anticipated that trial recruitment would begin soon after institutional approval was granted; however, this had to be delayed as a result of a change in the departmental chemotherapy treatment protocol, which necessitated a subsequent ethics application for approval of the minor change in the trial protocol. We initially envisioned that recruitment would run over a 2-month period with the trial completed within 10 months of commencement. The recruitment time target was not met, with the number of eligible patients only being recruited after 18 months and the study concluded after approximately 20 months of commencement.

The reasons for the delay in recruitment include a higher than anticipated proportion of patients receiving neo-adjuvant chemotherapy, which was prioritised for a faster than usual treatment start date; this often meant that hair sampling and classification could not be completed in time for chemotherapy commencement. If the turnaround time for hair classification was accelerated, this could potentially reduce the recruitment time period in a future definitive trial. Another reason is that only two scalp cooling devices were available for the trial and if patients were booked to start chemotherapy on a day on which two trial patients randomised to scalp cooling were already booked, these patients had to be excluded because of the possibility of them being randomised to scalp cooling, as a machine would not be available. In a future trial, the use of more scalp cooling devices could help to reduce recruitment timelines.

Once randomised, eight patients declined to actively participate before even beginning the intervention. To avoid early withdrawal in a definitive study, a suggestion would be to spend more time explaining the trial and the implications of the outcomes, including potential benefits for future patients, during the consent process. A further 31 patients dropped out of the study (through the subsequent seven cycles of chemotherapy) for various reasons after receiving at least one cycle of chemotherapy. Because of time constraints, as the investigator was in an active clinical training programme at the time of the pilot trial, patient counselling sessions were often brief. For the definitive trial, we believe retention rates may be improved by allocating a dedicated investigator to ensure adequate counselling of patients at each treatment visit. An emphasis would need to be placed on addressing the potential reasons for study withdrawal, as identified in the pilot trial, including highlighting the possibility of device-related side effects and encouraging patients to report these as soon as they occur to allow early management; examples include the early use of analgesics and body warmers. Dedicating more time to probing reasons for patient withdrawal (from the pilot trial) may have assisted in determining such in the patients that chose not to offer a reason for withdrawal; however, this had to be balanced with the ethics of respecting the right of patients not to offer a reason. Most of the patients that chose to shave their hair did so because of patchy CIA patterns that had a negative cosmetic effect; encouraging patients to use head covers instead of shaving may have reduced the need to shave in these patients. With regard to the missing pictures, the camera used for the trial was a shared resource within the department and some information was lost during the camera exchange process. A suggestion for a future trial is to obtain a camera that is solely dedicated to the study so as to limit the risk of losing information.

Generalisability

Although our data reflect the activities of only a single pilot trial, we believe that the findings and methods used are well suited to serve as a template for a future definitive RCT as well as for analysing other studies with different designs in other research settings.

Limitations

There are several limitations to this trial. It was a single-blinded design (because of the cooling) that had a relatively small sample size. Although it was determined that a relatively small number of patients (46) were required to provide adequate data, given that the chemotherapy regimens used are known to cause marked alopecia, we were unable to attain 46 as the ITT sample size. Eight participants (four in each group) dropped out before study initiation and clinical pictures of three participants in the cooling group could not be found leaving only 37 with analysable results at the end of the trial. There was additional patient drop out through the cycles of chemotherapy, with a differential attrition noted in favour of the non-cooling group. It was not determined if this differential dropout led to biased results.

Conclusion

Our study findings suggest that scalp cooling is effective, as evidenced by a statistically significant reduction in the overall mean CIA severity in patients who underwent scalp cooling compared to the control group. Hair curvature does not seem to impact the effectiveness of this intervention as a significant overall reduction in CIA could not be demonstrated between patients with straight and curly hair. A larger study is required to verify these findings.

Acknowledgements

The authors would like acknowledge the invaluable contribution of the following persons for making the research successful:

- Sister Juliet Esterhuizen, the study nurse, for her crucial role in the implementation of the study.
- Professor Jeannette Parkes, head of the Department of Radiation Oncology, as well as the doctors, nurses and administration staff in the Breast Clinic for their immense contribution in making the study a success.
- Dermatologists: Prof N.P. Khumalo, Dr Eugene Hirschfeld and Dr Tonderai Nyika, who assessed alopecia severity in the study photographs.

- The patients who agreed to participate in this trial; it is through their participation that this study was possible.

Competing interests

This is an investigator-initiated study; we requested a loan of Paxman Hair Loss Prevention System for the study.

Authors' contributions

O.O. conducted the research and wrote the initial draft of the manuscript. N.K. supervised the research and reviewed the manuscript drafts. T.N. and T.T. reviewed and edited the manuscript.

Funding information

Paxman Coolers Ltd. have agreed to engage in a loan agreement for two Paxman Scalp Cooling Systems for the duration of the study. Funding was also received from the South African Research Chairs Initiative (SARChI) Chair (Dermatology and Toxicology) and the South African Medical Research Council.

Data availability

Raw data were generated at Groote Schuur hospital. Derived data supporting the findings of this study are available from the corresponding author on request.

Disclaimer

The facts and opinions expressed in this article are solely those of the respective authors.

Ethical considerations

Ethical approval to conduct the study was received from the Human Research Ethics Committee at the University of Cape Town, Faculty of Health Sciences (JREC reference: 892/2016. Scalp cooling is an established safe method of reducing and even preventing CIA. The method is associated with minimal adverse effects (related to the cold cap); the intervention is not associated with scalp metastasis or poorer treatment outcome. All personal and clinical data of the patients were kept confidential. No participants below the age of 18 were enrolled in the study and thus all participants were able to sign their own written consent. The consent form was translated into isiXhosa and Afrikaans for the study.

Participants were able to, at any time during the study period, terminate their participation without any negative consequences to them. The study is investigator initiated and no monetary sponsorship was provided by a third party.

References

1. Ghoncheh M, Pournamdar Z, Salehiniya H. Incidence and mortality and epidemiology of breast cancer in the world. Asian Pac J Cancer Prev. 2016;17(S3):43–46. https://doi.org/10.7314/APJCP.2016.17.S3.43
2. Hershman DL. Scalp cooling to prevent chemotherapy-induced alopecia: The time has come. JAMA. 2017;317(6):587–588. https://doi.org/10.1001/jama.2016.21039
3. Nangia J, Wang T, Osborne C, et al. Effect of a scalp cooling device on alopecia in women undergoing chemotherapy for breast cancer: The SCALP randomised clinical trial. JAMA. 2017;317(6):596–605. https://doi.org/10.1001/jama.2016.20939
4. Massey CS. A multicentre study to determine the efficacy and patient acceptability of the Paxman scalp cooler to prevent hair loss in patients receiving chemotherapy. Eur J Oncol Nurs. 2004;8(2):121–130. https://doi.org/10.1016/j.ejon.2003.10.006
5. Lemieux J, Maunsell E, Provencher L. Chemotherapy-induced alopecia and effects on quality of life among women with breast cancer: A literature review. Psycho-Oncol. 2008;17(4):317–328. https://doi.org/10.1002/pon.1245
6. Luanpitpong S, Rojanasakul R. Topics in cancer survivorship. London: IntechOpen Limited; 2012.
7. De Souza BF, Pires FH, Dewulf Nde L, Inocenti A, Silva AE, Miasso AI. Patients on chemotherapy: Depression and adherence to treatment. Rev Esc Enferm USP. 2013;47(1):61–68. https://doi.org/10.1590/S0080-62342013000100008
8. Kruse M, Abraham J. Management of chemotherapy-induced alopecia with scalp cooling. J Oncol Pract. 2018;14(3):149–154. https://doi.org/10.1200/JOP.17.00038
9. Eldridge SM, Chan CL, Campbell MJ, et al. CONSORT 2010 statement: Extension to randomised pilot and feasibility trials. BMJ. 2016;355:i5239. https://doi.org/10.1136/bmj.i5239
10. Rugo HS, Klein P, Melin SA, et al. Association between use of a scalp cooling device and alopecia after chemotherapy for breast cancer. JAMA. 2017;317(6):606–614. https://doi.org/10.1001/jama.2016.21038