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Clinical Trial Results

Does Scalp Cooling Have the Same Efficacy in Black Patients Receiving Chemotherapy for Breast Cancer?

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Key Words. Paxman scalp cooling device • Chemotherapy-induced alopecia • Breast Cancer

Trial Information

- **ClinicalTrials.gov Identifier:** NCT04626895
- **Sponsor:** Paxman Scalp Cooling
- **Principal Investigator:** Asma Ali Dilawari
- **IRB Approved:** Yes

Lessons Learned

- Despite FDA approval to reduce alopecia, data on efficacy of scalp cooling in Black cancer patients is limited due to lack of minority representation in prior clinical trials.
- Scalp cooling devices may have less efficacy in Black patients; additional studies are required to explore the possible causes for this, including hair texture and cap design.

Abstract

Background. The Paxman scalp cooling (SC) device is FDA-approved for prevention of chemotherapy-induced alopecia (CIA). Studies report 50%–80% success rates and high patient satisfaction, yet there have been no studies of SC in Black patients. We conducted a phase II feasibility study of Paxman SC with a planned enrollment of 30 Black patients receiving chemotherapy for stage I–III breast cancer.

Methods. Black patients who planned to receive ≥4 cycles of chemotherapy with non-anthracycline (NAC) or anthracycline (AC) regimens were eligible. Alopecia was assessed by trained oncology providers using the modified Dean scale (MDS) prior to each chemotherapy session. Distress related to alopecia was measured by the Chemotherapy Alopecia Distress Scale (CADS).

Conclusion. SC may not be efficacious in preventing alopecia in Black women. Differences in hair thickness, hair volume, and limitations of cooling cap design are possible contributing factors.

Results. 15 patients enrolled in the intervention before the study was closed early due to lack of efficacy. Median MDS and CADS increased after SC suggesting increased hair loss ($p < .001$) and alopecia distress ($p = .04$). Only one participant was successful in preventing significant hair loss; the majority stopped SC before chemotherapy completion due to grade 3 alopecia (>50% hair loss). ***The Oncologist*** 2021;9999:• •

Discussion

The Paxman cooling device has been in use for over 20 years in Europe but only obtained FDA approval in the U.S. in 2017. Several studies have demonstrated the reduction in chemotherapy induced alopecia with the use of SC [1-2]. Higher success rates are reported with taxane, NAC regimens; however, AC regimens have had growing success in reduction of alopecia with SC [1-3]. Differences in hair texture amongst diverse populations may translate to

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different outcomes from the use of SC; however, the majority of SC trials were conducted with few Black patients and no analysis by hair type [2-4]. We report one of the first studies examining scalp cooling in Black women undergoing chemotherapy for breast cancer (Figure 1). The median number of sessions of SC for the intervention group was 3. Overall, median MDS increased from grade 0-1 (no hair loss) at baseline to grade 3 (50-75% hair loss) after SC ($P < 0.001$, Wilcoxon signed-rank test), suggesting a lack of efficacy of SC in preventing alopecia. Self-reported CADS also increased from a median score of 2.5 at baseline to 9 after SC ($P=0.04$) suggesting increased distress associated with alopecia. Five participants were treated with AC regimens which reportedly have less success with SC, yet median differences in alopecia grade and CADS did not differ between patients on AC versus NAC regimens. Several limitations are important to consider. Cap fitting may have been a unique challenge due to hair type. Participants complained that the required dampening of their hair actually expanded its volume making it difficult to have the cap fitted onto the scalp. After 5 participants experienced significant alopecia, a follow-up site visit was conducted by the Paxman training team to assess all procedures, machines, and cap fitting; no lapses were noted. Paxman's usual recommendation to avoid hair products was also amended to allow for products to control hair volume that could help with cap fitting. Regardless, inadequate contact of the cap with the scalp could have contributed to lack of efficacy. The time for cooling was also a challenge with a required pre- and post-cooling of 45 min. and 90 min. respectively, occupying chair time. One participant dropped SC because of the extended time requirement. Most participants did not use SC until the end of chemotherapy and 11 dropped SC early due to alopecia [Figure 1]. Despite their benefit in preventing chemotherapy-induced alopecia, SC costs are not usually covered by most insurance carriers in the U.S. [5]. There is limited use of SC in underserved, minority patient populations such as those at our cancer center, suggesting a disparity in care. Future studies of SC devices in Black and other ethnic hair types could explore improvements in cap design and potential barriers in access.

Trial Information	
Disease	Breast cancer
Stage of disease / treatment	Primary
Prior Therapy	None
Type of study	Phase II, single arm
Primary Endpoint	Toxicity
Secondary Endpoint	Chemotherapy Alopecia Distress Scale (CADS)
Additional Details of Endpoints or Study Design	Alopecia toxicity was measured by oncology providers using the Modified Dean Scale (MDS). Success was prevention of grade >2 alopecia (Table 1) [11]. Visual Analog Scale (VAS) was patient-reported hair loss with success defined as prevention of >50% hair loss (subjective assessment [the patient's perception of hair loss severity] 0-100 with 0=No hair loss and 100= Total hair loss.
Investigator's Analysis	Poorly tolerated/not feasible

Paxman Scalp Cooling Device	
Generic/Working name	Paxman Scalp Cooling Device
Company Name	Paxman Coolers
Schedule of Administration	Scalp cooling was delivered at the first chemotherapy cycle and repeated for each chemotherapy session or until participants dropped the intervention. The Paxman cooling device has been in use for more than 20 years but obtained FDA approval in the U.S. in 2017. It offers scalp cooling through a refrigeration unit weighing 79.4 lbs that is stored in an infusion center and a cooling cap. It spans a height between 60–165 cm and requires a power supply of 50/60 Hz. Specifications available at https://paxmanscalpcooling.com/practice/the-pscs/technical-specs/

Patient Characteristics

Number of patients, Control: 3 (female)

Number of patients, Scalp cooling group: 15 (female), median age: 56; cancer type: breast cancer; all patients had an ECOG 0–1

Patient Characteristics

Title	Control
Number of patients screened	3
Number of patients enrolled	3
Number of patients evaluable for toxicity	3
Number of patients evaluated for efficacy	3
Evaluation Method	Modified Dean Score (see Table 1)
Title	Scalp Cooling Group
Number of patients screened	24
Number of patients enrolled	15
Number of patients evaluable for toxicity	15
Number of patients evaluated for efficacy	15
Evaluation Method	Modified Dean Score (see Table 1)

Assessment, Analysis, and Discussion

Completion	Study terminated before completion
Investigator's Assessment	Poorly tolerated/not feasible

Despite advances in the treatment of side effects and prevention of nausea and vomiting associated with chemotherapy, chemotherapy-induced alopecia remains one of the most common and devastating side effects, with over 60% of cancer patients experiencing hair loss with chemotherapy [6]. About 10% of female patients will refuse chemotherapy due to risk of hair loss leading to poorer outcomes [7]. Several studies demonstrated a reduction in alopecia with the use of SC techniques, with some reporting up to 75% success rates in avoiding significant alopecia [8]. Higher success rates have been reported with taxane NAC regimens; however, AC regimens have also had up to 50-60% success rates in reduction of CIA with SC [2-3]. Meta-analyses and registry studies have not found an increase in scalp metastases in these patients, indicating the relative safety of this technique in preventing hair loss [9].

The Paxman SC device obtained FDA approval in the U.S. in 2017, although it has beendespite being used in Europe for decades; and recently results of prospective observational studies assessing SC in the U.S have been reported. Variations in hair texture amongst ethnic minorities in the U.S. may translate to differing outcomes from the use of SC; however, Black patients and those with ethnic hair types have been underrepresented in SC studies. The Scalp Cooling Alopecia Prevention (SCALP) trial was a multicenter, randomized trial enrolling 182 patients; only 12% were identified as Black [2]. One of the largest studies from the Dutch registry of SC had 1411 patients enrolled between 2006 and 2009, and only 11 (1%) were reported to have ''African'' hair type [4]. None of these trials presented results stratified by race. This is one of the first studies addressing the use of SC in Black women with breast cancer.

There were several challenges with SC procedures. Training was required for all nurses and research coordinators, but most had no prior experience with SC. Due to limitations in staffing, infusion nurses trained in SC were often unavailable, and study coordinators had to supervise SC, remaining with participants until cooling ended. Due to the need for pre- and post-cooling, occupied chair time was significantly increased due to SC; therefore, patients were scheduled on specific days and device access was limited to two participants daily.

Cap fitting was also reported as a challenge. Participants complained that dampening of the hair actually expanded its volume making it difficult to have the cap flushed against the scalp. To reduce operator variability with cap fitting, one research coordinator assessed size requirements for all the participants. After the initial 5 patients experienced significant alopecia, a follow-up site visit was requested from the Paxman training team to assess all procedures, machines, and cap fitting. No lapses in procedure were noted. The Paxman team recommended using the smallest cap size possible in order to ensure contact with the scalp, confirmed that sizing was done appropriately, and reviewed de-identified study photographs that were shared after the initial patients were treated. Their usual recommendation to avoid hair products was also amended after participant feedback to allow products that control hair volume leading to proper cap fitting. Regardless, inadequate contact of the cooling cap to the scalp could have contributed to lack of efficacy.

Study procedures did not include measurements of scalp temperature during chemotherapy, which could have helped assess cooling variability. Our inclusion of different chemotherapy regimens may be an additional limitation. We included AC and NAC regimens though reports of SC indicated better efficacy with NAC. However, in analyses stratified by regimen, the results remained unchanged (data not shown). We also included HER2 targeted therapies (administered during the post-cooling time) in our sample but did not expect that the presence of trastuzumab and pertuzumab would affect hair loss results. A majority of

participants requested SC discontinuation prior to completion of chemotherapy cycles. Median number of chemotherapy cycles with SC was 3 in our study. Eleven patients stopped SC before chemotherapy was completed due to alopecia. One had grade 1 alopecia but dropped out due to inconvenience (after 3 cycles) (Fig. 2). Results using patient-reported Visual Analog Scale for alopecia were similar to the provider measured MDS for 14 participants; 12 rated their hair loss 60-100%. There are limited validated patient-reported outcomes measuring the psychosocial effects of hair loss. The Chemotherapy Alopecia Distress Scale (CADS), a 17-question validated questionnaire to assess CIA distress, was administered every other session starting at cycle 2 [10]. However, the CADS has not been previously been studied in black women. CADS score continued deteriorating with chemotherapy cycles even with SC in our study. Paxman SC has reported improvements in efficacy with time and experience of sites, so it is possible that our institution's lack of prior SC experience contributed to these results. However, an informal survey of providers at another hospital in our network with predominantly White patients reported <5 failures with their first 45 patients treated.

Our results indicate the need for additional research on SC in Black patients and highlight the lack of minority representation in clinical trials. Average annual clinical trial enrollment at our institution is 33% of cancer patients, with 80% being Black and living in underserved areas. Interest in this trial was high with most patients expressing interest in SC despite not having prior knowledge of it. SC usually requires an out-of-pocket expense in the U.S. due to lack of consistent insurance coverage. Even with subsidies from organizations offering assistance for low income patients, there is limited use of this technique in underserved, minority patient populations such as those at our cancer center, and this illustrates a disparity in care. Our results address a gap in the literature; and an opportunity to work with SC device manufacturers to improve efficacy in diverse patient populations.

Disclosures

Asma Dilawari: Cardinal Health (H, SAB); Christopher Gallagher: Daiichi Sankyo, Seattle Genetics (SAB); Richard Paxman: Paxman Scalp Cooling (OI, E [CEO]). The other authors indicated no financial relationships.

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TABLE 1. Adverse events

Alopecia by MDS [11]	Hair Loss	Patients, N=15, *n* (%)
GRade 0	*No hair loss*	0
Grade 1	*>0- ≤25% hair loss*	1 (6)
Grade 2	*>25- ≤50% hair loss*	3 (20)
Grade 3	*>50- ≤75% hair loss*	8 (53)
Grade 4	*>75% hair loss*	3 (20)

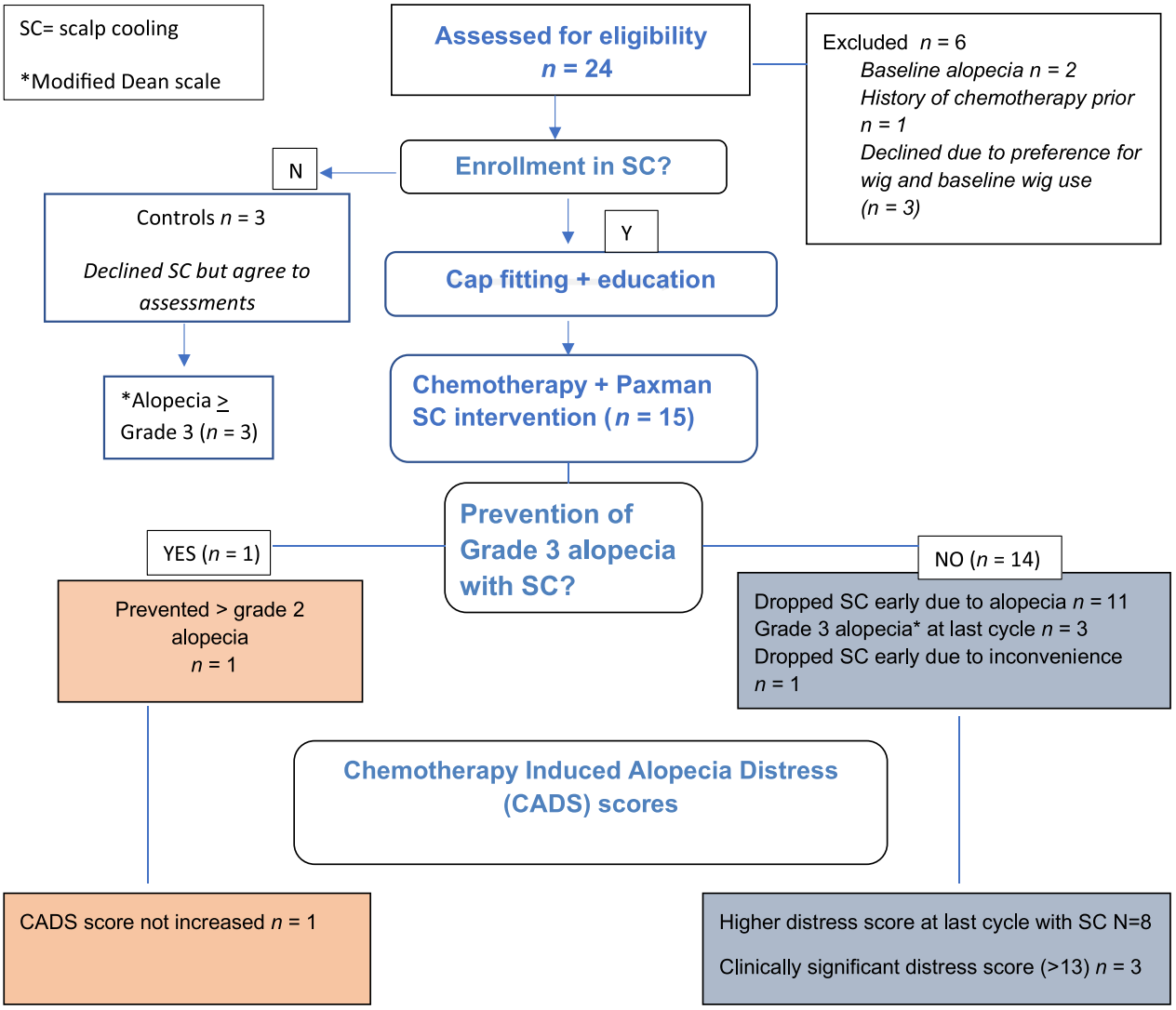

Figure 1. CONSORT flow diagram

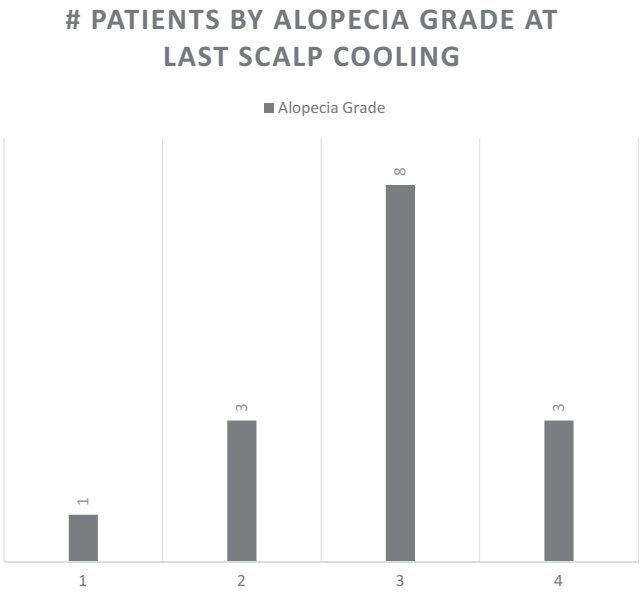

Figure 2. Alpecia grade results at last scalp cooling.