Racial Differences in Pain Reports between Black and White Participants with Chronic Venous Disorders Treated with Cryotherapy Compared to Usual Care

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Objective: To evaluate racial differences in pain and pain medication use in response to cryotherapy or usual care (UC) for leg skin inflamed by chronic venous disorders (CVDs).

Design: Randomized clinical trial.

Setting: Academic medical center in Charleston, South Carolina.

Participants: Sixty Black and White participants with severe CVDs randomized to receive cryotherapy or UC during the one-month study.

Intervention: Cryotherapy consisted of 30-minutes of cooling the most severely affected lower leg skin with a gel wrap while receiving UC (ie, elevating the legs and wearing compression stockings during the day).

Main outcome measure: Pain measured with the Leg Pain Questionnaire-Composite Score.

Results: 56 participants ($n=27$ cryotherapy; $n=29$ UC) completed the study: 52% African Americans (Blacks). Blacks in the usual care group ($n=15$) reported lower pain after 30 days compared to Blacks in the cryotherapy group ($n=15$) ($P=.02$). In Whites, there were no differences between cryotherapy ($n=13$) and usual care ($n=14$) ($P=.78$).

Conclusions: No statistically significant differences in pain were found between the cryotherapy group or UC group. Usual care in the Black group was found to reduce pain. (*Ethn Dis*. 2011;21(4):451–457)

Key Words: Pain, Cryotherapy, Chronic Disease, Blacks, Skin

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Introduction

Chronic venous disorders (CVDs) contribute to significant morbidity worldwide. In the United States, 600,000 individuals suffer from new leg ulcers each year while another 3 million live with chronic, non-healing leg ulcers.[1,2] Venous disorders are related to venous hypertension in the lower leg venous system, and, if unrelieved, vessel wall damage ensues, leading to skin breakdown.

Individuals with CVDs, including venous insufficiency, varicose veins, and venous leg ulcers, often report the presence of pain.[3] Leg heaviness, calf achiness and cramping, heat sensations, and sharp needle-like prickly pain are frequent complaints. The legs swell, become hyperpigmented, scaly, and weepy, and the skin becomes hardened. As CVDs worsen, the skin becomes inflamed with increased blood flow in the microcirculation and higher skin temperatures; as a consequence, the skin can ulcerate.[4] Compression stockings and layered wraps, the mainstay for the management of CVDs and ulcers, are considered difficult to do and have been reported as being painful to wear.[5] Thus, the effectiveness of this therapy is severely hampered by limited or inconsistent use and its tolerability, especially for ulcer prevention.

When new therapies are being sought for the management of CVDs, their impact on pain should be important research considerations. No less important are racial differences in pain responses to new therapies. A growing body of research suggests there are different experiences to pain across racial groups,[6] which is the focus of this study of a new treatment for CVDs, cryotherapy, that cools damaged lower leg skin.

Research studies related to pain in Blacks, Hispanics, and Whites revealed that Blacks and Hispanics have less tolerance for pain, including tolerance to cold, than Whites.[6–9] Blacks and Hispanics have higher levels and enhanced sensitivity to pain, describing pain as more unpleasant than Whites.[7–10] And Blacks have more pain-related disabilities than Whites.[7] Possible explanations for the racial disparities in the pain experience may include minorities' perceptions of a lack of control over pain[11] and underreporting of pain leading to inadequate pain treatment.[12] Other researchers attempt to explain minorities' greater pain experiences with pathophysiological reasons.[13] For example, increased melanin in the skin of Blacks slows the absorption of topical analgesia cream,[14] thus effectiveness may be limited.

Pain, a frequent symptom of CVDs, can impact healing when ulcers are present and affects function and quality of life.[15] A new approach to manage CVDs and its symptoms, cryotherapy – the application of cold to the skin – has potential long-term application to venous ulcer prevention. Cryotherapy's benefits for acute inflammation are well supported, but there is limited research on its benefits to chronically inflamed skin and its safety in CVDs. Cryotherapy can be uncomfortable or painful, especially during the first few minutes when it is applied to the skin. As part of a larger study to determine the impact of cryotherapy on microcirculation blood flow and skin temperature of chronically-inflamed skin,[16] this study's aim was to measure pain in the two

study groups: the experimental group received the cryotherapy intervention (cooling gel wrap) coupled with usual care (compression, leg elevation); the control group received usual care alone. Here, we report racial differences on pain, the outcome variable, between Blacks and Whites after the daily, one-month cryotherapy intervention applied to the lower leg most severely affected by CVDs. A major concern was that the cryotherapy might induce increased pain in the cooled lower leg over the course of the study. We were particularly concerned about Blacks' responses due to a lower tolerance for cold, as reported in the literature.

The research questions were: Does pain change from baseline after the four-week cryotherapy intervention? Are there differences in pain between Black and White participants receiving the cryotherapy intervention compared to usual care (UC)?

METHODS

Study Population and Design

The study was a randomized non-blinded clinical trial conducted with individuals diagnosed with CVDs who experienced the more clinically severe stages: stage 4 – skin damage and stage 5 – history of venous ulcers. Individuals who resided within a 75-mile geographic area of the study site in Charleston, South Carolina were recruited from wound clinics, physician offices, senior residential apartments, faith based community groups, and by word of mouth. Of 72 screened, 60 were enrolled and randomized to receive the cryotherapy (cooling gel wrap) or usual care only. The study group was representative of the recruitment area, which is 67% White, 32% Black, 1% Hispanic, as well as socioeconomic status (labor, technical, and professional occupations).

We report racial differences on pain, the outcome variable, between Blacks and Whites after the daily, one-month cryotherapy intervention applied to the lower leg most severely affected by chronic venous disorders.

Inclusion and Exclusion Criteria

Inclusion criteria included aged ≥21 years, skin changes consistent with severe clinical CVDs, and the ability to put on and agree to wear compression stockings during waking hours. As part of the study's safety processes to monitor for a cold response, participants had to be able to use a long-handled infrared, contact skin thermometer to measure leg temperature, and record information on the log sheet. Other inclusion criteria were ankle-brachial index of .80 – 1.3 mm Hg (intact arterial blood flow); skin and thermal sensation (normal neurological function); and venous refill time of ≤25 seconds (indicated chronic venous insufficiency).

Participants excluded from the study were unable or unwilling to wear compression stockings and to use the infrared thermometer to measure leg temperature or document on the log sheet. They were also excluded if leg ulcers were present, ankle-brachial index was <.80 or >1.3 mm Hg, skin and thermal sensation was impaired, or venous refill time was >25 seconds.

Sample Size Determination and Randomization

For this aim of the larger study, to test for differences in blood flow and temperature between the cryotherapy and UC groups, pain was a secondary outcome; thus, the study was not adequately powered to detect statistically significant differences in pain between the groups. However, for the between group (cryotherapy vs UC) comparison of pain change score, we had approximately 80% power to detect a difference of .8 SD units, based on a two-sided pooled *t* test comparison with level of significance $\alpha = .05$.

Participants were randomized to cryotherapy plus UC (Group 1) or UC (Group 2) by the study nurse using a computer-generated table of random numbers. The nature of the study prohibited the participants and study nurse, who consented and collected all data at two time points, baseline, then after the 30 day intervention, from masking/blinding. However, the principal and co-principal investigators were blinded to the treatment groups.

Intervention

The cryotherapy intervention used a cooling gel wrap (Southwest Technologies, Kansas City, Mo) made of a flexible, glycerin-based hydrogel that did not freeze to a solid state and accommodated various leg sizes. In addition, the wrap included two Lycra nylon coverings; the outer covering was washable and had a Velcro strap to secure it. Participants were asked to first remove compression stockings worn during waking hours and apply a protective polyethylene sleeve around the lower leg over which the cooling wrap was placed. This sleeve provided an additional safety feature to prevent frostbite. Participants were then asked to lie down and elevate both lower legs on a leg elevator pillow that was provided, gel wrap in place, for 30 minutes daily for four weeks. The UC group received the same intervention, minus the cooling wrap.

The participants were provided the infrared thermometer (TempTouch, Diabetica Solutions, San Antonio, TX) and taught to measure and record lower leg temperature. This procedure was used to monitor the legs before and after

the cooling treatment, or in the case of the UC group, before and after leg elevation, as a safety procedure. It was expected that the temperature would drop approximately 10 to 15°C from the participant's baseline in the intervention group, a safe yet therapeutic range established a priori.[16] There was no anticipated temperature decrease in the UC group; however, monitoring in both groups served as an adherence check as the logs were sent to and processed by study personnel each week.

Participants were instructed to store the cooling wraps in the home freezer at a temperature of 0°C, given freezer thermometers to monitor temperature, and asked to record these temperatures on the study log for tracking. If the freezer temperature dropped to −2°C, they were instructed to readjust the freezer temperature and delay using the gel wrap until the freezer temperature returned to 0°C.

Table 1. Demographic and clinical characteristics at baseline (total sample *N*=56)*

	Black (*n*=29)	White (*n*=27)	*P*
Age	56.5 ± 10.9	65.8 ± 12.8	.005
Age categories			.073
35–49 years	26.7% (8/29)	7.4% (2/27)	
50–69 years	53.3% (16/29)	55.6% (15/27)	
≥70 years	17.2% (5/29)	37.0% (10/27)	
Sex, female	72.4% (21/29)	66.7% (18/27)	.64
Occupation			.006
Professional	23.3% (7/29)	66.7% (18/27)	
Technical	36.7% (11/29)	14.8% (4/27)	
Labor	36.7% (11/29)	18.5% (5/27)	
Residence, urban	66.7% (19/29)	92.6% (25/27)	.023†
Body mass index	41.7 ± 12.3	34.8 ± 9.9	.026
BMI categories			.381
Normal (18.5–24.9)	3.5% (1/29)	22.2% (6/27)	
Overweight (25.0–29.9)	20.0% (6/29)	11.1% (3/27)	
Obese (30.0–39.9)	23.3% (7/29)	33.3% (9/27)	
Morbidly obese (≥40.0)	50.0% (15/29)	33.3% (9/27)	
Calf circumference	44.2 ± 7.2	42.8 ± 5.4	.407
Ankle circumference	26.3 ± 5.3	26.2 ± 3.2	.939
Compression stockings	62.1% (18/29)	70.4% (19/27)	.512
Over-the counter pain medication	44.8% (13/29)	55.6% (15/27)	.422
Prescription pain medication	13.8% (4/29)	14.8% (4/27)	.999†
Pain medication within 24 hours	27.6% (8/29)	18.5% (5/27)	.532†

* mean ± SD or % (*n*).
† from Fisher's exact test.

Demographic and History

A demographic and health history questionnaire provided information about race/ethnicity, sex, age, occupation, and residence (urban or rural). Health history information was obtained, such as body mass index (BMI), and calf and ankle circumferences. Participants were asked about the use of compression stockings (yes/no). Use of pain medication questions included prescription and over-the-counter medications for leg pain.

Leg Pain

Leg pain was measured with the Leg Pain Questionnaire Composite Score (LPQ-CS).[17] Participants were asked three questions: "How much pain in your legs are you having now?" "What is the worst pain you have had in your legs in the past 24 hours?" and "What was the average level of pain in your legs in the past 24 hours?" The responses were measured on an 11-point rating scale ranging from 0 (no pain) to 10 (worst possible pain). A composite leg pain score was calculated as the average of the 3 ratings as reported by Pieper et al.[18] The Cronbach's alpha for the scale is reported as .89 to .92.[18] For this study, Cronbach's alpha was .92 at baseline, .89 at follow-up, and .90 overall.

Statistical Analysis

Demographic (age, sex, occupation, residence) and clinical characteristics (BMI, calf and ankle circumference, use of compression stockings, over-the-counter and prescription pain medications) are reported using measures of central tendency or frequency distributions; groups were compared using pooled *t* test or chi-square tests. The outcome variable for this arm of the study, pain, is reported as the Leg Pain Questionnaire Composite Score (LPQ-CS) calculated as the average of three items: how much pain the participants reported as having at the time of measurement, the worst pain they had over the prior 24 hours, and the average pain over the prior 24 hours. Means of the composite pain score at baseline and follow-up and mean change from baseline to follow-up were compared across groups using pooled *t* tests (or Wilcoxon rank sum tests) and paired tests (or Wilcoxon Signed Rank tests). Use of pain medication including prescription pain medication (yes/no), over-the-counter (OTC) pain medication (yes/no), and a question as to whether or not participants used pain medication within the 24 hours prior to the assessment visit (use of pain medication within 24 hrs: yes/no) are reported in Table 1.

RESULTS

Demographics

Of the 60 participants enrolled, 56 participants (*n*=27 cryotherapy; *n*=29 usual care) provided data at the follow-up visit. Age ranged from 37 to 87 years. Black participants were aged an average of 56.5 years, while White participants

Table 2. Leg pain as measured by the Leg Pain Questionnaire Composite Score (LPQ-CS) by race

	Overall (*n*=56)	Black (*n*=29)	White (*n*=27)	Difference	*P**
LPQ-CS at baseline	2.51 ± 2.93	2.95 ± 3.19	2.05 ± 2.59	.90 ± 2.92	.252
LPQ-CS at follow-up	2.32 ± 2.74	3.11 ± 3.21	1.46 ± 1.83	1.66 ± 2.64	.021†
Difference in LPQ-CS from baseline to follow-up	.20 ± 2.18	−.16 ± 2.09	.59 ± 2.24	.75 ± 2.16	.198
P‡ (comparing baseline to follow-up)	.490	.681	.181	–	–

* From pooled *t* test.
† From Satterthwaite *t* test.
‡ From paired *t* test.

were 65.8 years. Although both sexes were represented, females had a higher representation; 72.4% of Black and 66.7% of White participants were female. Participants described their occupations as professional, technical, or labor. The majority (66.7%) of White participants reported professional occupations compared to 23.3% of Blacks (*P*=.006). Almost all White participants (93%) lived in urban areas compared to 67% of Blacks (*P*=.02). Black participants had statistically significantly higher body mass indexes (BMIs) than their White counterparts (42±12 vs 35±10, *P*=.02). Half of the Black participants were morbidly obese and more than 95% were overweight, obese, or morbidly obese compared to 78% of White participants (Table 1).

Leg pain

Pain scores measured by the LPQ-CS at baseline were higher for Blacks compared to Whites though not statistically significant. White participants reported somewhat lower pain at the follow-up visit compared to Blacks who had slightly increased leg pain scores with a difference between the groups of 1.6 ± 2.6 (*P*=.02). Differences from baseline to follow-up within the groups were not statistically significant (Table 2).

Pain scores among participants randomized to cryotherapy were higher at baseline than among participants randomized to UC regardless of race though not statistically significant (Table 3). Among Blacks in the cryotherapy group at follow-up, leg pain had increased while scores had decreased for the UC group (4.5 ± 3.4 vs 1.8 ± 2.4, *P*=.02). This relationship did not hold for Whites in either group. White participants started with lower pain scores at baseline and showed a further decrease at follow-up in both treatment groups (top panel of Table 3).

The bottom panel of Table 3 shows differences in leg pain scores by race and use of leg pain medication. Leg pain scores were statistically significantly higher among Black participants taking pain medication at baseline compared to those not taking leg pain medication (*P*<.0001). Leg pain scores were similar at follow-up (*P*<.001) though pain had decreased slightly among Blacks taking pain medication at baseline but increased for Blacks who did not take pain medication at baseline. Changes in leg pain from baseline were not statistically significant in either group. Among White participants in the group taking pain medication, leg pain scores were higher than for the group not taking medications but below the pain scores observed for the Black group. No statistically significant differences in leg pain scores were found between Blacks and Whites regardless of use of pain medication at baseline.

DISCUSSION

A goal of this study was to explore whether cryotherapy treatment for participants with CVDs would cause increased or decreased pain in the lower legs being cooled to reduce blood flow and skin temperature. Furthermore, this study sought to determine if Black and White participants treated with cryotherapy had different reports of pain before and after the cryotherapy treatment compared to UC. Overall, cryotherapy had minimal affect on the pain responses compared to UC; however, there were statistically significant differences between racial groups.

Leg Pain Before and After Intervention

The first research question was "Does pain change from baseline after the four-week cryotherapy intervention?" Overall, there was no change in pain. Participants entered the study with low pain scores (mean at baseline was 2.5 out of a possible maximum of 10) and no clinically significant increases or decreases in pain during the course of the study were observed. Furthermore, there were no indications that cryotherapy caused harm (a major concern) as

Overall, cryotherapy had minimal affect on the pain responses compared to usual care; however, there were statistically significant differences between racial groups.

Table 3. Leg pain as measured by the Leg Pain Questionnaire Composite Score (LPQ-CS) by race and treatment and use of pain medication

Leg pain by treatment by race	Cryotherapy (*n*=14)	Usual care (*n*=15)	Difference	*P**
African American or Black (n=29)				
LPQ-CS at baseline	3.64 ± 2.98	2.31 ± 3.35	1.33 ± 3.18	.269
LPQ-CS at follow-up	4.52 ± 3.42	1.80 ± 2.42	2.72 ± 2.94	.019
Difference in LPQ-CS from baseline to follow-up	−.88 ± 2.30	.51 ± 1.67	1.39 ± 2.00	.072
P† (comparing baseline to follow-up)	.182	.250	–	–
White (*n*=27)	(*n*=13)	(*n*=14)		
LPQ-CS at baseline	2.31 ± 2.04	1.81 ± 3.07	.50 ± 2.63	.232
LPQ-CS at Follow Up	1.46 ± 2.03	1.45 ± 1.70	.01 ± 1.87	.757
Difference in LPQ-CS from baseline to follow-up	.85 ± 2.49	.36 ± 2.06	.49 ± 2.27	.782
P† (comparing baseline to follow-up)	.211	.570	–	–
*P** (comparing difference in LPQ-CS between AAs and Whites)	.073	.826		
Leg pain by use of pain medication (within 24 hrs) by race	**Taking pain meds (*n*=8)**	**Not taking pain meds (*n*=21)**	**Difference**	***P****
African American or Black (*n*=29)				
LPQ-CS at baseline	6.83 ± 1.51	1.48 ± 2.27	5.36 ± 2.10	<.0001
LPQ-CS at Follow Up	6.25 ± 2.65	1.92 ± 2.55	4.33 ± 2.58	.0004
Difference in LPQ_CS from baseline to follow-up	.58 ± 3.12	−.44 ± 1.54	1.03 ± 2.07	.398
*P** (comparing baseline to follow-up)	.523	.203	–	–
White (*n*=27)	(*n*=5)	(*n*=22)		
LPQ-CS at baseline	4.60 ± 2.10	1.47 ± 2.36	3.13 ± 2.32	.012
LPQ-CS at Follow Up	2.53 ± 2.50	1.21 ± 1.62	1.32 ± 1.79	.149
Difference in LPQ-CS from baseline to follow-up	2.07 ± 3.99	.26 ± 1.60	1.81 ± 2.17	.372‡
P† (comparing baseline to follow-up)	.313	.509	–	–
*P** (comparing difference in LPQ-CS between AAs and Whites)	.163†	.151		

* From pooled *t* test.
† From Wilcoxon Signed Rank test.
‡ From Satterthwaite *t* test.

adverse events, such as frostbite, were not reported.

Leg Pain Differences between Racial Groups

The second research question was "Are there differences in pain between Black and White participants receiving the cryotherapy intervention compared to UC?" The experiences of White participants included lower pain at baseline, though not statistically significant and lower pain at follow-up compared to Black participants (statistically significant *P*=.021). Whites experienced less pain regardless of treatment group. In contrast, Black participants had different reports of pain. The cryotherapy treatment increased the pain experience for Blacks. Black participants who received the cryotherapy treatment had an increase in pain at follow-up, whereas Black participants who received UC had a decrease in pain at follow-up, though not statistically significant. In addition, Black participants taking pain medications reported higher pain compared to White participants taking pain medications. Overall, Black participants, compared to Whites, had higher pain at baseline, higher pain at follow-up, higher pain when taking pain medications, and higher pain after receiving cryotherapy treatment. However, we believe these were not clinically significant differences because the pain scores both fall on the lower third of the pain scale. For Black participants, only UC participants at follow-up reported decreased pain. However, the treatment was thought to be only minimally associated with pain overall as Black participants started with higher reported pain.

In addition, Blacks who received cryotherapy rated pain statistically significant (*P*=.019) at follow up compared to Blacks who received UC. Although these pain scores varied for cryotherapy (4.52 out of 10) compared to UC (1.80 out of 10), we believe the clinical benefits of cryotherapy treatment outweigh the increased pain score of 2.72 points. In essence, although there were statistically significant results, we believe cryotherapy is an important clinical treatment, and Blacks should not be excluded from receiving cryotherapy treatment because of racial differences in pain reports.

Black participants in this study experienced more pain than White participants at the start of the study. These findings are consistent with previous studies where Blacks are described as having enhanced pain and higher sensitivity to pain.[9,10,19]

Cold Tolerance for Blacks

Lower cold tolerance and higher sensitivity to pain may explain why Blacks receiving cryotherapy reported more pain compared to Whites.[6–9] In a study conducted by Grewen et al, Black women had lower plasma oxytocin levels compared to White women.[19] A positive correlation between oxytocin levels and cold tolerance was found. White women with higher oxytocin levels had increased tolerance to cold whereas Black women with lower oxytocin levels were less tolerant to cold.[19] ''Oxytocin is a hormone that helps relax and reduce blood pressure and cortisol levels. Oxytocin increases pain thresholds, has anti anxiety effects, and stimulates various types of positive social interaction. In addition, it promotes growth and healing.''[20] Grewen et al also found that the hormones norepinephrine and cortisol worked to control pain in Whites while Blacks experienced negative correlations between these hormones and their pain regulatory systems.[19] In our study, we did not find differences in pain experiences between Black and White women.

Physical and Psychosocial Contributors to Pain in Blacks

Other studies offer possible physical reasons for why Blacks in this study experienced more pain. Querlex et al found that Blacks have increased skin thickness.[21] Thus, it is plausible that increased skin thickness may be richer in cutaneous nerve fibers thereby increasing the susceptibility to pain. The literature also offers psychosocial explanations for Blacks' increased pain experience, including underreporting, perceived lack of control, and less adequate treatment.[11–12,22] Shavers et al identified reasons Blacks endure greater pain, including lack of access to health care providers and medical specialists, decreased ability to obtain pain medications, miscommunication between patient and provider, and cultural beliefs and practices that influence the expression of pain and the acceptance of treatment.[23]

Based on our observations, cooling the skin does not produce a clinically significant increase in discomfort in Black individuals, who had higher reports of pain at the start of the study. However, it is important for clinicians to recognize that there are differences in pain, perhaps in response to cryotherapy; thus, Black patients for whom cryotherapy is recommended, should be warned they might experience a slight increase in discomfort during the treatment and should not be excluded from treatments that involve cryotherapy.

As part of the study exit debriefing, all participants were asked whether they would use the cooling wrap after the study concluded; 89% of Blacks said they planned to continue to cool the skin compared to 78% of Whites. The major reason cited by both groups for continuing the treatment was that they believed it might halt further skin damage and thought it might prevent another ulcer in those with an ulcer history. While the participants were informed that there was not sufficient evidence to make these conclusions, they said they would do anything that might offer a benefit. We are currently undertaking a much larger, adequately powered 9-month clinical trial to determine whether cooling the skin offers these benefits, including ulcer prevention.

Limitations

There are several limitations to the present study. Because the intent of the study was to examine feasibility of a cryotherapy intervention for chronically inflamed skin, we collected data for one month only. Pain reports might have been different over a longer period of time. This study included a small sample size of 56 participants. In addition, the participants in the group receiving cryotherapy reported a higher pain score at baseline, although not statistically significant. An additional pain scale that is used almost ubiquitously in clinical settings, the Visual Analog Scale, should be included in a future study.

SUMMARY

Participants of different racial backgrounds had discrepant pain experiences when treated with cryotherapy. This study validated previous research that Blacks have greater pain sensations and experiences including Black participants with CVDs treated with cryotherapy. Although cryotherapy is an important treatment for patients with CVDs, clinicians should consider the patient's race when recommending additional pain relieving measures. Researchers are advised to continue to test new devices that might have the potential to cause discomfort to determine if there is a racial (and even sex) differential response.

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