Effect of Optically Modified Polyethylene Terephthalate Fiber Socks on Chronic Foot Pain Study

Dr. Ian L. Gordon M.D., Ph.D.
University of California Irvine
Medical Center
101 The City Drive
Orange, CA 92868
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Robyn M. Burgess York, M.S.

Ian L. Gordon, M.D., Ph.D.

Division of Vascular Surgery

Department of Surgery

University of California Irvine Medical Center, Orange CA

Correspondence: Ian L. Gordon

UCI Medical Center

101 The City Dr.

Orange, CA 92868

FAX 714 456 8919 [??]

Email ilgordon@uci.edu

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ABSTRACT

Objectives: To evaluate whether socks made from polyethylene terephthalate (PET) incorporating optically active particles (Celliant™) ameliorate chronic foot pain resulting from diabetic neuropathy and other disorders.

Methods: A double-blind, randomized trial with 55 subjects (38 men, 17 women) enrolled (average age 59.7 ± 11.9 years), 26 with diabetic neuropathy and 29 with other pain etiologies. Subjects twice completed the Visual Analog Scale, Brief Pain Inventory, McGill Pain Questionnaire, and SF-36 a week apart (W_{1+2}) before receiving either control or Celliant™ socks. The same questions were answered again one and two weeks (W_{3+4}) later. Mean W_{1+2} and W_{3+4} scores were compared to measure pain reduction.

Results: More pain reduction was reported by Celliant™ subjects for 8 of the 9 pain questions employed, with borderline ($p < 0.10$) significant or significant ($p < 0.05$) differences between controls and Celliant™ for 3 questions (McGill III, Pain Severity, and SF-36 Bodily Pain). Removing two outliers led the VAS results favoring Celliant™ to borderline significance and enhanced differences in favor of more pain reduction by Celliant™ in the other questions. In neuropathic subjects, Celliant™ caused more pain reduction in 6 of the 9 questions, but not significantly. Removing outliers led to improvement in 7 of the 9 questions favoring Celliant™ and one result (SF-36 Bodily Pain) became borderline significant. In non-neuropathic subjects 8 of 9 questions showed more pain reduction with the Celliant™ socks; one difference (VAS) was borderline significant. Removing outliers enhanced the differences in pain reduction in favor of Celliant™, and three of the differences were significant or borderline significant (McGill II and III and VAS).

Conclusions: Socks with optically modified PET (Celliant™) have a beneficial impact on chronic foot pain. The mechanism could be related to the effects seen with illumination of tissues with visible and infrared light.

INTRODUCTION

Celliant™ is a polymer fabric constructed from polyethylene terephthalate (PET) yarn containing optically active particles – a proprietary mixture of natural and inorganic materials – which scatter and reflect visible and near infrared light. Garments constructed with such optically modified fibers are thought to influence transmission and reflectance of electromagnetic energy into underlying tissue and skin. Numerous anecdotal reports from patients with a variety of chronic pain syndromes indicate that wearing Celliant™ garments for even a few days leads to dramatic improvement or complete resolution in subjective pain. We report here the results of a prospective, blinded study designed to substantiate the ability of Celliant™ socks to ameliorate chronic pain resulting from diabetic neuropathy and other disorders of the foot.

MATERIALS AND METHODS

This study was conducted at the Veterans Administration Medical Center Long Beach and approved by the local ethics board. Fifty-five subjects (38 men, 17 women, age 59.7 ± 11.9) were enrolled, 26 with diabetic neuropathy and 29 with other causes of foot pain. Inclusion criteria included age $\geq$21, foot pain for at least six months, and a score of $\geq$ 3 on question III of the McGill Short Form Pain Questionnaire (MPQ) at screening. Subjects with diabetic neuropathy (DPN) had a minimum of 2/6 anesthetic points by Semmes-Weinstein filament testing on one foot. Subjects without DPN had 0/6 anesthetic points. Exclusion criteria included severe peripheral arterial disease (PAD) (ABI < 0.5), inability to ambulate, chronic ulceration, and severe psychiatric disorders. For subjects without DPN, etiologies included arthritis, erythromelalgia, Parkinson's disease, and PAD (Table 1). The most common foot pain etiology was arthritis.

At screening (week 1) subjects underwent physical examination including monofilament testing and completed a series of four questionnaires (Visual Analog Scale[1], Brief Pain Inventory[2,3] [BPI], MPQ[4], and SF-36 Quality of Life Inventory[5]). Subjects completed the same questionnaires a week later (week 2) and were given 3 pairs of socks in a closed container and asked to wear them exclusively for the next two weeks. One (week 3) and two weeks (week 4) later they filled out the same panel of questions. Controls received socks made from standard 1.2 denier PET fabric, while the Celliant™ group received otherwise identical socks except PET containing Celliant™ particles was used to fashion the bottom (plantar) half of the garments. Both study personnel and subjects were blinded to the treatment assigned.

Mean scores for individual questions were calculated for the first two (W_{1+2}) and final two visits (W_{3+4}). Differences between W_{1+2} and W_{3+4} scores reflected changes in perceived pain resulting from wearing socks. Non-parametric t-test analysis (Mann-Whitney) was used to compare changes in scores [(mean W_{1+2}) – (mean W_{3+4})] for individual questions reported by control and Celliant™ subjects. Analyses were performed on all 55 subjects as well as DPN and non-DPN subgroups. Outlier analysis was performed for each question by removing the two subjects in each group or subgroup with the most improvement reported for that question.

RESULTS

Control and Celliant™ subjects had comparable age and gender distributions upon entry into the study (Table 2). Except for the BPI questions in the non-DPN subjects, there

were no significant ($p < 0.05$) differences in the mean scores for individual questions at screening.

Both control and Celliant™ subjects reported decreased subjective pain after wearing socks for every question based on comparing W_{1+2} scores to W_{3+4} scores (see Figures). The differences between W_{1+2} and W_{3+4} scores were significant ($p < 0.05$, Mann Whitney) in 6 of 9 questions for Celliant™ subjects and in 4 of 9 questions for controls. The improvement in controls is characteristic of a strong placebo effect often seen in pain studies. For most questions, however, more improvement was reported by the Celliant™ group based on the magnitude of differences in $[W_{1+2} - W_{3+4}]$ scores.

Questions Ia and Ib of the MPQ rate the intensity of various aspects of pain: Question Ia rates 11 sensory aspects of pain such as throbbing or cramping as absent, mild, moderate, or severe. Question Ib similarly rates four affective dimensions (e.g., fearful). Question II is a simple scale where the intensity of present pain is marked on a line. Question III rates overall pain on a 0 (absent) to 5 (excruciating) scale. For control and Celliant™ groups, little difference between the improvements in mean scores for questions Ia, Ib, and Ia+b were found ($p > 0.405$, data not shown). In question III (Figure 1), pain reduction for Celliant™ subjects was significantly greater (0.50 versus 0.00) than for controls ($p = 0.043$). Removing two outliers did not alter the greater improvement seen with Celliant™ socks, but the p decreased to 0.024. For subjects with DPN, questions Ia, Ib, and Ia+b showed no significant differences in pain reduction between the two treatment groups, with or without outliers removed ($p > 0.566$, data not shown). In question II, 19% more improvement was seen with Celliant™ in DPN subjects ($p=0.703$);

removing outliers increased the difference to 130% (p=0.888). For question III, DPN subjects wearing Celliant™ socks showed a reduction of pain of 0.50 versus 0.00 in controls (p = 0.148); removing outliers did not alter the result. In non-DPN subjects, no significant differences were observed for questions Ia, Ib, and Ia+b (p > 0.571, data not shown). For question II, however, a nearly two-fold difference in pain reduction was seen with Celliant™ socks compared to controls (1.20 vs. 0.65, p = 0.371, data not shown). Removing outliers led to a four-fold difference with Celliant™ which was borderline significant (1.20 vs. 0.30, p = 0.087, data not shown). For question III in non-DPN subjects, more reduction in pain was reported with Celliant™ (0.50 versus 0.00, p = 0.154) and removing two outliers led to borderline significance (p = 0.075; Figure 1).

Two scores are derived from the BPI. The severity score rates pain over the previous 7 days, past 24 hours, and present between 0 (absent) and 10 (worst possible). The interference score measures interference with activities such as walking and working from 0 (none) to 10 (complete). Celliant™ subjects reported a borderline significant 30% more reduction in severity compared to controls (p = 0.077, Figure 2). Removing outliers increased the difference to 40% with p decreasing to 0.058. For interference, the Celliant™ group reported 18% more reduction than controls (p = 1.000). Removing outliers did not change the result (data not shown). Celliant™ subjects with DPN reported a reduction in pain severity of 0.75 compared to 0.50 in the controls (p = 0.211); removing outliers had no affect (Figure 2). For interference, controls demonstrated a greater reduction compared with the Celliant™ group (0.35 vs. 0.03 respectively), but this was not significant (p = 0.644) and removing outliers did not affect the result (p = 0.504, data not shown). In non-DPN subjects a 40% greater reduction in severity was

observed in Celliant™ subjects (p=0.230). Removing outliers amplified the reduction to 56% (p = 0.157). Non-DPN Celliant™ subjects reported 34% more reduction in interference compared with controls (p = 0.760) and removing outliers had little effect (p = 0.415, data not shown).

The Visual Analog Scale (VAS) rated foot pain from 0 (none) to 10 (worst possible) during the previous week. The entire Celliant™ group reported 45% greater reduction in pain compared to controls (p = 0.127; Figure 3). Outlier removal enhanced the difference to 58% which became borderline significant (p = 0.097). Changes between W_{1+2} and W_{3+4} VAS pain scores did not vary significantly between Celliant™ and control DPN subjects (0.10 compared to 0.00, p = 0.849) (Figure 3). Removing outliers had no effect (p = 0.860). In the non-DPN group, Celliant™ subjects exhibited borderline significant 54% more reduction in pain compared to controls (p = 0.060). Removal of outliers led to a significant 75% greater improvement in Celliant™ subjects (p = 0.024).

The SF-36 questionnaire has 10 categories measuring health and wellness. The bodily pain score measures a subject's attitude towards pain. Higher scores reflect less pain and lower scores more. Reduced pain correlates with negative [$W_{1+2} – W_{3+4}$] results. Figure 4 shows the Celliant™ group had 62% more improvement compared to controls, which was borderline significant (p = 0.058). Removing outliers resulted in 91% more improvement with Celliant™ (p = 0.032); after removing outliers more pain was reported by the controls. In DPN subjects, there was 99% greater improvement in the pain score with Celliant™ compared to controls (p = 0.109). Removal of outliers increased the improvement with Celliant™ to 109% versus controls; this difference was borderline

significant ($p = 0.065$). For non-DPN subjects, pain improvement with Celliant™ was 29% greater compared to controls ($p = 0.275$). Removing outliers resulted in 105% greater improvement with Celliant™ versus controls ($p = 0.157$).

DISCUSSION

This is the first trial assessing the impact of optically modified PET garments on pain. The pain questionnaires employed have been validated in previous studies[1-7], and were modified only by asking subjects to consider foot pain in their replies (except for the SF-36). Although a placebo effect was observed for most questions (controls reported improvement in 7 out of 9, 3 significantly), more reduction in pain was reported by subjects wearing Celliant™. In several instances the greater pain reduction seen with Celliant™ compared to controls was either significant (MPQ question III) or borderline significant. Removing outliers in the attempt to filter out placebo effects on the analysis tended to enhance the differences in pain reduction in favor of Celliant™ and decrease p values. Three questions failed to show greater improvement with Celliant™ compared to placebo: MPQ questions Ia, Ib, and Ia+b. These questions employ multiple complex scales and are designed more to measure sensory and affective aspects of pain rather than improvements. Table 3 shows the aggregate result when MPQ questions Ia, Ib, and Ia+b are removed from the analysis. All six remaining questions showed results in favor of Celliant™ except for the BPI pain interference question in the DPN subgroup, where more improvement in controls was found ($p > 0.566$). Outlier analysis also shows more of a therapeutic effect with Celliant™, as eliminating two paired outliers tended to enhance the differential effect of Celliant™ on pain compared to controls, in many

instances resulting in decreased p values. We believe the data in Table 3 strongly indicates that wearing Celliant™ socks reduces foot pain.

In general, non-DPN subjects showed more sensitivity to the beneficial effect of Celliant™ than subjects with DPN. Assuming the effect of Celliant™ on tissue is relatively localized, one might expect less of an effect to be seen in neuropathy, as only a portion of the diseased neuron fibers are in close proximity to the plantar aspect of the socks, and thus likely subject to the effect of the modified fabric.

This raises the question of what mechanism accounts for the beneficial impact of optically modified fiber garments. Two unpublished studies, one in healthy subjects and one in diabetics, demonstrated significant increases in transcutaneous oxygen tensions in the skin of the hands and feet when Celliant™ garments were worn compared to placebo garments[8,9]. The increased oxygen tensions were observed by 10 minutes and persisted during repeated measurements over 60 minutes. The increase in healthy subjects ranged from 10 to 24%; diabetic subjects showed an average increase of 10%. It is conceivable that some interaction of the Celliant™ particles with light increases reflection or transmission of light in the visible or near infrared portion of the spectrum into the skin, leading to vasodilation of the microcirculation and enhanced perfusion of tissue, which plausibly could ameliorate some causes of chronic pain. Alternatively, the enhanced illumination of the skin and underlying tissues could influence the biologic activity of endogenous chromophores (cytochromes, flavins, and poryphyrins) involved in energy metabolism in a manner leading to anti-inflammatory or anti-nocioceptive effects.

A large body of evidence suggests that short periods of illuminating skin, tissue, and cells with visible or infrared light has positive effects on pain, injury recovery, and wound healing. A number of studies have looked at joint pain such as temporomandibular joint pain[10], finding that near infrared light (810 nm) appears to reduce pain compared to sham illumination regimens. A meta-analysis of 20 trials employing laser therapy for chronic joint disorders found that when sufficiently intense light was employed, such therapy had a direct anti-inflammatory effect on the joint capsule[11]. A study of the effects of infrared (950 nm) on sural nerve conduction showed significant impact of illumination on nerve conduction velocity and negative peak latency compared to sham illumination[12]. Several studies on diabetic neuropathy showed a favorable impact of intermittent illumination with infrared at 890 nm on sensation and pain[13,14]. Low intensity laser therapy at 810-820 nm combined with exercise regimens has been shown to benefit patients with chronic back pain and Achilles tendonopathy[15,16]. Several studies using animal models of wound healing or cell cultures have examined the effects of short exposures to red (e.g., 632nm, 670 nm) or infrared light (e.g., 830 nm), finding wound healing to be significantly accelerated or increased expression of genes and proteins associated with proliferation[17-22].

Previous studies generally entailed short illumination periods of a few minutes at intensities of 1 to 20 Joules/cm which are much higher than the possible low intensity optical effects of Celliant™ garments. Our subjects were wearing socks under ambient light conditions and often shoes. Past demonstrations of interactions between tissues and external light, nonetheless, support the possibility that Celliant™'s effect is due to prolonged exposure of underlying structures to an altered electromagnetic environment.

Given the putative anti-inflammatory effects of infrared light, the ability of longer wavelengths to penetrate more deeply, and the likelihood that Celliant™ particles significantly reflect and scatter infrared light, plausibly the Celliant™ effect is mediated by perturbations in the infrared portion of the spectrum. Conceivably, but we think unlikely, the Celliant™ effect may be due to higher skin temperatures resulting from more efficient reflection of infrared wavelengths, but this requires further investigation.

CONCLUSIONS

Our data supports the hypothesis that wearing Celliant™ fabric socks leads to a reduction in pain associated with chronic foot disorders. Future studies looking at other chronic pain conditions such as carpal tunnel syndrome and knee arthropathies are warranted as well as attempts to elucidate the mechanism by examining the influence of the modified garments on tissue perfusion, temperature, oxygen levels, and inflammation.

ACKNOWLEDGMENTS

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AUTHOR DISCLOSURE STATEMENT

No competing financial interests exist for all authors.

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Ian L Gordon, MD

Department of Surgery, UCI Medical Center

101 The City Drive South

Orange, CA 92868-3298

Charts

Figure 1

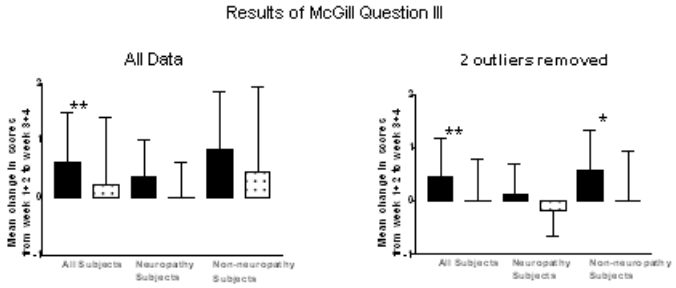

Figure 1: The difference between mean W_{1+2} and mean W_{3+4} scores is depicted. Solid bars report Celliant™ and stipled bars report control subjects. *p < 0.10; **p < 0.05

Figure 2

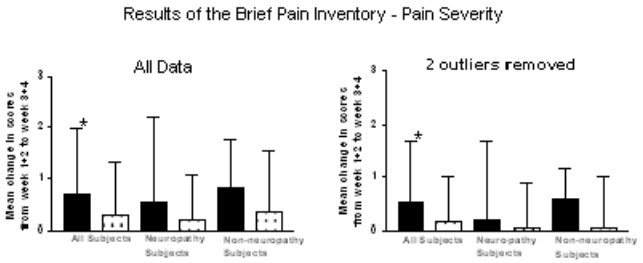

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Figure 3

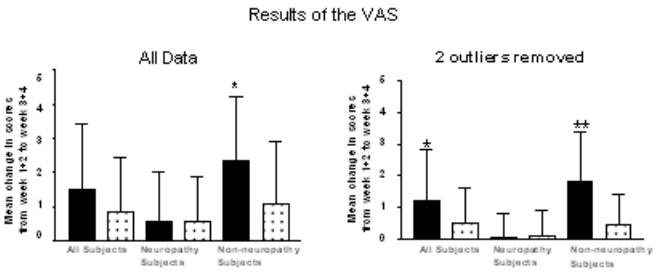

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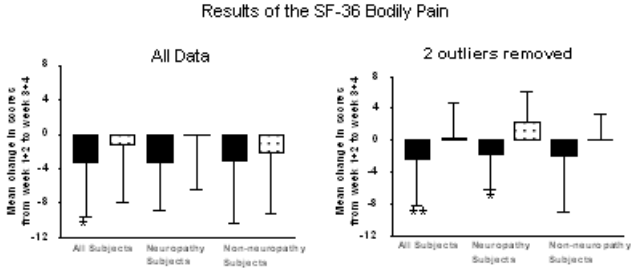
Figure 4



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Tables

Table 1: Pain etiologies in non-DPN subgroup

Etiology	**Celliant™**	**Control**
Arthritis	45%	40%
Edema	7%	0%
Erythromelalgia	0%	7%
Parkinson's Disease	0%	12%
PAD	0%	7%
Plantar Fasciitis	0%	7%
Previous Chemotherapy	7%	0%
Previous Surgery	7%	7%
Other Causes	36%	20%

Table 2: Subject Characteristics Prior to Treatment

	Demographics		McGill					Brief Pain Inventory			
All Subjects	**Age**	**% male**	**I-a**	**I-b**	**I-a+b**	**II**	**III**	**Pain Severity**	**Pain Interference**	**VAS**	**SF-36: Bodily Pain**
Celliant™	57.7±11.8	70%	1.2±0.8	0.6±0.7	1.9±1.5	4.7±2.4	2.6±1.0	4.4±2.0	4.2±2.4	5.8±2.4	37.8±8.1
Control	61.6±11.8	68%	1.3±0.7	1.1±1.0	2.4±1.6	5.4±2.8	3.1±1.1	5.2±1.9	5.5±2.6	6.4±1.8	34.6±7.8
DPN group											
Celliant™	63.0±7.7	85%	1.2±0.9	0.6±0.7	1.9±1.5	5.1±2.6	2.7±1.1	4.9±2.0	4.7±2.5	5.9±2.4	34.2±7.4
Control	63.9±11.0	77%	1.4±0.7	1.2±1.1	2.5±1.7	5.2±2.9	2.9±0.9	5.1±2.3	5.5±2.9	6.1±1.9	36.1±7.5
Non-DPN group											
Celliant™	52.7±13.1	57%	1.2±0.8	0.6±0.8	1.9±1.5	4.4±2.3	2.4±0.9	3.9±1.9	3.8±2.3	5.8±2.5	40.8±7.7
Control	59.5±12.3	60%	1.3±0.8	1.1±1.0	2.3±1.6	5.6±2.8	3.3±1.2	5.3±1.6	5.6±2.3	6.6±1.8	33.3±8.1

Table 3a: Results of selected questions – all subjects

Question	All Subjects	DPN subgroup	Non-DPN subgroup
McGill II	+	+	+
McGill III	+**	+	+
BPI Pain Severity	+*	+	+
BPI Pain Interference	+	-	+
VAS	+	+	+*
SF-36 Bodily Pain	+*	+	+

Table 3b: Results of selected questions – two outliers removed

Question	All Subjects	DPN subgroup	Non-DPN subgroup
McGill II	+	+	+*
McGill III	+**	+	+*
BPI Pain Severity	+*	+	+
BPI Pain Interference	+	-	+
VAS	+*	+	+**
SF-36 Bodily Pain	+**	+*	+

(+) Celliant™ showed greater improvement; (-) Controls showed greater improvement

* $p < 0.10$; ** $p < 0.05$