Effect of Ceramic-Impregnated "Thermoflow" Gloves on Patients with Raynaud's Syndrome: Randomized, Placebo-Controlled Study

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Abstract

OBJECTIVE: To determine the efficacy of ceramic impregnated gloves in the treatment of Raynaud's syndrome. DESIGN: Double-blind, placebo-controlled study. SETTING: Teaching hospital outpatient clinic. PARTICIPANTS: Ninety-three patients meeting the "Pal" criteria for Raynaud's syndrome. INTERVENTIONS: Treatment period of three months with use of ceramic-impregnated gloves. MAIN OUTCOME MEASURES: Primary end points: Pain visual analogue scale ratings and diary; Disabilities of the Arm, Shoulder, Hand questionnaire; Jamar grip strength; Purdue board test of hand dexterity. Secondary end points: Infrared skin temperature measurements; seven-point Likert scale rating of treatment. RESULTS: In 60 participants with complete data, improvements were noted in the visual analogue scale rating (P=0.001), DASH score (P=0.001), Jamar grip strength (p=0.002), infrared skin fingertip temperature (p=0.003), Purdue hand dexterity test (p=0.0001) and the Likert scale (p=0.001) with ceramic gloves over the placebo cotton gloves. CONCLUSION: The ceramic-impregnated "thermoflow" gloves have a clinically important effect in Raynaud's syndrome.

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Introduction

Raynaud's phenomenon is a syndrome of episodic attacks of vasospasm involving the small arteries/arterioles of the fingers, toes, and less frequently, the nose, tongue, and ears. The attacks are classically described triphasic with initial pallor (white), followed by a cyanotic phase (blue), and lastly by hyperemia (redness). Onset is often provoked by cold but may also be brought on by emotional stress or tobacco. It is a common condition that affects 10-15 percent of the female population.[1] Primary Raynaud's is of idiopathic origin. Secondary Raynaud's is related to connective tissue diseases, arterial occlusive disease, blood dyscrasias, drugs (e.g., ergot derivatives, beta-blockers, nitroglycerine, chemotherapy agents), toxins, and other miscellaneous disorders.[2] It may also be brought on by repetitive trauma such as the use of vibration tools (vibration-induced white finger syndrome)[3] and is seen in a higher proportion of carpal tunnel syndrome patients.[4]

The pathophysiology in primary and secondary cases of Raynaud's is poorly understood. Theories include the "local fault"[5] within the arterial wall, endothelial cell injury[6] with subsequent activation of platelets,[7] vasoconstrictors (serotonin, thromboxane),[8] free radicals,[9] and decreased vasodilators (nitric oxide[10] and calcitonin gene-related peptide[11]). More severe cases such as those in systemic sclerosis are characterized by fibrous intimal proliferation, peri-

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ungual capillary abnormalities, photoplethysmographic evidence of arterial occlusion, and angiographic evidence of narrowing and organized intraluminal thrombi.[12,13] Milder idiopathic cases due to sympathetic over-activity may improve with psychophysiological approaches.[14]

The usual treatment of primary Raynaud's syndrome involves keeping warm, smoking cessation, medications (long-acting calcium-channel-blocking drugs,[15,16] prostacyclin analogues[17]), and psychophysiological therapy (hypnosis,[18] behavior modification,[19] skin temperature biofeedback[20,21]). Thermal biofeedback has also been reported to be effective in diabetic claudication.[22] More aggressive approaches include sympathetic blocks and surgical sympathectomy. Newer approaches include a nitric-oxide generating topical jelly.[23] There is one randomized trial using traditional Chinese acupuncture.[24] In one previous study published by the same authors, acupuncture and biofeedback were the two most common alternative therapies recommended by physiatrists (physical medicine and rehabilitation medical specialists).[25]

Another treatment originating in the Institute of Hematology and Hospital for Blood Diseases (Chinese Academy of Medical Sciences) involves the use of ceramic-impregnated garments (95% polypropylene and polyethylene; 5% ceramic) that absorb ambient far-infrared radiation (0.76 to 4 micrometers wavelength) from the environment and body. This results in thermal energy being reflected into the underlying tissues, resulting in elevation of the dermal and subcutaneous tissue temperatures. Secondary improvement occurs via vasodilation and improved circulation.

One double-blinded study with 30 patients performed at the Chinese Academy of Medical Sciences documented increased blood volume and flow with impedance plethysmography for the active limb versus the control side (30 minutes of wear) with p-value < 0.01 for the lower leg and <0.05 for the forearm. Clinical effectiveness for pain (arthritis, peripheral vascular disease) was correlated with the duration of use per day. Side effects were minimal with two patients stopping due to the development of skin irritation.[26]

Table 1. *Pal Questionnaire*

Have you ever had episodes when your fingers, toes, ears, tongue, or nose have turned white or very pale? (2 points)
Do the involved areas become numb or tingle? (1 point)
Does the area throb? (2 points)
Does the white area later turn blue or red? (1 point)
Does the area sweat more when involved? (1 point)
Are there episodes provoked by tobacco? Cold air or water? Emotion? (2 points)

These products, known as "thermoflow garments," were approved in May 1997 by the Health Protection Branch in Canada. A randomized, controlled trial was approved by the hospital ethics committee and conducted from December 1999 to May 2000 in the section on Complementary and Alternative Medicine Research, Division of Physiatry, Department of Medicine at Sunnybrook and Women's College Health Sciences Centre (University of Toronto).

Participants and Methods

Patients

Subjects with Raynaud's phenomenon were recruited from newspaper advertisements. Out of a total of 132 telephone respondents, 93 met the "Pal" criteria for Raynaud's. This screening tool has been validated and requires a mandatory yes to question 1 and a total score greater than 4 (Table 1).

Of the subjects who passed, 93 were assessed at the outpatient departments of Sunnybrook and the Canadian Centre for Integrative Medicine. The clinical diagnosis was confirmed by medical evaluation and note made of previous rheumatologist assessment and peripheral Doppler studies done with cold stress. One female was excluded from the study due to fingertip skin ulceration and infection. Three subjects did not want to complete the study because they did not want to wear gloves while vacationing in Florida. Other exclusions included one subject with severe pulmonary disease, one with recent myocardial infarction, and another subject with terminal cancer. All subjects were also assessed for a history of connective tissue disease (scleroderma, systemic lupus erythematosus, rheumatoid arthritis, dermatopolymyositis, mixed connective tissue disease, etc.), endocrine disease (hypothyroidism, diabetes mellitus), and hematologic disease (blood dyscrasia, paraproteinemias).

They were also assessed for coexistent conditions such as carpal tunnel syndrome, fibromyalgia,[27] and thoracic outlet syndrome.[28] Use of cigarettes, caffeine, and alcohol was recorded. Medication use including birth control pills, chemotherapy, cold remedies with pseudoephedrine, and migraine pills (ergotamine) was recorded. Use of vibrating tools, occupation, and handedness were recorded. Also documented was use of other medications, such as calcium channel blockers, and herbal products, such as *Ginkgo biloba* and vitamin E, that could affect circulation. Other treatments, such as physiotherapy, biofeedback and surgical sympathectomy, were noted.

Males and females were included and all subjects were at least 18 years of age. Pregnant females were excluded.

The study protocol and consent form for participation were approved by the university-based teaching hospital's ethics committee. All subjects provided written informed consent for their participation in the study.

Treatment

Ceramic-impregnated "thermoflow" gloves were supplied to half of the participants who were instructed by a blinded consultant as to appropriate use (including duration of wear, hygiene, and application technique). Placebo gloves supplied to the other half were identical in appearance, odor, and texture.

Allocation to a treatment group (active or placebo) was carried out by assigning to the subject the next available randomization number (inner label) in the sequence given to the center. The sequence of treatments in the randomization list was determined by previous computer-generated random sequence for the pairs of gloves.

Study Design

The study consisted of two blocks of three months. The first group was recruited and assessed in December 1999, followed by a telephone call two weeks later to encourage compliance and reassessment in February 2000. A second group of subjects were assessed in March 2000 and reassessed in May 2000 using the same protocols. The treatment and follow-up periods were double blind.

Clinical Outcome Variables

All subjects were required to complete the following: pain diagram, short-form McGill Pain questionnaire, and visual analogue scale for pain over past week on day of assessment, and a diary of Raynaud's attacks. The previously validated functional questionnaires known as the DASH (Disabilities of the Arm, Shoulder, Hand) questionnaire[29] and the FIQ (Fibromyalgia Impact Questionnaire)[30] were also completed.

Table 2. *Demographics of Treatment and Placebo Groups*

Demographics		Placebo	Active	Statistical Significance
Sex	Male	4	10	
	Female	26	20	p=0.64 Likelihood ratio chi-square
Age average in years (standard deviation)		51.8 (12.3)	54.1 (12.1)	p=0.47 T-test with unequal variances
Body mass index (standard deviation)		22.0 (3.7)	24.5 (4.l)	p=0.01
Normal body mass index is classified as 18 to 25. Our subjects on average fell in this range.				

All subjects at the pre- and post-treatment assessment were examined by trained nurses for the following:

1. Exergen skin temperature measurements done over the fingertips and the finger dorsum (between the nail bed and the distal interphalangeal joint) of the 2nd to 5th digits. The distal-dorsal difference was calculated based on previous findings suggesting that a difference > 1°C is specific for underlying connective tissue disease.[31]
2. Jamar grip strength (average of three trials with each hand).
3. Purdue board test (hand dexterity).
4. Tinel's sign (percussing over the carpal tunnel) rated as absent, present:mild, or present:marked (patient withdraws hand).
5. Phalen's sign (passive flexion of the wrist over 60 seconds).

At the pre-treatment evaluation, height and weight were also recorded and the body mass index calculated. Blood pressure and pulse were recorded for each arm. The short-form McGill Pain questionnaire and pain diagrams were completed.

At the post-treatment evaluation, subjects also rated their response to treatment using the 5 point Likert scale.

Mean weekly outdoor temperatures were determined for each subject from data provided by the local meteorological center (Toronto). Mean changes were recorded for each group.

Test-Retest Reliability

Test-retest reliability was carried out on eight subjects for subjective and objective outcome measures (done over two consecutive days). The intra-class correlation coefficients were extremely high for the DASH (90.996), FIQ (0.984), Jamar average grip (0.993), and Purdue percentiles (0.997).

Tolerability and Safety

Subjects were asked during the follow-up telephone call and the post-treatment assessment to report any adverse events. Three subjects complained of skin irritation. Otherwise, there were no serious side effects reported.

Statistical Analysis

Statistical methods followed an intention-to-treat principle and corrected for possible bias caused by differences in missing data among groups by using a regression equation based on baseline variables to impute values for subjects

Table 3. *Outcome Measures at Baseline in Treatment and Placebo Groups*

Outcome Measure	Placebo	Active	Statistical Measure
Visual analogue scale (VAS) for average pain 0-100	55.1	56.9	p=0.65
Pain diagram:			
Bilateral hands	14	15	p=0.95
Hands and feet	12	10	likelihood ratio chi-square
Short-form McGill Pain	14.6	15.8	p=0.66
Disability of the Arm, Shoulder and Hand (DASH) score	21.5	24.4	p=0.85
Fibromyalgia Impact Questionnaire (FIQ)	1.46	1.98	p=0.43
Average fingertip skin Temperature °C	25.9	26.5	p=0.04
Average finger dorsum Temperature °C	26.3	27.2	p=0.03
Jamar Grip Strength			
Average of left hand in kg	25.0	29.4	p=0.10
right hand	25.5	29.6	p=0.10
Purdue Board Test			
Average percentile rating			
left	34.9	33.7	p=0.28
right	36.4	35.9	p=0.21

with missing data. Analyses were performed using SAS routines and were conducted by independent statisticians at the Institute of Clinical and Evaluative Sciences.

Results

Of the 93 subjects initially assessed, 60 (65%) completed the necessary forms and followed through with the post-treatment evaluation. Thirty subjects used active gloves over the three months and 30 subjects used placebo gloves. Of the 33 individuals who did not complete the study, 19 were on active and 14 were on placebo.

The demographic characteristics of the subjects were similar in the treatment and placebo groups (Table 2).

For the likelihood ratio chi-square, there were also no significant differences between the two groups for the mean PAL criteria (p = 0.61),

Table 4. *Post-Treatment Results for Active and Placebo Groups*

	Before	After	pvalue
VAS (SEM)	56.9 (4.5)	50.8 (4.3)	0.001
Placebo	55.1 (4.1)	57.9 (4.1)	0.20
DASH	24.4 (4.0)	19.1 (3.9)	0.001
Placebo	21.5 (3.2)	23.9 (3.2)	0.18
FIQ	1.99 (0.50)	1.64 (0.43)	0.75
Placebo	1.46 (0.37)	1.28 (0.45)	0.32
Fingertip temp	26.46 (0.37)	27.54 (0.37)	0.003
Finger dorsum	27.20 (0.51)	28.13 (0.44)	0.09
Placebo	25.87 (0.25)	26.39 (0.38)	0.29
	26.35 (0.37)	26.47 (0.46)	0.19
Jamar left	29.4 (3.1)	34.6 (2.8)	0.002
Jamar right	29.6 (3.1)	36.3 (2.8)	0.0001
Placebo	25.0 (3.1)	25.0 (3.1)	
	25.5 (3.4)	26.0 (3.3)	
Purdue left	33.7 (0.9)	42.0 (1.3)	0.0001
Purdue right	35.9 (0.9)	44.0 (1.3)	0.0001
Placebo	34.9 (1.6)	36.9 (1.8)	
	36.4 (1.6)	38.6 (1.8)	
Likert active		5.66	0.001
placebo		4.13	

Likert scale scoring is:
1. markedly worse
2. moderately worse
3. somewhat worse
4. no change
5. somewhat improved
6. moderately improved
7. markedly improved

presence of associated diseases (p = 0.09), smokers (p = 0.09), caffeine intake (p = 0.22), alcohol use (p = 0.19), relevant medication use (p = 0.08), and herbals such as Ginkgo or vitamin E (p = 0.13). There was a difference in use of vibratory tools with three in the active group compared to none in the control group (p = 0.04). One of the active and four of the placebo group were left-hand dominant (p = 0.15).

With regard to concurrent use of medication for Raynaud's, in the active group 17 were not taking any drugs, 10 were on a calcium channel blockers, and one on a prostacyclin analogue. One subject was on both types of drugs. In the control group, 20 were not taking drugs, eight were on a calcium channel blocker alone, and two were taking both types. The likelihood ratio chi-square p value was 0.47, which is not significantly different. There was also no significant difference between the two groups in the use of physiotherapy, biofeedback, and alternative medicines. No subjects had had surgical sympathectomies. Baseline outcome measures were similar between the two groups prior to treatment as listed in Table 3.

Tinel's sign, which is a screening test for carpal tunnel syndrome, was present in 21 of 60 subjects.

Results, which were statistically significant for the active group, are outlined in Table 4 for both treatment and control groups.

Discussion

These findings indicate that ceramic-impregnated "thermoflow" gloves are superior to placebo gloves in the management of Raynaud's symptoms. Significant improvements were documented in both subjective measures of pain and discomfort and in objective measures of temperature, grip, and dexterity.

The episodes of Raynaud's attacks recorded by diary also suggested improvement in the actively treated group. However, incompletely filled diaries prevented a statistical analysis. The subjective rating by the Likert scale suggests the active group had somewhat to moderate improvement, whereas the placebo group overall experienced no change.

Limitations to this study include the lack of more advanced measurements of peripheral vascular flow. Technology such as digit photoplethysmography and cold stressor tests would add more to the objective measures. Future studies would be helpful in documenting response rates over a longer period of time and with a larger number of subjects.

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