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ADDITION OF LOCAL CRYOTHERAPY FOR TREATMENT OF POST-MASTECTOMY LYMPHEDEMA

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ABSTRACT

Worldwide, lymphedema can present as a significant health issue. Left untreated, it can have long-term medical and psychological consequences for patients. Cryotherapy is a new physical therapy modality used for many purposes including reduction of pain, inflammation, and edema. It is thought to decrease interstitial fluid volume through many mechanisms. Therefore, it is reasonable to think that cryotherapy might have a positive effect in treatment of lymphedema. The goal of this study was to investigate how local cryotherapy in combination with standard therapy affects patient outcomes. Forty post-mastectomy female patients aged 40-60 years old with lymphedema were referred to the outpatient clinics of the Faculty of Physical Therapy at South Valley University for medical treatment and follow-up by the vascular surgery department. Patients were randomly divided into two groups of equal size. Traditional physical therapy programs (manual lymphatic drainage, pneumatic compression, bandaging, breathing exercises, circulatory exercises, shoulder mobilizations, and ROM exercises) were combined with pulsed local cryotherapy three times per week for 12 weeks in Group (A). For 12 weeks, Group (B) received only traditional physical therapy three times per week. Patients were evaluated using circumferential measurement with tape at the wrist, below the elbow, and above the elbow level, as well as ultrasonography to assess skin thickness before the start of physical therapy, 6 weeks later, and at the end of the treatment (after 12 weeks). Results indicate that cryotherapy is an effective adjunct modality for the treatment of secondary lymphedema and should be added to physical therapy protocols for lymphedema rehabilitation.

Keywords: Cryotherapy, lymphedema, post-mastectomy, treatment

Lymphedema is an incurable, debilitating, and progressive condition that is characterized by swelling of one or more parts of the body. It develops due to impaired lymph transport and is a major healthcare problem in many countries. Lymphedema may be present in all body parts (extremities, trunk, abdomen, head and neck, external genitalia, and internal organs). It is an important issue due to its long-term physical and psychosocial effects for the patient if left untreated (1,2).

About 200 million cases of lymphedema are estimated worldwide with filariasis, a parasitic infestation, being the most common cause (1,3). There are 2 types of lymphedema: a) primary due to the congenital dysfunction of the lymphatic system and can be diagnosed at different stages in life without definite cause; and (b) secondary forms that mostly develop after cancer surgery and/or radiation therapy for various cancers comprising breast, endometrium, cervix, ovary, melanoma, prostate, and bladder (1,3).

Cryotherapy is a new physical therapy modality used for many purposes including pain, inflammation, and edema. Skin cooling initially leads to local vasoconstriction (4) and decreases the normal post-ischemic hyperemic response caused by tissue indentation loading (5). Skin cooling also leads to systematic vasoconstriction (6,7). The local vasoconstriction also leads to decreased capillary to fluid filtration and increase post-capillary fluid reabsorption. All of this results in decreased interstitial fluid volume. Lymphedema is also often associated with inflammation and fibrosis, so cryotherapy which produces cooling to depth about 2-4 cm (8), might be having a positive effect on this condition.

There are different modalities utilized in the treatment of lymphedema such as compression therapy (pneumatic compression, bandaging), manual lymphatic drainage, shockwave therapy, breathing exercise, and circulatory exercise. In this study, we examine the effect of adding a new physical therapy modality called cryotherapy to the treatment of post-mastectomy secondary lymphedema.

PATIENTS AND METHODS:

Patients

Forty post-mastectomy female patients (aged 40-60 years old) with lymphedema were referred to the outpatient clinics for physical therapy at South Valley University from the vascular surgery department. Patients were treated and followed up from January 2020 to September 2021. Patients with active cancer, neuropathy, metastasis, blood vessels diseases, infection, renal disease, heart disease, lung disorder, on any medications that alter body fluids, or were pregnant were excluded from the study. Patients were divided randomly into two equal groups. Group (A) received a traditional physical therapy program (manual lymphatic drainage, pneumatic compression, bandaging, breathing exercise, circulatory exercise, shoulder mobilization, and ROM exercise) combined with pulsed local cryotherapy 3 times per week for 12 weeks. Group (B) received only traditional physical therapy 3 times per week for 12 weeks. Patients were assessed by circumferential measurement using a tape and ultrasonography before beginning of physical therapy treatment, after 6 weeks (Post I), and after 12 weeks of treatment (Post II, at the end of the treatment).

Assessment Tools and Procedures

Circumferential measurements (arm girth measurement):

A plastic tape was utilized to capture circumferential measures at the wrist, 10 cm below the elbow, and 15 cm above the elbow on both the affected and non-affected sides. Comparison for treatment results was obtained by subtracting the non-affected side from the affected side before treatment, after 6 weeks, and at the end of treatment (9).

Ultrasonography:

Ultrasonography was carried out using a Toshiba Xario prime ultrasound device. Before assessment, the most fibrotic point in the upper arm was identified by thumb palpation and marked for assessment. Then the ultrasonography assessment procedure was carried out by the radiology specialist before treatment, after 6 weeks, and after 12 weeks (at the end of treatment). The radiological specialist was the same person for each assessment. Thickness was determined for both the epidermis and dermis.

Treatment procedures:

Both groups received traditional physical therapy programs as follows: 1) A pneumatic compression device for 15 minutes; 2) Segmental manual lymphatic drainage from distal to proximal for 15 minutes; 3) Circulatory exercise for upper limb (from distal to proximal, slow-fast-slow rhythm); Breathing exercises (lateral costal and diaphragmatic); and 4) Bandaging.

Cryotherapy was added to group (A) by a cryo-air machine, (cryo-air mini brand) which utilizes cryo-air cold air therapy technology. This is a mature and safe-to-use

system that cools the air to -32°C. Steps of application included: 1) Apply oil or cream to moisture the skin before cryotherapy application; 2) Initialize the mini cryo-air equipment at level 6; 3) Apply for 5 minutes at the hand, wrist, forearm, and arm in a distal to proximal direction at each point which mirrors the direction of lymphatic fluid transport.

Ethical approval

The Ethical Committee of Faculty of Medicine, South Valley University, approved the study (approval 176/4/2021/4/VAS015/ MED/SVU) and written informed consent was obtained from every patient.

Statistical analyses

Statistical analysis was performed using SPSS statistical software version 25 for Windows (SPSS Inc., Chicago, IL, USA). An unpaired t-test was used for the comparison of patients' age between groups. The normal distribution of data was checked using the Shapiro-Wilk test for all variables. Levene's test for homogeneity of variances was used to test the homogeneity between groups. Mixed MANOVA was performed to compare within and between groups effects on ultrasonography and circumferential measurements. Post-hoc tests using the Bonferroni correction were carried out for subsequent multiple comparisons. A p-value of < 0.05 was considered statistically significant.

RESULTS

Mean age of study participants of group A was 48.75 (± 5.73 SD) years and that of group B was 50.2 (± 5.29 SD) years. There was no significant difference between groups ($p = 0.41$).

Effect of treatment on the thickness and circumferential measurement of the wrist, below the elbow, and above elbow revealed that there was a significant relation of treatment and time ($F = 14.82$, $p = 0.001$, $\eta^2 = 0.79$). In addition, there was a significant main effect of time ($F = 263.57$, $p = 0.001$, $\eta^2 = 0.98$) and a significant main effect of treatment ($F = 7.26$, $p = 0.001$, $\eta^2 = 0.45$). *Table 1* displays descriptive statistics of thickness and circumferential measurement of the wrist, below the elbow, and above the elbow as well as the comparison between groups and comparison before and after treatment in each group.

Within Group Comparison

Within group comparison showed that there was a significant decrease in thickness and circumferential limb difference at the wrist, below the elbow, and above the elbow of groups A and B at post treatment (Post II = after 12 weeks of treatment) compared with that pretreatment and Post I (after 6 weeks of treatment) ($p < 0.001$). In addition, there was a significant decrease in thickness and circumferential limb difference at the wrist, below the elbow, and above the elbow of groups A and B at Post I compared with that pre-treatment ($p < 0.001$) (*Table 1*).

Between Group Comparison

There was no significant difference in thickness and circumferential measurement between groups at pre-treatment ($p > 0.05$). But comparison between groups post-treatment revealed a significant decrease in thickness and circumferential limb difference at the wrist, below the elbow, and above the elbow of group A at Post I (after 6 weeks) ($p < 0.01$) and Post II (after 12 weeks) ($p < 0.001$) compared with that of group B (Fig. 1-2, *Table 1*).

DISCUSSION

Lymphedema is a major healthcare problem in several countries. It is a hot spot due to its long-term physical and psychosocial effects for the patient if left untreated. The objective of our study was to investigate the impact of adding cryotherapy traditional therapy on patient outcomes.

The first important result of our study is that local cryotherapy has a positive effect on post-mastectomy lymphedema treatment

TABLE 1
MEAN THICKNESS AND CIRCUMFERENTIAL MEASUREMENT OF WRIST, BELOW ELBOW, AND ABOVE ELBOW AT PRETREATMENT, POST I, AND POST II TIME PERIODS FOR GROUPS A AND B

	Pre-treatment	Post I	Post II	p-value		
	mean ± SD	mean ± SD	mean ± SD	Pre- vs Post I	Pre- vs Post II	Post I vs Post I
Thickness (mm)						
Group A	2.13 ± 0.57	1.41 ± 0.47	1.12 ± 0.39	0.001	0.001	0.001
Group B	2.02 ± 0.45	1.76 ± 0.42	1.45 ± 0.42	0.001	0.001	0.001
MD (95% CI)	0.11 (-0.22: 0.44)	-0.35 (-0.63: -0.06)	-0.33 (-0.59: -0.06)			
	p = 0.5	*p = 0.01*	*p = 0.001*			
Wrist (cm)						
Group A	3.87 ± 0.78	2.11 ± 0.68	1.01 ± 0.76	0.001	0.001	0.001
Group B	3.93 ± 0.69	2.68 ± 0.66	1.9 ± 0.68	0.001	0.001	0.001
MD (95% CI)	-0.06 (-0.53: 0.4)	-0.57 (-0.99: -0.13)	-0.89 (-1.35: -0.43)			
	p = 0.78	*p = 0.01*	*p = 0.001*			
Below elbow (cm)						
Group A	6.1 ± 1.08	3.52 ± 0.92	1.96 ± 0.53	0.001	0.001	0.001
Group B	6.25 ± 0.79	4.89 ± 0.71	3.46 ± 1	0.001	0.001	0.001
MD (95% CI)	-0.15 (-0.76: 0.46)	-1.37 (-1.89: -0.84)	-1.5 (-2.01: -0.99)			
	p = 0.62	*p = 0.001*	*p = 0.001*			
Above elbow (cm)						
Group A	8.06 ± 0.96	5.1 ± 0.93	2.61 ± 0.48	0.001	0.001	0.001
Group B	8.29 ± 0.8	6.3 ± 0.94	4.68 ± 0.89	0.001	0.001	0.001
MD (95% CI)	-0.23 (-0.79: 0.34)	-1.2 (-1.8: -0.6)	-2.07 (-2.53: -1.61)			
	p = 0.42	*p = 0.001*	*p = 0.001*			

shown by comparison between groups post-treatment. A significant decrease in thickness and circumferential limb difference at the wrist, below the elbow, and above the elbow of group A at Post I and Post II ($p < 0.001$) was found compared with group B (*Table 1*).

In agreement with our study, Mizeva et al interpreted this effect as topical skin cooling leading to local and systematic vasoconstriction which together leads to capillary- to- interstitial fluid filtration and enhance post-capillary fluid reabsorption. This process tends to decrease the interstitial fluid (10).

In concurrence with our study also

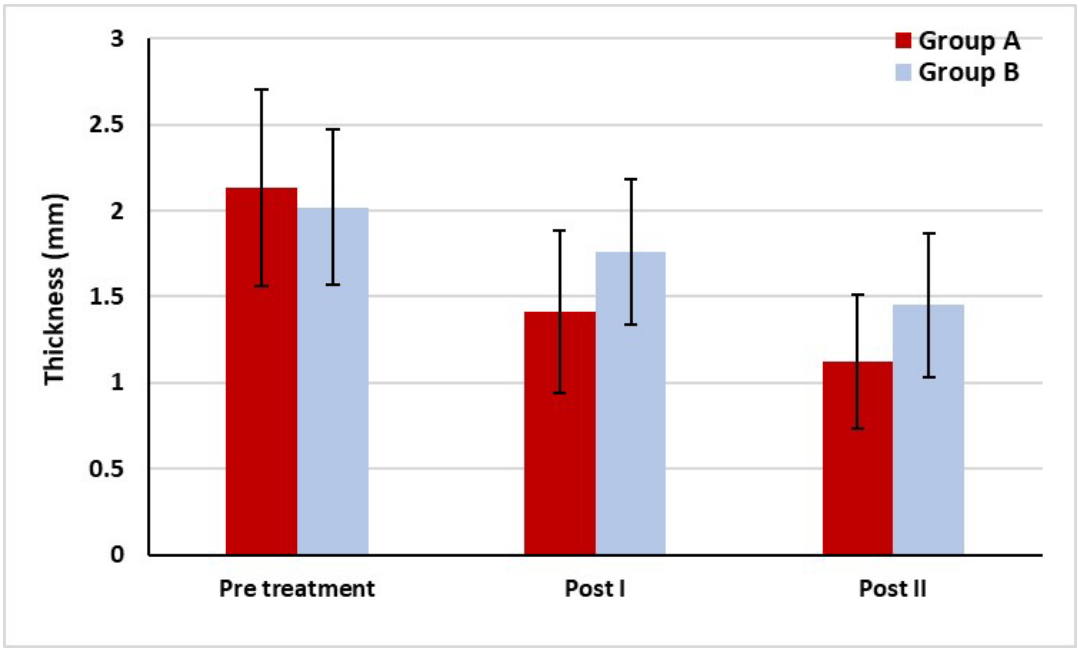

Fig. 1. *Mean thickness of skin (epidermis +/- dermis) of combined wrist, below elbow, and above elbow points at pretreatment, Post I, and Post II time points determined by ultrasound for groups A and B.*

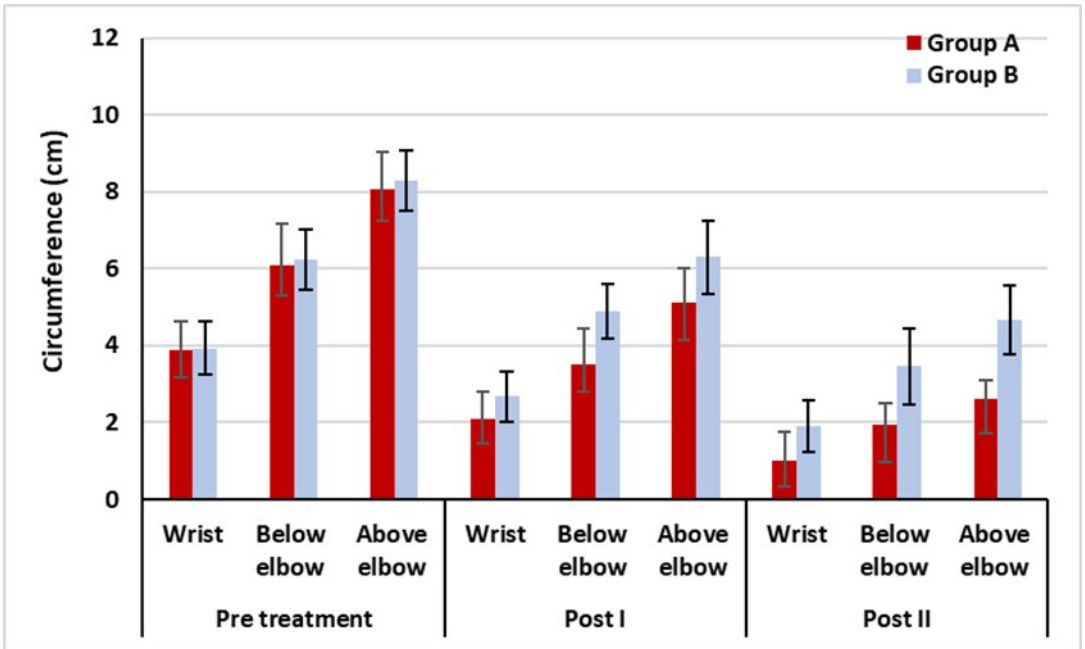

Fig. 2. *Mean circumferential measurement of wrist, below elbow, and above elbow at pre-treatment, Post I, and Post II time periods for groups A and B.*

Mayrovitz and Yzer showed that skin cooling of the upper limb softens lymphedematous and fibrotic tissue by about 24% to 28%. This tissue softening leads to decrease pressure on the underlying nerve ending and decrease input to the sensory nerves that interrupt the pain cycle. As softer tissues become more pliable and movable, myofascial mobilization, scar, and fibrous tissue release, and treatment techniques are easier for the therapist to perform (11).

Ho SS et al reported that cold therapy decreases cell metabolism and tissue blood flow. Their study using bone scanning showed that an ice wrap application to one knee for 20 minutes decreased soft tissue blood flow by 26%; arterial blood flow by 38%; and bone uptake, which reflects changes in bone blood supply and metabolism, by 19% (12).

In harmony with our study, Stockle et al found that both intermittent compression therapy and continuous ice application treatment were more effective than intermittent cool pack therapy for foot and ankle injuries. After 24 hours of treatment, decrease of edema was highest (47%) in the intermittent compression group, while the continuous ice water treatment group provided 33% decrease in swelling and conventional intermittent ice pack treatment only reduced swelling by 17%. After four treatment days, the intermittent compression and continuous ice water application were equivalent with an approximately 70% edema reduction, compared with a 45% edema reduction with intermittent ice pack treatment (13).

Concerning the duration of our treatment, according to a study by Kwiecien et al, extending the positive effects of cryotherapy by extending the duration of cooling can improve recovery. Furthermore, current recommendations in standard textbooks on the clinical use of ice have many flaws, and the majority of physicians rely on empirical evidence (14).

In a clinical setting, parameter selection is still made pragmatically, with recommendations in review articles ranging from 10 to 20 minutes, 2 to 4 times per day for up to 20 to 30 minutes, or every 2 hours for 30 to 45 minutes. Recent clinical practice surveys have revealed differences in the best mode, duration, and frequency of cryo application. The duration and frequency of cryotherapy treatments were not consistent across studies. With such a wide range of cryo protocols, the total treatment time subjects received was extremely variable. It is not possible to provide instructions for when to use cryo because it is dependent on the characteristics of each device (15).

Within clinical practice, ice is commonly combined with compression and elevation, making it difficult to determine the value of cryotherapy alone (14,16). Several studies have compared various cryo and compression combinations to determine their relative efficacy. Only one study compared ice and compression together to ice alone. This study does little to separate and quantify the individual effects of ice and compression because the modes and durations of cold treatments applied across groups were starkly different. This is consistent with our study limitation in that the inclusion of cryo with the standard treatment may have caused the improvement, and a future study that can isolate and identify cryo alone may be of interest (17,18).

Our study had several other limitations. First, the methodology of the study is invariably associated with missing data due to a longer follow up duration. Second, lack of a placebo control group makes it difficult to distinguish true treatment effects. Third, this study utilized a relatively small sample size, and we recommend larger sized studies to confirm these results.

CONCLUSION

Study results demonstrate that cryotherapy is an effective adjunct modality in the treatment and rehabilitation of post-mastectomy lymphedema, and it should be added to the protocol of lymphedema physical therapy rehabilitation to improve patient outcomes over traditional therapy alone.

CONFLICT OF INTEREST AND DISCLOSURE

The authors declare no competing financial interests exist.

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