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COMPARING TWO TREATMENT METHODS FOR POST MASTECTOMY LYMPHEDEMA: COMPLEX DECONGESTIVE THERAPY ALONE AND IN COMBINATION WITH INTERMITTENT PNEUMATIC COMPRESSION

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ABSTRACT

There is no cure for breast cancer related lymphedema. This study was conducted to compare two treatment methods for postmastectomy lymphedema: Complex Decongestive Therapy (CDT) and Modified CDT (MCDT) combined with Intermittent Pneumatic Compression (IPC). One hundred and twelve patients referred to the Lymphedema Clinic of the Iranian Center for Breast Cancer in 2008, were included in a randomized clinical trial. They were randomly allocated into two equal groups receiving daily CDT alone or in combination with IPC. The volume reduction of the upper limb was measured by water displacement volumetry. No statistically significant differences in demographic and clinical variables between the two groups were observed. During the intensive phase (phase I) of treatment, CDT alone yielded a significantly higher mean volume reduction than the combination modality (43.1% vs. 37.5%; p = 0.036). Limb volume measured three months following treatment, showed 16.9% volume reduction by CDT alone, and 7.5% reduction by MCDT plus IPC. This study demonstrated that the use of CDT alone, or in combination with IPC significantly reduced limb volume in patients with post mastectomy lymphedema. CDT alone provided better results in both treatment phases. Further studies will help to define the role of multidisciplinary approaches in the management of postmastectomy lymphedema.

Keywords: breast cancer, lymphedema, complex decongestive therapy, intermittent pneumatic compression, Iran

Lymphedema is an external manifestation of insufficiency of the lymphatic system (1). It is characterized by an accumulation of fluid in the interstitial tissue that causes swelling, most often in the arms or legs.

Lymphedema following treatment for breast cancer has received attention in multiple studies. The overall incidence of arm lymphedema can range from 8% to 56%, within 2 years following surgery, depending on the extent of axillary surgery and the use of radiotherapy (2). Breast cancer mortality rates have declined in recent years, reflecting advances in early detection and more widespread application of effective adjuvant therapies. Many women diagnosed with breast cancer today can expect survival that is similar to age-matched women without breast cancer. The National Cancer Institute estimates that one in seven women in the

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USA have a lifetime risk of being diagnosed with breast cancer, and mortality occurring in one in 33 (3). In Iran, there are 7,700 new cases of breast cancer diagnosed in females annually, with the Age Specific Incidence Rate of approximately 25 per 100,000 (4). As the life expectancy for women with breast cancer improves, more women are at risk for complications resulting from treatment. Complications including lymphedema can impair function and quality of life. For this reason effective prevention and management of breast cancer treatment related sequelae have taken on increasing importance (5).

No curative treatments for lymphedema are currently available. Therefore, the goal of treatment is to decrease the excess volume as much as possible and maintain the limb at its smallest size and best function (6). Failure to control lymphedema may lead to repeated infections (cellulitis/lymphangitis), progressive swelling and trophic changes in the skin, sometimes crippling invalidism and on rare occasions, the development of a highly lethal angiosarcoma (Stewart-Treves syndrome) (1).

Varying methods for controlling lymphedema have been prescribed. The gold standard treatment for lymphedema is Complex Decongestive Therapy (CDT) (6). Complex Decongestive Therapy, also known as Combined Physical Therapy (CPT), Complete or Complex Decongestive Physiotherapy (CDP), is backed by longstanding experience and generally involves a two-stage treatment program that can be applied to both children and adults.

A large study on CDT for the treatment of upper and lower extremity lymphedema, found an average edema volume reduction of 59.1% in upper extremities, and 67.7% in lower extremities. Patients in that study underwent an average of 15.7 days of treatment. Volume measurements were taken at the beginning and end of the treatment phase, and at six and 12 month follow-up visits. Patients both with upper and lower extremity lymphedema who were adherent during the maintenance phase retained 90% of the initial reduction, whereas non-adherent patients regained on average 33% of the initial reduction (6).

Pneumomassage or Intermittent Pneumatic Compression (IPC) is another modality for controlling lymphedema. In this method, the extremity is inserted into a sleeve that is then inflated by a pump. This exerts pressure on the extremity which shifts edema into the root of the limb and into the adjacent trunk quadrant. It has been documented that pneumomassage transfers the edema from the lymphedematous limb into the lymphedematous trunk quadrants since the adjacent trunk quadrant belongs to the tributary area of the axillary (or inguinal) lymph nodes (7). If high protein fluid accumulates in the trunk quadrant, fibrosclerosis impairs the interaxillary and axillo-inguinal anastomoses. As a consequence, the lymphedematous limb, decongested by pneumomassage, is at risk for re-swelling.

According to the International Society of Lymphology (ISL) consensus in 2009, displacement of edema proximally with subsequent development of a fibrosclerotic ring at the root of the extremity potentially obstructs lymph flow. This should be avoided through careful monitoring of the limb. Combining pneumatic compression with manual lymph drainage has been reported but not sufficiently evaluated (1). Some studies report that limb volume can effectively be reduced with pump therapy (8-10) while others suggest that better limb volume reduction occurs when pneumatic compression therapy is combined with other treatment modalities (11-12). Recent reviews of studies on post- mastectomy lymphedema management methods have reported a need for more clinical trials in this area (13-14). Increased information on the effectiveness of different lymphedema management methods can help many patients and health care providers decrease the morbidity associated with lymphedema. Patient's quality of life can be improved by minimizing cosmetic, functional, psycho-emotional, and potentially life-

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threatening complications. Therefore the aim of this study is to compare the effects of two available modalities for the management of post mastectomy lymphedema: CDT alone and the combination of CDT and IPC.

MATERIAL AND METHODS

Trial Design

In this randomized clinical trial of patients with breast cancer associated lymphedema, treatment with pneumatic compression therapy combined with MCDT was compared to CDT alone. Recruited patients were assigned randomly to one of the treatment arms. A parallel group design was used with block randomization. Block size of four patients was done by a person who was not involved in patients' treatment.

For study purposes, the CDT group alone was the standard or control group, and the combined treatment of MCDT plus IPC was the intervention group.

At the conclusion of the intensive phase (phase I) of treatment, both groups were educated in maintenance phase (phase II) activities of CDT to perform at home. Edema volume in both groups was assessed three months later.

Inclusion and Exclusion Criteria

All patients with postmastectomy lymphedema referred for treatment to Lymphedema Clinic of the Iranian Center for Breast Cancer in 2008 were considered eligible to enter the study. Postmastectomy lymphedema was defined as a ≥10% increase in the volume of affected arm compared to that of the contralateral arm. The minimum interval between the completion of breast carcinoma treatment (surgery, chemotherapy or radiotherapy) and enrollment in the study was three months. Agreement with the informed consent, willingness to be treated in the clinic, and having moderate level of physical stamina for activities of daily living were other criteria for enrollment. Patients with the following problems were excluded from study: active malignancy, breast cancer recurrence, active infection, patients with bilateral disease or bilateral lymphedema, venous insufficiency, low physical activity and unable to perform daily tasks, or female athletes with higher than normal physical activity, history of previous treatment for lymphedema, neuromuscular diseases especially in arms and any absolute contra-indications for CDT.

Treatment Methods

Treatments were implemented in two phases:

Phase I (intensive phase)

In this period, daily treatment was administered 5 days a week for 10-15 sessions in accordance with that recommended by ISL.

CDT Group: Phase I consisted of skin care, 45 minutes of a specific light manual massage (manual lymph drainage; MLD with Vodder technique), remedial exercises, and compression applied by multi-layered short-stretch bandages (Lohmann Rauscher lymphedema bandage set).

MCDT plus IPC Group: In the MCDT plus IPC group, lymph drainage was first stimulated in the trunk by applying 10-15 minutes MLD on the abdomen, chest, and axillary, inguinal and cervical lymph nodes. Following MLD, a four chamber pneumatic sleeve and intermittent pneumatic compression pump set at 40 mm Hg pressure for 30 minutes was used to promote lymph drainage of arm. Lymph drainage of the arm was completed with five minutes of arm MLD. The other three components of CDT (Skin Care, remedial exercises and bandaging) were identical to the CDT group. Because of this difference with standard CDT, we called it Modified CDT or MCDT.

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Phase II (maintenance phase)

This Phase, which was initiated promptly after Phase I, aimed to conserve and optimize the results obtained in Phase I. In the maintenance phase, both groups were educated to apply phase II of CDT methods. These consisted of compression by a low-stretch elastic stocking or sleeve with compression class of three worn during the day and bandaging at night, skin care, continued remedial exercise, and repeated light self massage one or two times daily.

Measurement Tools

Demographic and clinical characteristics were obtained from a questionnaire, through personal interview and from data recorded in the pathology report.

The volume of edema was measured by water displacement method with measurements performed by a blinded investigator not engaged in treatment of patients. The edema volume (defined as the volume difference between affected and unaffected arms) was recorded at the initial session, the final session of phase I, and at the end of three months follow up. The percent of volume reduction (PVR) was calculated as below:

PVR at the end of phase I =

$$\frac{Start\ volume - End\ volume}{Start\ volume} * 100$$

PVR after three months follow up =

$$\frac{End\ volume - 3\ months\ follow\ volume}{End\ volume} * 100$$

Subjective symptoms (pain, heaviness and paresthesia) were recorded on a four point scale questionnaire ranging between 0-3, indicating no symptoms, low, moderate and severe intensities. The score of these symptoms were assessed at three measurement times.

Statistical Analysis

Data were gathered on the 112 patients who completed three months of follow up. Two patients in CDT group and one person in MCDT+IPC group had been excluded from the study because of incomplete follow up and low compliance. Categorical variables were compared using the Chi-square (χ^2) test, and continuous variables were compared by the Student's t test. Mean difference of PVR in two groups was studied by Student's t test. Mann-Whitney test was used to show the symptom variations of two groups. Two-sided p-values <0.05 were taken as evidence of statistical significance. Statistical procedures were performed using the statistical package SPSS 17 for Windows.

RESULTS

Comparison between demographic and clinical characteristics of patients are shown in *Tables 1 and 2*. According to these data, most of the patients in the CDT and MCDT+IPC groups were married (87.5% vs. 83.9%, respectively, p=0.594) and had stage IIB of disease (57.1% vs. 53.6%, p=0.594). The mean age of those in the CDT and MCDT+IPC groups was 53.4 (±11.4) vs. 52.7 (±10.8) years, respectively (p=0.728), and the mean volume of edema in two groups at the beginning of the study was 1326 cm^3 vs. 1167 cm^3, respectively (p=0.239).

Data analysis in *Table 3* displays mean volume reductions of 43.1% (±13.7) in CDT and 37.5% (±14.4) in MCDT+IPC groups at the end of intensive treatment (phase I). This difference was statistically significant (p= 0.036). Compared to the end of phase I, and after three months follow up, additional volume reduction was 16.9% (±32.3) and 7.5% (±39.4) for the groups, respectively (p=0.167).

The intensity of symptoms such as pain, heaviness and paresthesia were also assessed by a repeated measures analysis from three points (start, end of treatment and after three

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TABLE 1
Demographic and Clinical Characteristics of Patients

Variable	CDT No. (%)	MCDT+IPC No. (%)	χ^2	p-Value
Education			0.786	0.853
Illiterate	5 (8.9)	7 (12.5)		
Primary School	20 (35.7)	21 (37.5)		
High school	19 (33.9)	19 (33.9)		
University	12 (21.5)	9 (16.1)		
Marital Status			1.042	0.594
Single	1 (1.8)	3 (5.4)		
Married	49 (87.5)	47 (83.9)		
Widow/divorce	6 (10.7)	6 (10.7)		
Dominant limb = involved limb			0.572	0.449
No25 (44.6)	29 (51.8)			
Yes	31 (55.4)	27 (48.2)		
Stage of Disease			1.854	0.396
I	1 (1.8)	4 (7.1)		
IIA	11 (19.6)	11 (19.6)		
IIB	32 (57.1)	30 (53.6)		
Unknown	12 (21.4)	11 (19.6)		
Breast Surgery			2.036	0.154
MRM	48 (85.7)	42 (75)		
B. preservation	8 (14.3)	14 (25)		
Radiation Therapy			1.924	0.165
No	5 (8.9)	10 (17.9)		
Yes	51 (91.1)	46 (82.1)		
Chemotherapy			4.265	0.039
No	3 (5.4)	10 (17.9)		
Yes	53 (94.60)	46 (82.1)		
Co-morbid disease			3.480	0.062
No	44 (78.6)	35 (62.5)		
Yes	12 (21.4)	21 (37.5)		
History of Trauma/Infection			4	0.261
No	39 (69.6)	39 (69.6)		
Yes	17 (30.4)	17 (30.4)		

months follow up). The score of these symptoms decreased in both methods of treatments during the time of study ($p<0.001$).

Mean of the score difference of those symptoms at the end of the phase I (score at the start of treatment - score at the end of treatment) and after three months of follow up (score at the end of phase I - score at the three months of follow up) was compared between the two groups (*Table 3*). Reduction of heaviness in the CDT group was more than the other group during the phase I of treatment ($p=0.04$), but no significant difference was observed in the score reduction of the other symptoms.

DISCUSSION

CDT is an effective method for controlling

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TABLE 2
Mean Comparison of Demographic and Clinical Variables of Patients

Variable	CDT Mean (±SD)	MCDT + IPC Mean (±SD)	student t	p-value
Age	53.4 (±11.4)	52.7 (±10.8)	0.349	0.728
Number of excised lymph nodes	10.6 (±5.5)	10.7 (±6.2)	-0.099	0.922
Number of involved lymph nodes	3.8 (±4.4)	3 (±3.8)	0.955	0.342
BMI	29.9 (±4.1)	30.9 (±4.3)	-1.270	0.207
Duration of lymphedema (months)	34 (±36.9)	35 (±41.6)	-0.128	0.898
Start volume (cm^3)	1325.7 (±723.7)	1160.7 (±749.8)	1.185	0.239

TABLE 3
Outcome Difference Between Two Groups of Patients

	CDT Mean (±SD)	CDT Range	MCDT+IPC Mean (±SD)	MCDT+IPC Range	Test Statistics	p-value
A. Percent of Volume Reduction					**student t**	
End of treatment	43.1 (±13.7)	8.89 -66.67	37.5 (±14.4)	14.29-72.97	2.122	0.036
3 months follow-up	16.9 (±32.3)	(-87.57)-100	7.5 (±39.4)	(-100)-78.57	1.391	0.167
B. Symptom Score Reduction (end of treatment)					**Mann-Whitney U**	
pain	0.7 (±0.8)	0 - 3	0.5 (±0.7)	(-1) - 2	1433.5	0.389
heaviness	1.2 (±0.9)	(-1) -3	0.8 (±0.8)	(-1) - 2	1268.5	0.063
paresthesia	0.4 (±0.8)	(-1) - 3	0.3 (±0.7)	(-1) - 3	1506.5	0.667
B. Symptom Score Reduction (3 months follow up)					**Mann-Whitney U**	
pain	0.1 (±0.6)	(-1) - 3	0.1 (±0.5)	(-1) - 2	1519	0.690
heaviness	0.3 (±0.6)	(-1) - 3	0.4 (±0.6)	(-1) - 2	1376	0.189
paresthesia	0.2 (±0.5)	(-1) - 2	0.2 (±0.4)	(-1) - 2	1487	0.502

lymphedema, which is used in many countries. Some clinics and therapists have introduced IPC as an adjunctive method of treatment used alone or in conjunction with CDT. In this randomized clinical trial, the efficacy of these two methods of treating lymphedema was compared. There was no statistically difference in demographic and clinical characteristics between the two treatment groups except for those receiving chemotherapy. The results showed that in the first phase of treatment, both methods significantly reduced limb volume in comparison to previous status. Comparison of the two methods revealed that CDT alone can be more effective. Even though no significant difference between the two treatment modalities was noticed during phase II of

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treatment, the effect of CDT was maintained to a greater extent than the other group (16.9% volume reduction vs. 7.9%) after 3 months of follow up.

Some researchers have investigated whether the combination of CDT and pneumomassage is more effective than the use of CDT alone. The results are contradictory. Rockson et al found that pneumomassage increased the effect of CDT in patients with arm lymphedema (15), while Szolnoky did not find such an effect in patients with leg lymphedema (16).

Szuba et al (11), in a randomized trial, studied the effect of decongestive lymphatic therapy (DLT) alone and compared the treatment results obtained by DLT with daily adjunctive IPC. Twelve patients were randomized to DLT plus IPC, and 11 patients were randomized to DLT alone. Following two weeks of treatment, the mean percent reduction in volume of the edematous arm was 45.3% for combination therapy and 26% for DLT alone ($p=0.05$). In another trial (12), manual lymph drainage (one of the CDT components) and sequential pneumatic compression each significantly decreased arm volume (14 cases in each group) but there was no statistically significant difference between the two treatment methods during two weeks of daily treatment. In this present study with a larger population (56 cases in each group), percent of volume reduction was significantly higher in the CDT group compared to MCDT+IPC at the end of treatment in the phase I (43.1±13.7% vs. 37.5 ±14.4%, $p=0.036$).

Szuba et al (11) reported that after the completion of intensive therapy, at Day 40, the mean volume reduction was 30.3% (range, 13% to 83%) for DLT in combination with IPC and 27.1% (range, 23% to 59.5%) for DLT alone. These results were not significantly different compared with the outcomes noted at Day 10. They showed 32.7±115.2 ml volume reduction in DLT alone and 89.5±195.5 ml in DLT and IPC at the end of maintenance phase of treatment (11).

In this study, with a longer follow up time (3 months), percent of volume reduction was higher with CDT alone compared to MCDT+IPC (16.9±32.3% vs. 7.5±39.4%, respectively). Even though this difference was not statistically significant, it is noteworthy that in phase II, volume reduction due to CDT alone was maintained better than MCDT with IPC. A consideration when designing this study was the high cost of the time spent by trained lymphedema therapists performing CDT in phase I, so replacement of some components of CDT with IPC could be cost effective. Furthermore, providing pumps to each patient at home is expensive and not possible. With these considerations in mind a parallel design of CDT with and without IPC in phase I, and CDT alone in both groups in phase II was implemented. Thus the role of IPC in the second phase cannot be evaluated in this study.

In addition to the above mentioned limitations, large standard deviations due to wide ranges of volume reductions similar to that found in other studies was noted (11). Designing studies with larger sample sizes and using IPC in the second phase of treatment may be necessary to provide more accurate evidence regarding the effectiveness of these modalities.

In this study, volume reduction in phase II was measured independently of phase I. This could indicate the role of patients in the maintenance phase and may reflect somewhat the effect of education in first phase.

Reduced quality of life (QOL) and restriction in activities of daily living is another issue of importance to patients undergoing surgical treatment for breast cancer. Significant changes from before to two years after surgery for breast cancer were found in almost all assessments of shoulder function, activities of daily living and several quality of life subscales by Rietman et al (17). Improving QOL along with reduction of volume are primary goals in dealing with lymphedema. It has been shown that both quality of life and pain are

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improved by CDT and continue to improve after the treatment has ended (6,18). A comparison of symptom scores of pain, heaviness, and paresthesia from before to after treatment by a repeated measures analysis, showed decreased symptoms from both treatment methods ($p<0.001$).

Reduction of heaviness was more apparent by CDT alone than the MCDT+IPC during the phase 1 of treatment ($p = 0.04$), but other symptom relief did not show significant difference between the two groups.

In conclusion, this study suggests that the use of CDT either alone or in combination with IPC, significantly reduces edema volume effectively in patients with postmastectomy lymphedema. CDT alone provided better results in both treatment phases of I and II. With this information, combined efforts of health professionals and medical equipment companies are recommended to increase the number of CDT trained personnel, educate patients in the techniques of CDT, and to utilize IPC in conjunction with CDT. These efforts should provide patients with better treatment results and improved quality of life.

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