

INTERMITTENT PNEUMATIC COMPRESSION ACTS SYNERGISTICALLY WITH MANUAL LYMPHATIC DRAINAGE IN COMPLEX DECONGESTIVE PHYSIOTHERAPY FOR BREAST CANCER TREATMENT-RELATED LYMPHEDEMA

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ABSTRACT

The application of intermittent pneumatic compression (IPC) as a part of complex decongestive physiotherapy (CDP) remains controversial. The aim of this study was to investigate whether the combination of IPC with manual lymph drainage (MLD) could improve CDP treatment outcomes in women with secondary lymphedema after breast cancer treatment. A randomized study was undertaken with 13 subjects receiving MLD (60 min) and 14 receiving MLD (30 min) plus IPC (30 min) followed by standardized components of CDP including multilayered compression bandaging, physical exercise, and skin care 10 times in a 2-week-period. Efficacy of treatment was evaluated by limb volume reduction and a subjective symptom questionnaire at end of the treatment, and one and two months after beginning treatment. The two groups had similar demographic and clinical characteristics. Mean reductions in limb volumes for each group at the end of therapy, and at one and two months were 7.93% and 3.06%, 9.02% and 2.9%, and 9.62% and 3.6%, respectively ($p < 0.05$ from baseline for each group and also between groups at each measurement). Although a significant decrease in the subjective symptom survey was found for both groups compared to baseline,

no significant difference between the groups was found at any time point. The application of IPC with MLD provides a synergistic enhancement of the effect of CDP in arm volume reduction.

Keywords: pneumatic pump, breast cancer, lymphadenectomy, lymphedema, physiotherapy

One of the complications of breast cancer surgery and postoperative irradiation is lymphedema of the ipsilateral arm. Lymphedema is caused by an impaired lymph drainage and can result in deformity of the limb, decreased functional ability, diminished joint movements, physical discomfort, recurrent episodes of microbial infections and psychological distress. Lymphedema may be acute, forming shortly after the surgical intervention, and in most cases is transient, or it may be chronic and more resistant to therapy. The incidence of lymphedema secondary to breast cancer treatment ranges between 5% and 80% (1) depending on extent of axillary surgery, use of radiotherapy, increase in body mass index (2), and previous alterations in lymph flow. Sentinel lymphadenectomy for breast cancer patients has lowered the risk of lymphedema but the number of new lymphedema cases is

still significant, and earlier cases need continuous follow-up and treatment (3,4). Lymphedema has three stages: the first is characterized by the reversible protein rich-edema; the second is designated as the spontaneously irreversible protein rich-edema, often associated with fibrosclerotic alterations due to the protein-induced chronic inflammation, secondary fibroblast proliferation, and the inflammatory cytokine network; and the third is elephantiasis, where the most severe form of lymphedema is accompanied by massive hyperkeratosis, diffuse fibrosclerosis and a marked increase in limb volume. Persistent lymphedema can have multiple consequences and must be treated as early as possible. CDP is a widely used treatment and has proved effective in reducing lymphedema and in improving the related subjective complaints (5). CDP involves a combination of intensive treatment with special MLD, compression with multi-layered short-stretch bandages, physical exercise to enhance the lymph flow, and meticulous skin care. The intensive phase of the treatment is followed by the maintenance phase with addition of daily use of standard or individually sized compression garments.

The use of pneumatic devices is somewhat controversial and no real consensus has been achieved concerning proper application. In the early use pneumatic devices, several therapeutic protocols have been introduced, and inappropriate treatment was linked with certain side effects (6). Some studies have corroborated the usefulness of these devices, while another randomized study has discounted their effectiveness. A few schools of lymphedema therapy support their utilization as part of a combined treatment regimen (7,8), whereas others oppose their use (6,9). The 1997 American Cancer Society Workshop on Breast Cancer Treatment-Related Lymphedema declared that future research was necessary to determine the relative efficacy of each of the components of the CDP treatment protocol (10). The latest ISL consensus includes IPC as a treatment

option and suggests that studies combining these devices with MLD are needed (11). The aim of the present study was to investigate whether the combination of pneumatic pump with MLD compared to MLD alone in standard CDP treatment can improve outcomes in women with stage 2 lymphedema after treatment for breast cancer. A secondary aim was to examine whether the use of pneumatic pumps in our hands was safe and harmless for the subjects.

MATERIALS AND METHODS

Subjects

This study included 27 women who had developed unilateral arm lymphedema after treatment for early breast cancer. Subjects were first seen at the lymphedema outpatient care unit of the Department of Dermatology and Allergology. Prior to enrollment, subjects underwent physical examination, laboratory tests including tumor markers, mammography, chest X-ray, and ultrasonography of the axillary, breast and abdominal regions to rule out malignant lymphedema and existing metastasis. Inclusion was limited to subjects more than 12 months after surgery or adjuvant treatment in order to have a reliable follow-up period to detect any possible metastasis. Exclusion criteria included subjects with any sign of local recurrence or distant metastases or if they were within the obligatory treatment-free period of one year. The study was carried out in accordance with the Helsinki II Declaration and was approved by the Institutional Review Board of the University of Szeged, Hungary, and each patient gave informed consent before inclusion.

Treatments

Subjects were randomly enrolled into either 60 min MLD (n=13) or 30 min MLD+30 min groups. No subjects withdrew or were withdrawn from the study. Median

TABLE 1
Characteristics of Study Subjects

	CDP	CDP+IPC	P value
Number of subjects	13	14	ns
Mean age (years)	54.83	56.6	ns
Left/right involved arm	5/8	7/7	ns
Chemotherapy	12	12	ns
Irradiation	8	10	ns
Mean duration of lymphedema (months)	16.3	11.8	ns

lymphedema volumes at baseline were 380 ml (range: 120-1780 ml) and 367 ml (range: 50-1560 ml) respectively, and subject characteristics were not significantly different between the groups (*Table 1*). Even though duration is not significant, this has not been shown to impact the efficacy of lymph drainage (1,12). No correction was made for asymmetry in these patients, as there was no significant difference between groups regarding operation on the right or left side or the dominant or non-dominant arm.

In both treatment groups, each subject underwent a once daily 2-week cycle (10 consecutive working-days) of treatment. Normally, CDP consists of 60 minutes of MLD by Vodder's method, performed by a specially trained physiotherapist followed by skin care with moisturizers, multilayered short-stretch bandaging with appropriate padding, and exercise under compression (13). The MLD extends to the neck, breast, and abdomen with application of light pressure (30-40 mmHg) and moving only the skin. Subjects in the MLD+IPC group received MLD for 30 minutes followed by IPC for 30 minutes with a Lympha Mat device (Bösl Medizintechnik, Aachen, Germany) at our standardize maximum pressure of 50 mmHg. The Lympha Mat is a multi-chamber device with 12 overlapping cells and sequential inflation progressively from distal to proximal.

Assessment

Subject assessment was completed at baseline, beginning of therapy, end of therapy, and 1 and 2 months after the start of the therapy. Limb volume measurements were made according to the disk model of Kuhnke (13) using tape measurements of circumferences at every 4 centimeters. The percentage reduction in total arm volume at each point was calculated via the formula: $\Delta V\% = [(pre-treatment\ arm\ volume - post-treatment\ arm\ volume) / pre-treatment\ arm\ volume] \times 100$. A subjective symptom questionnaire measuring function, heaviness, tension, and pain and their effects on related activities, was scored by each subject (*Table 2*). The questionnaire was designed in our department and includes 14 lymphedema-related questions with scores ranging from 1 to 5 (most severe= 5). Percentage improvement in the subjective complaints was calculated as follows: $\Delta S\% = [(total\ sum\ of\ pre-treatment\ scores - total\ sum\ of\ post-treatment\ scores) / total\ sum\ of\ pre-treatment\ scores] \times 100$.

Statistical Analysis

Statistical analyses were performed with the Student t-tests for paired samples and differences were accepted as significant when $p < 0.05$.

TABLE 2
Questionnaire for Lymphedema-Related Subjective Symptoms

	No (1)	Mildly (2)	Moderately (3)	Severely (4)	Extremely (5)
Do you feel strong pain in your arm?					
Does this pain affect your work?					
Does the pain cause sleeplessness?					
Is your life affected by sleeplessness?					
Is it exhausting to keep your arm in the same position?					
Do you find exhausting the housework?					
Do you find it disturbing and exhausting to participate in social programs?					
Do you find it disturbing and exhausting to do active physical exercise or sports?					
Are you nervous because of lymphedema?					
Do you easily become easily irritated?					
Do you feel that you impose on people or your family?					
Are you disturbed if your arm is visible?					
Do you have to put your arm in comfortable position?					
Do you feel disabled?					

RESULTS

Measurement of limb volume reduction is a common approach to quantify the extent of lymphedema and evaluate the therapeutic success. In the MLD group at the end of therapy, and 1 and 2 months after the start of the therapy, 3.06%, 2.9%, and 3.6% mean volume reductions were achieved. All volume reductions were significant compared to baseline ($p < 0.05$). In the MLD+IPC group, mean percentage reductions were 7.93%, 9.02% and 9.6%, respectively (all $p < 0.05$ compared to baseline). A significant difference was found between the groups at each time point ($p < 0.05$; *Fig. 1*).

At each visit, scores from the subjective questionnaire were summed and compared to

baseline (*Fig. 2*). All patients completed the questionnaire at all time points and analysis demonstrated a significant reduction in symptoms for each group at each point. There was a trend for improvement in both groups over time, but this did not prove to be significant. There were no significant differences between the groups at any time point.

DISCUSSION

Literature reports state that between 5% and 80% of patients who undergo treatment for breast cancer develop lymphedema, depending to some extent upon whether or not they receive radiation therapy. The introduction of sentinel lymphadenectomy has greatly reduced the overall number of

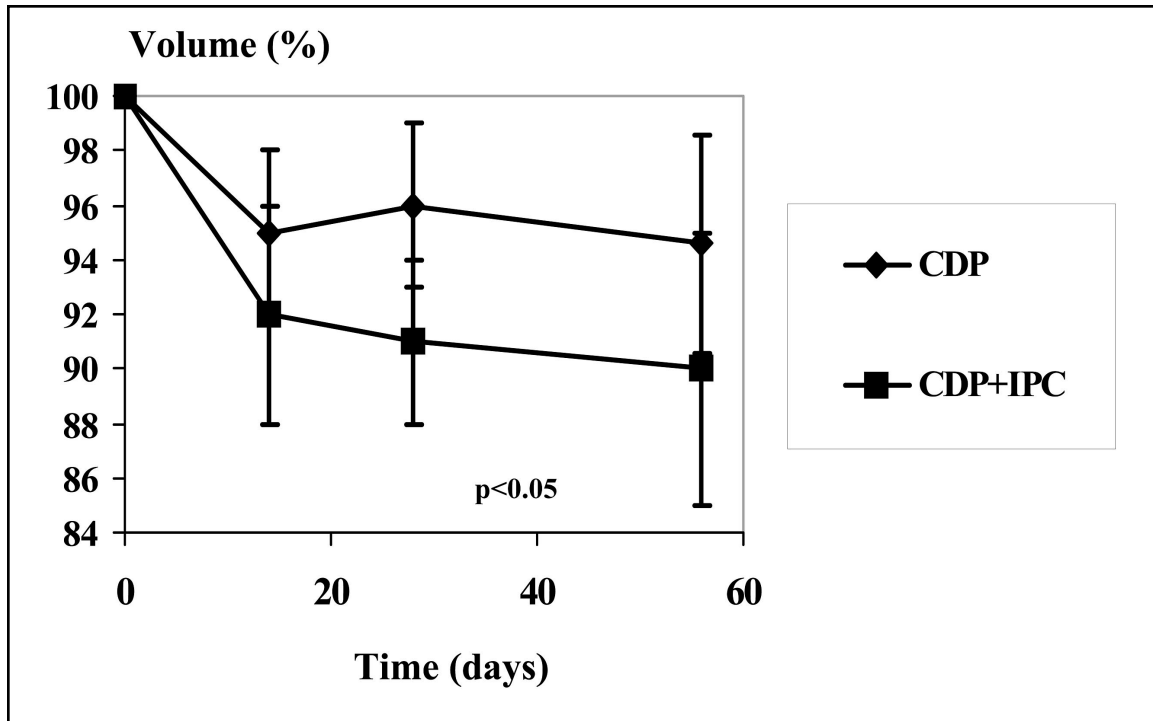


Fig. 1. Alterations in limb volumes of involved arms following the 2-week treatment and at 1 and 2 months after the start of therapy. Both MLD and MLD+IPC CDP treatment groups significantly reduced arm volumes ($p < 0.05$). The MLD+IPC group was significantly better than the MLD group at each time point after therapy onset ($p < 0.05$). MLD=manual lymphatic drainage, IPC=intermittent pneumatic compression, CDP=decongestive lymphatic therapy.

new lymphedema cases although breast carcinoma is gradually increasing in frequency (3,4). Lymphedema can be a serious and disabling complication and can cause significant psychologic distress associated with the status of cancer and appropriate treatment (14). Although there is no cure for lymphedema, conventional management with CDP is currently a popular, widespread, and successful approach to reduce swelling and alleviate symptoms (15). A crucial part of CDP is MLD. MLD is a technique of gentle massage, which stimulates lymphangiomotoric activity. It is thought to open and dilate uninvolved lymphatic anastomoses and to direct lymph away from edematous areas and therefore reduces volume of the limb by diminishing persistent lymph fluid and fibrosis. Short-stretch compression bandages have a double

effect. They can exert a low resting pressure and a significant high working pressure during physical exercise when the muscle pump is active. The intensity of application of the individual components of CDP depends on the initial severity of lymphedema.

Richmand et al safely used IPC pumps for upper limb lymphedema at relatively high pressure (80-110 mm Hg) for prolonged periods (6-8 hours) (16). Despite these conditions, no signs of tissue destruction were detected. A similar procedure was applied by Pappas et al for 4-8 hours with positive long-term responses reported (17). Yamazaki et al utilized a different protocol in which IPC was performed every second day for a year (18). They used a maximum pressure of 80 mmHg and achieved a significant edema reduction in 57% of the cases. Zanolla et al treated 60 postmastectomy patients with lymphedema

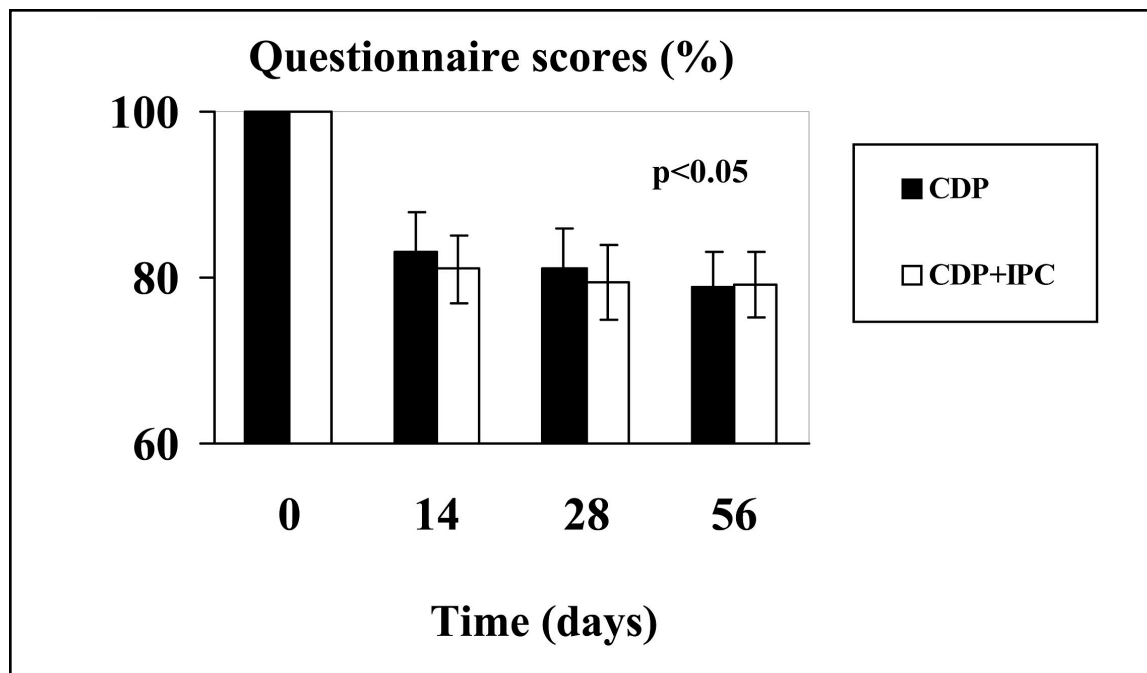


Fig. 2. Changes in sums of scores for lymphedema-related subjective symptom questionnaire after therapy. Both therapeutical modalities significantly alleviated the symptoms ($p < 0.05$), but no significant difference was found between the groups at any time point.

using IPC and pressures up to 90 mm Hg for 6 hours for 7 days (19), and they reported a noteworthy edema reduction. In none of the previous studies was the use of pneumatic pumps accompanied by MLD. Numerous side-effects are attributed to use of pumps (6) including: pumps do not evacuate fluid from the ipsilateral body quadrant; in lower extremity lymphedema, pumps can cause swelling of the external genitalia; and pumps may traumatize the superficial lymphatics. Some patients who use pneumatic pumps claim that the lymphedema worsens as time passes and therefore they stop using them. However, neither extensive clinical experience nor our own observation support these claims. Leduc et al and Miller always apply pneumatic pumps as an adjuvant treatment to MLD (7,8). Our belief is that pumps must be used at relatively low pressure to avoid collapse of the superficial lymphatics (20) and as part of a comprehensive program including

MLD, bandaging, exercise and skin care. The report of Szuba and his co-workers greatly supported the use of pneumatic pumps as an adjunctive treatment in breast-cancer-related lymphedema, achieving significant improvement in arm edema reduction compared to contralateral healthy upper extremities (21). Our work is in a good accordance with those findings and further recommends the application of IPC in secondary arm lymphedema.

In summary, MLD alone or in conjunction with IPC as part of a CDP protocol resulted in notable reductions in arm lymphedema and subjective complaints. Treatment with pneumatic pumps added a significant synergistic effect to the already significant volume decrease. During application and in the post-treatment follow-up, side effects such as swelling in the ipsilateral body quadrant or pain were not observed. The same results were not attained in lower limb lymphedema, irrespectively of whether the

lymphedema was primary or secondary (unpublished data). As far as we are aware, only one similar study has been previously reported in the literature concerning the efficacy of IPC as an adjunctive therapy to MLD in CDP treatment, and this area deserves further investigation.

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REFERENCES

1. Ramos, SM, LS O'Donnell, G Knight: Edema volume, not timing, is the key to success in lymphedema treatment. *Am. J. Surg.* 178 (1999), 311-315.
2. Werner, RS, A McCormick, JA Petrek, et al: Arm edema in conservatively managed breast cancer: obesity is a major factor. *Ther. Radiol.* 180 (1991), 177-184.
3. Sener, SF, DJ Winchester, CH Martz, et al. Lymphedema after sentinel lymphadenectomy for breast carcinoma. *Cancer* 192 (2001), 748-752.
4. McLaughlin, SA, MJ Wright, KT Morris, et al: Prevalence of lymphedema in women with breast cancer 5 years after sentinel lymph node biopsy or axillary dissection: Objective measurements. *J. Clin. Oncol.* 26 (2008), 5213-5219.
5. Cohen, SR, DK Payne, RS Tunkel: Lymphedema: Strategies for management. *Cancer* 192 (2001), 980-987.
6. Lerner, R: Complete decongestive physiotherapy and the Lerner lymphedema services academy of lymphatic studies (the Lerner School). *Cancer* 83 (1998) (12 Suppl American), 2861-2863.
7. Leduc, O, A Leduc, P Bourgeois, et al: The physical treatment of upper limb lymphedema. *Cancer* 83 (1998) (12 Suppl American), 2835-2839.
8. Brennan, MJ, LT Miller: Overview of treatment options and review of the current role and use of compression garments, intermittent pumps, and exercise in the management of lymphedema. *Cancer* 83 (1998) (12 Suppl American), 2821-2827.
9. Kasseroller, RG: The Vodder School: The Vodder Method. *Cancer* 83 (1998) (12 Suppl American), 2840-2842.
10. Rockson, SG, LT Miller, R Senie, et al: Workgroup III: Diagnosis and management of lymphedema. *Cancer* 83 (1998) (12 Suppl American), 2882-2885.
11. The Diagnosis and Treatment of Peripheral Lymphedema. 2009 Consensus Document of the International Society of Lymphology. *Lymphology* 42 (2009), 51-60.
12. Rockson, SG: Precipitating factors in lymphedema: Myths and realities. *Cancer* 83 (1998), 2814-2816.
13. Földi, M, S Kubik (Eds): *Textbook of Lymphology*. Urban and Fischer Publisher, 2005.
14. Avrahami, R, E Gabbay, B Bsharah, et al: A severe lymphedema of the arm as a potential cause of shoulder trauma. *Lymphology* 37 (2004), 202-205.
15. Moseley, AL, CJ Carati, NB Piller: A systematic review of common conservative therapies for arm lymphoedema secondary to breast cancer treatment. *Ann. Oncol.* 18 (2007), 639-646.
16. Richmand, DM, TF O'Donnell, A Zelikovski: Sequential pneumatic compression for lymphedema. *Arch. Surg.* 120 (1985), 1116-1119.
17. Pappas, CJ, TF O'Donnell, Jr: Long-term results of compression treatment for lymphedema. *J. Vasc. Surg.* 16 (1992), 555-562.
18. Yamazaki, Z, Y Idezuki, T Nemoto, et al: Clinical experiences using pneumatic massage therapy for edematous limbs over the last 10 years. *Angiology* 39 (1988), 154-163.
19. Zanolli, R, C Monzeglio, A Balzarini, et al: Evaluation of the results of three different methods of postmastectomy lymphedema treatment. *J. Surg. Oncol.* 26 (1984), 210-213.
20. Eliska, O, M Eliskova: Are peripheral lymphatics damaged by high pressure manual massage? *Lymphology* 2 (1995), 21-30.
21. Szuba, A, R Achalu, SG Rockson: Decongestive lymphatic therapy for patients with breast carcinoma-associated lymphedema. A randomized, prospective study of a role for adjunctive intermittent pneumatic compression. *Cancer* 95 (2002), 2260-2267.

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