Effects of Complete Decongestive Therapy on Primary and Secondary Lymphedema of Lower Extremity

Komplet Dekonjestif Tedavinin Primer ve Sekonder Alt Ekstremite Lenfödemi Üzerine Etkisi

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ABSTRACT Objective: To investigate the outcome of complete decongestive therapy (CDT) on primary and secondary lymphedema of the lower limb (LL). **Material and Methods:** Included 40 patients with LL lymphedema were retrospectively analyzed. Age, gender, diagnosis, extremity volume, subtype of lymphedema, radiotherapy chemotherapy history of all the patients were noted. The amount of limb edema was calculated with volumetric measurements before and after the treatment for each patient. Bilateral circumferential measurements were carried out at the level of metatarsophalangeal joints, mid-dorsum of the feet, ankle and every 10 cm till the inguinal level. Afterwards, a computer program was used to convert these values into limb volumes in milliliters. **Results:** It is found out that CDT causes a significant improvement in the average volume of the LL p=0.01). Nonetheless, the statistics showed significance (p= 0.008) only in secondary group. Moreover, there were no significant difference in percentage changes betwen both groups showed no significance after treatment (p>0.05). We also determined that initial volumes were significantly correlated with volume reduction rates (r= 0.670, p= 0.000). **Conclusion:** CDT is an effective, safe and well tolerated treatment for lymphedema of lower extremity limb. There was significant improvement in clinical outcomes particularly in secondary lymphedema group; whereas, percentage change in limb volumes of both groups showed no significance. Hence, our results suggest that the volume reductive effects of CDT is not correlated with the lymphedema (ethiology). Future studies comprising greater population with various ethiology are needed.

Key Words: Complex decongestive therapy; lower extremity; lymphedema; rehabilitation

ÖZET Amaç: Primer ve sekonder alt ekstremite lenfödeminde kompleks dekonjestif tedavinin (KDT) etkinliğini araştırmak. **Gereç ve Yöntemler:** Çalışmaya dahil edilen 40 alt ekstremite lenfödemi tanılı hastanın verileri retrospektif olarak analiz edildi. Hastaların yaş, cinsiyet, tanı, ektremite volümü, lenfödem subtipleri ve kemoterapi/radyoterapi öyküleri kayıt edildi. Bacaklardaki ödem tedavi öncesi ve tedavi sonrasında volümetrik ölçümler ile hesaplandı. Ayak sırtından başlayarak 10'ar cm aralıklarla inguinal seviyeye kadar bilateral olarak çevresel ölçümler yapıldı. Ardından bilgisayar programı ile bu ölçümler volümetrik değerlere çevrildi. **Bulgular:** KDT'nin alt ekstremite lenfödem tedavisinde anlamlı gelişmeler sağladığı görüldü (p=0,01). Ancak istatiksel anlamlılığa yalnızca sekonder lenfödem grubunda ulaşıldı (p=0,008). Bununla birlikte yüzde değişim oranlarına bakıldığında iki grup arasında anlamlı farkın olmadığı saptandı (p>0,05). Tedavi öncesindeki volümlerin, volüm azalma oranları ile anlamlı oranda korele olduğu da (r=0,670, p=0,000) saptandı. **Sonuç:** KDT, alt ekstremite lenfödem tedavisinde etkili, güvenilir ve iyi tolere edilebilen bir tedavidir. Ancak her nekadar istatiksel anlamlılığa sekonder lenfödem grubunda ulaşılmış olsa da yüzde değişim oranlarına bakıldığında gruplar arasında anlamlı farklılığın olmadığı görülmüştür. Bu nedenle KDT'nin volüm azaltıcı etkisinin lenfödem etyolojisi ile korele olduğunu söyleyememekteyiz. Değişik etyolojilere sahip bireylerle yapılacak daha çok sayıda hastayı içeren prospektif çalışmalara ihtiyaç olduğunu düşünmekteyiz.

Anahtar Kelimeler: Kompleks dekonjestif tedavi; alt ekstremite; lenfödem; rehabilitasyon

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Lymphedema (LE) has been defined as an abnormal accumulation of capillary filtrate with proteins, cytokines and chemokines, recirculating lymphocytes, products of parenchymatous cells, and debris of senescent cells.[1] Deterioration of lymphatic drainage can be classified as either primary or secondary. Primary lymphedema results from abnormal formation of lymphatic vessels before birth; thus, it has been shown to be an inherited disorder.[2] Besides, secondary lymphedema may occur as a result of obstruction or interruption of the lymphatic system due to surgery, radiotherapy, trauma, infection, malignancy or chronic venous insufficiency.[3]

LE is associated with feeling of discomfort or heaviness, functional limitation (especially difficulty with walking for lower extremity lymphedema (LEL), disfigurement, psychological distress, depression, decreased quality of life and self-esteem, and elevated risk of recurrent infection;[4-6] therefore, regardless of the stage or severity of the disease, treatment protocol should be commenced immediately after diagnosis.

Various treatment protocols targeting the management of the excessive edema through the limb, relief of the symptoms or minimizing the risk of complications have been developed for LE; however, efficiency or success of these treatment strategies have been a matter of debate.[7] Treatment alternatives may comprise drug therapy, surgical intervention or physical therapy.

Complete decongestive therapy (CDT), the most widely used physical therapy method for LE, incorporates skin care, manual lymphatic drainage (MLD), compression therapy, and exercise.[8] This method is applied in two consecutive phases: intensive phase and maintenance phase. Intensive phase primarily aims an initial reduction in extremity volume, and it includes skin care. This phase comprises application of a compression bandage after 30-45 minute-MLD treatment and exercise. After reducing the excess limb volume as far as possible, maintenance phase therapy should be carried out. Maintenance phase therapy includes use of compression garments, "remedial exercises" and application of additional MLD treatment, if needed.

A review of the literature regarding the efficacy of physical therapy in the management of lymphedema involving lower limbs demonstrated us a narrow knowledge and previous published studies were limited to some case reports concerning lymphedema emerging subsequent to treatment of gynecologic malignancies.[9-11] In this context, we designed this study to investigate the efficacy of CDT in patients with primary or secondary lymphedema of lower extremity.

MATERIAL AND METHODS

PATIENTS

Participants were recruited from the outpatient clinic of Physical Medicine and Rehabilitation Department. All 48 participants who were included in this study were aged between 13 and 78 and had either primary or secondary lymphedema of lower limb(s). These patients had undergone complete medical evaluations in level one or two centers, and other causes of extremity swelling, particularly tumor recurrence or metastases that may be presented with secondary lymphedema had been ruled out. Then, patients were referred to our third level of care-outpatient hospital service. Through a comprehensive retrospective scanning of the medical files, previous data comprising age, gender, diagnosis, period of radiotherapy (RT) or chemotherapy (CT) (if present) and type of lymphedema of patients were noted and analyzed. Exclusion criteria for this study were; acute inflammation, history of recurrent infections, ulceration(s) in ipsilateral extremity, significant congestive heart failure, and acute deep vein thrombosis. Medical files of 48 patients, who were included in the rehabilitation program at the lymphedema unit, were reviewed. Since eight patients were excluded from the study for inconsistent or lack of information in their files, forty patients (forty-nine legs) were eligible for analysis. All participants read and filled the written informed consent form and were willing to participate in the physical therapy program.

EVALUATION OF THE EDEMA

The amount of edema involving the limbs was calculated with volumetric measurement before and after the treatment protocol. Bilateral circumferential measurements were carried out at the level of metatarsophalangeal joints, mid-dorsum of the feet, ankle and every 10 cm till the inguinal level. Then a computer program (Limb Volumes Professional version 5.0) was used to convert these values into limb volumes in milliliters.

TREATMENT PROTOCOL

CDT was applied for a total number of twenty sessions (5 days/ week for 4 weeks), and each session lasted for nearly one hour. This program was comprised of patient education, manual lymphatic drainage (MLD) (self), compression therapy with a short-stretch bandage for 23 h per day, exercise, and skin care. After 4 weeks of initial therapy, Phase 2 therapy was commenced. At this point patients were told to use compression garments, do regular exercise, self-apply regular MLD and skin care to guarantee a sustainable reduction of limb volume. Patients were advised to lose weight; moreover, requested to read some detailed brochures that contain useful information about the treatment protocol, prevention techniques for lymphedema and details about the exercise program.

The local ethics committee of our University approved this study, and the authors obtained informed consent from all the patients that participated (Decision number: 16-5/8).

STATISTICAL ANALYSIS

All analyses were performed using SPSS Version 20.0 for Windows (SPSS Inc., Chicago, IL, USA). Continuous variables were described using means, standard deviations; categorical variables were described with proportions. Comparisons of pre- versus post-intervention values for continuous variables were made using paired, two-sided Student's T-tests. The categorical variables were analyzed by independent T-test and one-way ANOVA. Pearson correlation analyses were conducted to determine associations between the reduction in volume and age, chemotherapy and radiation therapy. A *p*-value of less than 0.05 was considered significant.

RESULTS

Forty-nine limbs of forty individuals were evaluated. The demographic and clinic data are shown in Table 1. Of all the patients, 33 were female (82.5%) and 7 were male (17.5%). Mean age of the participants was calculated as 52.47 ± 17.40, and 31 patients (77.5%) were diagnosed secondary lymphedema mostly caused by treatment for gynecologic malignancies (18 patients had urogenital cancer, 5 patients had venous insufficiency, 3 patients had malignant melanoma, 2 patients had filariasis, 1 patient had renal transplantation, 1 patient had neurofibromatosis, and 1 patient had inguinal hernia operation).

To mention about the efficacy of the treatment, we determined a statistically significant reduction in the volume of the involved limbs afterwards. Nonetheless, the statistics showed significance (p= 0.008) only in secondary LEL group (Table 2). An average reduction of limb volume in patients with primary lymphedema was found 6.1 %; however, the difference was not statistically significant (p=0.079). Rate of percentage change (posttreatment volume- pretreatment volume/pretreatment volume) in limb volumes of both groups showed no significance after treatment (p>0.05) (Table 3).

TABLE 1: Baseline characteristics of patient's.

	N	%	Mean	SD
Age (years)	40		52.47	17.40
Gender				
Female	33	82.5		
Male	7	17.5		
Etiology				
Primary	9	22.5		
Secondary	31	77.5		
Cancer treatment				
Chemotherapy	11	27.5		
Chemotherapy cure			2.32	5.10
Radiation therapy	13	32.5		
Radiation therapy session			9.02	13.43

SD: Standart deviation

TABLE 2: Therapeutic results during the treatment phase.

	Affected extremity volume before therapy (mean ± SD) (ml)	Affected extremity volume after therapy (mean ± SD) (ml)	p^b
Primary	9298.70 ± 2567.26	8727.40 ± 2200.96	0.079
Secondary	11276.72 ± 4547.14	10214.84 ± 3427.13	0.008*
p^a	0.195	-	

SD: Standart deviation, p^a Comparisons between groups before treatment, p^b Comparisons within groups regarding pre and post treatment results * <0.05.

TABLE 3: Comparisons between groups according to Δ value.

	Primary LE	Secondary LE	p
Δ (mean ± SD) (ml)	0.069 ± 0.067	0.094 ± 0.109	0.501

Δ: Delta value (posttreatment volume- pretreatment volume/pretreatment volume), LE: Lymphedema, SD: Standart deviation.

As opposed to patients with RT or CT, reduction of limb volume in patients without RT (p=0.01) or CT (p=0.004) was found statistically significant.

When we evaluated the correlations, we determined that initial volumes were significantly correlated with volume reduction rates (r= 0.670, p= 0.000); however, there was no correlation with age (r= 0.095, p= 0.559). No adverse effects were noted regarding our therapy, and no additional drugs were used for lymphedema during our study.

DISCUSSION

The results suggest that CDT can achieve an efficient reduction of limb volume in patients with either primary or secondary LEL; nonetheless, the statistics showed significance only in secondary LEL group. However rate of percentage change in limb volumes of both groups showed no significance after treatment (p>0.05).

LE is considered to be an incurable but treatable condition by the most, and its treatment strategy mainly involves reducing the limb volume as well as relief of the symptoms and minimizing the risk of complications.[12-14] Early treatment is beneficial since it efficiently reduces loss of functionality.

Previous reports have suggested that clinicians usually have inadequate knowledge and lack of interest in the evidence-based management of lymphedema, particularly when it is secondary to non-breast malignancies.[15-18] However, it has been shown that treatment of LEL is much more complicated than upper limb lymphedema, and LEL can have pretty strong negative impact on quality of life.[19]

Although CDT is generally announced to be the gold standard treatment method for LE, vast majority of previous studies were performed on patients with upper limb lymphedema that is secondary to breast cancer. A very limited number of retro and prospective studies have investigated efficacy of CDT in LEL which, in deed, mostly occurs subsequent to gynecological malignancies.[9-11] These few studies have reported the benefits of CDT in LEL, with a reduction of excess volume between 31% and 73.4%, varying on different stages of lymphedema and the number of CDT sessions.[9,20,21] Additionally, same researchers report that CDT helps to restore functionality such as independent ambulation or sitting or rising from a chair and improves quality of life, as well.

A prospective cohort study, conducted in 2008, evaluated the outcomes of CDT in 57 patients with gynecologic cancer. The results suggested the mean difference between the affected and the contralateral limb volume was decreased from 56% to a baseline value of 32% after one month ($P < .05$). Besides, significant improvements were reported in quality of life evaluated by Short Form-36, physical function, social function and mental health ($P = .043$, $P = .013$, and $P = .005$, respectively).[9]

Ko et al. conducted a prospective study in 1998 and evaluated the success of CDT in 150 patients with LEL.[22] They found that limb volume was reduced by an average of 68% after the treatment phase ($P < .05$), and these reductions were maintained during the maintenance phase (at six and twelve months; $P < .05$). A retrospective cohort study by Liao et al (11) also reported similar results suggesting that intensive CDT program is effective and successful in patients with LEL that is emerged

after treatment of pelvic malignancies. Forty-four women with LEL were included in the study, and CDT was performed consecutively for 4 to 21 days to achieve reduction of limb volume within a range of 68.1% ± 35.9%. Another clinical trial evaluating the outcomes of CDT in 56 patients with one affected arm and 38 patients with one affected leg reports a volume reduction of 62.6% and 68.6% respectively.[23]

Our results also demonstrate significant correlation between baseline volume and absolute volume change. To clarify, higher baseline volumes were associated with better outcomes. A previous study has also reported that the most important predictor of the volume reducing effect of CDT is the amount of initial swelling at the time of presentation.[12] This point of view is also supported Liao et al. who have reported results that suggest initial percent excess volume (PEV) ($p<0.001$) is a predictive factor for CDT efficacy.[11]

It is unclear whether the etiology of lymphedema have any implications on the response to treatment. In contrast to our study, a recent study evaluating the efficacy of CDT in patients with primary and secondary LEL reported that all groups had close amount of reduction in percentage of excess limb volume (PCEV) and CDT effectively promoted reduction of lymphedema volume.[12] There was significant improvement in clinical outcomes particularly in secondary LE group; whereas, percentage change in limb volumes of both groups showed no significance ($p>0.05$). There were only nine patients in primary LE group; therefore, this result can be attributed to insufficient number of patients that can have negative impact on proper statistical analyses. We infer that, the volume reductive effects of CDT can not be correlated with the cause of lymphedema (primary or secondary).

This study has significant limitations. First of all, this study was a single-center, retrospective study; therefore, readers should bear in mind that our results are not decisive and it is not possible to reach a definite conclusion. Moreover, we were not able to evaluate the influence of therapy on quality of life since the study was designed as retrospective. Other limitations are short follow-up period and lack of comparison with other treatment methods for LEL.

Despite these limitations, our study has unveiled the affect of CDT on patients with primary and secondary LEL. There have been limited number of studies focused on the outcomes of treatment in both subgroups of LEL (primary and secondary). We believe that future studies should therefore be focused on all the subgroups of LEL since more information on this subject will help us to establish a greater degree of accuracy on the treatment of LEL.

CONCLUSION

CDT is an effective, safe and well tolerated treatment for LEL. There was significant improvement in clinical outcomes particularly in secondary LE group; whereas, percentage change in limb volumes of both groups showed no significance ($p>0.05$). Therefore, the volume reductive effects of CDT can not be correlated with the cause of lymphedema (primary or secondary). Nevertheless, we think that prospective, randomized controlled trial studies comprising larger samples with different etiologies of LE are needed to propose more effective and successful treatment protocol.

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