

The effects of lymphatic massage on serum lipid levels and venous flow in patients with lymphedema

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Abstract. Interstitial fluid proteins play an important role in cholesterol homeostasis. Accumulation of protein rich fluid in interstitial tissue leads to lymphedema. Current study aimed to evaluate the effects of manuel lymphatic drainage (MLD) on the serum cholesterol and trigliserid levels and venous flow changes.

Our study included thirty patients with lower limb lymphedema. MLD treatment was performed after measurements of pretreatment serum cholesterol and triglyceride levels of the patients. Four to ten days after MLD treatment serum cholesterol and triglyceride levels were measured again. The caliber of femoral vein and mean flow velocity changes were also examined by venous Doppler ultrasonography. The statistical comparisons were done by using paired sample t-test. $P < 0.05$ values were accepted as significant.

There were six male and twenty-four female patients ranging in age from 34 to 70 years. Pre-treatment, mean serum cholesterol levels was 182 ± 39 mg/dl and triglyceride levels was 123 ± 47 mg/dl. Post-treatment mean serum cholesterol and triglyceride levels were 196 ± 42 mg/dl, and 127 ± 52 mg/dl respectively. Post-treatment serum cholesterol and triglyceride levels were found to be significantly high. The caliber and mean flow velocity of femoral vein were also significantly increased after MLD.

MLD effectively decreases the interstitial lymphatic fluid volume, alleviates the symptoms and improves the quality of life. MLD also significantly increases mean serum cholesterol and triglyceride levels and increases venous flow.

Key words: Lymphedema, lymphatic massage, venous flow

1. Introduction

Lymphedema is defined as extremity swelling due to excessive lymphatic fluid accumulation in subcutaneous tissues. Primary lymphedema is the malfunction of the lymphatic vessels due to a congenital pathology whereas secondary lymphedema becomes evident after a local infection, trauma or malignancy with impairment in lymphatic channels. It is most commonly encountered in the lower limbs (1-3).

The importance of lymphedema management is increasing as the prevalence of it steadily increases due to the viral, bacterial and parasitic infections of the soft tissues, bone fractures and

oncological surgery (4). Lymphedema management aims to minimize swelling and prevent recurrent infections (5). The optimal lymphedema management consists of a physical therapy program combined with Manual lymphatic Drainage (MLD), skin care, exercise and compression therapy. MLD is a form of massage and acts on reducing edema. Recently, MLD management has been accepted as the treatment of choice for lymphedema by great number of centers around the world (4-6).

Compared with plasma high density lipoprotein cholesterol (HDL) levels, lymphatic fluid had an increased HDL levels and contained proportionately more phospholipids and free cholesterol levels (7). Previous studies showed that during the Sequential Intermittent Pneumatic Compression treatment; the serum cholesterol levels increase due to entrance of edema fluid (8). Our study aimed to compare serum total cholesterol and triglyceride levels and venous flow changes in patients with lower limb lymphedema before and after MLD treatment.

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2. Material and methods

After the protocol was approved by ethic committee of Bozok University, the study was carried out according to the principles of the Helsinki Declaration at the Hospital of Bozok University between October 2012 and October 2013. A consecutive series of thirty patients suffered from unilateral secondary lower limb edema were included in the study. The informed consent was obtained from all participating patients. The exclusion criteria were renal insufficiency, congestive heart failure, hepatic failure, chronic venous insufficiency of lower extremities and peripheral arterial disease. Patients with cardiovascular disease were not included in the study to avoid possible risks related to increased levels of cholesterol and triglyceride due to MLD. The diagnosis of lymphedema was based upon physical examination and confirmed by using isotopic lymphoscintigraphy in all patients (Figure 1).



Fig. 1. Massive stasis of the radionuclide substance (dermal backflow) and dilated lymphatic channels in the right lower limb and partial lymphatic obstruction in the left lower limb are shown.

The minimum time interval between the onset of the symptoms and the diagnosis was 2 years. All patients were examined to rule out previous deep venous thrombosis with color Doppler ultrasonography of lower limbs. Serum albumin, creatinine, blood urine nitrogen and urine analysis were assessed to rule out the renal failure, hypoalbuminemia, and protein-losing enteropathy. Only patients with unilateral lower limb lymphedema were included in the study. The cross-sectional area and mean flow velocity changes of the femoral vein were evaluated by venous Doppler ultrasonographic examinations before MLD therapy and during follow-up in all patients (Table 1).

Subjective complaints including hardness of the skin, edema of the involved lower limb and sensory impairments were noted. Objective findings such as the volume of the lower limb, thickness of the skin and circumference of the lower limb were also recorded. Throughout the study patients remained on the same diet to balance the influence of dietary factors on serum cholesterol and triglyceride levels.

All patients were treated with MLD after a basal serum cholesterol and triglyceride level measurement. After 4-10 days, post treatment serum cholesterol and triglyceride levels were measured in all patients. The statistical analyses were done by comparing the pre- and post-treatment values using paired sample t-test. $P < 0.05$ values were accepted as significant.

3. Results

There were six male and 24 female patients ranging in age from 34 to 70 years with a mean age of 45.2 years. Seventeen (57%) patients had lymphedema of the left leg and 13 (43%) patients had lymphedema of the right leg. Impaired mobility of the involved extremity was recorded in six (20%) patients. Skin findings were dermal thickness in 13 (43%) patients, dryness in 16 (53%), hair loss in 4 (13%), lymphangitis in 3 (10%) and epidermal shining and thinning in 3 (10%).

The cross-sectional area and mean flow velocity of femoral vein were increased using MLD therapy ($p < 0.05$).

The pre-treatment mean serum cholesterol and triglyceride levels were 182 ± 39 mg/dl and 123 ± 47 mg/dl, respectively, while the post-

Table 1. Cross-sectional area and blood flow changes related with MDL in femoral vein

Femoral vein	Before MDL	After MDL	p value
Cross-sectional area (cm ²)	0.45 ± 0.18	0.52 ± 0.21	< 0.05
Mean flow velocity (cm/s)	13.4 ± 6.5	14.5 ± 5.1	< 0.05

treatment mean serum cholesterol level was 196 ± 42 mg/dl and the post-treatment mean serum triglyceride level was 127 ± 52 mg/dl. Post-treatment serum cholesterol levels were significantly ($p<0.002$) high in 25 (83%) of the patients when compared to pre-treatment values. Additionally, post-treatment serum triglyceride levels were found significantly ($p<0.001$) high in 27 (90%) patients when compared to pre-treatment levels. However, considerable clinical improvements were observed in all patients.

During the follow up period extending to 15 months, lower limb lymphedema significantly reduced and mean limb circumference considerably decreased in all patients. Cosmetic and functional problems had completely resolved. Thus, MLD therapy was intermittently continued.

4. Discussion

Lymphedema is regional swelling of one or more limbs because of a blockage in lymphatic vessels effecting lymphatic drainage and seen in the lower limb in eighty percent of cases (2). The lymphedema can be serious in mild or severe forms and if untreated it may impair the quality of life by skin changes, loss of function and discomfort due to swelling, pain and chronic infections due to inadequate lymphatic drainage (9). Malignancy and related treatments such as radiotherapy, chemotherapy and surgery are the leading factors causing lymphedema in industrialized countries (10, 11). Post infectious lymphedema was the most commonly encountered form in our patients. Currently, there are not any exact data about the prevalence of lower limb lymphedema. There is no guide for clinicians to identify those most at risk of developing this condition. Lymphedema occurs in both sexes. However, females seem to be more likely to develop lymphedema (10, 12). Our findings were consistent with this, lymphedema was more frequently encountered in females.

Capillary pressure, negative interstitial pressure, interstitial fluid colloid osmotic pressure and plasma colloid osmotic pressure alterations can cause lymphedema. The first stage of lymphedema is accumulation of protein rich products towards the interstitial space. Pooling of fluid and protein in the interstitial compartment reshapes the cellular composition. Soft pitting edema is principle clinical manifestation. The number of cells found in the interstitial space such as fibroblasts, histocytes and neutrophils increase gradually. Progressive inflammation occurs by the further accumulation of fibroblasts, adipocytes and macrophages. In this stage of lymphedema, tissue edema is more pronounced.

In the last stage, the inflammation is so destructive that lymphatic vessels are damaged by inflammatory response and recurrent infectious attacks. These changes finally lead to subcutaneous tissue fibrosis (3, 10, 13).

Two thirds of lymphedema are unilateral. The distal parts of the extremity are affected earlier and it progresses towards proximal segments in the later periods of the disease. The swelling may be in different levels and commonly unnoticed in the early stages whereas in later stages becomes more obvious and serious disabled enlargement occurs in the affected limb. Unilateral painless swelling on the dorsum of the foot is common presenting symptom of the patients with lower extremity lymphedema. The patient may also suffer from a feeling of heaviness in the lower limb. On initial examination the swelling is observed as pitting edema, but lately fibrosis develops in the subcutaneous tissues and leads to the classical nonpitting signs (2, 10, 14). Painless swelling of the involved limb was the most common presenting symptom in our patients. Skin changes were also common presenting symptoms of the patients in our series.

Although there are many suggested treatment alternatives, there are no any standard and exact treatment procedures (8, 15). Early diagnosis is very important for minimizing the complications and necessary for a successful treatment (9). The principal goals of the treatment modalities are to prevent the progression of disease, to improve the symptoms, and avoiding skin changes. The main goal of the lymphedema therapy is to minimize the lymphedema, restore the functionality and the cosmesis of the limb and prevent complications (2, 10). Conservative or pharmacological treatment strategies are tailored to the severity of the condition and symptoms (2, 15). Currently, it is widely accepted that complete decongestive therapy (CDT) is the gold standard for the conservative treatment of lymphedema (9, 11). MLD is a principal component of CDT (11, 16, 17). The actual techniques of MLD are well described and keenly debated and MLD is preferred first-line conservative treatment. MLD stimulates lympholymphatic and lymphovenous anastomoses, and alleviates the symptoms related with lymphedema (11,17). Randomized controlled trials reported that the effects of MLD on breast-cancer related lymphedema is controversy (6). However Ko et al. (18) have showed that CDT with MLD is highly effective treatment for both primary and secondary lymphedema. Besides, many authors have reported that MLD improves clinical stages, hemodynamic parameters and quality of life in

patients with chronic venous disease (19). In this study MLD was the preferred treatment model in patients with lymphedema.

Lymphatic vessels play an important role for homeostasis and transport of immune cells, inflammatory molecules and dietary lipids (20). The surrounding tissues are affected adversely by the malfunction of the lymphatic system. Hemodynamic changes also occur in extremities with lymphedema. Increased arterial blood flow has been noted in lymphedematous arms when comparing with the contralateral arms (3). Peripheral cell cholesterol metabolism is regulated primarily by interaction with lipoproteins in the interstitial space. Lymph transport is one of the factors that affect the composition of interstitial fluid. It has been postulated that specific receptors for interstitial fluid lipoproteins may exist and plays an important role for cholesterol homeostasis (7).

There are many skin ligaments connecting skin and deep fascias on thigh, popliteal area and leg. These ligaments support the skin during the movement. Stretching of the skin during MLD creates pressure to the dermal structures and increases the venous blood flow (21). Although the precise mechanisms for increase in femoral venous blood flow are not clear, the possible mechanism would be due to traction of the lower limb causing increased superficial venous flow velocity. The increase in superficial venous flow would lead to the increased flow in across perforating venous system and deep venous system (21). Similarly, our study demonstrates that MLD significantly increases the mean flow velocity in femoral vein.

Mostafa et al. (8) showed increased serum lipid levels following Sequential intermittent pneumatic compression (SIPC) treatment. SIPC therapy leads to transport of large molecules from interstitial space to the blood vessels. MLD leads to the contraction of lymph collectors. Therefore it may also increase the blood serum lipid levels via transport of lipid rich lymphatic fluid (15). Our study showed that these large molecules can also pass into circulating blood after MLD, similar to SIPC treatment effect.

Conclusively, lymphedema is a common problem and carries high morbidity risk in patients without any treatment. There are many treatment options which are suggested but none is definitive treatment. MLD seems to be an effective conservative treatment model and significantly reduces the painless swelling, alleviates the symptoms and improves the quality of life. It may be more useful particularly in patients with coexisting chronic venous disease.

Serum cholesterol and triglyceride levels should be carefully monitored during and following MLD therapy to prevent any complication related to increased hypercholesterolemia and hypertriglyceridemia levels, especially in patients suspected with cardiovascular disorders.

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