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Possibilities of conservative treatment of patients with lymphedema of the extremities (literature review)

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ABSTRACT

The literature review describes various methods for treating patients with lymphedema of the extremities. Statistics show an increase in the incidence and disability of patients with this pathology. However, the possibilities of therapeutic measures in lymphedema are far from perfect.

The analysis of literature data showed that the basis of treatment for lymphedema of the extremities is comprehensive conservative therapy with the use of pathogenetically grounded physical, mechanical, and medical methods. In complex schemes of conservative treatment for lymphedema, physiotherapy methods occupy a prominent place. The most common technique among them is regular combined decongestive therapy. This method is recognized by leading experts as the main one in treating patients with lower extremity lymphedema. Commitment of patients to treatment and their social and psychological counseling are of great importance. The choice of the volume and method of surgical intervention requires a difficult and individual assessment of pathological changes developing throughout the course of the disease.

Despite certain improvements in treatment methods, lower extremity lymphedema is still an unsolved issue. The experience of most specialists involved in lymphedema treatment demonstrates a reasonable balance between basic conservative and surgical treatment methods. Undoubtedly, results of evaluation of these methods will improve the choice of an optimal technique for treating patients with lymphedema of the extremities.

Key words: lymphedema of the extremities, conservative treatment, physiotherapy.

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Возможности консервативного лечения пациентов с лимфедемой конечностей (обзор литературы)

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РЕЗЮМЕ

Представлен обзор литературных источников, посвященных различным методам лечения пациентов с лимфедемой конечностей. Статистические данные свидетельствуют о росте заболеваемости и инвалидизации

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пациентов с этой патологией. Вместе с тем возможности лечебных мероприятий при лимфедеме оставляют желать лучшего.

Анализ литературных данных показал, что основу лечения лимфедемы конечностей составляют комплексные консервативные мероприятия, которые должны обеспечить применение патогенетически обоснованных физических, механических и медикаментозных методов. В комплексных схемах консервативного лечения лимфатических отеков значительное место занимают физиотерапевтические методы. Ведущим среди них является регулярная комплексная противоотечная терапия. Этот метод признается ведущими специалистами в качестве основного в лечении пациентов с лимфедемой. Большое значение имеют приверженность пациентов к лечению, их социальная и психологическая поддержка. Выбор объема и метода оперативного вмешательства требует осуществления трудной, индивидуальной оценки патологических изменений, развивающихся при заболевании.

Несмотря на определенные достижения, результаты такого лечения далеки до удовлетворительных значений. Опыт большинства специалистов, занимающихся лимфедемой, свидетельствует о разумном балансе между базовой консервативной терапией и хирургическими способами лечения. Несомненно, результаты оценки этих методов позволят улучшить выбор оптимального метода лечения пациентов с лимфедемой конечностей.

Ключевые слова: лимфедема конечностей, консервативное лечение, физиотерапия.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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INTRODUCTION

The current level of care for patients with lymphedema of the extremities is quite high. New methods of conservative and surgical treatment are being developed and implemented in clinical practice. At the same time, observations show that with an obvious increase in the incidence of lymphedema associated with cancer, inflammatory diseases, and malformations, the effectiveness of therapeutic measures is far from perfect [1, 2]. The peculiarities of the pathogenesis and clinical course of lymphedema result in a dubious prognosis and the opinion of some doctors about the futility of treating patients with lymphedema [3]. Undoubtedly, lymphedema of the extremities is a chronic disease, but its effective treatment is a difficult, but quite solvable task [4–7].

The main principles of the treatment strategy are complexity and phasing. Experience shows better results when treatment starts early. In treatment of patients, it necessary to take into account medical, psychological, and social rehabilitation [8]. Patient's commitment to treatment and systematic coopera-

tion between the doctor and the patient are of great importance. A special role is attributed to the system of training patients to fight against their disease [9].

Currently, conservative therapeutic measures occupy a prominent place in the treatment of patients with lymphedema of the extremities [2, 3, 6, 10]. They should ensure correction of all interrelated pathogenetic links of this disease and be complex and step-by-step, including preoperative preparation and postoperative care [3, 5].

CONSERVATIVE TREATMENT OF LYMPHEDEMA

Compression therapy. Compression therapy is one of the basic methods recommended for daily use in treatment of patients with lymphedema of the extremities [1, 2, 4]. Using elastic compression garments leads to an increase in pressure in the interstitial space with increased reabsorption of fluid and proteins into lymphatic capillaries. A decrease in the diameter of superficial and deep veins of the limb results in acceleration of venous blood flow and lymph

outflow in the supra- and subfascial spaces with a moderate fibrinolytic effect [4, 6, 7].

When using elastic bandages, short-stretch bandages are recommended, as they create a more pronounced increase in the pressure during motor activity, contributing to the work of the skeletal muscle pump and providing a high decongestant effect. The structure of elastic bandages, which is constantly being improved, is of great importance. So, one of the studies shows that using single-layer silicone bandages with stretchability of 35% provides optimal pressure not only in the horizontal, but also in the vertical body position and during movements of patients. This reduces the volume and consistency of the limb tissues by up to 40% [11].

The use of therapeutic compression garments has a number of advantages. It is advisable to use flat-knit compression garments, which creates sufficient working pressure, has increased strength and wear resistance, and prevents formation of folds [4, 12]. For stage I lymphedema, class 2 compression is recommended. Class 3 compression garments are indicated for stage II lymphedema, class 4 compression (pressure over 49 mm Hg) is indicated for stage III—IV lymphedema with fibredema.

Inelastic compression in lymphedema is more effective than elastic one, as it improves emptying of veins and outflow of lymph by creating a stiff shell around the limb and high working pressure. For example, the CIRCAID device consists of a series of nylon strips wrapping a leg and connected together via a Velcro system, which allows the patient to dose pressure on the limb. Products are sold ready-made or are tailor-made to a given size for the entire limb or for its individual segments [13].

Recently, there have been reports on using special Kinesio tapes on the limbs in patients with lymphedema [14, 15]. According to studies, fan cut taping can be used as additional treatment for lymphedema in order to reduce edema and pain by stimulating proprioception, blood flow, and lymph outflow. However, despite the fact that this technique gives positive results, its use requires detailed scientific justification.

Massage. Lymphatic massage or manual lymphatic drainage in comprehensive treatment of patients with lymphedema of the extremities in recent decades has received universal recognition due to its practical effectiveness and scientific confirmation of its usefulness [1–4, 12]. The main effects of manual

lymphatic drainage are to improve the transport function of the lymphatic system by stimulating lymphangions, increasing collateral lymphatic outflow, and allowing for lymphatic vessel and lymphovenous anastomoses. The effect of fluid reabsorption, and most importantly, removal of proteins from the interstitial space, which is essential for reducing fibrotic changes in soft tissues in lymphedema, is of great importance [3, 7, 12, 16].

Manual lymphatic drainage is very different from traditional types of massage techniques. Massage movements should be slow, eliminating the friction of the skin. The pressure exerted on the tissues by the hands is much lower than in other types of massage (no higher than 30–40 mm Hg), since the main area of influence is the lymphatic network of the skin and subcutaneous tissue. The sequence of massage movements is of particular importance. Initial movements are performed in the area of regional lymph nodes with a gradual movement to the peripheral areas of the limb. Each movement in a certain zone is carried out in the proximal direction, based on the principle that the lymph should move to the area from where it is displaced [12, 16].

Recently, new, clinically proven and objective markers have been developed to assess the effectiveness and scientific validity of manual lymphatic drainage. The data of bioimpedance spectroscopy, tonometry, and short-wave diathermy determine with sufficient accuracy movement of fluid on different segments of the limb, depending on the applied massage manipulations.

Course application of professional manual lymphatic massage creates a temporary effect, although with a certain aftereffect. Therefore, patient's mastering this method for its regular use in complex self-treatment is of great importance [4]. Reports on introduction in recent years of devices that allow for dosed lymph massage are worth noting. Thus, the Linforoll device consists of a handpiece with a roller attached to the tip and connected to a computerized system that allows for real-time optimization of pressure exerted by the roller on the main tissues of the limb and improves results of treatment [17, 18].

Exercise therapy. Various physical exercises are aimed at activating extralymphatic stimulation of lymph outflow, since a significant increase in lymph transport in the limb has been proven during active and passive muscle movements and respiratory gymnastics [2, 3, 6]. In the horizontal body po-

sition, light-intensity movements in the joints of the extremities are performed with alternating vertical walking on the spot, toe lift, and performing 'swallow' position. Swimming has a significant positive effect on lymphedema. With severe forms of lymphedema, being in a water pool becomes problematic for patients. In this regard, classes in a dry pool are essential, which is a tank filled with special plastic balls. In the dry pool, the patient can perform any movement, including simulated swimming. Unlike in a water pool, the patient does not need to remove the compression bandage [12]. Recently, there have been reports on the positive effect of dosed Nordic walking in the comprehensive treatment of patients with lower extremity lymphedema [19].

A combination of manual lymphatic drainage, compression bandaging, and physical therapy forms the basis for combined decongestive therapy. This method is recognized by leading experts as the main one in the treatment of patients with lymphedema [2, 3, 9, 10, 12].

PHYSIOTHERAPY METHODS

In the complex schemes of conservative treatment for lymphedema, physiotherapy methods occupy a prominent place [2, 3, 4, 9].

Intermittent pneumatic compression. The method of intermittent pneumatic compression (IPC) or pneumatic massage of the extremities is widely used [2, 6, 20, 21]. The effect of regional pneumatic compression mainly consists in significant reabsorption of fluid and, to a lesser extent, proteins from the edema into the lymphatic bed. There is also a decrease in hydrostatic pressure and tissue tension. Standard equipment allows for regular IPC sessions from distal to proximal parts of the limb in the modes from 30 to 50 mm Hg, lasting 25–30 minutes [9]. Recently, to increase the efficiency of this method, IPC devices with retrograde velocity signals with constant pressure parameters of 40 mm Hg have been introduced [22].

The study of tissue fluid pressure during IPC in patients with stage II-IV lymphedema guided by electronic manometry and plethysmography was carried out. It was noted that pressure in the tissue fluid in IPC reached 40–100 mm Hg, and the volume of displaced tissue fluid varied from 10 to 30 ml in proximal parts of the limb during the compression cycle, and in some cases – up to 100 ml [23, 24]. Studies using fluorescence lymphography showed

that IPC accelerates lymph flow in the superficial lymph vessels of the extremity with faster and more efficient flow during relaxation than during compression.

In the treatment of patients with lymphedema, a positive effect is provided by a combination of IPC and manual lymphatic drainage, exercise therapy, and respiratory gymnastics [2, 3, 7]. One of the advantages of IPC is a possibility of using this method by the patient at home adhering to all indications and contraindications. For this purpose, small-sized and inexpensive devices have been developed [4, 7].

Laser therapy. Among physiotherapy methods, laser therapy has become a common method of treating patients with lymphedema in the outpatient setting [25]. Under the influence of low-intensity laser radiation, changes occur at all levels of a living organism. At the subcellular level, a stereochemical rearrangement of molecules and activation of redox processes occur. At the cellular level, a change in the membrane potential and an increase in proliferative activity are observed. At the tissue and organ levels, blood and lymph circulation are activated. At the systemic and organizational levels, adaptive neuro-reflex and neuro-humoral reactions take place [26, 27]. For treatment with low-intensity laser radiation, helium-neon lasers with a wavelength of 0.63 um and power of 20 mW and semiconductor infrared lasers with a wavelength of 0.89 µm, a frequency of 70-100 Hz, and radiation power of 10-11 mW are used.

Photodynamic therapy is a special method of laser therapy based on the photochemical reaction of an injected photosensitizer that selectively accumulates in cancer or microbial cells and exposure to laser radiation of a certain wave for damaging pathological formations [25]. In patients with lower extremity lymphedema, complicated by recurrent erysipelas, antimicrobial photodynamic therapy has been recognized. After a course of photodynamic therapy, histological studies show a significant decrease in the number of lymphocytes and histiocytes, reduction of lymphatic lacunation, and, most importantly, almost complete elimination of microbial cells. This contributes not only to relief of exacerbations of erysipelas, but also to stabilization of the clinical presentation of lymphedema [25].

Magnetic therapy. Currently, magnetic fields are widely used as a powerful physiotherapy method in various pathologies. The therapeutic effect of

magnetic fields is primarily associated with positive changes in the morphofunctional state of vessels in the microcirculatory bed: vasodilation, increased blood flow and lymph outflow, improved blood rheology. Clinically, this is manifested through anti-inflammatory, trophotropic, antispasmodic, decongestant, and disaggregating effects [25].

With lymphedema of the lower extremities, using of a constant magnetic field at initial stages of the disease is the most effective. So, patients subjectively report a decrease in the feeling of heaviness and pressure sensations in the lower extremities. In lymphedema, characterized by significant fibrotic changes in the soft tissues of the limb, the effect of magnetic therapy is not observed [25]. The obtained data confirm reasonability of the therapeutic use of pulsed low-frequency magnetic fields in treatment of patients with lymphedema [26]. The effectiveness of the method is due to various synergistic actions (diamagnetic force acting on a liquid medium, thermal effect and stimulation of transport of macromolecular compounds).

Good results were noted both according to clinical and instrumental studies. In particular, in the experimental group, the authors observed clinical improvement compared with the control group, as evidenced by improved quality of life on the clinical severity scale, as well as results of echographic studies [26].

Electrophoresis with enzymes and calcium chloride. Anti-edematous and anti-inflammatory effects of electrophoresis with these substances are mainly effective at stages I and II of lymphedema, which is due to stimulation of human lymphatic pacemaker and an increase in contractility of lymphangions [28, 29]. Disadvantages of the standard electrophoresis technique are the superficial effect on tissues, inability to create a drug depot in this lymphatic region, and rapid elimination of the drug from the focus.

Ultrasound therapy. Using low-frequency ultrasound in combination with thermocontrast absorption of drugs (hyaluronidase, ronidase) increases permeability of the skin and reduces density of the subcutaneous fat due to loose connective tissue and depolymerization of hyaluronic acid [7]. In addition, direct and indirect effects of ultrasound lead to emergence of acoustic flows, cavitation, and variable sound pressure, which increases the functional activity of the cell and ultimately leads to improved

drainage function of lymphatic vessels and increased lymphatic and venous outflow.

Electrical stimulation of lymphatic vessels. This method can significantly enhance the drainage function of lymphatic vessels by normalizing their tone, restoring and accelerating rhythm of their contractile activity, and stimulating additional lymph outflow pathways in order to influence the crucial link in the pathogenesis of lymphedema – impaired lymphangion function [2, 4, 7, 28, 29]. Developments on the application of electrical stimulation in treatment of lymphedema using the Lymphavision stimulator are of great interest. The device is based on generation of currents similar to impulses of human nervous system [7].

Follow-up of patients using anthropometry, rheolymphovasography, and thermal imaging showed significant reduction of edema at all levels of the affected limb by an average of 12%, a decrease in thermal symmetry of healthy and affected limbs by 48.2%, and an increase in the rate of lymphatic outflow on the affected side by more than 2 times. There is successful experience of using the Body Drain device for treatment of lower extremity lymphedema, designed to provide a combined effect of electrical stimulation of lymphatic and venous systems and vacuum therapy [7].

The effect on lymphatic outflow in the region of the pathological process is achieved due to electrical stimulation of smooth muscles in the lymphatic vessels and striated muscles in the extremities. Creation of negative pressure in projection of main lymph nodes leads to stimulation of their drainage function and an increase in the intensity of extravascular fluid movement.

Ultraviolet blood irradiation. In clinical practice, ultraviolet blood irradiation (UBI) has a powerful biostimulating effect on the immune system, tissue regeneration, and improvement of blood rheology. This method is of great importance for patients with lymphedema of the extremities, complicated by recurrent erysipelas [4, 7, 25, 28]. The most pronounced effect of using UBI is observed in exacerbation of the pathology, and its cycle application prevents development of relapses of erysipelas. Results of using UBI show a good immediate result in 32.6% of patients, satisfactory result in in 59.1% of patients, and unsatisfactory result in 8.3% of patients [27, 28].

Gravity therapy. The main mechanism of the therapeutic effect of this method is the action of centrifugal forces of craniocaudal direction, created by a special artificial gravity unit [30]. Moderate hypergravity (1.5 G) causes an increase in pressure in the interstitial space and increases lymphatic pumping. Increased lymph outflow stimulates lymph formation and activity of preserved lymphangions. Improvement of microcirculation under the gravitational influence with activation of metabolic processes in cells reduces the degree of dystrophic changes and growth of connective tissue. Stimulation of lymphatic drainage in tissues promotes destruction and removal of macromolecular substances from the interstitial space and reduces the degree of fiber rearrangement of soft tissues [31]. The rotation speed of the artificial gravity unit is 29–34 revolutions per minute, the number of sessions is 10-12, the duration of each session is 8–10 minutes [31].

Observations indicate that in comprehensive treatment of patients with lymphedema, the use of gravity therapy is advisable at the initial stages of the disease. According to volumetric data obtained at the end of a treatment cycle, a decrease in the volume of the limbs on average by 14% is observed mainly in the distal parts in patients with stage I lymphedema, by 12% – in stage II lymphedema, and by 8% – in patients with stage III lymphedema. According to computed tomography performed in patients after completion of the comprehensive treatment, there is a decrease in the thickness of the subcutaneous tissue to an average of 12.7 ± 1.22 mm and a decrease in its density with the value of 123.46 ± 3.03 HU [30].

Shockwave therapy. A report on using shockwave therapy is of interest [32]. Electro-pneumatically generated radial shock waves stimulate metabolism, accelerate neoangiogenesis, have an anti-inflammatory effect, and increase transfer of interstitial fluid. In the course of treatment in patients with lymphedema, a decrease in edema density upon palpation and reduction of limb circumference are identified. Ultrasound examination records a decrease in the epifascial thickness of tissues with a decrease in their hyperechogenicity. It should be noted that prescription of certain physical factors (pneumatic compression, shockwave therapy, electrical stimulation) is a contraindication in patients with suspected acute venous thrombosis and acute erysipelas of extremities.

DRUG TREATMENT

Possibilities of medical treatment of lower limb lymphedema are limited. Different groups of drugs affect individual links in the pathogenesis of the disease and its complications with different, often insignificant, degrees of effectiveness. Benzopyrones (coumarin), stimulating the activity of macrophages, promote removal of proteins from tissues in protein-rich lymphatic edema [33, 34].

Along with this, benzopyrones increase lymph outflow and reduce capillary fragility [35, 36]. Flavonoid derivatives (diosmin, hesperidin) affect three main components of interstitial space drainage disorders in edema: microcirculation and venous and lymphatic outflow. One of the most effective drugs according to numerous studies and a large body of evidence is detralex. Its micronized purified flavonoid fraction has certain advantages that increase the pathophysiological orientation of this drug [4, 5, 7].

Feasibility of systemic enzyme therapy (wobenzym, phlogenzym) in lymphedema is determined by its positive effect on blood rheology, reduction of platelet aggregation, increase in fibrinolysis, modulation of the activity of monocytes and macrophages, and reduction of tissue damage. Clinically, this is mainly manifested through immunomodulatory, anti-inflammatory, and decongestant effects, improvement of reparative processes, and reduction of thrombotic complications [4, 6, 37].

Additionally, segmental lymphotropic injections are of particular interest. This method consists in a sequential, step-by-step lymphostimulating effect at various levels of the limb in conditions of lymphatic edema. Administration of drugs with lymphostimulating properties should help restore normal passage of lymph in the affected limb. A course of segmental lymphotropic lymphostimulating injections includes 3 injections with an interval of 48 hours. The composition of injections is the following: lidase 32 units, lidocaine 100 mg, actovegin 200 mg, tramal 50 mg, 40% glucose solution as a filler and solvent [7].

Recurrent erysipelas often leads to formation of persistent lymphedema, and severity of edema is always directly related to the frequency and severity of recurrent erysipelas. [2, 4]. In case of exacerbations of erysipelas, various groups of broad-spectrum antibiotics are used in clinical practice. Lymphotropic and endolymphatic methods of administration of antibiotics provide a more long-term bactericidal

concentration of the drug in the lymphatic vessels and lymph nodes, which reduces the total dose of the drug and side effects of antibiotic therapy [4, 6, 24, 28]. Implementation of long-term preventive antibacterial therapy in the outpatient setting using penicillins (bicillin-1, bicillin-5, retarpen) for 6–12 months, is of great importance.

The combined use of physiotherapy methods and drugs is worth noting. Thus, ultratonotherapy for lymphatic edema in combination with the application of chitosan-based gel allows to optimize non-specific activation of local defense mechanisms of the body and contributes to strengthening of the barrier function of the skin. Chitosan promotes activation of macrophages and can also be used as an adjuvant for immunostimulating agents in order to increase production of antibodies [7].

Long-term experience of leading specialists shows that patients' adherence to independent therapeutic measures recommended by doctors is an indispensable part of comprehensive conservative treatment of lymphedema. The therapy includes skin care, self-massage, wearing compression garments, physical and breathing exercises, creating an elevated position of the limb, and, if possible, using portable pneumatic compression devices. [38-40]. Follow-up of 348 patients with lymphedema showed that self-treatment is an essential and important part in management of this group of patients. The methods are easy to use at home and, therefore, allow to solve difficulties in availability of specialized, systematic, and frequent care, saves time, and strengthens patient's awareness of their own responsibility for participating in results of comprehensive treatment.

CONCLUSION

Thus, conservative treatment of patients with lymphedema of the extremities, taking into account a chronic course of the disease, is indicated for all types and stages of the disease, should be carried out constantly, and be comprehensive. Monotherapy for lymphedema is ineffective. It is advisable to step-by-step combine several methods for treatment simultaneously [2, 3, 7, 38, 41]. In general, the success of treatment in patients with lymphedema of the extremities depends on its early diagnosis and, consequently, early use of preventive and therapeutic measures. These measures, primarily of a conservative nature, are aimed at reducing the accumulation of

tissue fluid and lymph and preserving and maintaining the function of lymphatic vessels and designed to slow down the progression of the disease to the greatest extent, achieve a stable positive effect, and improve the quality of life of the patient.

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Authors contribution

Katorkin S.E. – conception and design of the study, editing of the article. Myshentsev P.N., Yarovenko G.V. – collection and processing of the material, drafting of the manuscript.

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