LASER THERAPY AND UNLOADING THERAPEUTIC GYMNASTICS IN THE TREATMENT OF DYSLIPOPROTEINEMIA

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Based on clinical practice, some patients with lipid metabolism disorders (LMD) are resistant to lipid-lowering therapy (LLT) — in such patients, taking optimal doses of LLT drugs does not reduce levels of cholesterol and its fractions to target levels and using LLT at higher doses is associated with increased odds of adverse events. To optimize the treatment, 58 patients with ischemic heart disease with LMD resistant to LLT were examined. The patients were divided into two groups: in the main group, 29 patients received laser therapy and unloading therapeutic gymnastics; in the control group, 29 patients continued to take their usual medications. The obtained results showed a significant lipid-lowering effect of the treatment in the main group: we observed a significant decrease in total cholesterol (by 27.7%, $p < 0.01$) as well as low-density lipoprotein cholesterol (by 34.7%, $p < 0.01$), a significant increase in high-density lipoprotein cholesterol (28.1%, $p < 0.01$), a significant decrease of atherogenic coefficient (by 50.2%, $p < 0.01$) and in the levels of triglycerides (by 49.6%, $p < 0.01$). At the same time, no significant positive changes in lipid profile were observed in the control group. In patients of the main group, tolerance to physical activity increased significantly, with statistically insignificant changes in the control group accordingly.

Keywords: Ischemic heart disease, lipid metabolism disorders, resistance to lipid-lowering pharmacotherapy, total triglycerides, low-level laser therapy, unloading therapeutic gymnastics, cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol

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ЛАЗЕРОТЕРАПИЯ И РАЗГРУЗОЧНАЯ ЛЕЧЕБНАЯ ГИМНАСТИКА В ЛЕЧЕНИИ НАРУШЕНИЙ ЛИПИДНОГО ОБМЕНА

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В клинической практике встречаются больные с нарушениями липидного обмена (НЛО), резистентные к гиполипидемической терапии (ГТ), у которых прием оптимальных доз этих препаратов не приводит к снижению уровня холестерина и его фракций до целевого уровня, а повышение дозы препаратов способствует появлению побочных эффектов. Для оптимизации лечения таких больных было обследовано 58 больных ишемической болезнью сердца с НЛО, резистивных к ГТ. Исходно больные в зависимости от метода лечения были разделены на две сопоставимые группы: в основной 29 больных получали лазеротерапию и разгрузочную лечебную гимнастику; в контрольной — 29 больных продолжали принимать базовое медикаментозное лечение. Полученные результаты свидетельствуют о достоверном гиполипидемическом действии проведенного лечения в основной группе: отмечены достоверное снижение общего холестерина на –27,7% ($p < 0,01$) и холестерина липопротеидов низкой плотности на –34,7% ($p < 0,01$), достоверное повышение холестерина липопротеидов высокой плотности на 28,1% ($p < 0,01$), достоверное снижение коэффициента атерогенности на –50,2% ($p < 0,01$) и триглицеридов на –49,6% ($p < 0,01$). В то же время в контрольной группе достоверной положительной динамики липидограммы не наблюдали. У больных основной группы толерантность к физической нагрузке достоверно повышалась, а в контрольной группе изменялась недостоверно.

Ключевые слова: ишемическая болезнь сердца, нарушение липидного обмена, резистентность к гиполипидемической лекарственной терапии, холестерин, липопротеиды высокой плотности, липопротеиды низкой плотности, триглицериды, лазеротерапия, лечебная гимнастика

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Diseases of the cardiovascular system (CVS) are among the most important problems in the world. In the treatment of patients with ischemic heart disease (IHD), along with pharmacotherapy (PT), surgery methods are widely used: stenting and coronary artery bypass grafting (CABG). Using these treatment methods have a positive effect for a time and then it is gradually lost due to progressing atherosclerosis and IHD [1–3].

In recent years, significant progress has been made in PT of lipid metabolism disorders (LMD) in IHD patients. In most cases, PT has a good effect and target levels of cholesterol (CS) and its fractions are achieved [4–15]. Lipid lowering drugs (LLD) are known to be prescribed for continuous use, and this can cause side effects in the form of liver cell damage (elevated levels of transaminases: alanine aminotransferase (ALT), aspartate aminotransferase (AST)). Other side effects include myopathy, myalgia, diarrhea, nausea, liver discomfort, constipation, insomnia, headaches, etc. [16]. Dose reduction or discontinuation of LLD leads to an increase in levels of cholesterol and its atherogenic fractions. In clinical practice, some IHD patients with LMD are resistant to lipid-lowering therapy (LLT) — in such patients, taking optimal doses of the LLD does not reduce levels of cholesterol and its fractions to target values [16–19].

The above suggests that the trigger mechanisms of atherosclerosis and IHD have not yet been fully understood and require in-depth study. The existing treatment methods do not fully affect all etiopathogenetic mechanisms of atherosclerosis and IHD that contributes to the progression of the disease.

In earlier studies, it was shown that taking medications improve peripheral blood circulation at rest to normal values however, the reserve blood flow is not fully restored. Such structural changes of vessels are considered to be irreversible and serve as the most important factor in progression of cardiovascular pathology. Treatment of atherosclerosis, IHD and LMD relies on pharmacotherapy. For a more complete recovery of cardiovascular reserve and relieving the heart burden, it is advisable to use non-medication methods of treatment along with drug therapy [1–3].

It is known that laser therapy (LT) [20–24] and especially LT in combination with unloading therapeutic gymnastics (UTG) [25] can have a significant positive effect in the treatment of cardiovascular diseases (CVD). The mechanisms of such positive effect are described in many publications [20–24]. Intravenous laser blood irradiation (ILBI) at red spectrum is more often used to achieve a systemic effect while the infrared range is used for a local effect. When these two ranges are used in combination, the positive effects are cumulated.

Our observations demonstrated that the course treatment with LT did have a positive effect in the short-term period. However, four months after the course of LT, the achieved positive effect was leveled out and laboratory parameters returned to the initial values (before LT treatment course). It should be noted that antianginal therapy and LT, separately and in combination, increase blood flow and reduce peripheral vascular resistance at rest however, the reserve blood flow is not fully restored. This proves that the mentioned methods of treatment never completely recover the reserve exchange surface of capillaries. To maintain the effect of laser therapy, patients must receive a course of LT at least two or three times a year. Since such patients need lifelong treatment, they may experience certain inconveniences, difficulties or distrust and after the first or a few next courses of treatment, may not proceed with the treatment.

The main factor in restoring CV reserve is a proper selection of motor regimen for the patients. In all clinical recommendations on non-drug treatment of atherosclerosis and IHD, physical activity is of great importance. The risk of developing CVD in people leading a sedentary lifestyle is 20–50% higher than in physically active people [16]. In patients with CVD, exercise tolerance (ET) is significantly reduced due to a limited CV reserve.

The limited reserve exchange surface of capillaries can be recovered effectively with the use of UTG only. Loading exercises cause an increase in heart rate, blood pressure, respiratory rate, activation of the sympathoadrenal system undesirable for cardiac patients while unloading exercises have a normalizing effect. Severe and/or elderly patients cannot do loading exercises due to limited cardiovascular reserve and/or severity of condition but they can easily perform unloading exercises that expands the indications for the use of UTG. Such exercises are performed systematically on a daily basis, and the achieved effect lasts for a long time [1–3]. So the patients' life quality significantly improves and the number of medications taken regularly decreases accordingly — subject to our further long-term observations.

Another UTG advantage is that significant part of the heart pumping function is performed by the muscular system. The reserve capillary exchange surface area is restored and maintained due to angioneogenesis, the reserve blood flow increases, and peripheral vascular resistance is significantly reduced. Under these conditions, the heart strain is reduced [1–3]. This technique is effective even in those cases when patients develop resistance to PT. Consequently, the technique can be used for patients with coronary artery disease with LMD, in whom, despite taking LLD, it is not possible to lower blood lipids to the optimal levels due to various circumstances.

In this regard, the development and scientific substantiation of new treatment methods for common somatic diseases is one of the important and promising areas of modern medicine [26–28]. The problem is of particular importance in the case of cardiovascular pathologies, primarily atherosclerosis and coronary artery disease, especially with resistance to PT [28–32]. Using invasive treatment methods is often unjustified, and it is ineffective in the presence of severe multifocal atherosclerotic vascular lesions.

Thus, the problem of using LT and UTG in a comprehensive program of physical rehabilitation of IHD patients still contains many unresolved questions that require further investigation — the present study is an attempt to answer some of them.

The aim of the study was to develop effective ways of using red and infrared laser irradiation and UTG in rehabilitation treatment of IHD patients with LMD resistant to lipid-lowering drug therapy, with ongoing maintenance therapy.

METHODS

The study involved 58 IHD patients with stable angina pectoris II and with LMD resistant to LLT aged between 40 and 60 years (93.1% men, 6.9% women), with disease duration of 2 to 6 years. Patients with obesity, diabetes mellitus type II, arterial hypertension, chronic kidney disease and chronic renal failure were not included in the study. The distribution of IHD patients with LMD resistant to LLT by gender and age in the main group (MG) and control group (CG) is shown in Table 1.

Depending on treatment method, all patients were randomized into two groups comparable in clinical and functional characteristics and maintenance pharmacotherapy (MPT): 29 patients of the main group received a complex consisting of combined LT (ILBI and cutaneous exposure to infrared laser radiation) and kinesiotherapy in the form of UTG on MPT background; 29 patients of the control group

Table 1. Distribution of IHD patients with LMD resistant to LLD by gender and age

	Groups of patients			
	Main group (MG)		Control group (CG)	
	Number of patients	%	Number of patients	%
Men	27	93.1	27	93.1
Women	2	6.9	2	6.9
Total	29	100	29	100
Average age, years	56.5 ± 2.1		54.9 ± 2.0	

received MPT only. In both groups, if side effects occurred, LLD doses were reduced until the side effects disappeared. In each group, 12 patients (41.4%) received rosuvastatin and 17 patients (58.6%) received atorvastatin. The daily dose of statins in tablets for oral administration was 38.8 ± 2.83 mg in MG, and 39.0 ± 2.41 mg in CG.

The patients were examined using standard clinical and laboratory methods.

Before starting treatment, patients underwent laboratory examination including the detailed analysis of lipid spectrum: levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG). Atherogenic coefficient (AC) was calculated. Blood samples were drawn from peripheral elbow veins using disposable syringes. After collection, whole blood (4.5 mL) was added to a tube with 0.5 mL of 3.8% sodium citrate and mixed thoroughly. The blood was then centrifuged at 3000 rpm for 15 min. After centrifugation, plasma was collected into a clean tube and stored at –20°C. The main fractions of plasma lipids (TC, TG, HDL-C) were determined by enzymatic method using Humalyser-2000 (Human; Germany) with the following reagents from Human: cholesterol with antilipid factor (Human; Germany); triglycerides with antilipid factor (Human GmbH; Germany); HDL-cholesterol without precipitation (Human GmbH; Germany). LDL-C content was calculated using the Friedewald's formula, provided that plasma TC concentration did not exceed 4.5 mmol/L:

$$\text{LDL-C, mol/L} = (\text{TC}) - (\text{HDL-C}) - (\text{TG}/2.2)$$

according to National recommendations NSSC and SSCI (Third revision, 2007).

The results were presented in mmol/L.

Veloergometric test (VEM) was performed on a bicycle ergometer (Elema; Sweden) according to a common method of continuous stepwise increasing load according to the method developed by D. M. Aronov.

ILBI and percutaneous LT were performed using the Mustang-2000 laser therapy device (NPLC Technika LLC; Russia). We used combined LT consisting of ILBI and external infrared LT performed alternately every other day at the rate of 3 procedures per week. The total course of treatment consisted of 15 procedures (8 procedures — ILBI with 15 min exposure and 7 procedures — infrared LT with 6 min exposure). The duration of treatment was 1.5 months. For ILBI, we used a semi-conductor red laser emitting head with a wavelength of 0.63 μm, with output power of the light pipe 2 mW. For percutaneous irradiation, a semiconductor infrared laser emitting heads with a wavelength of 0.89 μm were used. The infrared radiation dose was 0.6 J/cm^2. Percutaneous LT was performed in the following zones: aorta projection — second intercostal space on the right parasternal line — 1 min; pulmonary artery projection — second intercostal space on the left parasternal line — 1 min; projection of absolute cardiac bluntness — 1 min; thoracic spine — 6 zones — 3 zones on the right and left parasternal line — 30 s each.

UTG was performed using a patented method with monitoring of blood pressure (BP), pulse and clinical condition of the patient [1, 3]. Exercises were done in portions until BP and pulse rate increased. A patient performed the first exercise by smooth bending forward in a sitting position on a chair, at a rate of up to 5 bends per minute, then had a break of 15 s, and repeated the exercise. The total number of bends on the first day was limited to 100 while each subsequent day the number of bends was increased up to 50 times bringing the total number of bends to 150–200 times per day. The patient's hands were placed on the knee joints while performing the bends. At the same time, the patient simultaneously performed flexion and extension of the arms with elements of upper limb extension. When straightened up, the patient simultaneously retracted the anterior abdominal wall and thus facilitated movement of the diaphragm, respiratory muscles and pelvic muscles. At the same time, the patient smoothly tilted his neck and head forward and backward with periodic turns to the right and left. Total daily number of exercises was performed in fractions of up to five sessions per day. Next, the patient was prescribed to perform flexion and extension of the lower extremities (without taking the legs off the bed) fractionally in the supine position with the frequency described above. Their total number was increased from 50 to 100 times a day. Then the patient was

Table 2. Initial parameters of lipid metabolism and ET in healthy individuals and LLT-resistant IHD patients (M ± *m*) with ongoing maintenance pharmacotherapy

Lipid metabolism parameter	Healthy individuals	Patients of main group	Patients of control group	p^2
TC, mMol/L	5.26 ± 0.12	8.06 ± 0.11**	8.01 ± 0.10**	NS
HDL-C, mMol/L	1.85 ± 0.06	1.14 ± 0.05**	1.15 ± 0.05**	NS
LDL-C, mMol/L	3.13 ± 0.16	5.31 ± 0.14**	5.25 ± 0.14**	NS
AC	1.84 ± 0.07	6.47 ± 0.44**	6.40 ± 0.38**	NS
TG, mMol/L	1.14 ± 0.11	3.59 ± 0.21**	3.52 ± 0.19**	NS
ET, kgm /min	658.0 ± 35.4	408.6 ± 27.1**	424.1 ± 30.8**	NS

Note: ** — statistically significant differences between initial values in patients compared to values in healthy individuals ($p^1 < 0.01$); NS — differences between OG initial values and CG initial values are statistically insignificant (p^2); TC — total cholesterol; HDL-C — high-density lipoprotein cholesterol; LDL-C — low-density lipoprotein cholesterol; AC — atherogenic coefficient, TG — triglycerides; ET — exercise tolerance.

Table 3. Dynamics of lipid metabolism parameters and ET in IHD patients resistant to LLT in MG and CG (M ± *m*)

Lipid metabolism parameter	Patients of MG, initial values	Patients of MG, values after LG and UTG	Patients of CG, initial values	Patients of CG, values after PT	*p*
TC, mMol/L	8.06 ± 0.11	5.83 ± 0.10**	8.01 ± 0.10	7.87 ± 0.12	NS
HDL-C, mMol/L	1.14 ± 0.05	1.46 ± 0.04**	1.15 ± 0.05	1.21 ± 0.05	NS
LDL-C, mMol/L	5.31 ± 0.14	3.47 ± 0.14**	5.25 ± 0.14	5.22 ± 0.13	NS
AC	6.47 ± 0.44	3.22 ± 0.19**	6.40 ± 0.38	6.26 ± 0.37	NS
TG, mMol/L	3.59 ± 0.21	1.81 ± 0.11**	3.52 ± 0.19	3.54 ± 0.20	NS
ET, kgm /min	408.6 ± 27.1	501.7 ± 27.6**	424.1 ± 30.8	439.7 ± 31.7	NS

Note: ** — $p < 0.01$; NS — difference between values before and after treatment is not significant; TC — total cholesterol; HDL-C — high-density lipoprotein cholesterol; LDL-C - low-density lipoprotein cholesterol; AC — atherogenic coefficient, TG — triglycerides; ET — exercise tolerance.

prescribed squatting — he leaned forward, rested his hands on the corresponding knee joints, squatted smoothly and rose in the reverse order. Squatting was performed in portions. The total number of squats was from 10 to 50 times a day.

Data statistical processing was performed using Microsoft Excel and SPSS Statistics. Values of arithmetic mean (M), standard deviation (δ), and arithmetic mean error (m) were determined. For estimating the statistical significance of differences, *t*-test was used. P-values less than 0.05 were considered to be statistically significant.

RESULTS

In patients of both groups, despite taking LLD, dyslipidemia was originally reported: hypercholesterolemia, increased LDL-C, decreased HDL-C, increased AC and triglyceridemia. Based on the baseline VEM test data, a significant decrease in ET compared to norm values was reported for both groups, indicating a decrease in the reserve capacity of the cardiovascular system (Table 2).

The comparative evaluation of the initial parameters of blood lipid spectrum and ET in patients of the two groups showed that differences in the levels of total cholesterol, HDL-C, LDL-C, AC, TG as well as ET were statistically insignificant (Table 2). The two groups were therefore initially comparable in terms of the mentioned parameters.

Thus, the examined patients of MG and CG had confirmed LMD resistant to lipid-lowering pharmacotherapy and decreased ET indicating the impaired CV reserve.

The obtained data (Table 3) demonstrated a significant lipid lowering effect of the treatment in MG patients who received treatment with ILBI and external LT in the infrared range as well as physical rehabilitation in the form of UTG. In this group, we found a significant decrease in the levels of total cholesterol (by 27.7%, $p < 001$), LDL-C (by 34.7%, $p < 001$), AC (by 50.2%, $p < 001$) and TG (by 49.6%, $p < 001$), and a significant increase in HDL-C level (by 28.1%, $p < 001$). These positive changes in MG patients were accompanied by a significant increase in ET. At the same time, no positive dynamics of the lipid profile parameters and ET were observed in CG patients (Table 3).

Thus, using the therapeutic complex including percutaneous and intravenous LT in combination with UTG physical rehabilitation in IHD patients with LMD refractory to LLT contributes to significant improvements in blood lipid parameters and increase of ET. The developed treatment complex including ILBI and external infrared LT in combination with UTG physical rehabilitation is recommended for use in IHD patients with LMD resistant to LLT.

DISCUSSION

A long-term increase in the level of atherogenic lipids in blood is believed to contribute to progressing atherosclerotic vascular damage while the decrease can inhibit the development of the pathological process and improve the course and prognosis of the disease. The examined patients of MG and CG had significant impairments in blood lipid metabolism resistant to LLT and decreased ET indicating the impaired CV reserve. This confirms that IHD patients with LMD resistant to LLT also have cellular, tissue and microcirculatory disorders that cannot be cured by using pharmacotherapy only. For their proper treatment, UTG is recommended for use as well.

Blood-to-cell metabolism occurs at the level of capillaries. In earlier studies it was shown that microcirculation damage in atherosclerosis and IHD is systemic. The number of functioning capillaries in atherosclerosis and IHD was found to be significantly lower compared to the norm, i.e. the total exchange surface of capillaries was reduced significantly [33].

Capillaries form the basis of cardiovascular reserve. Normally, about 20% of the capillary network is functioning at rest while the remaining 80% is in a reserve state. This means that the heart, due to its pumping function, maintains blood supply of only 20% of the exchange surface of capillaries. To maintain the performance of 80% of capillary exchange surface area, proper levels of physical activity are required [1–3].

In case of significant decrease in the total exchange surface of capillaries, not only the level of cholesterol but also some other substances in blood are elevated including insulin and glucose levels (type II diabetes mellitus); blood viscosity and clotting, blood pressure, peripheral vascular resistance may increase as well. The limited total exchange surface of capillaries results in insufficient cholesterol supply in cells and elevated cholesterol levels in blood accordingly [1, 3].

Increased cholesterol level and dyslipoproteidemia are believed to result from the reduction of the total exchange surface of capillaries due to a decrease in a number of not only reserve capillaries (80%) but also active capillaries (total exchange surface of capillaries decreases by 3 or 4 times). Low-density lipoproteins cannot pass through the limited exchange surface of capillaries sufficiently so their level in the blood increases. Cholesterol acts as essential building blocks of the plasma membranes. Insufficient supply of cholesterol to cells slows down the growth and development of young and stem cells leading to a slowdown of regenerative processes accordingly. Low-density lipoproteins pass through the capillary network releasing cholesterol to body cells and converting into HDL-C. High-density cholesterol in the liver is used for production of bile acids entering the duodenum as part of bile for food digestion. In patients with atherosclerosis and IHD with manifestations of dyslipoproteinemia, on the one hand, have less high-density cholesterol, and on the other hand, they are used for synthesis of bile acids excreted as part of bile into the duodenum. Therefore, in atherosclerosis and IHD the level of atherogenic cholesterols is increased while the level of anti-atherogenic cholesterols is decreased. Consequently, restoring and maintaining the reserve and total exchange surface of capillaries using the unloading exercises has an important pathogenetic significance in case of atherosclerosis, IHD, lipid metabolism disorders, type II diabetes mellitus, arterial hypertension, circulatory insufficiency, etc. [1–3].

We consider it undesirable to overload the liver with high doses of LLD which when taken for a long time, may cause liver cell damage and other side effects, requiring biochemical control of liver cell functions since there is a new simple physiologic technique for regulating metabolism and blood lipid spectrum that can be used along with the maintenance PT. Many patients have various concomitant chronic diseases — in practice, 3 or 4 different groups of medications can be prescribed independently by different physicians for long-term use, and a patient sometimes should take up to 12 tablets per day that leads to polypharmacy. The treatment method developed by us can significantly reduce the pharmacological burden on patients.

Performing UTG daily helps to restore and maintain the total and reserve exchange surface of capillaries, relieve the work of the heart and keep its positive effect for a long period of time in cases of LMD resistant to LLT in IHD patients [1, 3]. In this case, cholesterol reaches the cells in sufficient quantities, the level of cholesterol and its atherogenic fractions in blood decreases and the level of anti-atherogenic fractions increases. This facilitates faster recovery and regenerative processes and slows down the damage processes [1, 3] as demonstrated in our study. Thus, we have developed the effective way to regulate cholesterol metabolism and control dyslipoproteidemia.

CONCLUSIONS

In IHD patients with LMD resistant to lipid-lowering pharmacotherapy, using laser therapy in combination with unloading therapeutic gymnastics makes it possible to correct disorders in blood lipid spectrum — the levels of high-density lipoprotein cholesterol are increased while the levels of total cholesterol, low-density lipoprotein cholesterol and triglycerides are decreased significantly. The atherogenic coefficient values are decreased as well in case of such treatment. These positive changes favorably affect the functional state of patients as evidenced by the increase in exercise tolerance serving as a marker of CV reserve recovery.

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