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Research Article

Lipid Metabolism Disorders and its Correction in Patients with Critical Lower Limb Ischemia During Revascularizing Osteotrepanation with Intramedullary Laser Irradiation Using Intravenous Laser Irradiation and Cytokine Therapy in the Perioperative Period

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Abstract

Background: Given the pathogenetic role of dyslipidemia in the development of chronic critical ischemia, correction of lipid metabolism is important in complex surgical treatment.

Purpose: To study the state of lipid metabolism and the possibility of its correction in patients with critical ischemia of the lower extremities with indirect revascularization

Material and Methods: Studies were conducted in 65 patients with critical ischemia of the lower extremities of atherosclerotic and thrombangiitic genesis. In 34 patients, indirect revascularization was performed with generally accepted conservative treatment in the perioperative period. (control group). In 31 patients, revascularizing osteotrepanation with intraosseous laser irradiation with intravenous laser irradiation and cytokine therapy in the perioperative period in parallel with generally accepted treatment. (main group). In dynamics, the parameters of lipid metabolism were studied - total cholesterol, low and very low density lipoproteins, high-density lipoproteins, triglycerides, atherogenic coefficient. The reference group consisted of 48 practically healthy individuals. The obtained data were processed by parametric and non-parametric statistics. The compared groups were the same in terms of age and sex, the level of arterial damage, the duration of arterial damage and the duration of the development of critical ischemia, the nature and volume of generally accepted conservative treatment in the perioperative period.

Results: Upon admission to the clinic, a sharp violation of lipid metabolism was revealed - dyslipidemia: a significant increase in the pro-atherogenic fraction ($p = 0,023-0,004$) a significant decrease in the anti-atherogenic fraction ($p = 0.0005$) of the lipid spectrum. At the end of in patient treatment, patients of the control group observed an unreliable ($p = 0,322-0,066$) correction of dyslipidemia. In the main group, before discharge from the hospital, a significant decrease ($p = 0,003-0,000007$) of proatherogenic fractions and an increase ($p = 0,0038$) of the antiatherogenic fraction were detected. Correlation-statistical analysis revealed a significant dependence ($p < 0.001$) of lipid spectrum correction on the method of treatment in the perioperative period with a pronounced correlative relationship ($r = 0.6-0.7$).

Conclusion: The obtained data make it possible to assert that the use of intravenous laser irradiation of blood and cytokine therapy with a recombinant interleukin-2 preparation in the perioperative period with revascularizing osteotrepanation with intramedullary laser irradiation significantly levels the studied parameters of lipid metabolism, except for total cholesterol.

Keywords: Critical Lower Limb Ischemia; Lipid Metabolism; Revascularizing Osteotrepanation with Intramedullari Laser Irradiation; Intravenous Laser Irradiation of Blood; Cytokine Therapy

Introduction

Chronic obliterating diseases of the arteries of the lower extremities account for more than 20% of all types of cardiovascular diseases, which corresponds to 2-3% of the total population [1]. According to the largest national registries, the incidence of critical lower limb ischemia (CLLI) reaches 150 new cases per 100,000 population per year [2]. Altin., *et al*. [2] analyzed the results of 1,276,745 hospitalizations for CLLI in the United States between 2012 and 2015. In 29% of cases, the age was less than 66 years, in 56% of cases 66-85 years, and another 15% of patients were over 85 years old. Patients with CLLI represent the most difficult population for medical, surgical, and endovascular treatment. The prevalence of CLLI in the U.S. is estimated to be about 2 million. Hospitalization of CLLI patients is common, and up to 60% of them are readmitted within 6 months [3].

Lipid metabolism disorders and modification of low-density lipoproteins, endothelial dysfunction, immune and inflammatory processes play an important role in the pathogenesis of CLLI. Hyperlipidemia, as well as other risk factors that increase oxidative stress (the formation of reactive oxygen species), cause the accumulation of oxidized low-density lipoproteins, which is the first step in the development of atherosclerosis [4-6].

In recent years, statins have been widely used to correct lipid metabolism disorders, non-drug methods such as plasmapheresis, ultraviolet irradiation of blood, intravenous laser irradiation of blood [7-12].

The purpose of the study

To study the state of lipid metabolism and the possibility of its correction in patients with CLLI during revascularizing osteotrepanation with intramedullary laser irradiation using intravenous laser irradiation and cytokine therapy in the perioperative period.

Material and Methods of Research

The studies were carried out in 65 patients with critical lower limb ischemia of atherosclerotic and thromboangiitic genesis aged 31 to 74 years. The study was approved by the Ethics Committee of the Scientific Center of Surgery. M.A. Topchubashova and the written consent of patients. (27 March 2004, protocol No. 3). Doppler ultrasound and multispiral computed tomography angiography diagnosed distal arterial lesions in all patients. In 34 patients in the perioperative period with indirect revascularization (lumbar sympathectomy, revascularizing osteotrepanation, lumbar sympathectomy + revascularizing osteotrepanation), conventional conservative treatment (control group) was performed. The age of the patients was 62.7 ± 9.6 years. In 31 patients with revascularizing osteotrepanation with intramedullari laser irradiation in the perioperative period, intravenous laser irradiation of the blood + cytokine therapy with recombinant interleukin-2 (rIL-2) - the drug Roncoleukin was used in conjunction with conventional therapy (main group). The dosage of the drug was similar in patients in this group. The age of patients in this group was 61.4 ± 8.9 years. Intravenous and intramedullary laser irradiation was carried out with the Mustang 2000 and Mustang 2000+ devices in the following parameters: for intravenous laser irradiation, the wavelength of laser beams is 0.63 μm, the power of laser radiation at the end of the quartz light guide is 5 mW, and the laser exposure is 30 min [13]. A disposable sterile nozzle (240 ± 20) mm with a needle for a set of products for low-intensity laser radiation KIVL-01 was used for VLOC. A laser light guide was inserted into the cubital vein. For intramedullary laser irradiation, the nozzle of the same name was also used: two light guides (sterile) were inserted through 2 upper osteotrepanation holes into the medullary canal and fixed for laser irradiation in the postoperative period. The wavelength of laser beams is 0.63 μm, the power of laser radiation at the end of the quartz light guide is 1.5-2 mW, the exposure to laser irradiation is 15 min. For cytokine therapy, 1 ml (1000000 IU) of Roncoleukin (BioTech, St. Petersburg) was injected subcutaneously into both shoulders at 3-day intervals.

The state of lipid metabolism in patients with CLLI and the possibility of its correction during operations with revascularizing osteotrepanation with inutriosteromarrow laser irradiation using VLOK and CT in the perioperative period were studied. (total cholesterol – TX, low-density lipoproteins – LDL, very low-density lipoproteins – VLDL, high-density lipoproteins – HDL, triglycerides – TG, atherogenic coefficient – AC). The obtained results were compared with identical parameters of 48 practically healthy individuals (reference group).

The results of the research were processed on a personal computer using the Excel 2010 program and processed with the help of the analytical program SPSS Statistics. M ± m, t, p, and χ2, p, and r were <determined.

The Results obtained and their Discussion

Upon admission to the clinic, severe dyslipidemia was detected in both groups. The compared groups were similar in age and sex, the level of arterial damage, the duration of arterial damage and the duration of the development of critical ischemia, in the nature and extent of generally accepted conservative treatment in the perioperative period.

In comparison with the reference group, patients in the control group had an increase in TX by 29.9% (t = 2.30; p = 0.0241), LDL by 70.2% (t = 5.06; p = 0.000003), VLDL by 109.6% (t = 6.34; p = 0.000000), TG by 93.4% (t = 6.32; p = 0.000000), AC by 85.0% (t = 4.97; p = 0.000004) and a decrease in HDL by 35.8% (t = 3.60; p = 0.000559). Before discharge from the hospital, a repeated study of the lipid spectrum revealed a moderate insignificant improvement in the studied parameters. As a result, there was a decrease in TX by 4.9% (t = 0.43; p = 0.668147), LDL by 6.8% (t = 0.65; p = 0.519034), VLDL by 11.1% (t = 1.13; p = 0.263104), TG by 4.5% (t = 0.52; p = 0.602503), AC by 3.1% (t = 0.28; p = 0.779734) and an increase in the level of antiatherogenic HDL by 11.5% (t = 1.00; p = 0.322681) (Table 1 and Diagram 1).

Study Groups Parameters	Reference group n = 48	Control group n = 34			
		Before Treatment	After Treatment		
TX (mmol/L)	3,94 ± 0,28	5,12 ± 0,43	4,87 ± 0,39	t = 0,43	p = 0,668
LDL (mmol/L)	2,42 ± 0,17	4,12 ± 0,29	3,84 ± 0,32	t = 0,65	p = 0,519
VLDL (mmol/L)	0,52 ± 0,04	1,09 ± 0,08	0,97 ± 0,07	t = 1,13	p = 0,263
HDL (mmol/L)	1,62 ± 0,14	1,04 ± 0,08	1,16 ± 0,09	t = 1,0	p = 0,322
TG (mmol/L)	1,52 ± 0,12	2,94 ± 0,19	2,81 ± 0,16	t = 0,52	p = 0,602
AC (units)	2,67 ± 0,18	4,94 ± 0,42	4,79 ± 0,33	t = 0,28	p = 0,779

Table 1: Dynamics of the lipid spectrum in patients with critical lower limb ischemia in patients of the control group ((M ± m; t p).

Notes: TX– total cholesterol; LDL – low-density lipoproteins; VLDL – very low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; AC – atherogenicity coefficient.

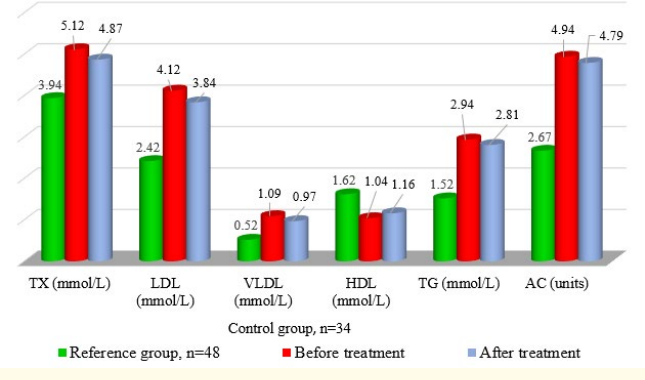

Diagram 1: Changes in lipid metabolism in control patients with critical lower limb ischemia.

Notes: TX – total cholesterol; LDL – low-density lipoproteins; VLDL – very low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; AC – atherogenicity coefficient.

In comparison with the reference group, the patients of the main group showed an increase in OCH by 28.2% (t = 2.32; p = 0.023137), LDL by 67.8% (t = 5.01; p = 0.000003), VLDL by 119.2% (t = 7.69; p = 0.000000), TG by 98.9% (t = 5.41; p = 0.000001), AC by 85.0% (t = 7.45; p = 0.000001) and a decrease in HDL by 35.8% (t = 2.94; p = 0.004252). In patients with CLLI during ROT with intramedullary laser irradiation (IMLI) with the use of intravenous laser irradiation of blood in the perioperative period +cytokine therapy with conventional treatment before discharge from the hospital A decrease in lipid spectrum was revealed during repeated examination of the lipid spectrum TX by 19.1% (t = 1.78; p = 0.080115), LDL by 34.0% (t = 4.08; p = 0.00126), VLDL by 48.2% (t = 6.82; p = 0.000000), TG by 45.7% (t = 4.90; p = 0.000007), CA by 33.6% (t = 3.61; p = 0.000620), and an increase in antiatherogenic HDL by 39.8% (t = 3.00; p = 0.003825) (Table 2 and Diagram 2).

Research Groups Parameters	Reference group n = 48	Main group n = 31			
		Before Treatment	After Treatment	t	P
TX (mmol/L	3,94 ± 0,28	5,09 ± 0,41	4,12 ± 0,36	1,788	0,080
LDL (mmol/L)	2,42 ± 0,17	4,06 ± 0,28	2,68 ± 0,19***	4,086	0,001
VLDL (mmol/L)	0,52 ± 0,04	1,14 ± 0,07	0,59 ± 0,04***	6,828	0,0000004
HDL (mmol/L)	1,62 ± 0,14	1,13 ± 0,09	1,58 ± 0,12**	3,00	0,0038
TG (mmol/L)	1,52 ± 0,12	3,02 ± 0,25	1,64 ± 0,13***	4,903	0,000007
AC (units)	2,67 ± 0,18	4,94 ± 0,40	3,28 ± 0,23***	3,61	0,00062

Table 2: Dynamics of the lipid spectrum in patients with critical lower limb ischemia in patients of the main group (M ± m; t p).

Notes:*- the difference between the values before and after treatment along the horizontal line is statistically significant** P < 0.01; P < 0,001).

TX – total cholesterol; LDL – low-density lipoproteins; VLDL – very low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; CA – atherogenicity coefficient.

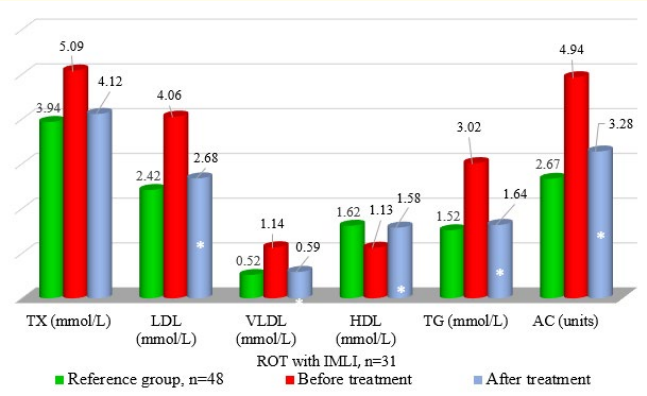

Diagram 2: Changes in lipid metabolism in patients of the main group with critical ischemia of the lower extremities.

Notes :*- the difference between the indicators before and after treatment within the group is statistically significant;

TX – total cholesterol; LDL – low-density lipoproteins; VLDL – very low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; CA – atherogenicity coefficient.

The obtained data indicate that the implementation of conventional drug treatment in the perioperative period without the use of VLOC + CT in patients with indirect revascularization in patients with CRC causes a partial improvement in lipid metabolism. And the use of intravenous laser irradiation of blood and cytokine therapy together with conventional conservative treatment in the perioperative period for 10-12 days in revascularizing osteotrepanation with intramedullary laser irradiation, in addition to the level of total cholesterol, causes a reliable correction of all other studied parameters of the lipid spectrum.

The dependence of the correction of lipid metabolism indicators on the treatment tactics in the perioperative period with indirect revascularization was studied. At the same time, it was revealed that, depending on the traditional method used with the use of IVLI and CT in the perioperative period, a significant correction of lipid spectrum indicators ($p < 0.001$) was observed in ROT with IMLI. . There is a pronounced correlation between the use of VLOC+CT in the perioperative period with ROT and correction of lipid metabolism (r = 0.6-0.7) (Table 3). Dyslipidemia in patients with atherosclerosis and critical lower limb ischemia has been observed by other researchers [3-6]. Studies by other authors [14-17] also revealed lipid metabolism disorders in patients with cardiovascular diseases and other pathologies and the leveling of these disorders with the use of intravenous laser therapy in complex treatment. However, a correlation and statistical analysis of the dependence of lipid metabolism correction on the applied complex measures has not been carried out.

Study Groups Parameters		Control group n = 34	Main group n = 31	
TX	Reduction	11	27	χ^2 = 20,011 p < 0,001 r = 0,6
	Unchanged	23	4	
VLDL	Reduction	12	25	χ^2 = 13,601 p < 0,001 r = 0,6
	Unchanged	22	6	
HDL	Upgraded	15	27	χ^2 = 13,101 p < 0,001 r = 0,6
	Unchanged	19	4	
TG	Reduction	14	27	χ^2 = 14,681 p < 0,001 r = 0,7
	Unchanged	20	4	

Table 3: Dependence of correction of some parameters of lipid metabolism on treatment tactics in the perioperative period with indirect revascularization (number of patients; χ2 ; p; r).

Notes: The main group is revascularizing osteotrepanation with intramedullary laser irradiation + conventional treatment + intravenous laser irradiation of the blood + cytokine therapy

TX – total cholesterol, VLDL – very low density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides

!!! This table shows the dependence of lipid metabolism correction on perioperative treatment in the study group.

The mechanisms of the antiatherogenic effect of laser therapy can be as follows. Under the influence of low-intensity laser radiation, an increase in antioxidant activity was noted, which reduces the ability of LDL to oxidize, and at the same time reduces the damaging effect of oxidized lipoproteins on the endothelium of the arteries. The stimulating effect of low-intensity laser radiation on lipoprotein lipase leads to an increase in oxidation and a decrease in the activity of fatty acid synthesis Since HMG-CoA reductase is also stimulated, there is no decrease in cholesterol in hepatocytes, which explains the increase in HDL. An increase in the receptor sensitivity of cells to lipoprotein lipase under the influence of laser therapy with a simultaneous increase in HDL stimulates the reverse transport of LDL to the liver, which is accompanied by a decrease in the content of triglycerides in the structure of lipoproteins [17]. The mechanism of the pathogenetic aspects of Roncoleukin's effect on the blood lipid spectrum needs further research.

Conclusion

The obtained data make it possible to assert that the use of intravenous laser irradiation of blood and cytokine therapy with the recombinant drug interleukin-2 (rIL-2) in the perioperative period during revascularizing osteotrepanation with intrabone marrow laser irradiation significantly neutralizes the studied parameters of lipid metabolism, except for total cholesterol.

Conflict of Interests

The authors declare that there is no conflict of interest in the submitted article.

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