DOI: 10.23934/2223-9022-2019-8-1-53-59

Low-intensive Laser Therapy for Management of Cerebral Dysfunction in Patients with Obstructive Jaundice of Non-tumor Origin

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BACKGROUND The liver's function is impaired above all others in the mechanical jaundice, which leads to the progression of endogenous intoxication and the damage of different organs and systems, including the brain. The development of hepatic encephalopathy undoubtedly aggravates the course of the disease, which requires its timely management.

AIM OF STUDY: to evaluate the efficacy of the low-intensity laser therapy when managing the cerebral dysfunction in mechanical jaundice of non-tumor origin.

MATERIAL AND METHODS A comprehensive study of 60 patients with obstructive jaundice of non-tumor origin was performed. The patients were divided into 2 groups: I (comparison) — the standard therapy (n=30); II (studied) group — inclusion of low-intensity laser irradiation of blood (n=30). On check dates (day 1 and 7), the severity of cerebral dysfunction was assessed in all patients using the psychometric tests ("Point in Circle, "Labyrinth"). The microcirculation was assessed with LACC 02 device (Russia). The coagulation/lysis system of blood was studied with TEG 5000 thrombelastograph (USA).

RESULTS In patients with obstructive jaundice, disorders of the functional state of the liver were noted, which resulted in the growth of total bilirubin, alanine and aspartic aminotransferases, and toxic products. All this was accompanied by cerebral dysfunction, which was shown by results of the psychometric study and extended performance of tests, in particular ("Point in Circle", "Labyrinth"). Significant changes and disorders of the hemostatic system were revealed in patients. The complex treatment of obstructive jaundice, which included laser therapy, allowed a relatively rapid recovery of the functional state of the brain to be observed, as evidenced by the shortening of the test time for the tests being studied. The positive effect of this kind of therapy was accompanied by a decrease in the severity of the syndrome of endogenous intoxication, improved microcirculation and hemostasis.

CONCLUSION The presence of pancreatic obstructive jaundice lead to the development of florid syndrome of endogenous intoxication, which was reflected in the growth of ALT, AST, amylase, and total bilirubin. During the entire period of the study, a decrease in studied blood parameters was observed in patients who had underwent low-intensity laser therapy sessions. Conducting a psychometric study in the initial periods revealed some violations, such as extended performance of tests ("Point in Circle", "Labyrinth").

Keywords: mechanical jaundice, laser therapy, cerebral dysfunction

For citation Vlasov A.P., Chigakova I.A., Timoshkin D.E., et al. Low-intensive laser therapy for management of cerebral dysfunction in patients with obstructive jaundice of non-tumor origin. *Russian Sklifosovsky Journal of Emergency Medical Care.* 2019; 8(1): 53–59. DOI: 10.23934/2223-9022-2019-8-1-53-59 (In Russian)

Conflict of interest Authors declare lack of the conflicts of interests

Acknowledgments The study had no sponsorship

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ALT — alanine aminotransferase
AST — aspartate aminotransferase
APTT— activated partial thromboplastin time
BI — bypass index
K — coagulation time
LDF — laser Doppler flowmetry
M — circulation index
MEI — microcirculation efficacy index
R — reactive time

INTRODUCTION

According to literary sources, obstructive jaundice constitutes from 47 to 88% of hepatopancreatoduodenal diseases complications [1–4]. At the same time, there is a steady upward trend in the indicated pathology [5-7]. With obstructive jaundice, the functional state of the liver suffers first, which leads to the progression of endogenous intoxication and, as a result, damage to various organs and systems, including the brain [8-10]. The development of hepatic encephalopathy certainly aggravates the course of the disease, which requires its timely management [11, 12]. In this regard, attention is drawn to the low-intensity laser irradiation of blood, which has a number of positive effects [13].

Objective: to evaluate the effectiveness of low-intensity laser irradiation of blood when managing cerebral dysfunction in obstructive jaundice of non-tumor origin.

MATERIAL AND METHODS

A comprehensive clinical, laboratory and instrumental examination of 60 patients with obstructive jaundice of non-tumor origin was performed. The cause of jaundice was acute pancreatitis. Criteria for inclusion in the study: the presence of clinical, laboratory and instrumental data to reliably diagnose obstructive jaundice of pancreatogenic origin; disease duration not more than 48 hours from initiation of the disease. Exclusion criteria: age over 70 and under 20; disease duration more than 48 hours; conducting surgery for emergency or urgent indications; the presence of severe pathology of other organs and systems. The patients were divided into 2 groups: I (comparison) where patients were given standard therapy (n=30); II (main) group where combined therapy included low-intensity laser irradiation of blood (n=30). Laboratory examination of patients was performed on day 2, 4, 6, 8, and 10. Psychometric tests were performed on day 1 and 7. All procedures were performed with the informed voluntary consent of patients to participate in the study in accordance with the international ethic requirements of the World Health Organization (*Good Clinical Practice* rules), imposed on medical research involving human patients (Geneva, 1993). The data used as a standard were obtained from 15 healthy volunteers of both genders (comparison group).

The surgery for obstructive jaundice was not performed. Patients received complex basic therapy, including infusion, antispasmodic, analgesic, antifermental, hepatoprotective components, etc. The Matrix device daily sessions were added in patients of the second clinical group for 10 days (registration certificate No. FSRR7) / 00589, certificate of conformity ROSS RU.AB35. D00082). The KLO3 head was used (radiation with a wavelength of 635 nm and a power of 2 mW). Transcutaneous laser irradiation of blood through tight pressing the output window of the laser emitter in the projection of cubital vein at the elbow for 15 min was performed, then in the projections of carotid arteries (carotid sinus area) and vertebral arteries (suboccipital area on CI-CII level) for 5 minutes in each area on both sides.

Psychometric research in all studied patients included an assessment of the severity of cerebral dysfunction using psychometric tests ("Point in Circle", "Labyrinth"). To establish the severity of jaundice and the functional state of the liver, a number of routine indicators (total bilirubin level, transaminase activity) were determined. Endogenous intoxication was assessed by definition of hydrophilic (medium weight molecules) (O.I. Pikuza, L.Z. Shakirova, 1994) and hydrophobic (total and effective albumin concentration with subsequent calculation of albumin binding potential and albumin toxicity index) (Y.A. Gryzunov, G.E. Dobretsov, 1998) toxicity. The state of microcirculation was assessed using the LAKK–02 laser diagnostic complex (Russia). The LDF was performed for 7–10 min at the *VB*–18 point located on the gall bladder meridian.

Evaluation of the state of the coagulation and lytic system of the blood was assessed using the *TEG*® 5000 *Thrombelastograph® (USA)* and routine laboratory tests (activated partial thromboplastin time (APTT) and fibrinogen). The obtained digital data were processed by the method of variation statistics using the Student's t-test and the *Microsoft* software package *Office* 2007.

RESULTS

A psychometric study revealed significant abnormalities in patients with obstructive jaundice in both groups. Two tests were performed. The first one determined the rate of cognitive activity (Labyrinth), where a patient had to hold the line without touching the walls of the labyrinth, guided by the direction of the arrow. The time spent to pass the test was estimated. When performing the test “Point in Circle,” a patient was asked to put a dot in the center of the circle. This action should be repeated 100 times.

According to the “Point in Circle” test (Table 1), patients of group I showed a slowdown in the cognitive function of the brain, which was expressed in the lengthening of the test time. So, 1 and 7 days later, it exceeded the normal values by 65.15 and 46.39% (p<0.05). In patients with laser therapy (group II), the time lengthened by this test by 73.11 and 21.26% (p<0.05) was also noted. However, 7 days later it was 17.16% shorter than in the comparison group (p<0.05), statistically significant in all 3 cases.

Table 1

The dynamics of tests results in the course of treatment

Tests	Normal values	Groups	Day of observation	
			1	7
Point in Circle	36.45±3.89 sec	I	60.20±6.25*	53.36±3.23*
		II	63.10±3.64*	**44.20±3.62***
Labyrinth	33.20±2.56 sec	I	58.25±5.23*	44.0±2.40*
		II	60.10±3.20*	**35.20±3.10**

Notes: * — significant difference of a parameter related to the normal value (p<0.05); bold — significant values related to the control group (p<0.05)

When assessing the “Labyrinth” test, the violation of constructive apraxia was noted, characterized by disturbed ability to draw or construct objects from various elements. The study revealed that in the initial terms in patients of I group, there was an excess of the test execution time in relation to the norm by 75.45% (p<0.05). Seven days later, in patients of this group, the excess of the test execution time was 32.53% (p<0.05). In group II of patients, the test execution time was also exceeded by 81.02% (p<0.05) on day 1, which corresponded to its values in the comparison group. It is worth noting that at the final stage (day 7) in patients of this group the test result closely approached the normal value. At the same time, in relation to the data in the comparison group, it was less by 30.10% (p<0.05), statistically significant in all the indicated comparisons. According to N. Shomerus et al. (1981), tests for the ability to move along the line are interesting because they give an idea of the patient's ability to navigate the terrain.

In the comparison group (Table 2), there was a significant statistically significant growth of the total bilirubin values compared with the norm from 4.7 to 12 times (p<0.05). In the main group, in the initial periods, it also statistically significantly exceeded the normal values by more than 12 times (p<0.05) with laser therapy, there were significant positive changes in this indicator: after 8 days of laser therapy, the excess compared to the norm was still 4.8 times (p<0.05) and was statistically significantly different, but at the same time its statistically significant decrease by 41.0% (p<0.05) was revealed relative to the data of the comparison group.

Table 2

The dynamics of bilirubin concentration and enzymes activity in blood plasma in the course of treatment

Parameter	Normal value	Group	Day of observation				
			2	4	6	8	10
Total bilirubin,mcM/l	10.25±0.51	I	150.72±7.49*	127.18±6.35*	100.17±4.98*	83.15±4.02*	64.86±3.23*
		II	149.45±7.47*	**98.15±5.07***	**71.52±3.52***	**49.42±2.48***	**25.01±1.26***
ALT, u/l	25.12±1.25	I	129.17±6.41*	103.22±5.1*	74.13±3.61*	41.23±2.03*	34.71±1.78*
		II	115.19±5.57*	98.82±4.99*	**61.02±3.73***	36.18±1.84*	**29.98±1.48***
AST, u/l	24.36±1.24	I	147.20±7.14*	113.34±5.56*	75.58±3.25*	42.25±2.01*	37.45±1.64*
		II	137.46±6.97*	109.01±5.62*	**64.09±3.33***	38.52±1.85*	34.28±1.71*
Amylase, u/l	75.0±3.75	I	540.02±21.52*	371.05±16.12*	213.04±10.07*	142.14±7.13*	81.24±4.02
		II	**453.47±23.06***	**302.61±15.29***	**176.58±7.91***	**124.11±6,22***	74.15±3.73

Notes: * — significant difference of a parameter related to the normal value (p<0.05); bold — significant values related to the control group (p<0.05). ALT — alanine transferase, AST — asparagine transferase

During the study, patients in the comparison group showed a significant statistically significant increase in the ALT activity values in the entire study period within 38.1–414.2% relative to the norm (p<0.05). In the main group, the ALT value from day 2 to day 10 was also statistically significantly higher than normal figures by 19.34–358.6% in the course of laser therapy (p<0.05). It should be noted that the activity of ALT in this group on day 2 and 4, corresponded values of the control group. However, from day 6 to 10, this figure remained statistically significantly higher than in the comparison group by 12.2–17.7% (p<0.05).

Patients of group I at all stages of observation had a statistically significant increase in AST activity by 49.8–488.8% (p<0.05). Patients in group II also had a statistically significant increase in AST values of 37.1–464.3% (p<0.05). At the same time, on day 2, 4, 8 and 10 they corresponded to the values in the comparison group, and on day 6 they were statistically significantly lower than the corresponding indicator by 14.1% (p<0.05) .

It was noted that in the I group of patients the blood alpha-amylase value was higher than the normal values throughout the observation period by 89.5–620% (p<0.05). In the final examination dates (day 10), this indicator was close to normal. In the course of laser therapy, alpha-amylase activity was also increased in patients of group II. So, it was statistically significantly higher than the normal value by 65.48–504.6% (p<0.05) by day 8 and only on day 10 it began to correspond to its values. In group II, on day 2, 4 and 6, the level of amylase was statistically significantly lower than its values in the comparison group, respectively, by 16.0, 17.1 and 12.7% (p<0.05).

In the examined patients, we revealed statistically significant increase in blood toxicity associated with the presence of toxic products, of both hydrophilic (by 45.3–112.2%, p<0.05) and hydrophobic (by 37.4–89.1 %, p<0.05) type. At the same time, the syndrome of endogenous intoxication persisted until day 10, even when laser therapy was included into the treatment. However, at all stages of the observation period, starting from the 4th day, a statistically significant decrease in the amount of toxic products in the blood plasma in relation to the comparison group by 14.3–26.2% (p<0.05) was observed. Thus, the level of medium molecules at λ= 280 nm (0.502 ± 0.018 units) in the comparison group after 4 days was statistically significantly different from that in the main group by 9.6% (0.454±0.014 units, p<0.05). This kind of dynamics was preserved 10 days later: the content of medium molecules with their general decrease in the comparison group was 0.417±0.016 units, whereas in the main group it was statistically significantly lower by 9.8% (p<0.05), amounting to 0.371±0.011 units. Effective albumin concentration after 4 days of combined therapy increased to 33.12±1.18 g/l, whereas in comparison group it was substantially and statistically significantly lower by 10.1% and was 29.12±0.82 g/l (p<0.05). Ten days later, this indicator increased to 42.47±2.02 g/l in the main group, which was statistically significantly higher compared to the data of the comparison group by 10.7% (p<0.05), which was 38.42±1.87 g/l.

When assessing the hemostasis system (Table 3) it was found that in patients of group I, the value of R (reactive time), an indicator that determines the blood coagulation period and characterizes the 1-2 phase of coagulation, it was statistically significantly reduced relative to the norm from day 2 to day 6 by 62.90, 40.60 and 21.80% (p<0.05), respectively. In the final study dates (day 8 and 10), the value of this indicator corresponded to the norm. In group II, patients also had a statistically significant excess of the values of R in relation to the norm from the 2nd to the 4th day by 59.39 and 32.33% (p<0.05). However, on day 6, 8 and 10, the value of this indicator corresponded to the values of the norm. When analyzing the data of hemostasis in patients of group II, the values of R correspond to such values in the comparison group on day 2, 6, 8, and 10, but were statistically significantly higher on day 4 of the study by 13.9% (p<0.05).

Table 3

The dynamics of hemostatis parameters in the course of treatment

Parameter	Normal values	Group	Day of observation				
			2	4	6	8	10
R, mim	3.99±0.29	I	1.48±0.07*	2.37±0.11*	3.12±0.15*	3.67±0.17	3.94±0.21
		II	**1.62±0.06***	**2.70±0.14***	**3.69±0.14***	3.79±0.19	3.97±0.20
K, mim	1.81±0.11	I	0.59±0.04*	1.02±0.05*	1.55±0.08*	1.63±0.09	1.78±0.09
		II	**0.90±0.07***	**1.35±0.12***	1.59±0.09*	1.76±0.08	1.82±0.09
α, deg	55.06±0.44	I	71.04±3.41*	67.02±1.78*	60.93±2.64	56.31±2.57	51.12±2.7
		II	67.11±3.39*	**61.25±2.12***	58.12±2.03	56.01±2.13	53.99±1.98

Notes: * — significant difference of a parameter related to the normal value (p<0.05); bold — significant values related to the control group (p<0.05). R — reactive time; K — time of clot formation; α — angle showing fibrinogen concentration in plasma

When analyzing the parameter *K*, the time of clot formation (coagulation time, thrombin constant), which characterizes the 3rd phase of blood coagulation, it was noted that in patients of group I, its value was statistically significantly lower than normal from day 2 to day 6 by 44.6–67.4% (p <0.05). At the same time in group II, a statistically significant decrease in *K* compared with the norm by 14.4–50.3% (p<0.05) was found. In the subsequent periods of the survey (day 8 and 10), the value of this indicator was within the normal range. In a comparative analysis of data in patients of group II, the value *K* on day 2 and 4 statistically significantly exceeded the values of the comparison group by 80.0 and 32.35% (p<0.05), respectively, and almost corresponded their values from day 6 to day 10.

The values of the indicator α-angle (characterizing the level of fibrinogen in plasma) in patients of group I increased statistically significantly by day 2 and 4 by 29.0 and 21.7% (p<0.05). In the subsequent survey dates (day 6, 8 and 10), the indicator corresponded to the normal values. In patients of group II, they statistically significantly increased by day 2 and 4 by 21.9 and 11.2% (p<0.05), respectively. By day 6, the value α- the angle corresponded to the normal values. Throughout the study period, the values of this indicator in patients of group II essentially corresponded to the values of the comparison group, with the exception of day 4, when this indicator was statistically significantly lower by 8.6% (p<0.05).

The effect of laser therapy on the hemostatic system was also indicated by the results of biochemical tests. Thus, in the comparison group, the APTT value was statistically significantly shortened relative to the norm on day 2 and 4 by 13.43 and 10.12% (p<0.05), respectively, while using combined therapy during these periods — only by 8.31% (p<0.05, statistically significant) and 5.23% (p>0.05), respectively. On the background of low-intensity laser therapy, positive changes in the content of fibrinogen in the blood plasma occurred. In the comparison group, its level increased by 12.3–22.9% (p<0.05) within 6 days, whereas in the main group of patients it increased only by 8.27–16.2% (p<0,05, statistically significant).

Regarding the state of microcirculation (Table 4), it should be noted that in patients of group I, the indicator of microcirculation (M) within the first 6 days was statistically significantly reduced by 13.5-26% (p<0.05). In the subsequent stages of observation (day 8 and 10) it was restored and on the 10th day it corresponded to the normal value. In patients of group II, less significant microcirculation disorders were noted in the course of laser therapy. Significant changes in the studied indicator were noted only within first 4 days, when its values were statistically significantly lower than the norm by 23.0 and 14.5% (p<0.05), respectively. In the period from day 8 to day10, M was normal. A comparative assessment established a significant effect of laser therapy on this indicator 4, 6 and 8 days later, when its values were statistically significantly higher than in the comparison group by 13.9, 10.0 and 11.9% (p<0.05).

Table 4

The dynamics of microcirculation parameters in the course of treatment

Parameter	Normal value	Group	Day of observation				
			2	**4**	**6**	**8**	**10**
M, perf. units	6.12±0.13	I	4.53±0.19*	4.59±0.15	5.30±0.17*	5.46±0.15*	6.02±0.24
		II	4.71±0.15*	**5.23±0.21***	**5.83±0.13***	**6.11±0.09**	6.19±0.08
MEI	1.32±0.07	I	0.70±0.08*	0.86±0.07*	0.99±0.03*	1.17±0.04*	1.29±0.02
		II	0.75±0.09*	0.92±0.06*	**1.15±0.04***	**1.31±0.05**	1.35±0.03
BI	1.14±0.05	I	1.31±0.05*	1.38±0.04*	1.33±0.03*	1.21±0.03	1.16±0.02
		II	1.29±0.08*	**1.28±0.03***	**1.24±0.05**	**1.15±0.03**	1.15±0.03

Notes: * — significant difference of a parameter related to the normal value (p<0.05); bold — significant values related to the control group (p<0.05). BI — bypass index; M — microcirculation index; MEI — microcirculation efficiency index

Values of efficiency microcirculation index (MEI), which characterizes the ratio of passive and active mechanisms regulation of microcirculation, were statistically significantly below normal figures in patients of group I from day 2 to day 8 by 11.4-47.0% (p<0.05). On day 10, this indicator became normal. In the course of laser therapy, a statistically significant decrease in the values of this indicator by 12.9–43.2% (p<0.05) was also noted at the first three control stages. In relation to the comparison group, a significant effect of laser therapy was detected 6 and 8 days later, when the MEI values were higher by 16.2 and 12.0%, respectively.

The values of the bypass index (BI) reflecting the degree of bypass and ischemia, were statistically significantly increased in the comparison group on day 2, 4 and 6 by 14.9–21.1% (p<0.05). In the subsequent study dates (day 8 and 10), this indicator was normal. In the course of complex (with laser therapy) treatment, a statistically significant increase in BI was diagnosed only in the first two stages of observation (day 2 and 4), when it was respectively increased by 13.2 and 12.3% (p<0.05). The value of BI significantly decreased and corresponded to those in the comparison group (p<0.05) 4 and 6 days later.

CONCLUSION

The findings of the psychometric study confirm the development of latent encephalopathy in patients with mechanical jaundice. In its pathogenesis, the development of endogenous intoxication is significant, and, as our studies have shown, significant microcirculation and hemostasis system disorders, caused by acute pancreatitis. Standardized therapy reduces the severity of diagnosed disorders. The improvement of therapy efficacy occurs with complex treatment using low-intensity laser irradiation. This kind of therapy allows to manage microcirculation hemostasis system disorders, and accordingly, reduce the severity of endogenous intoxication. It should be noted that complex therapy including laser sessions improves the clinical course of obstructive jaundice. In particular, a statistically significant reduction in the length of stay of patients in the hospital from 22.8±0.8 to 19.3±1.1 days (p<0.05) was noted.

FINDINGS

1. In case of mechanical jaundice of non-tumor origin, the development of hepatic encephalopathy is accompanied not only by significant endotoxicosis, but also by significant impairments of microcirculation and coagulation-lytic changes.

2. The use of low-intensity laser irradiation of blood reduces the severity of hepatic encephalopathy, based on its ability to reduce the severity of endogenous intoxication by improving microcirculation and managing the state of the coagulation-lytic system.

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Received on 07.11.2018

Accepted on 28.11.2018