

LASER THERAPY FOR MANAGEMENT OF CEREBRAL DYSFUNCTION IN CASES OF ACUTE SEVERE PANCREATITIS.

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Abstract:

Background. A persistently high mortality rate of patients with pancreatitis is the result of multiple organ failure which is in many aspects associated with developing endogenous intoxication. Pancreatic encephalopathy is one of particular manifestations of this syndrome.

Aim of study: to determine severity of cerebral dysfunction in cases of acute destructive pancreatitis, to assess the efficacy of laser therapy for this disease.

Material and methods: The research is based on the results of clinical studies, carried out at the Republican Clinical Hospital No.3. Clinical laboratory analysis of 60 patients was conducted. The patients were randomly split into two equal groups: the comparison group (standard therapy) and the basic group (standard therapy and laser therapy). The patients were examined upon admission to hospital and in dynamics (day 1, 3, 5, and 7). The severity of cerebral dysfunction was assessed within controlled terms with the help of RASS and psychometric tests: Number Connecting Tests (A and B), "Point in circle", "Labyrinth", test of symbols and numbers. The level of endogenous intoxication was evaluated by the amount of hydrophilic (medium mass molecules) and hydrophobic (common and effective albumin concentration) component.

Results. Acute severe pancreatitis led to a marked endogenous intoxication, which manifested itself as an increase in medium molecular weight peptides, decrease in common and effective albumin concentration, growth of toxicity index with regard to normal indices. During all research period the basic group (laser therapy) there was a decrease in medium molecular weight peptides, significant increase in common and effective albumin concentration and a decrease in index toxicity. Psychometric tests revealed a number of deviations from normal indices. At the beginning of the research, a reliable prolongation of time interval during examination tests (Number Connecting Test B, "Point in Circle", "Labyrinth") was noted, and less cells were filled during symbol and number test with regard to normal indices. The subsequent analysis of psychometric tests of patients from the basic group revealed a shortening of time interval during Number Connecting Test block B, "Point in circle" and "Labyrinth". More filled cells during symbol and numbers test were also observed.

Conclusion. Results of psychometric tests confirmed latent encephalopathy during endogenous intoxication, associated with acute severe pancreatitis. The laser therapy as a component of complex treatment promotes to decrease severity of endogenous intoxication and manifestation of encephalopathy.

Key words: pancreatitis, laser therapy, cerebral dysfunction, endotoxemia.

ECA – effective concentration of albumin

IT – index of toxicity

MMMs – medium mass molecules

NCT – Number Connecting Tests

PC – "Point in the Circle" test

TCA – total concentration of albumin

RABS – reserve albumin binding capacity

RASS – Richmond Agitation-Sedation Scale

INTRODUCTION

Despite introduction of new diagnosis and treatment methods, mortality of acute pancreatitis remains stably high and reaches 30% [1, 2]. Such high figures are largely associated with the development of systemic inflammatory response and multiple organ failure. One of the particular manifestations of this syndrome is pancreatic encephalopathy, associated with a higher level of mortality of patients [3]. Despite the fact that more than 70 years have passed since the description of pancreatic encephalopathy [4], there is still no clear idea of its pathogenesis [5, 6]. Some authors point

hyperactivation of phospholipase A₂ and activation of lipid peroxidation in this process [7].

The methods which increase oxygen saturation and inhibit lipoperoxidation allow the severity of encephalopathy to be reduced [8, 9]. Laser therapy, in particular, low-intensity laser irradiation of blood, has a significant antioxidant potential and has proved itself in the treatment of various diseases [10, 11]. We expressly indicate the economic effect of laser therapy as the use of this technique allows to shorten the duration of treatment in a hospital and thereby save state budget funds at least by 20-30% [12].

Aim of study: to establish the severity of cerebral dysfunction in acute destructive pancreatitis; to evaluate the efficacy of laser therapy for this disease.

MATERIAL AND METHODS

The work is based on data from a study conducted on the basis of the Republican Clinical Hospital No. 3. Criteria for inclusion in the study: the availability of clinical, laboratory and instrumental data that allow reliable diagnosis of acute severe pancreatitis; duration of the disease not more than 48 hours at the time of admission. Exclusion criteria: age over 70 and under 20; the duration of the disease more than 48 hours; the surgical operation according to urgent indications; presence of severe combined pathology.

Clinical and laboratory examination of 60 patients was conducted. Surgical intervention for acute severe pancreatitis was not performed. Patients were randomized into two equal groups: comparison group (standard therapy) and main group (laser therapy in addition to standart treatment).

The examination of patients of all groups was performed upon admission and over time (day 1, 3, 5, and 7). Scientific developments were carried out with informed consent of patients in accordance with international moral requirements of the World Health Organization (*Good Clinical Practice* rules) for medical research involving human subjects (Geneva, 1993). To obtain data that are accepted for the physiological norm, relevant studies were carried out in 14 healthy volunteers of both gender.

Patients received complex therapy, in accordance with standard algorithms of treatment for this pathology, including antibacterial, infusion, antispasmodic, analgesic and anti-enzymatic drugs.

In patients of the second clinical group (main), in addition to basic therapy for 10 days, daily laser therapy sessions were performed with the Matrix device (registration certificate No. FSR 2007/00589, certificate of compliance with ROSS RU.AB35.D00082). The radiating head KLO3 (wavelength 635 nm, power 2 mW) was used. Transcutaneous laser irradiation of the blood was performed by tightly pressing the exit window of the laser radiator in the projection of the cubital vein in the elbow fold for 15 min, then in the projection of the carotid (sinocarotid zone) and vertebral arteries (suboccipital zone, CI-CII level) for 5 min on each area from two sides.

In the control periods (day 1, 3, 5, and 7), the severity of cerebral dysfunction was assessed in all observed patients by evaluating the neurological status, *RASS* (*Richmond Agitation-Sedation Scale*), psychometric testing (Number Connecting Tests block A and B, "Point in Circle", "Labyrinth", symbolic and numerical tests). The endogenous intoxication was assessed by the level of hydrophilic toxic products (medium mass molecules, MMM) and hydrophobic substances (by the total and effective concentration of albumin). The total (TCA) and the effective (ECA) concentration of albumin in the blood serum were determined by the fluorescence method using the specialized analyzer AKL-01 "Zond". A set of reagents "Zond-Albumin" (Moscow) was used in according with instructions (G.Y. Dobretsov, 1992). The reserve albumin binding capacity (RABC) was then calculated: $RABC = ECA/TKA$ and plasma toxicity index (IT): $IT = TKA/ECA - 1$; (Y.A. Gryzunov, G.E. Dobretsov, 1994). MMMs were calculated according to the following procedure. The blood serum was mixed with a 10% solution of trichloroacetic acid in a ratio of 1:2 and centrifuged for 30 minutes at a rate of 3000 rotations per min. Then 0.5 ml of the supernatant was mixed with 4.5 ml of distilled water and the optical density was measured on SF-46 spectrophotometer at wavelengths 254 and 280 nm (O.I. Pikuza, L.Z. Shakirova, 1994). To determine the severity of the disease, the *APACHE-II* scale was used.

The obtained digital data was processed by the variational statistics method using the Student's test. Calculations were performed on *CPU 3, 10 GHz Intel® Core™ i3-2100* using the *Microsoft Office 2007* software package.

When patients arrived, the diagnosis of "acute severe pancreatitis" was based on clinical, laboratory and instrumental methods. When assessing the severity of the disease on the *APACHE-II* scale, it turned out that when examining the signs of the disease, the sum of scores in patients of the first group was 10.3 ± 0.2 , and 11.2 ± 0.3 in the second group. This indicated severe pancreatitis.

It was revealed that there were more men among patients with acute pancreatitis than women, in both groups patients of working age (20-40 years) prevailed. The first group ($n=30$) consisted of patients aged 32 to 63 years (53.1 ± 6.4), of whom 23 were male patientd (76.7%), and 7 (23.3%) were female. The second group ($n=30$) included patients aged 30 to 65 years (56.9 ± 7.1), of whom 25 were male patients (83.3%), and 5 (16.7%) were female patients.

In the major part of patients one or two days passed from the time of the first clinical manifestations to initiation of inpatient treatment.

Neurological status evaluation revealed no abnormalities in 28 patients (93.33%) of the comparison group and 29

patients (96.67%) of the main group. One patient (3.85%) of the comparison group had attack-like burning pain in the left cheek, painful palpation of the exit point of the second branch of the trigeminal nerve (left-sided trigeminal neuralgia during the last 3 years in the anamnesis). One patient (3.85%) has hyperesthesia in the innervation region of *n. cutaneus femoris anterior* due to previously experienced neuropathy of the above nerve. In 1 patient (3.85%) of the main group, bilateral horizontal large-scale nystagmus was observed (congenital, according to the patient, no dizziness or ataxia).

RESULTS AND DISCUSSION

Acute severe pancreatitis led to significant endogenous intoxication. In relation to indicators of healthy volunteers (concentration of MMM ($\lambda=254$ nm) was 252.6 ± 10.84 standard units, the concentration of MMM ($\lambda=280$ nm) was 325.6 ± 12.4 units), in the comparison group, the concentration of medium-molecular peptides determined at a wavelength of 254 nm statistically significantly exceeded the norm by 26.2-122.9% ($p < 0.05$), and by 38.3-89.3% ($p < 0.05$) for a wavelength of 280 nm. The progressive increase in the concentration of MMM was noted starting from day 3, and figures didn't became normal against the background of standard therapy at the final stage of the study.

The concentration of hydrophobic toxic metabolites in the blood plasma was assessed by TCA and ECA in blood plasma, as well as by IT. In the group of healthy volunteers, the parameters of TCA, ECA and IT, respectively, were 52.1 ± 2.5 g/l, 45.4 ± 2.2 g/l and 0.15 ± 0.01 standart units.

In the comparison group, a statistically significant decrease in TCA by 17.5-39.4% ($p < 0.05$) was found, ECA was lower normal figures by 43.7-64.5% ($p < 0.05$) and IT was increased by 11.7-14.2 times ($p < 0.05$) with respect to normal indicators.

During the entire study period, the concentration of MMM ($\lambda=254$ nm) in the main group was statistically significant by 9.1-22.1% ($p < 0.05$), and the concentration ($\lambda=280$ nm) was lower than in the comparison group by 13.3- 21.2% ($p < 0.05$) At the end of the studies in the main group, the titer of medium-molecular weight peptides ($\lambda=254$ nm and $\lambda=280$ nm) did not statistically significantly differ from the norm.

Comparing the results of the studies in the comparison group and the main group, we identified the notable difference between the studied indices of endogenous intoxication (Fig. 1). In the group receiving laser therapy, TCA increased by 16.3-29.4% ($p < 0.05$), ECA grew by 28.9-82.7% ($p < 0.05$) relative to the comparison group. In this group of patients, IT was also lower than in the ECA comparison group by 37.6-65.4% ($p < 0.05$); all these differences were statistically significant.

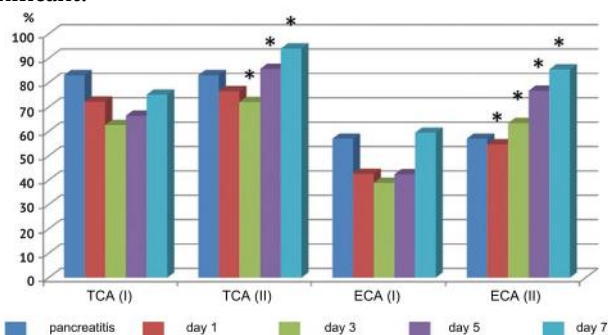


Fig. 1. The dynamics of total and effective concentration of albumin in the main group and the comparison group (the established norm is assumed to be 100%, I – the data of the comparison group, II – the data of the main group, * – the reliability of the difference in the indices relative to the comparison group, $p < 0.05$).

Thus, the use of supravascular laser irradiation of blood allowed the severity of endogenous intoxication to be reduced.

The duration of inpatient treatment of patients with acute pancreatitis in the comparison group was 15.5 ± 0.7 days. The stay of patients in the main group in the hospital was 13.7 ± 0.8 bed days, which was less by 12.9% compared to the comparison group ($p < 0.05$).

When examining patients with acute severe pancreatitis using the RASS scale, one or another degree of impairment at the time of admission was detected in 4 patients (13.3%) of the comparison group and in 5 (16.7%) patients of the main group. A study of the RASS indicator in dynamics revealed that the maximum number of patients with impaired consciousness was observed on the 3rd day of observation: in the main group and in the comparison group there were 8 patients (26.7%) who scored minus 1 or less according to RASS. It should be pointed out that starting from day 5 in the group of patients receiving low-intensity laser blood irradiation in addition to standard therapy, there were no patients who scored RASS minus 3 points. In the comparison group receiving standard therapy, on the 5th day of treatment, 1 patient (3.3%) scored minus 3 points on the RASS scale.

The psychometric study revealed some deviations from normal indices. Patients who scored minus 2 and minus 3 (RASS) during the study were not tested (in the comparison group, a psychometric study was not performed in 5 patients (16.7%), and in 4 patients (13.3%) in the main group. In patients of both the main group and the comparison group, no statistically significant deviations from the norm were observed when the "A" block of the Number Connecting Test was performed. The normal value 38.3 ± 13.7 sec was obtained in a group of healthy volunteers. At the same time, all patients showed a statistically significant increase in the duration of NCT-B, "Point in the Circle" and the "Labyrinth", as well as a decrease in the number of filled cells when performing symbolic and numerical tests). The normal values for NCT-B, "Point in the Circle" and "Labyrinth" were 55.8 ± 17.8 sec, 38.1 ± 5.8 sec and 33.3 ± 8.3 sec, correspondingly. Healthy volunteers filled 55.1 ± 14.3 cells during 90 sec.

In the course of further observation, statistically significant changes were noted in the comparison group: prolongation of the time of performance of the NCT-B by 124.9-136.5% ($p < 0.05$), by 41.1-51.5% ($p < 0.05$) for "Point in the Circle", by 82.4-94.1% ($p < 0.05$) for "Labyrinth", together with a decrease in the number of filled cells in the symbolic and numerical tests by 24.0-28.9% ($p < 0.05$) with respect to normal figures.

The obtained data as a result of research of the psychometric status in the comparison group confirm the development of latent pancreatic encephalopathy, and the basic treatment practically does not influence the studied indicators.

The analysis of psychometric tests in patients of the main group revealed statistically significant differences between the first and second clinical group at the final stage of the study. Thus, in patients of the main group the time of performing NCT-B, "Point in the Circle" and "Labyrinth" was statistically significantly shortened on day 7 by 15.8, 19.3 and 16.3% ($p < 0.05$) respectively. A statistically significant increase in the number of filled cells in the symbolic and numerical test was registered by 19.1% ($p < 0.05$) (Fig. 2).

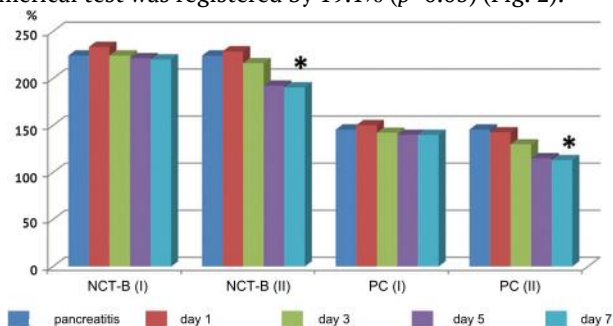


Fig. 2. The dynamics of indices of psychometric testing in patients of two groups with acute severe pancreatitis; I – the comparison group, II – the main group, NCT-B – the number connection test block B, PC – the "Point in the Circle" test; * – the reliability of the difference in indices relative to the comparison group ($p < 0.05$)

CONCLUSION

The findings of the psychometric study confirm the development of latent encephalopathy in endogenous intoxication caused by acute destructive pancreatitis. The use of laser therapy as part of complex treatment allows to reduce the severity of endogenous intoxication and manifestations of encephalopathy. The duration of psychometric indicators deviation from normal figures (on day 7 of observation there was no normalization of indices), which requires further research.

FINDINGS

1. Acute severe pancreatitis leads to an increase in the level of medium molecular weight peptides in blood, a decrease in the total and effective concentration of albumin in blood, and a dramatic increase in the toxicity index relative to normal indices. When comparing the results of dynamic observation of the observed changes to the comparison group and the main group, a significant difference in the values of the studied indices of endogenous intoxication was found. In the group receiving laser therapy, the total concentration of albumin increased by 16.3-29.3% ($p < 0.05$), the effective concentration of albumin grew by 28.9-82.7% ($p < 0.05$) if compared to the comparison group. In the group of patients receiving complex treatment, the toxicity index was also lower than in the comparison group by 37.6-65.4% ($p < 0.05$). The concentration of medium mass molecules in patients of the main group was lower than in the comparison group: MMM ($\lambda = 254$ nm) by 9.1-22.1% ($p < 0.05$), and MMM ($\lambda = 280$ nm) by 13.3-21.2% ($p < 0.05$).

2. In a psychometric study, in all patients with acute severe pancreatitis, a statistically significant increase in the duration of NCT-B, "Point in the Circle", and "Labyrinth" test was found, as well as reduction in the number of filled cells when the symbolic and numerical test was performed. The analysis of psychometric tests in dynamics revealed a statistically significant decrease in the time of performance of NCT-B, "Point in the Circle" and "Labyrinth" tests in patients of the main group by 15.8, 19.3 and 16.3% ($p < 0.05$), respectively. A statistically significant increase in the number of filled cells of the symbolic and numerical test was also registered by 19.1% ($p < 0.05$).

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