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Ozone: active forms of oxygen, nitric oxide, molecular hydrogen, and high-intensity physical factors in biology and medicine

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Abstract Book

Index

Fedorova TA, Bakuridze EM, Pyregov AV, Gavrilova TYu, Kozachenko IF, Yesayan RM, Khamidulina KG, Khachatryan NA, Ivanets TYu, Krechetova LV, Inviyaeva EV, Vtorushina VV, Beznoshchenko OS, Nechipurenko DYu, Beresneva EA. Possibilities of the use of systemic ozone therapy in patients with COVID-19 infection

Alyasova AV, Kontorshchikova KN. Influence of ozonized saline solution on the psychological status of patients with breast cancer

Bekezin VV, Korolyova AE. Features of free radical oxidation and vitamin d content in children with allergic rhinitis depending on body fat mass

Belyaev AN, Boyarkin EV, Bespalov NN, Kostin SV, Pankin PN, Babas DV. The use of negative aeroions in the treatment of mechanical jaundice

Belyaeva K, Didenko N, Pushkin A, Zagrekov V, Soloveva A. Comparative evaluation of the hyperbaric oxygenation application, admission of antioxidants and classic methods on the lipid peroxidation products dynamics in burn patients plasma

Bitkina OA, Parshina KS, Kuskova MO. Analysis of options for prescribing methods of systemic and local ozone therapy in the outpatient practice of a dermatovenerologist and trichologist

Bogodvid TKh, Muranova LN, Andrianov VV, Vinarskya AKh, Deryabina IB. The effect of the NO-synthase blocker L-NAME on the formation of long-term sensitization in terrestrial snail

Boyko EL, Malyshkina AI. Prevention of perinatal pathology in newborns in married couples with early pregnancy miscarriage in the anamnesis

Brichkin YuD, Medvedev AP, Fedorov SA, Deryugina AV, Danilova DA, Taranov EV, Nazarov EI, Pichugin VV, Makarov EV, Ryazanov MV, Bolshuhin GV, Smorkalov AYu, Tselousova LM. Prospects for the use of molecular hydrogen in cardiac surgery practice

Danilova DA, Skokova AA, Deryugina AV. The effect of molecular hydrogen on the functional stats of red blood cells and the oxidant properties of the blood of rats with simulated heart failure

Didenko NV, Belyaeva KL, Zagrekov VI, Pushkin AS, Soloveva AG. The effect of hyperbaric oxygenation on the state of antioxidant protection enzymes in burn patients

Domnin SE, Pichugin VV, Sandalkin EV, Deryugina AV. Efficiency of myocardial protection during inhalation and extracorporal ways of gaseous nitric oxide administration in surgery with cardiopulmonary bypass

Domnin SE, Deryugina AV, Pichugin VV, Sandalkin EV, Brichkin YuD. Supplying of nitric oxide into cardiopulmonary bypass circuit: clinical study of blood plasma oxidant indicators and aggregation properties of erythrocytes

Gainutdinov KhL, Kulchitsky VA, Andrianov VV, Yafarova GG, Zamaro AS, Tokalchik YuP, Bazan LV, Iyudin VS, Yurtaeva SV, Pashkevich SG, Dosina MO, Zavoisky EK. EPR study of nitric oxide content in the hippocampus of rats in the acute phase of ischemic stroke

Grechkanev GO, Strelets IO. Features of the use of ozone therapy in patients with bacterial vaginosis

Grechkanev GO, Uglanova NP. Experience in the treatment of genitourinary syndrome in combination with nonspecific vaginitis using ozonated oil

Khatkevich AS, Guzalov PI, Polinov AL. Rehabilitation of patients who had covid-19 in the conditions of a sanatorium

Kontorshchikova KN, Maslennikov OV, Okrut IE.Ozone therapy in the treatment of elderly patients with coronary heart disease

Kostina OV, Pushkin AS, Presnyakova MV, Zagrekov VI, Starikova MA. The effect of hyperbaric oxygenation on the biochemical status of burned patients

Martusevich AK, Karuzin KA, Golygina ES, Soloveva AG, Perunova AA. Some metabolic effects of reactive oxygen species on tissue fragments

Martusevich AK, Bocharin IV, Karuzin KA, Nikolaeva AV, Kovaleva LK. Modulating effect of the ozone of blood serum structurization

Martusevich AK, Kovaleva LK, Golygina ES, Nikolaeva AV, Andreeva M, Malysheva KS, Shumaev KV. Specificity of the response of the crystallogenic properties of blood to the action of various forms of nitric oxide

Martusevich AK, Golygina ES, Nazarov VV, Novikov AV. Cold plasma as a regulator of physical and chemical parameters of biological systems

Pedder VV, Golubitskikh AA, Peretyagin SP, Khrustaleva EV, Postolnik SI. Modern approaches to the treatment of patients with a dry form of age-related macular degeneration

Peretyagin PV, Boyarinov GA, Peretyagin SP, Soloveva AG. Heart rate variability with a prolonged course of infusions of ozonated saline solution

Peretyagin SP, Boyarinov GA, Sokolov SA, Struchkov AA, Peretyagin PV, Solovyova AG, Kiselevich VE, Bessonova NE. Sanogenetic possibilities of ozonated fish oil

Polyakova AG, Solovyova AG, Peretyagin PV. Influence of EMR at nitric oxide frequencies on vascular and metabolic adaptation in experimental trauma

Popovicheva AN, Martusevich AK, Fedulova EN, Sosnina LN. Assessment of the state of the antioxidant system of the blood in children with inflammatory bowel diseases

Rechkunova OA, Chernysheva TV, Guryanov AM. The effectiveness of the rehabilitation treatment of patients with gonarthrosis

Rozanov VV, Matveychuk IV, Panteleev IV. New approaches to the modernization of ozone generators to optimize the technology of bioimplants sterilization

Simutis IS, Boyarinov GA, Mukhin AS, Kuznetsov AB. Possibilities of organoprotection with ozone in severe blood loss

Soloveva AG, Peretyagin PV, Peretyagin SP, Dudar AI. The state of microcirculation during a burn in an experiment under the action of dinitrosyl iron complexes

Soloveva AG, Peretyagin SP, Peretyagin PV, Didenko NV, Belyaeva KL, Semin DA, Novopoltsev DE. The effect of singlet oxygen inhalations on the biochemical parameters of the blood biotransformation system in patients with thermal trauma

Sycheva EI, Terskikh ED. Experience in the use of ozone therapy in spa treatment of persons with carbohydrate metabolism disorders

Syomin D, Belyaeva K, Didenko N, Peretyagin P, Solovyova A, Novopoltzev D. Comparative assessment of the influence of terahertz radiation and generated no flux on the energy metabolism of erythrocytes in thermal injury.

Schwartz Adriana. Complementary application of the ozonized saline solution in mild and severe patients with pneumonia COVID-19:A non-randomized pilot study.

Terskikh ED, Sycheva EI, Koroma LA. Intravenous ozone therapy and diastolic function of the myocardium in persons with arterial hypertension

Zachvatov AN, Timoshkin VO, Parshina AYu, Kalabkin EA. Substantiation of the use of antioxidant and anti-inflammatory therapy in the correction of bioradical processes in experimental post-traumatic arthritis

Zhelezina EC, Bitkina OA, Grechkaneva OA. Clinical and laboratory monitoring of the condition of the skin of the face when using the cream "OZODERMIS 10%"

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Possibilities of the use of systemic ozone therapy in patients with COVID-19 infection

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The **aim of this stu**dy was to assess the efficacy and safety of the use of medical ozone in the complex therapy of patients with COVID-19 infection.

Materials and methods. The study included 139 patients at the age from 27 to 84 years with a confirmed diagnosis of COVID-19 admitted to the covid hospital in "National Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V.I. Kulakov». All patients were treated in accordance with the Interim Guidelines of the Ministry of Health of the Russian Federation "Prevention, Diagnosis and Treatment of New Coronavirus Infection (covid-19)" Version 6. Out of 139 patients, the first group consisted of 69 patients who were included in the complex treatment with systemic ozone therapy: intravenous infusion of 400 ml of ozonized saline solution was carried out every other day, for a total of 6 procedures. The ozone concentration in the solution was 4 mg / l. Out of 69 patients 1A group - 55 patients with an average course of infection, and group 1B - 14 patients with a severe course of the disease, all patients underwent infusions without complications. The second group - comparison consisted of 70 patients who received therapy without the use of medical ozone. Clinical, laboratory, special and statistical research methods were used. The indicators were evaluated at admission to the hospital and at the end of the course of treatment.

Results and discussion. When examining 139 patients aged 27 to 84 years with covid infection, the most frequent were noted: weakness and malaise, cough, shortness of breath, tachycardia, decreased saturation, bowel dysfunction, sore throat, headache, loss of smell, fever, pain in the muscles. In patients of 1st group , the clinical picture improved much faster: 95% of patients in the group with ozone therapy noted a significant improvement in general condition, "breathing relief", a surge of strength, a

decrease in weakness, muscle pain, improved sense of smell, normalization of body temperature. Laboratory parameters showed a significant increase in the relative and absolute content of lymphocytes, a significant decrease in the relative and absolute number of neutrophils, a pronounced decrease in the level of LDH, CRP, ferritin and fibrinogen, especially in patients with severe disease. A decrease in the coagulation potential of blood in the 1st group was revealed in the study of the hemostasis system according to the data of thromboelastography (TEG) and the "Thrombodynamics" test. The duration of a bed-day in the first group of patients was 11-16 days, and in the second group - 12-25 days. Significantly lower NEWS scores after treatment in the first group compared to the second group.

Conclusion: the results showed the expressed positive effect of ozone therapy on the clinical course of the disease, laboratory data indicating anti-inflammatory, immunomodulatory, rheo and coagulo-correcting, analgesic, antihypoxant effects, which contribute to a faster stopping of the process, improving the condition of patients and shortening the length of hospital stay. The use of ozone therapy should be considered as an additional adjuvant method in complex therapy in patients with SARS-CoV-2 infection. Further research is needed to optimize the ozone therapy protocols, the number and the start time of the treatments.

Key words: Ozone, ozone therapy, COVID-19, SARS-CoV-2, Ozonized saline solution, efficiency, safety

Influence of ozonized saline solution on the psychological status of patients with breast cancer

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Purpose of the study is to estimate the possibilities of the corrective effect of ozonized saline solution on the psychological status of patients with breast cancer (BC) in the course of antitumor therapy.

Materials and methods. The study included 203 patients aged 35-65 years with a histologically confirmed diagnosis of breast cancer, mainly with III-IV stages of the disease – 69,5% (141/203). Clinical and psychological interviewing of patients was carried out according to the method of A.E. Kolosov – N.B.Shipovnikov (1994), testing using the Spielberger – Khanin test and the SMOL test before and after the courses of antitumor therapy, supplemented, in 31.5% (64 / 203) of patients with the introduction of ozonized saline solution (OSS). The data obtained were processed using the statistical software package STATISTICA 6.0.

Results. In the cases of using O3SS, the patients were less worried about the symptoms of intoxication, there was a feeling of a surge of energy and strength, mood and sleep improved, working capacity and physical activity increased, patients' anxiety decreased, fixation on their own feelings. The score for the level of reactive anxiety (RT) in patients receiving O3SS was lower than the initial one (before treatment 38,62 ± 1,08 points, after treatment – 33,51 ± 1,0 points, $p < 0,05$). In the group receiving cytostatic therapy, patients complained of weakness, loss of strength, loss of interest in the environment, increased irritability. The score of the RT level did not change relative to its value before treatment (35,86 ± 1,31 and 35,05 ± 1,45 points, respectively). Psychological testing according to the SMOL questionnaire after the course of treatment revealed a decrease in the level of the personality profile in the patients receiving O3SS on the scales of the neurotic triad, the scales of paranoia and psychoasthenia. On the contrary, in women who did not receive O3SS during chemotherapy, the SMOL test showed an increase in most personality profile scales relative to their baseline values. This form of the profile indicated a high level of permanent anxiety combined with symptoms of depression. There was an increase in tension, anxiety about the state of their physical health, phobic phenomena, alienation and isolation from others by the presence of somatically conditioned difficulties, inadequate emotional response.

Thus, the use of anti-stress methods against the background of chemotherapy can be considered not only as a means of improving the quality of life of patients, but also as a way to increase the effectiveness of cytostatic therapy. One of such approaches may be the use of ozonized physiological solution, which has a corrective effect on the psychological status of patients with breast cancer in the course of antitumor therapy.

Key words: breast cancer, ozonized saline solution

Features of free radical oxidation and vitamin d content in children with allergic rhinitis depending on body fat mass

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Introduction. Currently, an active research on the role and interconnection of oxidative stress, vitamin D supply, and excess body fat mass in the pathogenetic processes of allergic diseases (including allergic rhinitis) is being done.

Purpose. The main purpose of the study is to determine oxidative status and vitamin D supply in children with allergic rhinitis, depending on their body fat mass.

Materials and methods. A comprehensive examination of 34 children aged 6-7 years with allergic rhinitis without exacerbation was carried out, including anthropometry, bioimpedansometry (Medass apparatus, Russia), induced chemiluminescence (ICL) of blood serum and determination of vitamin D in blood serum by ELISA (ELISA Kit, Belgium). Depending on the percentage of body fat mass (BFM percentage) according to bioimpedance data, all the examined children were divided into 2 groups. The 1st group included 11 children with more than +2SD BFM percentage, taking into account the age and sex of a child. The second group included 23 children with BFM percentage within ± 1SD, taking into account the age and sex of a child. There were no gender differences between groups 1 and 2. The indicators of free radical oxidation (FRO) were measured by the blood serum ICL method on a domestic biochemiluminometer BLM 3606 M-01 (Russia). The value of the total light sum ($S_{tot.}$ (arb. units)) and the first peak of induced chemiluminescence (H (arb. units)) were determined. Additionally, an integral indicator was calculated, namely the chemiluminescent oxidative coefficient (COC): $(S_{tot.} \times H)/10^6$ (arb. units), indicating the oxidative status of a child as a whole. Oxidative stress was determined at a COC level of more than 1352.9 arb. units.

Results and Discussion. The analysis of the average values of the FRO indicators, obtained by the method of induced chemiluminescence, showed that the children of the 1st group in comparison with the children of the 2nd group had higher values ($p<0,05$): H – by 1,33 times; $S_{tot.}$ – by 1,35 times and COC – by 1,81 times. Accordingly, oxidative stress was detected in 63,6% of children of the 1st group and in 21,7% of children of the 2nd group. In children of the 1st group, the average values of vitamin D were 1.48 times lower ($p<0.05$) than in children of the 2nd group. At the same

time, the correlation coefficient between vitamin D and COC testified to a negative correlation between these indicators and manifested most in children of the 1st group ($r = - 0,549$, $p<0,05$). The results revealed in the study indicate that oxidative stress ($\chi^2 = 5,720$; $p = 0,017$) and vitamin D deficiency / deficit (in 54.5% children of the 1st group compared with 17.4% of children of the 2nd group; $\chi^2 = 4,948$, $p = 0,027$) are more often recorded in children with allergic rhinitis against the background of excess body fat mass (the 1st group). An excess of body fat mass undoubtedly increases the intensity of FRO processes and reduces the antioxidant activity of serum (i.e., leads to oxidative stress). Taking into account the revealed correlation between the level of vitamin D and COC, it is pathogenetically justified to prescribe children with allergic rhinitis and excess body fat mass a vitamin D preparation in order to correct their oxidative stress.

Conclusion. Oxidative stress and vitamin D deficiency / deficit are 2,93 and 3,13 times, respectively, more likely to be recorded in children with allergic rhinitis against the background of excess body fat mass. Prescribing children with allergic rhinitis and excess body fat mass vitamin D will allow to improve their antioxidant protection.

Key words: oxidative stress, vitamin D, children, allergic rhinitis

The use of negative aeroions in the treatment of mechanical jaundice

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Experiments were conducted on 20 rats divided into an experimental (15) and a control (5) group. Reversible mechanical jaundice was stimulated to the rats by applying a loop-garrotte to the choledochal, which was removed on the 3rd day of mechanical jaundice. In the experimental group after decompression of choledochal on animals they were exposed to negative aeroions (10 thousand negatively charged aeroions in 1 cm3 with an exposure of 60 min.) during 15 days of observation. Aeroionotherapy was not performed in the control group after decompression of the choledochal. Negative aeroionotherapy, compared to the control group, contributed to a decrease in the level of alkaline phosphatase and an increase of catalase, which indicated to a stimulated production of its own antioxidant enzymes and reduction of hepatocyte cytolysis.

It is known that with obstructive jaundice, liver cells are damaged due to excessive stimulation of free radical oxidation processes and the development of oxidative stress The level of its own antioxidant enzymes significantly decreased, indicating insufficient protection of liver cells from the damaging effects of free radicals.

Experimental results have shown that negative air ions have a significant therapeutic effect in obstructive jaundice. After the use of negative air ions, the production of own antioxidant enzymes is stimulated, while the value of catalase increased by 41%, and intracellular enzymes indicating cytolysis of hepatic cells decreased (ALP - by 22%), while in the control group, without aeroionotherapy, catalase decreased by 9%, ALP - by 12%. In addition, negative air ions increase tissue oxygenation, stimulating regenerative processes. In our study, this was manifested by the acceleration of the healing of postoperative wounds.

Conclusion: Negative aeroionotherapy for obstructive jaundice reduces cytolysis of hepatocytes due to stimulation of the antioxidant system and promotes the acceleration of the regeneration of postoperative wounds.

Key words: mechanical jaundice, negative aeroions, antioxidant enzymes

Comparative evaluation of the hyperbaric oxygenation application, admission of antioxidants and classic methods on the lipid peroxidation products dynamics in burn patients plasma

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Severe thermal trauma of great depth and area contributes to the development of burn disease, characterized by hypoxia and oxidative stress (OS), which leads to lipid peroxidation (LPO). Among LPO products, there are diene conjugates (DC), ketodienes and conjugated triene conjugates (TC), Schiff bases (SB), and others. Diene conjugates (DC) are formed during free-radical oxidation of arachidonic acid, have a damaging effect on lipoproteins, and interact with other LPO products. Upon further addition of oxygen, secondary LPO products are formed to ketodienes and triene conjugates (TCs). Schiff bases (SB) are formed as a result of the interaction of secondary lipid peroxidation products with proteins, which are classified as end products of lipid peroxidation. To reduce OS and hypoxia, in addition to classical therapy, antioxidants and the method of hyperbaric oxygenation (HBO) were additionally used in the treatment regimen.

The aim of this work was to compare lipid peroxidation products dynamics under the application of classical burn treatment and in additional applying hyperbaric oxygenation (HBO) method or antioxidant admission.

Materials and methods. 28 patients with burns were examined, 8 patients were additionally prescribed a course of antioxidants *per oralis* and 10 patients were prescribed a course of hyperbaric oxygenation. The procedures were carried out in a reanimation pressure chamber for 14 days. Before and after each session, the content of LPO products in blood plasma was assessed on days 1, 7, and 14 of the therapy. The control group consisted of 60 healthy patients (normal). The spectrophotometric method was used to assess the content of LPO products.

Results and discussion. When comparing the results of therapy in the groups of combined treatment with the group of classical therapy, an increase in the content of DC in the group of antioxidants was obtained (by 18% on day 1 ($p = 0.027$) and 15% on day 14 ($p = 0.034$). A decrease in DC by 8% ($p = 0.048$) was found in the group after HBO procedure on day 14. An increase in the concentration of MC in the plasma of

burn patients for 1 day of taking antioxidants and HBO (before and after the procedure) was found in comparison with classical therapy by 15% ($p = 0.039$), 12% ($p = 0.042$) and 13% ($p = 0.036$), respectively. No statistically significant differences were found in the subsequent periods. When examining the SB content in the blood plasma of burn patients, no statistically significant differences were found in comparison with classical therapy. This may indicate the absence of negative consequences at the usage of antioxidants and HBO in addition to classical therapy, as well as classical therapy in the treatment of severe burns. This can also indirectly indicate an increase in the activity of aldehyde dehydrogenase.

Conclusion. The use of antioxidants in addition to classical therapy promotes the initiation of PUFA oxidation; the HBO method does not have a negative effect in the treatment of thermal injury. Presumably, HBO promotes an increase in the activity of oxidoreductases, e.g. aldehyde dehydrogenase.

Key words: burn, hyperbaric oxygenation, burn disease, dyene conjugates, tryene conjugates, Shiff base

Analysis of options for prescribing methods of systemic and local ozone therapy in the outpatient practice of a dermatovenerologist and trichologist

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Objective: To study the effectiveness of the use of external and systemic ozone therapy in patients with various diseases of the skin and scalp.

Materials and methods.166 patients with skin and scalp diseases were examined and treated using various ozone technologies on the basis of the outpatient reception room of the Alexandria Clinic. Clinical, laboratory and instrumental research methods were used to establish the diagnosis. Patients underwent complex treatment using courses of systemic and local ozone therapy.

Results and discussions. The main aspects of the use of medical ozone-oxygen mixture in dermatological practice for the current period are chronic immune-dependent dermatoses (allergodermatoses, psoriasis, lichen planus), dermatoses of infectious etiology (mycoses, herpes, HPV-associated dermatoses, pyoderma). The options for its use in cosmetology include pink and vulgar acne, correction of age-related skin changes, a combination of applications of external ozonide-containing drugs with destructive therapies. The trichological direction is actively developing in the form of treatment of seborrheic dermatitis and various variants of alopecia.

Conclusion. The methodology of using ozone therapy methods formed for the current period in the practice of a dermatologist, cosmetologist, trichologist is a promising alternative method of treatment in the presence of contraindications to the use of drug therapy. Of particular value are external ozonide-containing preparations due to the complexity of the effects in the form of moisturizing, bactericidal, virusocidal and fungicidal effects. A promising direction is the development of new methods of active physiotherapy (Ozotens therapy).

Key words: ozone therapy, dermatology, cosmetology, trichology, Ozotens therapy

The effect of the NO-synthase blocker L-NAME on the formation of long-term sensitization in terrestrial snail

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Nitric oxide (NO) is one of the most important mediators involved in the functioning of various body systems. NADPH d-positive neurons synthesizing NO were detected by histochemical method in various ganglia of the terrestrial snail *Helix lucorum*. There is a large amount of evidence of the participation of NO in the processes associated with plasticity. It was also shown that the intensity of NO production in the tissues of the nervous system and heart of the snail decreases after the formation of such a form of plasticity as long-term sensitization (LTS). LTS is a form of plasticity of a long-term nature, in which there are signs of both non-associative and associative learning. Therefore, the purpose of this work was to study the effects of the NO-synthase blocker L-NAME on the process of LTS formation in a terrestrial snail.

The effects of the NO-synthase blocker L-NAME at a dose of 100 mg/kg of animal weight were studied. L-NAME was injected with a syringe into the internal cavity of the animal (in a liquid volume of 0.1 ml) in the sinus node area once a day for 4 days, 30 minutes before the start of LTS formation. During the experiment, it was found that when the NO-synthase blocker L-NAME was introduced with subsequent sensitization (n=15), the indicators of defensive behavior increased from 19.8±0.6 s to 40.8±1.8 s. In the LTS group, the duration of the closed state of the pneumostome increased from 15.2±0.6 to 61.7±2.8 s. Thus, in the group with the introduction of L-NAME before the formation of LTS, the severity of LTS is weaker than in the group of sensitized animals.

Key words: nitric oxide, L-NAME, long-term sensitization

Prevention of perinatal pathology in newborns in married couples with early pregnancy miscarriage in the anamnesis

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Introduction. One of the conditions for reducing perinatal pathology is a comprehensive approach to improving the health of married couples in preparing them for a new pregnancy.

Materials and methods. 200 married couples with a history of early pregnancy miscarriage taken under observation were divided into groups comparable to their clinical characteristics. The first group (n=100) included married couples whose preparation for pregnancy was carried out with the use of traditional drug therapy with antibacterial, anti-inflammatory drugs, vitamins according to the recommended regimens. The second group (n=100) included married couples who, in addition to drug therapy, had ozone therapy in the form of small autohemotherapy with the concentration of ozone in an ozone-oxygen mixture at 30 μg/mL in combination with local procedures with an ozonated saline solution with the concentration of ozone at 9-10 micrograms/ml in both spouses. Additionally, all men were recommended to use the barrier method of contraception (condom) on a regular basis.

Results and discussion. The use of traditional drug-based methods of rehabilitation of the reproductive health of women and men from married couples with miscarriage made it possible to favorably complete the subsequent pregnancy in 61.2% of cases, while complex pre-pregnancy preparation with the ozone therapy in both spouses increased the frequency of carrying out the pregnancy to 86.7% ($p<0.01$). Special attention should be paid to married couples in which, when planning a subsequent pregnancy, only a woman underwent comprehensive training, and a man refused rehabilitation treatment. With complex rehabilitation of women and men together, the frequency of birth of healthy children increased to 72.2%, whereas with complex pre-pregnancy preparation carried out only in women, healthy children were born in 47.1% of cases ($p<0.01$). These mothers were more likely to have children with perinatal pathology ($p<0.01$), including in a state of moderate and severe asphyxia, with perinatal lesions of the central nervous system ($p<0,01$). In order to correct the detected

violations, these children were more often detained in the maternity hospital, more often transferred to the pathology department or to the second stage of newborn nursing ($p<0.01$).

So, pre-pregnancy preparation is necessary for both future parents. This approach enables spouses to prepare for pregnancy, improve their own health, and conceive in the most optimal period for them. A wide range of effects of medical ozone - from the antimicrobial effect to the metabolic adaptation of the body as a whole, makes it possible to increase the effectiveness of pre-pregnancy preparation of married couples for childbirth.

Key words: pre-pregnancy preparation, family planning, prevention of perinatal complications

Prospects for the use of molecular hydrogen in cardiac surgery practice

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Introduction. The postoperative complication rate stay high despite the all improvements in the surgery technique and modern methods of diagnosis and management. That is why searching for factors affecting on critical links of development of complication in patients after cardiac surgery so important.

Materials and methods. The study includes 20 patients who got surgeries with the acquired heart defect. All patients were randomized into two groups. The first group includes twelve patients with using of molecular hydrogen (H2) like an inhaled treatment during the surgery.H2 supplied into circuit of the ventilator and produsedby “Bozon-N H2 device (NPP “EKONIKA” Odessa, Ukraine). The second group includes eight patients without H2 inhaled treatment. The study was endorsed by Ethics Committee of Cardiac and Vascular Hospital after by B.A. Korolev (№2; 02.19.2019) and accordance with Declaration of Helsinki. The blood tests were performed four times: Just after induction of anesthesia, before bypass, after bypass and in 24 hours after surgery. We examined diene (DC) and triene (TC) conjugates, Schiff bases (OR), malondialdehyde (MDAO) in blood plasma and catalase in erythrocytes which were determinated by Volchegorsky method (1989).

Results. There were found that TC and OR decrease in blood tests performed just after induction of anesthesia and in 24 hours after surgery. The rate MDAO decreases in the group patients. The growth rate of OR was registered in second group of patients (without H2) especially in the blood tests before bypass.

Conclusions. Using of H2 in cardiac patients can be effective in the fight with oxidative stress.

Key words: molecular hydrogen, oxidative stress, cardiac surgery

The effect of molecular hydrogen on the functional stats of red blood cells and the oxidant properties of the blood of rats with simulated heart failure

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Introduction. According to the World Health Organization, diseases of the cardiovascular system have been the leading cause of death worldwide for 20 years. The most common syndrome of this group of diseases is chronic heart failure (CHF), accompanied by disorders of peripheral and systemic circulation, which leads to the development of hypoxia and oxidative stress.

Material and methods of research. The study of the effect of molecular hydrogen (H2) on the aggregation, electrokinetic parameters of red blood cells and the concentration of MDA in the blood plasma of rats with chronic heart failure (CHF) was carried out. CHF in rats was modeled by intraperitoneal administration of an 1 mg/ml epinephrine hydrochloride solution of 0,3 mg/kg of rat's body weight. Inhalation of 2% H2 was carried out 40 minutes repeatedly (for 5 days daily) and 40 minutes once. The control rats were not inhaled. The dynamics of the studied parameters were studied on the 1^{st}, 3^{rd}, 7^{th} and 14^{th} days after the modeling of CHF.

Results. Using of H2 caused an increase in electrophoretic mobility of RBC, a decrease in aggregation and the concentration of MDA in both research groups by 14 days relative to 1 day of registration with a significant change in these indicators in the control group.

Conclusion. Thus, using of H_2 in CHF led to a decrease in oxidative stress, an increase in the electronegativity of red blood cells and a decrease in their aggregation, which improves microcirculation and allows to recommend H_2 for protection against ischemic and reperfusion tissue damage.

Key words: molecular hydrogen, chronic heart failure, red blood cells

The effects of a donor of nitric oxide on the process of reconsolidation of contextual conditioning in terrestrial snail

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Results. The obtained results showed that the blockade of NO-synthase reduces the effect of anisomycin on the "forgetting" of the conditioned reflex, demonstrating the process of reconsolidation of long-term memory.

When forming a memory for any events, abundant traces first appear, which are consolidated through the synthesis of new proteins into a stable memory. It has been shown that memory amnesia can occur if consolidated and stable long-term memory (LTM) is reactivated before amnestic exposure. The process by which reactivated labile memory is stabilized over time is known as memory reconsolidation. Contextual memory reconsolidation has also been shown in invertebrates. NADPH d-positive neurons synthesizing nitric oxide (NO) were detected by histochemical method in the nervous system of the terrestrial snail. It has been demonstrated that NO is necessary for both learning and memory erasure in reconsolidation processes. Thus, the study of the role of NO in the formation and consolidation of LTM is an urgent task within the framework of the problem of the neurobiology of learning and memory.

Material and methods. The terrestrial snail Helix lucorum was chosen as an object for experiments. It was formed the conditioned situational reflex (CSR), when the animals could distinguish the test signals applied in different situations (on a ball and flat surface). For the formation of CSR snails for 5 days showed 5 electrical stimuli per day when they are on the ball. Behavioral reactions were tested in 2 contexts: 1) on a ball (i.e., in standard conditions), 2) on a flat surface (i.e., in conditions other than standard). It was demonstrated a significant increase in defensive reactions when snails was on the ball, which demonstrates learning. The day after the test, a session of "reminders" was conducted and then immediately blocked protein biosynthesis by injection of anisomycin (AN). A study was conducted on the effects of the influence of L-NAME on the reconsolidation of CSR in a terrestrial snail caused by the use of AN. The results obtained show that the injection of SS after recalling the situation does not lead to a change in the magnitude of the defensive reaction of the snail ommatophores to tactile

irritation when tested on a ball, at the same time, injections of AN (n=10) led to a significant decrease in the defensive reaction, i.e., to complete forgetting of the formed memory. The obtained results showed that the blockade of NO-synthase reduces the effect of anisomycin on the "forgetting" of the conditioned reflex, demonstrating the process of reconsolidation of long-term memory.

Key words: nitric oxide, learning, long-term memory, reconsolidation of memory

The effect of hyperbaric oxygenation on the state of antioxidant protection enzymes in burn patients

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An important factor of high mortality in burn disease is the development of oxidative stress (OS), occurs as a result of an imbalance between the formation and neutralization of free radicals. In this regard, it is necessary to provide timely and effective therapy for burn disease, which resists the development of free radical oxidation, as well as having anti-inflammatory and wound-healing effects. The usage of hyperbaric oxygenation (HBO) in the treatment of patients with burns shows an improvement in the gas exchange at the tissues of the burn patients, and also activates the metabolic processes subsequently.

The aim of this work was to evaluate the antioxidant status in red blood cells in burn patients before and after the use of hyperbaric oxygenation (HBO) on the 1st, 7th and 14th days of therapy**.**

Materials and methods. 10 patients with burns who were prescribed a course of hyperbaric oxygenation were examined. The procedures were carried out in the intensive care chamber for 14 days. Before and after each session, the activity of antioxidant defense enzymes was evaluated on the 1st, 7th and 14th days of the therapy. The control group consisted of 60 healthy patients (norm). To assess the antioxidant status of red blood cells of burn patients, spectrometric methods were used to determine the activities of the following antioxidant enzymes: superoxide dismutase (SOD), catalase and glutathione reductase. The obtained data were processed statistically in the software package Statistica 6.1 for Windows.

Results and discussion. We found a significant decrease in the activity of the enzyme of the first link of antioxidant protection - SOD in burn patients before HBO application that indicates the stress response of the body, and also be accompanied by an increase in the number of active forms of O_2. However, it should be noted that the HBO sessions at all the studied periods were accompanied by a significant increase in the specific activity of the enzyme compared to the level of the indicator before the HBO. A similar data was noted for other antioxidant enzymes under study. Thus, the specific activity of catalase in the red blood cells of burn patients increased significantly by an average of 9-14% on the 1st and 7th days and by 35.87% on the 14th day of the HBO in comparison with the level of the indicator before the procedure on the

corresponding day. The study also showed an increase in the specific activity of GR on the 1st day of the HBO by 11.74% ($p<0.05$), and on the 7th day by 11.942% ($p<0.05$) compared with the activity of the enzyme before the HBO procedure.

Thus, the data of the HBO effect on the antioxidant status of red blood cells in patients with contact-thermal trauma, it was found that the HBO procedure (14 days) in burn patients, it increases the specific activity of all the studied antioxidant enzymes (SOD, catalase, GR), thereby reducing the likelihood of the development of oxidative stress characteristic of this pathology.

Conclusions. The obtained data showed the timely implementation of the HBO procedure (14 days) increases the antioxidant status of red blood cells of patients with thermal injury (an increase in the specific activity of antioxidant enzymes taken into this study), thereby reducing the probability of oxidative stress.

Key words: burn, hyperbaric oxygenation, antioxidant enzymes

Efficiency of myocardial protection during inhalation and extracorporal ways of gaseous nitric oxide administration in surgery with cardiopulmonary bypass

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Aim of the study. To increase the efficiency of myocardial protection during operations on the heart valves by supplying gaseous NO by inhalation, as well as into the extracorporeal circulation circuit.

Materials and methods. The study included 93 patients who underwent cardiopulmonary bypass surgery were randomized into 3 groups: the first (30 patients) - control, the second (30 patients) - inhalation supply of NO (20 ppm) throughout the operation, the third (33 patients) - supply of gaseous NO (20 ppm) to the oxygenator. We investigated the activity of troponin I (cTnI) after surgery; studied changes in myocardial contractile function; clinical markers of the postoperative period in patients.

Results. Preoperative cTnI levels were not statistically significant between groups. In the postoperative period (at the end of the operation, 12, 24 and 48 hours after the operation), the levels of cTnI in patients of groups 2 and 3 are statistically significantly lower than in the control group. Changes in LVEF revealed its more intact values after cardiopulmonary bypass and early postoperative period in patients of the 2nd and 3rd groups. The length of ICU stay was shorter in the patients of the study groups. There was no statistically significant difference between the patients of the 2nd and 3rd groups for all the studied parameters.

Conclusion. Nitric oxide, used for anesthesia and cardiopulmonary bypass during cardiac surgery, has a cardioprotective effect; no statistically significant differences were found between the technologies of NO application.

Key words: nitric oxide, myocardial protection, cardiopulmonary bypass surgery

Supplying of nitric oxide into cardiopulmonary bypass circuit: clinical study of blood plasma oxidant indicators and aggregation properties of erythrocytes

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Background. The effect of nitric oxide (NO) on the state of oxidative processes during operations with cardiopulmonary bypass (CPB) has not been studied. The state of erythrocytes, which determine the oxygen homeostasis, and in particular the analysis of their aggregation properties, with the supply of NO into the extracorporeal circuit has also not been studied.

The aim of the study was to investigate the state of oxidative parameters of blood plasma and the aggregation properties of erythrocytes during the supply of gaseous NO into the extracorporeal circuit during the heart valves surgery in conditions of cardiopulmonary bypass.

Materials and methods. The study included 63 patients who were randomized into 2 groups: control (30 patients), study (33 patients) —gaseous NO (20 ppm) was supplied to the CPB circuit. The “Tianox” apparatus (Russian Federation) was used as a NO generator. The intensity of the processes of lipid peroxidation (LPO) was investigated by the content of diene (DC) and triene (TC) conjugates, Schiff's bases (SB) in blood plasma. Aggregation of erythrocytes was studied by optical microscopy by counting single erythrocytes and their aggregates. Research stages: 1- before surgery, 2- before CPB, 3- 5 min by CPB, 4- 30 min by CPB, 5- 60 min by CPB, 6- 90 min by CPB, 7-end of the operation.

Results. In the control group, the concentration of DC and MC increased statistically significantly by 30 min of CPB, remained elevated by 60 min of CPB relative to the indicators of the 1st and 2nd stages, and it was restored to the values of the 1st stage by the end of the operation. A significant increase in SB was recorded by 60 min of CPB, although by the end of the operation, recovery of values to the indicators of the 1st stage was also observed. The study of prooxidant processes in the study group revealed the absence of statistically significant changes in the concentration of DC and TC throughout the entire study, the concentration of SB increased statistically

significantly by 30 min of CPB, but was significantly lower compared to the control group, and from 60 min of CPB to the end of the operation decreased below initial level (values of the 1st stage). Analysis of the aggregation properties of erythrocytes showed that in the group using NO, the percentage of aggregation decreased starting from the 4th stage of the study, while in the control, from 60 min of CPB, an increase in erythrocyte aggregation was observed, which remained until the end of the study.

Conclusion. The supply of gaseous NO into the extracorporeal circuit during the heart valves surgery in conditions of cardiopulmonary bypass allowed limiting LPO activation and reducing the aggregation of erythrocytes, which is an important factor contributing to the improvement of oxygen supply to tissues and tissue perfusion. Probably, in low concentrations of NO, acting as a scavenger of oxygen radicals, it determines the detoxification of potentially dangerous ROS, limiting lipid peroxidation processes and restoring the state of cell membranes.

Key words: nitric oxide, oxidative parameters, aggregation of erythrocytes, operations with cardiopulmonary bypass

EPR study of nitric oxide content in the hippocampus of rats in the acute phase of ischemic stroke

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Introduction. Hypoxia is a pathological process that occurs when there is insufficient supply of oxygen to the tissues of the body. With hypoxia and ischemia of the brain, the functioning of neurotransmitter systems, including the system of nitric monoxide (NO), is disrupted. NO, synthesized by constitutive isoforms of NO-synthase, provides adequate blood supply to brain regions, affects the activity of neurons, regulates cell metabolism. The role of NO in the functioning of the cardiovascular and nervous systems is particularly significant in the vital activity of animals. The participation of NO in the mechanisms of development of various pathological conditions of the body attracts great interest. Recently, the electron paramagnetic resonance (EPR) method has become one of the most effective methods for detecting and quantifying EPR in biological tissues. The aim of this work was to study the effects of experimental ischemic brain stroke on the NO content in the tissues of the hippocampus of the brain by EPR spectroscopy using the spin trap technique.

Material and methods. When modeling an ischemic stroke, the animals were subjected to 5-minute hypobaric hypoxia (conditional ascent to an altitude of 4500 m above sea level). The NO content in rat hippocampal tissues was studied 5 and 24 and 72 hours after the presentation of the hypoxic stimulus. The technique of spin traps was applied, which allows detecting NO in low concentrations, a complex of Fe^{2+} with diethyldithiocarbamate (DETC) was used. EPR measurements were carried out in the X-band on the EPR ER-200 spectrometer of the Bruker company at a temperature of 77 K. The amount of NO was estimated by the intensity of the characteristic EPR signal belonging to the complex $(DETC)_2$-Fe^{2+}-NO. We found that the amount of NO decreases after modeling an ischemic stroke. After 5 hours, the NO content in the hippocampus decreases by 2-3 times. This decrease in NO production persists 24 and 72 hours after a stroke.

Results. Using EPR spectroscopy, it was found that the amount of NO decreases after modeling an ischemic stroke. After 5 hours, the NO content in the hippocampus decreases by 2-3 times. This decrease in NO production persists 24 and 72 hours after a stroke.

Key words: nitric oxide, hippocampus, ischemic stroke, electron paramagnetic resonance

Features of the use of ozone therapy in patients with bacterial vaginosis

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Introduction. Bacterial vaginosis (BV) remains one of the pressing problems of gynecology due to the wide spread of this pathology. Significant risks are presented by this disease for the gestational process, childbirth and the postpartum period, various types of surgical interventions. The recurrent nature of the disease has a negative impact on the quality of life of women. The aim of the study was to increase the effectiveness of the treatment of bacterial vaginosis through the use of ozone therapy.

Material and methods. In 2020 – 2021, 60 patients with a confirmed diagnosis of BV were examined. Group I patients (30 people) received eradication therapy, according to current clinical recommendations, in the form of: metronidazole 500 mg per os 2 times a day for 7 days. 30 women of group II simultaneously received rectal insufflations of ozone-oxygen mixture No. 7 and therapy with tampons with ozonated olive oil No. 10. All patients received a course of probiotics intravaginally at the end of the first stage of therapy.

Physical, bacterioscopic, bacteriological, and immunological studies were used before and 3 months after the end of the corresponding therapy. The total duration of follow-up was 1 year. The assessment of the level of local immunity was based on the determination of the levels of lysozyme, secretory immunoglobulin A (sIgA), interleukins 6 and 10 (IL-6, IL-10).

The results and discussion. A comparison of the immediate clinical results of treatment in the groups showed that the relief of complaints in group II patients occurred after 3 days of treatment, while in group I the effect was achieved only after the complete completion of the first stage of treatment (antibacterial therapy).

After the standard course (its first stage) of treatment of group I patients, the study showed the relief of BV. The analysis of the levels of local immune protection factors initially revealed no differences in the groups. A repeated study of them 3 months after the end of treatment showed that in group I, all the studied indicators of local immunity remained at the same level. In group II, on the contrary, there was an obvious dynamics-there was an increase in the level of lysozyme from 22.5±0.4% to 32.3±0.73%, i.e. by 43.6% ($p<0.05$), sIgA from 0.015±0.002 g/l to 0.024±0.001 g / l, i.e. by 60.0% ($p<0.05$). In the group, there was a decrease in the level of IL-6 from

240.3±10.2 pg/ml to 172.5±8.6 pg/ml, i.e. by 30.7% ($p<0.05$). The content of IL-10 increased from 24.7±0.7 pg / ml to 45.3±0.8 pg/ml, i.e. by 83.4% ($p<0.05$). As a result, the content of lysozyme in group II was 1.44 times, sIgA 1.85 times, IL-10 1.67 times higher than in group I, and IL-6, respectively, 1.4 times lower ($p<0.05$).

Subsequent clinical observation for 1 year showed that in group I, BV relapses occurred in 80% of patients. The use of ozone therapy as part of complex treatment in group II patients resulted in a lower frequency of BV relapses, which were noted in 50% of cases.

Conclusion. Based on the conducted studies, it can be concluded that the combination therapy using ozone technologies has a positive effect on the clinical and immunological parameters of patients with recurrent bacterial vaginosis. Studies to further improve the results of treatment are continuing.

Key words: bacterial vaginosis, immunity, ozone therapy

Experience in the treatment of genitourinary syndrome in combination with nonspecific vaginitis using ozonated oil

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Introduction. The current trend is an increase in the proportion of older women in the population, which inevitably leads to an increase in the prevalence of disorders associated with postmenopausal age. These include genitourinary menopausal syndrome, a frequent complication of which is the addition of nonspecific vaginitis. The aim of the study was to increase the effectiveness of the treatment of GUM, complicated by the development of nonspecific vaginitis, through the use of ozone therapy in the form of local applications of ozonated olive oil.

Material and methods. We examined 60 patients aged 48 to 52 years (the average age was 49.2±2.4 years) with a postmenopausal duration of 2.3±1.1 years with GUMS (without other signs of menopausal syndrome) in combination with nonspecific bacterial vaginitis. In group I (20 patients), applications of ozonated olive oil of the OTRI 6000 series on the vaginal walls were used for the relief of the pathological process with a course of 12-14 procedures that were lowered daily. In group II (20 patients), vaginal candles containing 0.5 mg of estriol were used for 14 days, 1 candle in the morning, followed by a gradual reduction of the dose to 1 candle 1 time a week (total duration 2 months). In parallel, in group II, vaginal candles containing antimicrobial components and prednisone were used for 1 candle in the evening for a course of 10 days. In parallel with antimicrobial therapy, a drug containing the lactobacillus strain LSR 35 was treated in the form of vaginal candles for a course of 14 days.

To assess the effectiveness of treatment, patients underwent a comprehensive clinical and laboratory study.

Research results and discussion. The assessment of the dynamics of clinical symptoms against the background of the compared methods of treatment showed that complaints of pathological white spots, discomfort during sexual intercourse, vaginal hyperemia disappeared in group I by the 8th day of treatment, in group II they persisted until 12-15 days from the start of therapy. According to bacterioscopy, the majority (80%) of patients after ozone therapy achieved a state of normocenosis, most patients of group II at the end of treatment had an intermediate type of smear, which is characterized by a moderate or insignificant number of representatives of the normoflora (lactobacilli) with the simultaneous presence of cocci, rods, leukocytes,

macrophages, epithelial cells. A bacteriological study of the vaginal discharge showed that ozone therapy has a greater suppressive effect on the conditionally pathogenic flora than drug therapy.

In women of group I, the vaginal pH decreased by 1.48 times to 4.2±0.2, in group II - by 1.2 times to 5.0±0.1 (the differences were considered significant at $p<0.05$). The feeling of dryness in the vagina and symptoms of dyspareunia were stopped in patients receiving ozone therapy after the end of the course of treatment, i.e. after 12-14 days, in several cases, therapy with ozonated olive oil was continued for up to 17 days. In patients of group II, these manifestations of GUMS persisted, gradually decreasing, for 20-25 days.

Conclusion. Applications of ozonated olive oil on the vaginal walls have a positive effect on the manifestations of nonspecific vaginitis associated with genitourinary menopausal syndrome.

Key words: genitourinary menopausal syndrome, nonspecific vaginitis, ozonated olive oil, vaginal biocenosis.

Rehabilitation of patients who had covid-19 in the conditions of a sanatorium

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Introduction. The introduction and development of new methods of rehabilitation for patients who have undergone COVID-19 with neurological and cardiovascular pathology is an urgent goal. In SOGAZ Medical Center, sanatorium White Nights, in addition to all the traditional methods of treatment and rehabilitation of neurological patients (massage, mud therapy, thermal therapy, balneotherapy, various types of physiotherapy including physiotherapeutic exercises), since February 2021, active forms of oxygen in the form of intravenous injections of ozone-oxygen mixture and hyperbaric oxygenation.

Materials and methods. Our study involved 243 patients after suffering a coronavirus infection with diagnosed post-COVID infectious syndrome. About 90% of patients presented neurological complaints: decreased memory, concentration, fatigue, irritability or drowsiness, apathy, depression, sleep disturbance, hair loss, instability of blood pressure and heart rate, shortness of breath during physical exertion. The patients were undergoing the program "Rehabilitation after COVID-19" program.

143 patients underwent a course of ozone therapy consisting of 10 procedures, the ozone concentration depended on the body weight and the patients' history (from 1.8 to 5 mg / l).

The course of the barotherapy procedures was carried out in 103 people and included 10 procedures, the duration of the stay was 45 minutes. The appointment of intravenous drip ozone therapy or hyperbaric oxygenation depended on the patient's contraindications.

Results. After the first two or three procedures, there was a clear improvement in the clinical picture in the form of a decrease in shortness of breath, increased physical activity (the patient can walk 2 times more distance on a walk without shortness of breath), improved sleep quality, improved memory and concentrated attention. There was an improvement in vegetative indicators - an indicator of adaptive compliance from 0.5 to 0.27 points and an index of functional changes from 4.25 to 3.1 points. Additionally, there was also an improvement in the quality of life indicators according to the SF-36 questionnaire.

Conclusions. Consequently, the use of a complex of physiotherapeutic and oxygen-protective methods for the rehabilitation of post-COVID infectious syndrome, including courses of ozone therapy and hyperbaric oxygenation, has a highly effective positive effect on the patient's condition and wellness. In order to prolong the effect and prophylaxis, 1-2 treatment courses are required.

The article examines the influence of various forms of oxygen in the complex treatment of patients who have undergone COVID-19 in a spa treatment. A positive effect on the effectiveness of patient rehabilitation through the use of ozone therapy, barotherapy and physiotherapy procedures has been noted. The clinical picture and ease of use of the procedures make it possible to recommend for expanding the possibilities of spa treatment for patients with neurological and cardiovascular disorders.

Key words: ozone therapy, hyperbaric oxygen therapy, various forms of oxygen, spa treatment, neurological symptoms, cognitive functions, cardiovascular system

Ozone therapy in the treatment of elderly patients with coronary heart disease

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The aim of this work was to evaluate the effectiveness of ozone therapy in elderly patients with coronary artery disease. The study involved 119 patients (age 65-63 years) with a diagnosis of ischemic heart disease, stable angina pectoris 2-3 FC.

The course of ozone therapy consisted of intravenous administration of ozonized physiological solution. In all patients, the parameters of the lipid profile, the intensity of free radical oxidation, the concentration of nitric oxide by the final metabolites - nitrates and nitrites, as well as the level of endothelin and ADP –induced platelet aggregation - were assessed.

After a course of ozone therapy, good results were achieved in 91% of patients. The improvement in the patient's condition was expressed in a decrease in the number of pain attacks and in the intake of nitrates. Completely anginal attacks were stopped in 50% of patients, in 41% - their number was reduced by more than half. All patients reported subjective improvement after each procedure. After a course of ozone therapy, there was a decrease in total cholesterol levels by an average of 10%, LDL cholesterol by 12.5%, TG by 22%, and the atherogenic coefficient by 12%. At the same time, the duration of the treatment effect lasted up to three months. All patients showed positive dynamics in improving blood rheology, characterized by a decrease in ADP-induced platelet aggregation from 13.37% to 7.26%. In the development of atherosclerosis, free radicals are of great importance, and the decisive role is played by peroxidized atherogenic lipoproteins — LDL. Our data testified to the strengthening of the antioxidant defense system and a decrease in the activity of free radical oxidation. Intravenous administration of low concentrations of ozone improved endothelial function by reducing high levels of nitric oxide and endothelin.

Key words: ozonized saline solution, lipid metabolism, free radical oxidation, nitric oxide, endothelin

The effect of hyperbaric oxygenation on the biochemical status of burned patients

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Introduction. Hypoxia, which develops in severe burn disease, is accompanied by oxidative stress, which contributes to multiple organ failure. One of the methods that stimulate regenerative and reparative processes in burn disease is hyperbaric oxygenation (HBO), the use of which is pathophysiologically justified by the need to eliminate local and general hypoxia, reduce bacterial contamination, normalize microcirculation. It seems relevant to study the effect of HBO on the parameters characterizing the biochemical status of burned patients.

Materials and methods. The study included 19 patients with burns of I-II-III degree on an area of 31-80% of the body surface: 10 patients - a group of standard therapy (control) and 9 patients-a group with an additional appointment of HBO sessions with an extended isopression regimen of 1.3 Ata with a total session duration of 50-60 minutes. The observation period was 14 days. The number of sessions varied from 4 to 7. Blood sampling for biochemical studies was performed before the hyperbaric oxygenation session and immediately after its completion.

Results and discussion. The assessment of changes in indicators before the HBO session and immediately on the same day after the HBO session revealed the following features. There were no differences between the medians of lactate concentration before and after the HBO procedure. After the HBO sessions, there was a statistically significant increase in LDH activity - by 1.2 times ($p=0.009$), which probably explains the lack of differences between the medians of lactate concentrations before and after the session: since the enzyme promotes its utilization, and lactic acid accumulation does not occur. Immediately before and after the session, we found no significant differences between the concentrations of CRP, total protein, albumin, prealbumin, bilirubin, urea, creatinine, zinc, ALT and AST activity. Nevertheless, the examination of patients in dynamics showed that the course effect of hyperoxia was manifested by a tendency to normalize the level of albumin and total protein, cholesterol, urea, and an increase in the concentration of zinc by the 9th day of the study period. A decrease in the level of C-reactive protein was revealed by almost 2 times compared to the control group. It was found that hyperbaric oxygenation to the greatest extent contributed to an increase in the level of prealbumin, which is a negative

marker of the acute phase of inflammation, which also reflects the protein-synthetic function of the liver. The evaluation of the obtained results showed that the number of HBO therapy sessions had an effect only on the level of this protein – i.e., the longer the course of HBO therapy, the higher the level of prealbumin in the patient's blood serum. The effect was noted by the 7th and 14th days of follow-up ($0.01<p<0.004$), apparently, there was a cumulative effect of HBO therapy, consisting in a gradual stimulation of the synthesis of prealbumin in the liver. The content of this metabolite by 14 days of follow-up was statistically significantly different from the level in the control group of patients ($p=0.009$), in whom there was no normalization of this indicator.

Conclusion. Based on the data obtained, it can be concluded that the use of hyperbaric oxygenation with an extended isopression regimen in patients with extensive thermal trauma is safe and has a positive effect on the biochemical status of patients with burns.

Key words: hyperbaric oxygenation ,hypoxia

Some metabolic effects of reactive oxygen species on tissue fragments

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The aim of the work was a comprehensive assessment of the effect of reactive oxygen species and nitric oxide on a fragment of scar tissue ex vivo.

Materials and methods. The study was performed using fragments of scar tissue (n=10) removed intraoperatively in patients with Dupuytren's contracture. Each fragment was divided into 2 equal parts, the first of which was not manipulated, the second was treated with singlet oxygen. The duration of the tissue treatment period was 5 minutes for all factors. Singlet oxygen was created in the mode of 100% power of the corresponding apparatus. Each portion of the tissue was homogenized using the "Ultraturrax" apparatus according to the standard procedure. In the obtained homogenates, the parameters of oxidative metabolism were studied by Fe-induced biochemiluminescence: the intensity of free radical oxidation processes and the overall antioxidant activity.

Statistical processing of the obtained results was carried out using the Statistica 6.1 for Windows program.

Results. It was found that the treatment of a fragment of scar tissue by sources of radicals for 5 minutes leads to significant shifts in the state of free radical processes. Thus, the treatment of tissue fragments with singlet oxygen provided moderate stimulation of radical reactions (1.21 times; $p<0.001$ compared to the control sample, which was not manipulated). According to the effect on the overall antioxidant activity of the biomaterial, both evaluated factors demonstrate a tendency to increase the value of the parameter. Exposure to singlet oxygen also leads to an increase in the antioxidant activity of tissue homogenates, but these shifts are less pronounced (+15.7%; $p<0.05$ relative to a fragment of biomaterial that was not affected). In this case, it can be assumed that the influence of the factor on the state of the pro- and anti-oxidant systems of the biological sample is balanced.

Conclusion. The experiment made it possible to establish that the treatment of fragments of scar tissue with a gas stream from singlet oxygen generators leads to a change in the intensity of free radical processes in it, and the nature of the response is specific with respect to the nature of the influencing factor.

Key words: reactive oxygen species, nitric oxide, oxidative metabolism

Modulating effect of the ozone of blood serum structurization

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The aim of the work was to establish the characteristics of the reaction of the crystallogenic properties of human blood to ozonation.

Material and methods. Venous blood sampling (4 ml) was performed in 15 practically healthy volunteers. Next, the samples were saturated with a saline solution treated with an ozone-oxygen mixture with an ozone concentration: without ozonation (control); 1000 mcg/l; 3000 mcg/l; 6000 mcg/l; 10000 mcg/l; 20,000 mcg/l and 40,000 mcg/l (saturation rate of 30 mcg/l*min; duration - 3-5 min). We studied the nature of the initiated crystal formation in the system "blood serum - ozonated saline solution" with the concentration of the latter increasing in the above range, for which freshly prepared blood serum was mixed with an aliquot amount of 0.9% ozonated or control sodium chloride solution (component ratio 1: 1). It should be emphasized that with such an experiment it is possible to conduct only a tesigraphic test, because its mandatory conditions are the introduction of a solution of sodium chloride into the biological fluid, which is a good crystal-forming agent and in this case acts as a base substance. Evaluation of the results of the initiated crystallogenesis of blood serum was carried out visuametrically according to the traditional algorithm using a system of basic (the main thesigraphic coefficient Q, the coefficient of elucidation P) and a number of additional (uniformity of the distribution of elements in the micropreparation R; the severity of cellular C; zones of the dried sample (Z), including the marginal (Kz); the clarity of the texture of T) criteria. The application of visuometry to the description of the result of dehydration structuring allows us to quantitatively study the changes in both the initiating potential of the biological medium and the correctness of the formation of crystalline and amorphous elements of the facies of the biological medium.

Statistical processing of digital data was performed using the SPSS 16.0 program.

Results. By modeling the biosystems "blood serum - ozonated saline solution", the nature of the response of this biofluid to ozonation under in vitro conditions was studied. Based on the conducted studies, it is shown that with an increase in the saturation dose of ozone, a nonlinear dynamics of changes in the parameters of the tesigraphic test with an extremum corresponding to 6000 mcg/l is observed, which,

taking into account the analysis of all applied criteria, is interpreted as optimum. Thus, low concentrations of ozone have a dose-dependent stabilizing effect on human blood serum normally, and the optimal concentration is 6000 mcg/l, while high-dose effects (20000-40000 mcg/l) have a negative, disorganizing effect on the studied biofluid.

Key words: blood serum, crystallogenesis, ozone

Specificity of the response of the crystallogenic properties of blood to the action of various forms of nitric oxide

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The purpose of this work was a comparative analysis of the effect of various forms of NO on the nature of the dehydration structuring of human serum samples.

Materials and methods. Blood samples from 15 healthy people served as the research material. For the experiment, the blood was divided into 8 portions (intact, which was not affected, and 7 experimental, treated). The volume of each serving was 5 ml. Were six experimental blood samples directly bubbled with nitrogen oxide gas generated by the Plason apparatus at standard power (concentration NO - 800 ppm) and a tenfold diluted flow from this device (80 ppm), as well as an experimental apparatus for the synthesis of nitric oxide (at concentrations of 20, 50, 75 and 100 ppm). Bubbling time - 3 min., exposure after exposure - 5 min. 0.1 ml of an aqueous solution of dinitrosyl iron complexes with glutathione ligands (the concentration of the compound was 3 mmol/l) was added to the seventh blood sample. The synthesis of dinitrosyl iron complexes was carried out according to the method of A.F. Vanin et al. (2005). At the end of the exposure, all samples were centrifuged at 1500 rpm for 15 minutes. The resulting blood serum in the volume of 100 ml was applied to a slide and micro-preparations of dried biological fluid were prepared in accordance with the method of crystalloscopy, which allows to evaluate the intrinsic crystallogenic activity of the biological medium. The dried micro-preparations were evaluated morphologically (by describing the features of the structuring of the dried sample of biological fluid) and visuametrically (using their own system of parameters).

The data obtained were processed statistically in the Statistica 6.1 for Windows package.

Results. It was found that when processing samples of biological fluid with a gas stream from the Plason apparatus, there is a distinct inhibition of the intrinsic crystallization of the biological medium, which manifests itself in a significant decrease in both crystallizability and the structural index of the crystallograms ($p<0.05$ for both cases). Tenfold dilution of the latter with air reduces the severity of this effect, but both

indicators do not reach the level of the control sample ($p<0.05$). On the contrary, when exposed to a gas stream from another generator containing a similar amount of nitric oxide (75 versus 80 ppm) without admixture of reactive oxygen species, primarily ozone, the crystallization result practically does not differ from the facies of an intact biological fluid. This suggests that the inhibition of structuring observed during blood processing by the flow from the "Plason" is determined not only by the concentration of NO, but also by the formation of peroxynitrite, which has a negative effect on the conformation and structure of plasma macromolecules.

Key words: nitric oxide, dinitrosyl iron complexes, blood plasma, crystallogenic properties, biocrystallomics

Cold plasma as a regulator of physical and chemical parameters of biological systems

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Plasma medicine is one of the most modern synthetic scientific directions, born at the junction of plasma physics and biomedicine, dealing with fundamental and applied issues of the interaction of plasma and living matter. At the same time, the field of plasma medicine, associated with the disclosure of biological and sanogenetic effects of cold plasma, attracts the greatest attention of researchers. This circumstance is due to the fact that the plasma generated under standard environmental conditions has a temperature of 3000-5000^{0}C, which has an absolute destructive effect on biological objects.

Currently, cold plasma is commonly understood as ionized gas of various compositions, cooled to a temperature comparable to physiological (30-400C). It is for this factor that a number of potentially useful effects for medical tasks have been experimentally and clinically demonstrated in recent decades. Among them, the antibacterial activity associated with the direct damaging effect of cold plasma on the cell wall of microorganisms is the well studied and described. On the other hand, a more thorough analysis of even this aspect of the problem reveals numerous poorly studied issues, among which are the selectivity of action, the absence of significant damage to the macroorganism's own tissues, etc.

Of particular interest are the bioregulatory properties of cold plasma in relation to the functional and metabolic parameters of living systems. Thus, the pro-regenerative activity of the factor, its ability to inhibit tumor growth, etc., has been previously demonstrated. Of course, these empirical facts require multi-stage verification, but the very presence of such data indicates the presence of secondary, indirect biological effects in cold plasma, which makes it possible to consider it as a potential bioregulator.

It should be emphasized that there are a significant number of undisclosed aspects regarding the elucidation of the biological effects of cold plasma. In particular, the absolute majority of specialists apply and study the so-called atmospheric cold plasma obtained from atmospheric air at normal pressure. The multicomponent nature of the initial gas flow and the impossibility of its standardization necessitate the search

for alternative options, one of which is a monocomponent plasma formed during the ionization of inert gases of a high degree of purification (for example, argon or helium). At the same time, studies of the effect of such plasma on biological objects are isolated and mostly concern argon plasma.

In our previous studies performed both in vitro and in vivo, the existence of secondary bioregulatory properties in cold plasma was shown and verified. In particular, even a short treatment (1-3 min.) of blood samples with a stream of helium cold plasma led to the formation of a biosystem response (according to metabolic and physico-chemical criteria), and it is important to emphasize the dose dependence of the detected shifts. The nature of the changes was significantly different from the "pattern" of the response to a similar effect of an unionized helium stream from the same source. Interestingly, the reaction of isolated blood from the body as a simple model biosystem as a whole turned out to be co-directed to shifts in the same blood parameters of rats exposed to short-term (1-2 min.) exposure to cold plasma on pre-epilated areas of the back. As with in vitro experiments, in this case a moderate antioxidant effect of the factor is shown, its positive effect on the intermediate of energy metabolism, etc. In addition, a modulating effect on the parameters of systemic and local hemodynamics was demonstrated.

On the other hand, these empirical findings should be supported by deciphering the mechanisms of the identified secondary effects. In particular, messengers and methods of transmitting a signal about the effects of cold plasma through intact skin and further to other organs and tissues, including peripheral blood, and the internal environment of the body as a whole need to be disclosed. This should become one of the most significant areas of plasma biomedicine.

Thus, plasma biomedicine is a promising, dynamically developing direction that integrates biophysical and biomedical approaches and is able to form fundamentally new medical technologies that are potentially useful for the correction of various diseases, pathological conditions, injuries and burns.

Key words: cold plasma, biological effects, plasma medicine

Modern approaches to the treatment of patients with a dry form of age-related macular degeneration

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Introduction. The age-related macular degeneration (AMD), which occurs in patients aged 35-40 and older and is characterized by a damage to the eye retina macular zone, is nowadays one of the causes of vision disability.

One distinguishes between a dry and a wet form of AMD. The dry form of AMD affects up to 90% of patients with AMD, however, the range of remedial measures is severely limited for this form of AMD. The absence of sufficiently effective methods for the treatment of the AMD dry form stimulates the search for new methods that use a combined effect on the pathologically altered eye tissues involving both pharmacological and instrumental treatment.

Materials and methods. The proposed treatment method of patients with AMD is implemented according to a multi-stage medical technology adopting a hardware system "Ophtalmoton-MM" (SPE Metromed, LLC, Omsk), which uses a photochromic-ultrasonic method combined with ozone-/NO-containing substances and antioxidants.

Twelve men and women (aged 40-65 and older) suffering from the AMD dry form took part in the clinical testing of the proposed method, that was implemented on the basis of the Medical Center "Blik" in the manner prescribed. The patients of the main group (6 persons) were treated according to the method proposed using 10 daily procedures. At the same time, the patients were prescribed to take tablets of succinic acid 100-200 mg 3 times a day after meals on a daily basis. The patients of the control group (6 persons) received a 15-day course of standard treatment (Omega-3 fatty acids – up to 1600 mg, vitamin C – 500 mg, vitamins B_6 – 50 mg and B_{12} – 1 mg a day).

Results and discussion. The ophthalmologic indicators of the main group after the treatment performed were as follows: the visual acuity increased by 18% at an average; the eye retina electrical sensitivity threshold reduced from 199.67 to 144.52 μA; the eye retina electrical lability increased from 30 to 38 Hz; according to the OCT data, the eye retina edema reduced in all patients, as well as there was a reduction in the size and number of druses, which fact evidenced the efficacy of treatment using the

method. As for the control group, the visual acuity remained almost the same; the eye retina electrical sensitivity threshold reduced from 198.32 to 171,32 μA; the eye retina electrical lability insignificantly increased from 30 to 34 Hz; the OCT data showed a moderate decrease in the size of druses, while their number remained unchanged.

Conclusions. In our opinion, the positive results of treating the patients with the AMD dry form using the hardware system “Ophtalmoton-MM», which adopts a photochromic-ultrasonic method combined with ozone-/NO-containing substances and antioxidants, are potentially productive and can be used in the clinical ophthalmology.

Key words: age-related macular degeneration, ozone, ultrasonic, photochromic radiation, antioxidants

Heart rate variability with a prolonged course of infusions of ozonated saline solution

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The systemic effect of ozone therapy, primarily its effect on the functional state of vital body systems, in particular on the cardiovascular system, has not been studied in sufficient detail. In this regard, the study of the adaptation of the heart rate to a long course of administration of ozonated saline solution was relevant. The experiment was performed on 40 Wistar rats, randomized into 4 groups of equal numbers. Animals of the first (control) group (n=10) received daily intraperitoneal infusions of oxygenated saline solution (1 ml) for 30 days. The rats included in the second, third and fourth groups (10 animals each) were injected with 1 ml of ozonated saline solution (saturating concentrations of ozone in the ozone-oxygen mixture – 3000, 10000 and 40,000 micrograms/l, the received doses of ozone – 0.6, 2 and 8 micrograms, respectively) also daily for 30 days. ECG registration and calculation of HRV parameters in rats were performed on the Poly-Spectrum-8 / V hardware and software complex. Long-term use of an oxygen-containing saline solution in a chronic experiment is associated with the phenomena of bradycardia. In contrast, the use of low and medium doses of ozone in saline solution is accompanied by stimulation of the heart rhythm. When using high doses of ozone dissolved in saline solution (especially – 8 micrograms/day), the activity of the heart did not undergo significant changes.

Key words: ozone, infusions, heart rate variability

Sanogenetic possibilities of ozonated fish oil

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The use of ozone in practical medicine is accompanied by a multifactorial mechanism of its therapeutic action, which is due to the redox potential that is twice that of oxygen. The starting point of its effect on the body during primary reactions with biological substrates is the effect on the pro- and antioxidant balance, after which the main restorative processes unfold, which form the basis of the body's readaptation in a variety of pathologies, including the biocidal effect on the infectious presence, the reaction of oxygen homeostasis, the anti-inflammatory effect, vasodilator, microcirculation restoring effect, immunomodulatory effects, increased energy metabolism in cells, correction of the hemostasis system, dehydration effect, detoxification effects (S.P. Peretyagin, 1991; 2003)

The mechanisms of action and the possibilities of ozone therapy in the processes of restoration of disturbed organs and systems of the body in various kinds of pathological processes, especially those associated with hypoxic and ischemic disorders, are known (A.V. Gustov, S.A. Kotov, K.N. Kontorshchikova, Yu.P. Potekhina, 1999; G. A. Boyarinov, V. V. Sokolov. 1999; A. V. Zmyzgova, V. A. Maksimov. 2003, T. S. Kachalina, G. O. Grechkanev, 2007; O. V. Maslennikov, K. M. Kontorshchikova, B. E. Shakhov., 2018). The resulting moment in the mechanisms of the therapeutic effect of ozone is the modulation of its energy production due to the mobilization of enzymatic reactions. This is a key link that triggers and supports adaptation processes in rehabilitation treatment. An intensification of the utilization of carbohydrates and lipids serves as a substrate supply and a source of energy-generating processes (S.P. Peretyagin., 2016).

The task of this development was to create a new means-a complex of ozonized unsaturated fatty acids based on fish oil, which can be used for metabolic stimulation of energy production processes in the body during pathological processes of vital organs and systems accompanied by hypoxic disorders (central nervous system, respiratory organs, cardiovascular system, organs of the gastrointestinal tract and others).

Material and methods. An original technology was developed for obtaining a complex of ozonized unsaturated fatty acids based on ozonized fish oil (ORF), a feature

of which was the content of an increased amount of short-chain and medium-chain fatty acids in it, while maintaining a certain status of OMEGA-3 fatty acids. (Patent No. 2725980).

Pilot studies were carried out on volunteers, which consisted first in determining the effective dose of ROS in the PCF with different peroxide numbers (PP 500, 2500 and 5000 megO2 / kg) in a 3-day intake of capsules with the complex substrate. Then the studied complex of ozonized FA was taken by a group of volunteers for 30 days. The subjects initially underwent functional and laboratory studies: general clinical, endoscopic, morphological, microbiological, immunological, study of LPO and AOS, microcirculation by laser fluometry, determination of central and systemic hemodynamics by tetrapolar rheography, external respiration parameters by spirography. A repeated complex functional laboratory study was carried out on the 30th day after the end of the course of taking the complex and in the long-term period 3 months after taking the ORF.

Results. It was found that all tested variants of the created fatty acid complex based on ORF with different doses of active oxygen from 500 megO2 / kg to 2500 megO2 / kg and up to 5000 megO2 / kg have biological activity in relation to oxygen-dependent metabolic processes in the body and the associated functional state of life. - important systems (in particular - microcirculation).

For the course tests of the therapeutic and health-improving effect of the developed complex, a dose of ROS with an IF = 2500 megO2 / kg in a volume of 0.67 ml of a gelatin capsule was chosen. Long-term (within a month) intake of ORF with a frequency of 2500 megO2 / kg caused an intensification of carbohydrate utilization in the blood of the subjects (a decrease in glucose and lactic acid to 83% and 51%, respectively, an increase in LDH - up to 148%), antioxidant potential (AOA -145 %, SOD -117%), unchanging reaction of the medium. Carrying out a course intake of the ORF complex with OMEGA for 30 days was accompanied by an increase in cardiac output. The stroke volume of the heart a month after the daily intake of the complex increased to 115% of the initial and remained at this level for more than 3 months of observation. At the same time, there was no significant increase in the cardiac output, which was evidence of an increase in myocardial contractility due to an increase in its internal adaptive capabilities, provided primarily by an increase in the energy potential of cardiomyocytes. This was evidenced by such indicators as the work of the left ventricle of the heart (LV LV - 140% after 3 months), the power of the left ventricle of the heart - 127%. After the end of the intake of the ORF complex, the total power of the

neurohumoral modulation spectrum is high. The state of neuro-humoral regulation is developed, with a high level of vagal and sympathetic influences in the modulation of the heart rate. The balance of the divisions of the autonomic nervous system was characterized by a mixed (balanced) type of autonomic modulation of the heart rate. The current functional state is good.

When studying the parameters of microcirculation of the examined patients who took the complex (OUFA) during the course of treatment, a significant increase in the volumetric microcirculation in the peripheral parts of the cardiovascular system was noted. The microcirculation index in patient 2 after the course of the complex was increased by 2.7 times compared to the initial level. The endothelial factor of active regulation (an increase in the bioradical activity of NO), increased by 2 times, exerted the greatest influence on the mechanism of microcirculation enhancement.

Enteral intake of capsules containing a complex of fatty acids based on ORF was accompanied by a systemic positive effect on the function of external respiration in the examined patients. It was found that after a course intake of a complex of FA, the indicator of the vital capacity of the lungs (VC) was at a higher level: 175% compared to the initial one. There were also marked positive changes in the frequency and depth of breathing: up to 134%, and the RR 120%, which was the optimal combination, in which the work of the external respiration apparatus increased - MOI 163%. In such a situation, energy consumption per 1 liter of minute ventilation is minimized and the ratio of alveolar ventilation to general ventilation of the lungs increases. The advantage of stimulating external respiration by enteral intake of a complex of FAs in the ORF containing reactive oxygen species with an energy substrate can be explained by the greater influence of ROS on oxygen-dependent processes of lung tissue metabolism, as well as on the changing energy potential of erythrocytes flowing through the pulmonary circulation, which together provides a large the effectiveness of the oxygen transport function in the body.

Key words: ozone, fatty acids, energy production, life support optimization

Influence of EMR at nitric oxide frequencies on vascular and metabolic adaptation in experimental trauma

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Introduction. An urgent medical problem is the introduction into practice of new non-drug technologies based on electromagnetic radiation (EMR) of the extremely high-frequency range of the extremely high-frequency (EHF) range with the frequency of nitric oxide (NO).

Material and methods of research. The study was conducted in compliance with the principles and rules of the European Convention ET/S 129, 1986 and Directives 86/609 ESC. The results of a two-stage study of the effect of broadband electromagnetic noise radiation of various frequency ranges: 53.57..78.33 GHz, 110.0...170.0 GHz and 150.176...150.664 GHz on the parameters of vascular and metabolic adaptation reactions under experimental ischemia and contact thermal burn (CTO) of the III degree on an area of 20% of the body surface were studied. The EHF therapy device "AMPHIT" (Russia) and two experimental noise signal generators of the specified ranges (Russia) were used. We studied the dynamics of microcirculation, lipid peroxidation and antioxidant protection in male Wistar rats (25 at each stage) in response to a seven-day course irradiation with a power of 1 MCW with a dose of 1.2 MJ (once a day) of the occipital protuberance at a distance of 0.5 cm from the skin. The injuries were inflicted under anesthesia (Zoletil+Xyl). The animals were divided into 5 equal groups (3 experimental ones according to the number of radiation sources used) and 2 control ones (intact and not irradiated after injuries). The area of ischemia was measured with a lined stencil, the total microcirculation index was measured by laser Doppler flowmetry (LDF) on a LACK-M laser analyzer (NPP "Lazma", Russia). The activity of peroxidation processes (POL) in plasma and red blood cells was studied by the method of induced biochemiluminescence on BHL-06 (N. Novgorod). Statistical processing was carried out using the Statistica 6.0 program.

Results and discussion. The frequency dependence of microvascular reactions, indicators of pro - and antioxidant protection is shown. Clinically, in experimental groups of animals exposed to radiation at frequencies containing nitric oxide (110.0-170.0 GHz and 150.176...150.664 GHz), a decrease in the area of ischemic manifestations and the necrosis zone was recorded to 26.3% compared to 31% in the group with EHF EMR of 53-78 GHz and 46.5% in the control, which was

confirmed by the results of LDF. In parallel, there was a decrease in the intensity of POL processes and an increase in the total antioxidant reserves of the blood with an increase in the activity of bio-radical protection enzymes, both in the case of an ischemic flap and against the background of thermal trauma. The obtained results confirm the role of nitric oxide as a biogenic vasodilator, and a regulator of the state of the body's pro - and antioxidant systems.

Conclusions. The registered fact can have a positive impact on the correction of post-traumatic ischemic and metabolic disorders in the clinic.

Key words: burn injury, ischemia, blood microcirculation, lipid peroxidation, EHF therapy

Assessment of the state of the antioxidant system of the blood in children with inflammatory bowel diseases

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The aim of the work is to assess the nature of changes in the antioxidant defense system in children with inflammatory bowel diseases.

Material and methods. The state of oxidative blood metabolism was studied in 40 children aged 6 to 17 years with inflammatory bowel diseases (20 with Crohn's disease and 20 with ulcerative colitis) and 35 healthy children of the appropriate age (control). The diagnosis of inflammatory bowel disease was verified on the basis of a comprehensive examination, including clinical and laboratory monitoring, as well as endoscopic examination of the intestinal mucosa with morphological analysis of biopsies.

The concentration of SH-groups in platelet-free blood plasma stabilized with sodium citrate was determined by the Hu (1994) method. Catalase activity in erythrocyte hemolysate was determined by the method of Aeble (1952). The content of reduced glutathione GSH in erythrocyte hemolysate was determined by the Beutler method (1990).

The study was approved by the Local Ethics Committee of the Federal State Budgetary Educational Institution "PIMU" of the Ministry of Health of Russia. Informed consent to participate in the study was obtained from the parents of the children (or from the children themselves over the age of 15) before taking samples.

The results were processed using the Statistica 6.0 program.

Results. Our study shows a malfunction of the antioxidant defense system of the body of children with inflammatory bowel diseases. A significant (1.3-fold) increase in the activity of catalase in erythrocytes is noted only during hospitalization of children with Crohn's disease, which continues even at the discharge of patients. The concentration of the main intracellular non-enzymatic antioxidant glutathione in patients also increases, and more pronounced in those suffering from ulcerative colitis. The concentration of reduced glutathione remains significantly elevated even when children with inflammatory bowel diseases are discharged. The level of total sulfhydryl groups characterizes the state of the body's antioxidant system, which, by regulating the mechanisms of free radical oxidation, ensures the prevention of oxidative degradation of biomacromolecules (Banne et al., 2003). According to our study, the level of SH-groups

of blood plasma of children with inflammatory bowel diseases tended to increase, and at discharge of patients with Crohn's disease exceeded the control values by 1.14 times.

Conclusion. Thus, violations of the antioxidant activity of the blood of children with inflammatory bowel diseases play a significant role in the pathogenesis of these diseases, while accompanying changes in hemorheology and hemostasis.

Key words: inflammatory bowel disease, Crohn's disease, ulcerative colitis, antioxidant defense system, catalase, glutathione, SH-groups

The effectiveness of the rehabilitation treatment of patients with gonarthrosis

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Introduction. Osteoarthritis is a joint disease characterized by cellular stress and degradation of the extracellular matrix arising from macro- and microdamages, followed by anatomical and physiological disorders (cartilage degradation, bone remodeling, osteophyte formation, inflammation, loss of normal joint function). In addition to drug treatment, physiotherapeutic methods are used in the complex therapy of arthrosis. Physiotherapy regimens are selected taking into account the stage of the pathological process, the leading symptom, the patient's age, and the presence of concomitant diseases. However, there is conflicting information about the effects of physiotherapy. One of the widely used methods of restorative treatment is ozone therapy. To date, information about the treatment of gonarthrosis by the method of ozone therapy is poorly covered in literary sources.

Objective of the study: to evaluate the effectiveness of complex rehabilitation treatment in patients with gonarthrosis.

Materials and methods: The study included 60 people (32 women and 28 men) aged 35-55 years with a diagnosis of stage I - II gonarthrosis, according to the criteria of Altman (1991). The patients were divided into three groups. The first group (21 people) was prescribed a course of ozone therapy (10 procedures). Ozone therapy was carried out 2 times a week with an ozone-oxygen mixture with a ozone concentration (5000 μ / l), obtained using the device "Medozon VM-03" (Russia). Oxygen supply to the ozonizer is carried out by the Longfian Scitech oxygen concentrator (China). The required volumetric flow rate of the oxygen-ozone mixture is 0.5 l / min. The ozone-oxygen mixture was taken into a 20 ml syringe. The injection was performed periarticularly into the trigger points with a 0.30 * 12mm BL / LB (30G * 1/2 ") needle. Group II (19 people) underwent 5 applications of kinesio taping of the knee joint using the method of lymphatic drainage and muscle correction. The tapes were applied once a week for a period of 5 days. Each patient received 5 applications, with intervals of two days. In group III patients (20 people) ozone therapy was combined with kinesio taping. The results of the study were evaluated according to clinical data, as well as according to the WOMAC questionnaire.

Discussion and results: In all groups, there was a positive effect of the treatment. If, before treatment, each of the patients had edema of the joint area, limitation of movement in the affected joint (mean WOMAC in all groups 6.4 ± 0.3 points), pain during exercise and at rest (mean WOMAC in all groups 11, 8 ± 0.5 points), then by the third procedure the pain indicators were represented by the following values: in the first group - 6.8 ± 0.3 points, in the second group - 7.6 ± 0.3 points, in the third group - 6, 5 ± 0.2 points.

Also, there was a positive trend in the stiffness scale of the WOMAC questionnaire: in the first group, the indicator decreased to 3.3 ± 0.3 points, in the second - to 3.5 ± 0.5 points, in the third - to 2.8 ± 0.3 points. ... The average value of the indicator of physical activity before the start of treatment in all groups was 45.6 ± 0.5 points. Against the background of the treatment in the first, this indicator decreased to 26.8 ± 0.3 points, in the second and third groups - to 33.8 ± 0.5 and 25.5 ± 0.3 points, respectively.

Conclusions: The conducted rehabilitation treatment of patients with gonarthrosis generally yields a positive result. In particular, ozone therapy helps to reduce pain and stiffness in the joint, kinesio taping, in addition to increasing the range of motion, has a lymphatic drainage effect, leading to a decrease in periarticular edema. Their combined use potentiates the effect of these techniques, which speeds up recovery and shortens the rehabilitation period for patients.

Key words: gonarthrosis, ozone therapy, kinesio taping

New approaches to the modernization of ozone generators to optimize the technology of bioimplants sterilization

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Introduction. Sterilization is the most important stage in the technological process of manufacturing bioimplants, the main task of which is the need to ensure the safety of the use of plastic materials when they are introduced into the recipient's body. The developments of recent years indicate the significant potential of combined technologies for sterilizing bioimplants, in which the stages of ozone and radiation exposure are combined within one process. Ozone sterilization is also promising as an independent technique, the development of which requires further improvement of ozone generators.

The purpose of this work is to develop a new control principle for a medical ozone generator with feedback to optimize the sterilization process.

Material and methods. In model experiments, fragments of the femur bones of a bull were used (the age of the animals is 1.5 ÷ 2 years). The samples obtained were stored in bags made of two-layer DGM Steriguard thermofilm sealed on an F70-400 thermocouple (Netherlands). The generator of medical ozone A-s-GOKSf-5-04-OZON with an IKO-50 ozone concentration meter (manufactured by JSC Lepse Electromachine-Building Plant, Kirov, Russia) and an oxygen concentrator Vision Aire (USA) were used for sterilizing the packaging and bone samples. The original developed equipment implements the ozone generation method based on a tubular ozonizer.

Results and discussion. In this investigation, to optimize the sterilization process, it was proposed to use the principle of closed-loop control of a medical ozone generator. The circuit for comparing the concentrations of the ozone-oxygen mixture at the inlet and outlet of the sterilization chamber generates a differential signal, upon reaching the minimum threshold value of which the device is turned off. The minimum value corresponds to the moment when ozone in the sterilizing gaseous medium of the working chamber is not consumed for interaction with the object to be sterilized. The permissible value of the threshold difference in concentrations is set taking into account the rate of natural dissociation of ozone molecules.

Conclusion. The principle of closed-loop control proposed and implemented in the created device for ozone sterilization makes it possible to process objects and optimize the sterilization process without setting a specific processing time in advance. Automatic accounting of the influence of current external parameters - temperature, humidity, illumination, fluctuations in the concentration of the gas mixture, and other process features allows saving time and energy costs during the sterilization process. The development is protected protected by the patent of the Russian Federation.

Key words: bone grafts, ozone, sterilization, ozone generators, closed loop control

Possibilities of organoprotection with ozone in severe blood loss

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Introduction. Hypoxia, along with an increasing imbalance of lipid peroxidation and antioxidant activity and endogenous intoxication, is a universal cause of the progression of organ dysfunction in hemorrhagic hypotension. The work is devoted to assessing the effectiveness of the use of ozonized autoerythrocytes for the prevention of organ dysfunction in severe blood loss.

Material and research methods. The study was carried out on 32 nonlinear rats, which were simulated acute severe blood loss, while in the study group it was compensated with 0.9% S. NaCl ozonized before transfusion with an ozone concentration of 2 mg / l autoerythrocytes, against standard autoerythrocytes in the control. On the 5th day of the post-transfusion period, all studied and 5 intact animals were decapitated, the liver was removed for morphological examination.

Results. In rats that underwent severe blood loss, on the 5th day of standard blood loss therapy, hypoxic damage and microcirculation disorders were formed in the liver, manifested in a decrease in the number of capillaries and an increase in their cross-section, impaired permeability of the microvascular wall, swelling and pericellular edema of endotheliocytes. Intravascular changes in microcirculation manifested themselves in the formation of hyaline thrombi, microaggregates and erythrocyte sludge in their lumen. Disturbances outside the vascular wall were detected in the form of diapedetic hemorrhages and pronounced perivascular edema. The hepatic triads were characterized by arteries with free-lying red blood cells, as well as veins with free lumen. In the hepatic cells surrounding the triad, pronounced hydropic dystrophy was noted, as well as moderate round-cell infiltration and an increase in the number of stellate cells. The structure of the hepatic lobule as a whole was preserved, and the interbeam spaces were unevenly expanded. Moreover, a significant part of them were erythrocytes. The above damage was resolved with the use of transfusion of ozone-treated autoerythrocytes. Against the background of a significant decrease in the severity of perivascular edema, a small number of free-lying erythrocytes is observed in the lumen of the arteries. Less pronounced phenomena of tissue dysergosis are also confirmed by a weakly expressed hydropic dystrophy of the hepatocytes surrounding

the triad, their pronounced cytoplasmic basophilia. There is a high structure of the hepatic lobule, as well as a uniform expansion of the interbeam spaces.

Conclusions. As a result of acute blood loss in rats, hypoxic disorders of microcirculation are formed in the liver, the number of nuclear profiles decreases, and the number of non-nuclear cells increases. These patterns are consistent with the earlier reported data on posthemorrhagic myocardial injury. Administration of ozonized autoerythrocytes to rats with blood loss prevents hypoxic and reperfusion liver damage and improves microcirculation.

Key words: blood loss, hypoxia, ozonized erythrocytes, organ failure

The state of microcirculation during a burn in an experiment under the action of dinitrosyl iron complexes

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Introduction. One of the most important problems in medicine is thermal trauma. Severe disorders of central, regional and peripheral hemodynamics develop during burn disease (Goldzon, Dolgikh, 2011). A promising type of NO donor suitable for biomedical use is dinitrosyl iron complexes (DNIC). The aim of the study was to evaluate the effect of DNIC on the state of microcirculation in experimental combined thermal trauma (CTT).

Material and methods. The experiment was carried out on 50 male rats of the Wistar line. Working conditions with animals were in accordance with the rules of the European Convention ET/S 129, 1986 and Directives 86/609 ESC. 5 groups of equal numbers were formed: intact; 1 experimental group – animals receiving 1 ml of saline solution; 2 experimental group-animals with CTT; 3 experimental group-animals with CTT receiving 1 ml of saline solution; 4 experimental group-animals with CTT receiving 1 ml of DNIC daily (0.3 micromol/l). CTT (contact burn on an area of 20% and thermal inhalation effect for 20-30 seconds) was applied under anesthesia (Zoletil + Xyl). DNIC was obtained by the method of A.F. Vanin (2015). The animals were removed from the experiment on the 10th day after CTT. Before removal, the state of microcirculation was evaluated using laser Doppler flowmetry (Krupatkin et al., 2004) on the "LAKK-M" analyzer. Statistical processing of the results was carried out using the program "Statistica 6.0".

Results and discussion. In CTT, the amplitude of the regulatory components increased compared to healthy animals, but in the group with DNIC, there was a decrease in active and passive regulatory factors, which may indicate the restoration of endothelial function, a decrease in sympathetic hyperregulation and congestion in the venous microvascular bed, optimization of the filling processes of arteries and arterioles of the microcirculatory link. A decrease in the vascular tone of arterioles (removal of spasm) due to a decrease in neurogenic activity increases the heart rate in the microcirculatory bed due to an increase in the flow of arterial blood, which introduces a pulse wave (Krupatkin et al., 2004).

The intensification of microhemodynamics under the influence of DNIC may be associated with the predominance of nutritive blood flow (bypass rate <1). In CTT, the

amplitude of the regulatory components increased, but in the group with DNIC, there was a decrease in active and passive regulatory factors in relation to animals with CTT without treatment. It is known that DNIC have a hypotensive effect, which is realized due to the release of NO from them (Vanin, 2015).

Conclusions. Thus, CTT showed an increase in the endothelial, neurogenic and respiratory components of microcirculation, microhemodynamics of the border area of the burn, bypass rate. The normalization of the microcirculation state was revealed after the use of 0.3 micromol/l of DNIC in CTT, which increases the adaptive potential of the body.

Key words: combined thermal trauma, dinitrosyl iron complexes, microcirculation.

The effect of singlet oxygen inhalations on the biochemical parameters of the blood biotransformation system in patients with thermal trauma

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Introduction. Thermal trauma (TT) is one of the most common types of domestic injuries, which is becoming more frequent in the conditions of an aggravation of the military situation. Currently, singlet oxygen (SO) inhalation under hypoxia conditions is promising, but poorly studied. The aim of the study was to study the effect of SO on the biochemical parameters of the blood of patients with TT.

Material and methods. The study examined 55 blood samples of patients with TT II-III degree with an area of more than 20% of the body surface. The patients were randomized into 2 groups: control - patients with TT and experimental-patients with TT and SO inhalations (intensity 100%, 10 days). The generation of the SO was carried out using the "Airnergy" device (Germany). The activity of aldehyde dehydrogenase (AlDH), lactate dehydrogenase (LDH), superoxide dismutase (SOD), catalase and their kinetic characteristics were determined in the blood, the intensity of free radical oxidation was evaluated using the method of biochemiluminescent analysis (total antioxidant activity (TAA); S – light sum of chemiluminescence for 30 seconds, reflecting the ability of a biological object to free radical oxidation) and determining the concentration of malonic dialdehyde (MDA). The lactate concentration was determined using an automatic analyzer Super GL Ambulance (Dr. Muller, Germany). Statistical processing of the results was carried out using the Statistica 6.0 program (Statsoft Inc., USA), using the Student's t-test.

Results and discussion. After a 10-day course of SO inhalations, normalization of the redox balance of blood was noted in patients with TT. The light sum S decreased in plasma and red blood cells by 29.19% ($p=0.033$) and 24.21% ($p=0.038$), the concentration of MDA in plasma decreased by 41.56% ($p=0.039$) compared with the indicators of lipid peroxidation in the blood of patients with TT without treatment. SO inhalations led to normalization of TAA in blood plasma, an increase in the activity of AlDH, SOD and catalase in red blood cells by 2.32 times ($p<0.001$), by 71.71% ($p=0.025$) and 39.17% ($p=0.031$), normalization of lactate levels due to an increase in LDH activity in direct and reverse reactions by 34.03% ($p=0.032$) and 14.49%

(p=0.041), respectively, and an increase in the energy reaction balance coefficient ((LDHdir/LDHrev) / (LDHrev/LDHdir) × 100) by 37.28% (p=0.026). Activation of SOD, catalase, LDH, AlDH in erythrocytes after SO inhalation in TT is due to a decrease in the half-conversion time of substrates for enzymatic reactions, an increase in the catalytic efficiency of enzymes.

Conclusions. Thus, in clinical conditions with TT, a favorable effect of SO inhalations for 10 days was demonstrated: normalization of TAA, lactate concentrations, a decrease in plasma MDA, activation of AlDH, LDH, SOD and catalase, while the increase in the activity of oxidoreductases is due to an increase in their affinity for reaction substrates and catalytic efficiency.

Key words: thermal trauma, singlet oxygen, blood biotransformation system

Experience in the use of ozone therapy in spa treatment of persons with carbohydrate metabolism disorders

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Diabetes mellitus has been and remains one of the most urgent problems of medicine. This pathology ranks third among the direct causes of death after cardiovascular and oncological diseases. Treatment of patients with diabetes mellitus is a complex treatment aimed at the underlying disease and its various complications that aggravate its course. Along with the main methods of treatment (diet therapy, drug treatment), therapeutic physical factors play an essential, although auxiliary role in complex therapy. In this regard, ozone therapy is a promising direction in medicine.

The aim of our work was to evaluate the effect of intravenous ozone therapy on the carbohydrate metabolism of patients with its violation.

Material and methods. 128 patients with carbohydrate metabolism disorders were examined: increased glucose tolerance (n=31 people); insulin-dependent diabetes mellitus of mild (n= 51 people) and moderate (n=46 people) severity. Women made up 56.2% (72 people); men-43.8% (56 people). The average age of the observed - 61.8+2.16 years. Patients who received intravenous ozone therapy in the complex of sanatorium-resort treatment made up the main group (n=82 patients); the control group included persons who received only traditional sanatorium treatment (n=46 patients).

Traditional spa treatment included diet therapy, climate therapy, balneotherapy, physiotherapy.

Ozone therapy was performed in the form of intravenous administration of ozonated saline solution of 200.0 ml 3 times a week. The physiological solution was ozonized on a medical ozonizer of the company "Medozons" (Nizhny Novgorod). The course of treatment consisted of 5 procedures.

The following parameters were evaluated in dynamics: clinical condition, fasting blood glucose, glycated hemoglobin; a postprandial test was performed, according to indications.

Results and discussion. Intravenous ozone therapy in combination with spa treatment significantly reduced the average fasting blood glucose by 18.7 %; glycated hemoglobin by 12.5%; postprandial glycemia by 14.8%. In the control group-without significant dynamics.

The positive effect of the treatment was expressed in a decrease in hyperglycemia, a decrease in thirst, the disappearance of polyuria, itching of the skin, weakness. When analyzing the effectiveness of treatment of patients with insulin-dependent diabetes mellitus in 40.2% of cases (39 people) after a course of intravenous ozone therapy, it was possible to achieve compensation for the condition, which is one of the main criteria for successful treatment.

Thus, ozone-oxygen therapy can be considered as an effective additional method of prevention and treatment of carbohydrate metabolism disorders in persons with its violation.

Key words: violation of carbohydrate metabolism, insulin-independent diabetes mellitus, intravenous ozone therapy, Spa treatment.

Comparative assessment of the influence of terahertz radiation and generated no flux on the energy metabolism of erythrocytes in thermal injury

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Severe thermal trauma developing as a consequence of burn disease, characterizes by hypoxia, lactic acidosis and oxidative stress. One of the most important indicators that play a role in burn disease is the activity of lactate dehydrogenase (LDH) in the direct (LDHdir), oxidizing lactate to pyruvate, and reverse (LDHrev), reducing pyruvate to lactate, reactions.

Previously were found that nitric oxide lead to normalization of metabolic state at burns.At the same time it is possible to regulate the activity and synthesis of endogenous NO by acting on the body with terahertz radiation. The mechanism is explained by the fact that when the frequencies of the produced rotation frequency of the polar molecules coincide, the transfer of energy is possible, which affects its reactivity. The rotational molecular spectrum of absorption and emission of NO, affecting SH-groups in the active center of enzymes, is 155 GHz.

The aim of this work was to compare LDH activity in direct and reverse reaction under the usage of nitric oxide (NO) and terahertz radiation of frequency matching in the peak of endogenous NO generation in the treatment of II degree burn. (155GHz).

Materials and methods. These studies were carried out on male Wistar rats. The animals under anesthesia underwent thermal injury of the II degree with an area of 15% of the surface area of the body. The animals of the experimental groups received daily therapy: the first experimental group - NO-therapy from the air-plasma coagulator "Plazon" (2 min), and the second - from the emitter of terahertz radiation (THR) with a frequency of 155 GHz (2 min). The animals were withdrawn from the experiment by decapitation with cutting the carotid artery under anesthesia ("Zoletil" + "Xyla") on the 7th day. The spectrophotometric method was used to assess the activity of LDH in direct and reverse reactions.

Results and discussion. The predominance of LDHrev activity by 41% ($p = 0.003$) compared with the norm were found in the group of burnt animals without treatment, that may indicate the accumulation of lactate and, accordingly, lactic acidosis.

The use of exogenous nitric oxide («Plazon») and THR 155 GHz contributed to a close to normal ratio of the activity of LDHdir and LDHrev: compared with a burn, LDHdir increased by 39% ($p = 0.006$), and LDHrev decreased by 47% ($p = 0.003$); relative to normal values, the enzyme activity was lower by 10% ($p = 0.008$) and 15% ($p = 0.011$), respectively. At the

same time, the use of 155 GHz THC promoted an increase in LDHdir by 50% ($p = 0.003$), and LDHrev by 23% ($p = 0.001$) compared with a burn, and no significant differences in LDHdir activity were found compared to the norm. Thus, the use of NO-therapy lead to reduce of the hypoxia, but the use of THR 155 GHz had a more pronounced effect. Both therapy options helped to reduce hypoxia and lactic acidosis, however, the more pronounced effect of the use of THR 155 GHz can be explained by the absence of losses of nitric oxide that occur with exogenous use of nitric oxide.

Conclusions. It was found that therapy with the use of nitric oxide helps to normalize energy metabolism and reduce hypoxia; the usage of THR 155 GHz, promoting the endogenous NO induction, lead to the most pronounced effect.

Key words: thermal injury, burn injury, nitric oxide, terahertz radiation, hypoxia, lactate dehydrogenase.

Complementary application of the ozonized saline solution in mild and severe patients with pneumonia COVID-19:Anon-randomized pilot study. Adriana Schwartz

Context: Currently, there is no effective antiviral therapy recommended for novel coronavirus pneumonia 2019 (COVID-19).

Aims: To assess the safety of ozonized saline solution (O3SS) used as a complementary therapy in adult COVID-19 patients.

Methods: Twenty-five adult patients hospitalized with mild to severe symptoms of COVID-19, who met the inclusion criteria and were treated from April 18 to April 26, 2020, at Virgen De La Paloma Hospital, Madrid, Spain were included in this study. Patients were assigned to receive standard care consisting ceftriaxone (250 mg – 2 g twice daily for 7 days) plus azithromycin (500 mg once daily for 5 days), of 200 - 400 mg hydroxychloroquine twice daily for 5-7 days plus tocilizumab 400 mg twice daily for 5 days, low molecular weight heparin and 40 to 60 mg metil-prednisone plus O3SS, 200 mL, 3-5 µg/mL per day for 10 days. No control group was included, the data was compared to clinical trials in this subject. Secondary endpoints assessed included the clinical status of participants, laboratory examinations, and duration of viral shedding.

Results: Patients with COVID-19 with mild to severe symptoms who received intravenous O3SS as an adjunct treatment experienced no side effects. The main results of O3SS treatment were a tendency to improve clinical symptoms without side effects. None of the patients treated died.

Conclusions: Early evidence of efficacy shown improvements in symptoms such as dyspnea, weakness, and reduction in body temperature were observed and corresponded to improvements in laboratory results including D-dimer, fibrinogen, lactate dehydrogenase, and C-reactive protein. These preliminary data will serve as the basis for a future study of the effectiveness of this therapy.

Intravenous ozone therapy and diastolic function of the myocardium in persons with arterial hypertension

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Patients with arterial hypertension are characterized by violations of the diastolic function of the left ventricle. Therefore, it is very important to identify early signs and variants of the disease and preventive measures. The aim of the study was to evaluate the effect of intravenous ozone therapy on the parameters of transmittal blood flow in people with arterial hypertension. After the course of sanatorium-resort treatment with the use of intravenous ozone therapy, according to the results of Dopplerographic assessment of the parameters of the transmittal blood flow, a shortening of the segmental time of isovolumic relaxation of the myocardium by 6.5% was revealed in dynamics, and there was a tendency to increase the ratio of the peak time of early to late filling of the left ventricle, which indicated a positive effect of medical ozone on the diastolic function of the heart.

To objectify the data obtained in the main and control groups, a clinical and instrumental examination was carried out, which included: an assessment of the clinical state, an analysis of the parameters of central hemodynamics by the method of echocardiography. In the course of the work, positive results of the influence of ozone therapy on the indicators of diastolic function were obtained.

Thus, against the background of the ongoing complex spa treatment with the use of intravenous ozone therapy, a 6.5% shortening of the segmental time of isovolumic relaxation was revealed, and a tendency towards an increase in the E / A index was noted. In the control group, there was no reliable dynamics.

Conclusion. The obtained positive results of the effect of parenteral ozone therapy on the indicators of diastolic function deserve attention and can be successfully used in a complex of preventive measures for arterial hypertension.

Key words: arterial hypertension, diastolic function of the left ventricle, intravenous ozone therapy

Substantiation of the use of antioxidant and anti-inflammatory therapy in the correction of bioradical processes in experimental post-traumatic arthritis

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The parameters of oxidative stress and antioxidant activity of 89 white non-pedigree rats under the conditions of complex therapy of post-traumatic osteoarthritis with nimesudide and ethoxidol were studied in dynamics. The model of puncture traumatization of the joint according to the method of G. M. Dubrovin was reproduced. Laboratory animals were divided into three groups: intact; control, without receiving treatment; experimental, with therapy in the form of intra-articular injections of ethoxidol at a dose of 5 mg/kg every other day, a course of 5 days and oral administration of nimesulide 2 mg/kg/day for 10 days. Laboratory examination of blood samples of the control group on the 28th day of the experiment recorded an increase in the indicators of oxidative stress by more than 71.8% of the norm, with a steady decrease in the activity of the antioxidant system. The combined use of ethoxidol and nimesulide revealed a decrease in markers of oxidative stress by more than 38.8% with an increase in the antioxidant potential by almost 2 times compared to the data of the control group.

The results obtained in the control group indicate the formation of pronounced oxidative stress after experimental traumatization of the joint, which cannot be suppressed by endogenous antioxidant system and is maintained independently under conditions of aseptic inflammation. At the same time, complex therapy with two drugs with different points of application in the pathogenesis of osteoarthritis made it possible to effectively reduce the intensity of bioradical processes, restoring the antioxidant potential. Thus, nimesulide, selectively inhibiting COX-2, suppresses the formation of prostaglandins in the secondary alteration zone, lowers the production of pro-inflammatory interleukins, thereby breaking the vicious circle and limiting inflammatory reactions, but to a lesser extent counteracting cytotoxic and protease activity. Ethoxidol, due to its pronounced antioxidant properties, contributes to the replenishment of antiradical enzymes, and also prevents phospholipid destabilization, inhibiting lipid peroxidation by inactivating reactive oxygen species, increasing membrane resistance and eliminating hypoxia. Thus, intra-articular administration of ethoxidol in combination

with oral administration of nimesulide successfully corrects the negative effects of oxidative stress and prevents the chronicity of post-traumatic arthritis.

Key words: post-traumatic osteoarthritis, ethoxidol, lipid peroxidation

Clinical and laboratory monitoring of the condition of the skin of the face when using the cream "OZODERMIS 10%"

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The **aim of the work** is to study the dynamics of laser Doppler flowmetry and ultrasound and functional parameters of the facial skin during the application of an ozonide-containing face cream and during glycolic peeling a month after application.

Materials and methods. The study was conducted in the period from December 2018 to September 2021 on the basis of the Alexandria clinic in 65 people aged 25 to 65 years, at room temperature of 22-23 degrees Celsius, lying down after a 20-minute rest. To establish the dynamics of facial skin parameters during the application of an ozonide-containing face cream, the following methods were used: macrophoto, dermatoscopy, laser Doppler flowmetry, study of functional parameters of the skin using the Multi Skin Test Center device.

Results and discussions

1. The study revealed a cumulative stimulating effect of the “Ozodermis 10%” cream on the microcirculation of the skin, which makes its use promising both in healthy people to improve the condition of the skin, and in people suffering from various diseases in the pathogenesis of which a significant role is played by a violation of microcirculation of the skin.

2. Combination therapy of the application of Ozodermis cream 10% together with Sesglicopeel Classic glycolic peeling, 52.5% glycolic acid, pH represents a new opportunity for an integrated approach to improve the condition of the skin.

3. Ozonide-containing cosmetics is a new direction of external preparations in dermatology that have a complex effect on the functional parameters of the skin

4. Further comprehensive evaluation of preparations from a series of ozonide-containing cosmetics with different values of peroxide numbers depending on the age of patients and skin type is necessary.

Key words: ozone therapy, ozodermis, cosmetology