

Содержание:

Goldman A., Wollina U., Machado D., Marinowic D. LONG-PULSED ND:YAG LASER TO TREAT TELANGIECTASIA OF THE NOSE: A COMPREHENSIVE 5-YEAR SINGLE CENTER STUDY	7
Бойко С.Ш.С., Русин В.И., Бойко С.А., Русин В.В., Попович Я.М. АНАТОМО-КЛИНИЧЕСКОЕ ИССЛЕДОВАНИЕ НИЖНЕЙ ПОЛОЙ ВЕНЫ И ВЕНОЗНОГО ВОЗВРАТА В УСЛОВИЯХ ОПУХОЛЕВОГО ВЕНОЗНОГО ТРОМБОЗА	13
Venher I., Kostiv S., Kolotylo O., Herasymiuk N., Nechytailo O. NONSPECIFIC DYSPLASIA OF THE CONNECTIVE TISSUE – A FACTOR IN VENOUS THROMBOEMBOLIC COMPLICATIONS OF HIP JOINTS' ENDOPROSTHETICS.....	21
Parfentiev R., Grubnik V., Grubnik V., Bugridze Z., Giuashvili S., Beselia L. STUDY OF INTRAOPERATIVE INDOCYANINE GREEN ANGIOGRAPHY EFFECTIVENESS FOR IDENTIFICATION OF PARATHYROID GLANDS DURING TOTAL THYROIDECTOMY	

Kuridze N., Rukhadze B., Bakashvili N., Verulava T., Aladashvili A. CARDIAC IMPLANTABLE ELECTRONIC DEVICE INFECTIONS - PREVENTION, DIAGNOSIS, TREATMENT AND IMPACT ON QUALITY OF LIFE.....	99
Iosebashvili D., Petriashvili Sh., Lolashvil N., Petriashvili A., Mamatsashvili I. PREVALENCE OF IRON DEFICIENCY AND ANEMIA IN PATIENTS ADMITTED TO HOSPITAL WITH CHRONIC HEART FAILURE	107
Goncharuk O., Matyukha L. CORRELATION BETWEEN THE LEVELS OF ADIPOSE-DERIVED HORMONE AND CARDIOMETABOLIC MARKERS IN PATIENTS WITH HYPERTENSION AND OBESITY	111
Naumova L., Milevska-Vovchuk L., Burak A., Krytsky T., Pankiv I. NEUROLOGICAL MANIFESTATIONS OF PROLACTINOMA (CASE REPORT).....	116
Gabritchidze S., Karanadze N., Charkviani N., Chokhonelidze A. MINERAL WATER „DZUGURI” AND TYPE 2 DIABETES MELLITUS: SCREENING RESULTS.....	121
Slyka N., Rusnak I., Zub L., Kulachek Y., Kulachek V., Al Salama M., Rovinskyi O. MODIFIED TREATMENT OF HEPATORENAL SYNDROME TYPE I DEPENDING ON THE STAGE OF ACUTE KIDNEY INJURY	125
Гнатишин Н.С., Буздыган Е.Н., Черначук С.В., Кульчицкая Е.Н. НЕКОТОРЫЕ ОСОБЕННОСТИ КОГНИТИВНЫХ НАРУШЕНИЙ ПРИ БИПОЛЯРНОМ АФФЕКТИВНОМ РАССТРОЙСТВЕ	129
Bondarenko I., Privalova E. THE ROLE OF HIGH-RESOLUTION ULTRASOUND IN THE DIAGNOSTICS OF FACIAL AND NECK SKIN AFTER LASER RESURFACING	134
Vasetska O., Zubko O., Prodanchuk M., Kravchuk O., Zhminko P. EFFECT OF 2,6-DIMETHYLPYRIDINE-N-OXIDE ON THE SEVERITY OF CYTOGENETIC EFFECTS INDUCED BY DIOXIDINE IN BONE MARROW CELLS OF MICE.....	139
Grigorenko A., Yeroshenko G., Shevchenko K., Lisachenko O., Perederii N. REMODELING OF THE RAT DUODENAL WALL UNDER THE EFFECT OF COMPLEX FOOD ADDITIVES OF MONOSODIUM GLUTAMATE, SODIUM NITRITE AND PONCEAU 4R.....	145
Tatarina O., Chulak O., Chulak Yu., Nasibullin B. CHANGES IN THE KIDNEY AND LIVER STRUCTURE AND FUNCTIONS DURING THE EXPERIMENTAL, NON-LETHAL LOAD OF CARBON TETRACHLORIDE (CCL ₄)	150
Гуцуляк А.И., Булик И.И., Пасько А.Я., Иванина В.В., Мищук В.В., Гуцуляк В.И. НАЛОЖЕНИЕ БИЛИОДИГЕСТИВНЫХ АНАСТОМОЗОВ МЕТОДОМ ВЧ-ЭЛЕКТРОСВАРИВАНИЯ	155
Кицюк Н.И., Звягинцева Т.В., Миронченко С.И. МОРФОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ КОЖИ МОРСКИХ СВИНОК ПРИ ВОЗДЕЙСТВИИ ЛОКАЛЬНОГО УФ А ОБЛУЧЕНИЯ.....	162
Чурадзе Л.И., Чагелишвили В.А., Кахетелидзе М.Б., Явич П.А., Мсхиладзе Л.В. ВОЗМОЖНОСТЬ ИСПОЛЬЗОВАНИЯ ДИОКСИДА КРЕМНИЯ, ПОЛУЧЕННОГО ИЗ ОТХОДОВ ПРОИЗВОДСТВА МЕТАЛЛИЧЕСКОГО МАРГАНЦА, В ПРОИЗВОДСТВЕ КОСМЕТИЧЕСКИХ КРЕМОВ И МАЗЕЙ.....	166
Салахетдинов Д.Х., Сысуев Б.Б. ФАРМАЦЕВТИЧЕСКАЯ РАЗРАБОТКА ТАБЛЕТОК С МОДИФИЦИРОВАННЫМ ВЫСВОБОЖДЕНИЕМ ЦИТИКОЛИНА И МЕМАНТИНА.....	172
Brkich G., Pyatigorskaya N. ANALYSIS OF THE PROPERTIES OF NEW PAM AMPA RECEPTORS BASED ON 3,7-DIAZABICYCLO[3.3.1]NONANE FRAME	179
Крупнова Л.В., Антонова Е.Р., Кохан В.П., Спивак И.В., Крикун В.Б. ОБЩЕСТВЕННЫЙ КОНТРОЛЬ КАК СРЕДСТВО ОБЕСПЕЧЕНИЯ РЕАЛИЗАЦИИ ПРАВА НА ОХРАНУ ЗДОРОВЬЯ.....	184

SEARCH FOR NEW CRITERIA AMONG THE BLOOD HEMOGRAM INDICES TO ASSESS THE CONDITION OF PATIENTS WITH CHRONIC WOUNDS AND EFFICACY OF THEIR TREATMENT

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Chronic wounds (CW) represent a serious global health care problem. The prevalence of lower extremities trophic ulcers in civilized countries is 4-5 patients per 1000 population. There is a steady tendency in this group of patients to increase [12]. A timely clarification of the CW causes is necessary to accelerate wound healing and prevent further complications. All traditional methods of treatment and diagnosis of such wounds do not allow achieving optimal results.

Therefore, there is a need to develop diagnostic and therapeutic innovations in treatment of chronic wounds [16].

Pathophysiology of wounds that do not heal for a long time is complicated and diverse, but they all have the only feature in common: it is a long course of inflammation. CW are characterized by increased activity of tissue enzymes that destroy the matrix, impaired vascularization and reduced ability of tissues to regenerate due to activation of tissue proinflammatory cytokines. Due to these factors, plastic closure of chronic wounds, as a rule, results in implants lysis [1].

To date, the main criterion for diagnosing the course of wound healing is the clinical characteristics of the wound process (general condition of the patient, signs of perifocal inflammation, necrosis, presence of granulations, wound contraction, marginal epithelialization), supplemented by various instrumental and laboratory study methods (general blood test (number of leukocytes, percentage of cellular elements in the leukocyte formula, ESR), biochemical, microbiological and cytological examination), most of which are unsuitable for dynamic monitoring of the wound process, do not permit to clearly establish the stage of the wound process and are frequently subjective [5].

Predictors are necessary prognostic elements of the condition and monitoring of physiological and pathological processes in the body. Their determination and selection are important for assessing the state of immunity in various pathologies and, in particular, for monitoring the course of the disease and the efficacy of chronic wounds treatment, in the development and healing of which immunopathogenetic mechanisms play a significant role.

Donetsk region is an old industrial region with multibranch industry, whose activities have led and is leading to accumulation of large amounts of toxic industrial waste, including xenobiotics [2]. The region's territory is subject to constant exposure to low-intensity ionizing radiation. [13, 7].

Aggression of the Russian Federation has been going on in the region since 2014, which has led to the partial occupation of the region's territory, significant destruction of the infrastructure in Donbass, deepening environmental and economic crisis [3]. To deter Russian aggression in the region, Joint Forces Operations (JFO) are being carried out, i. e. military operations.

Under these conditions, the psychoneuroimmune system and its compartment - the immune system is subjected to significant and prolonged versatile stress, which can lead to disruption of its adaptation. In this regard, there is a need to study the features of the immune system's status in patients with CW living in the Donetsk region during the period of JFO and to identify the predictors of changes in the immune system and assess the efficacy of treatment regimens.

The purpose of the work was to establish the features of the immune system in patients with CW living in the Donetsk region, to determine the predictors (parameters) of monitoring and treatment efficacy.

Material and methods. The total of 75 patients aged 21 to 92 years with CW of various etiologies were examined before and after treatment, at the in-patient department of Kramatorsk city hospital No. 3. Among patients there were 36 (48.0%) men and 39 (52.0%) women, with mean age of 60.5±1.7 years. Treatment of patients with CW was performed according to standard approaches, with additional local application of local negative pressure and hyaluronic acid. The hyaluronic acid preparation was injected into the perifocal area of ulcers (at a distance of 1 cm from the edges and deep under the skin, into subcutaneous fat), 6 and 3 days before surgery and intraoperatively. At the same time therapy of wounds with negative pressure was applied. Before and after treatment, the content of hemoglobin, erythrocytes, peripheral blood leukocytes and the relative content of peripheral blood leukogram elements were determined using conventional methods [4,6]. The obtained results were expressed in absolute numbers (g/l) and compared to the norm for a relatively healthy population [8,10].

Cytomorphological changes in the blood hemogram were analyzed by the total number of cell disintegrations, the content of giant platelets as a sign of increased lipid peroxidation, the percentage of cytomorphologically altered cells in individual leukocyte pools [15,17,19]. Changes in the cytomorphology of such major pools of leukocytes as neutrophilic leukocytes (microphages) and lymphocytes were studied. In the study of neutrophils' cytomorphological changes, the content of microphages with fragmented (FN), hypo (HN) - and hypersegmented (HrN) nucleus, the number of cells with ruptures in the cytoplasmic membrane and swelling of the nucleus (SN), with villous chromatin in the nucleus, cells with toxic cytoplasmic granularity (TG), neutrophil adhesion (NA) content were determined. When studying the cytomorphological changes of lymphocytes, the number of Botkin-Gumprecht decays, the content of aberrant lymphocytes (AbL), lymphocytes shaped as a mirror with a handle (MHL), young forms of lymphocytes (YFL), villous lymphocytes (VL), elongated lymphocytes (EL), spindle-shaped lymphocytes (SpL) and Ridder's lymphocytes (RL), cells with a bean-shaped nucleus (BShN) and a dry leaf shaped nucleus (DLN), plasmacytes (PIC), as well as large granular lymphocytes (LGL) were determined. In the analysis of cytomorphological changes of leukocytes and lymphocytes, their number per 100 cells of a particular pool was taken into account.

The obtained results were expressed as a percentage (%) and compared to the norm for a relatively healthy population [8]. The latent immunocompromise was determined by the indices of functionally capable and atypical lymphocytes [11,14]. Examination of blood smears was performed using an immersion trinocular MICROmed XS-4130 microscope on the basis of Donetsk National Medical University of the MOH of Ukraine (Kramatorsk). The obtained results were processed by methods of variation statistics and rank correlation using PCL. Statistica Windows software and a package of appropriate measurement software were used.

Results and discussion. Hemogram examination showed that red blood cells indices remained almost unchanged before and after the chronic wound treatment. The mean content of hemoglobin in patients with CW before treatment was 108.7 ± 6.7 g/l and was reliably lower than the regional norm (RN) – 138.10 ± 3.00 g/l ($P < 0.05$). In the dynamics of the study, the hemoglobin content had a slight tendency to decrease and averaged 106 ± 7.9 g/l. In all patients before and after treatment, a decrease in hemoglobin was determined in the range of 25 – 35%.

The content of erythrocytes before treatment in patients with CW was 3.85 ± 0.36 T/l and had no significant differences from the RN indices – 4.30 ± 0.06 T/l ($P > 0.05$). After treatment, this figure in patients with CW did not change and was 3.9 ± 0.3 T/l. Hemogram studies showed that red blood cells remained almost unchanged before and after treatment of the chronic wound, and indices such as hemoglobin and erythrocytes could not be predictors for monitoring the condition of patients with CW.

The performed studies of immunity indices by methods of level I testified to their features in patients with CW and to considerable and natural change in the course of treatment.

Fig. 1 shows data on the content of leukocytes, neutrophils and peripheral wound lymphocytes in patients with CW before and after treatment.

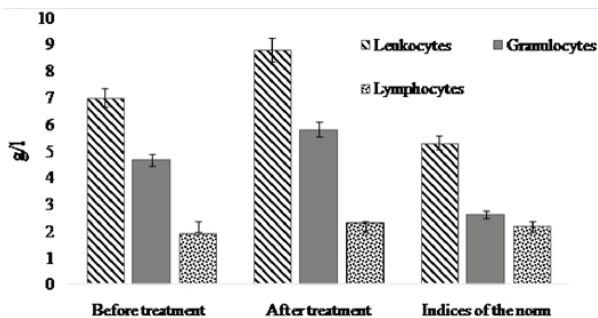


Fig. 1. Content of leukocytes, granulocytes and lymphocytes of the peripheral wound in patients with CW before and after treatment

As it can be seen from the above data, the content of leukocytes tended to increase compared to normal. At the same time in 57.1% of patients increase in the content of leukocytes was registered, and in 14.2% - their decrease. The mean content of leukocytes in CW before treatment was 7.0 ± 1.6 g/l and was significantly, but not reliably higher than the RN indices – 5.3 ± 0.1 g/l ($P > 0.05$). After treatment, the content of leukocytes in patients significantly, but not reliably, increased compared to the baseline and made 8.8 ± 1.3 , but was significantly and reliably higher than the RN ($P < 0.05$).

The results obtained showed an increase in the content of leukocytes mainly due to granulocytes. Their total content significantly exceeded the RN values before treatment and increased even more after it.

Fig. 2. shows data on changes in the content of granulocyte populations in patients with CW before and after treatment.

Metamyelocytes were registered in 14.2% of patients at the beginning of the treatment. The summarized content of neutrophilic granulocytes increased in total in 71.4% of patients with CW.

The content of stab neutrophils before treatment was 0.3 ± 0.06 g/l and was probably increased compared to RN – 0.12 ± 0.01 g/l ($P < 0.05$). After treatment, the content of stab neutrophils decreased slightly, but remained more than twice and reliably higher than the RN indices and was 0.25 ± 0.1 g/l ($P < 0.05$). The

dynamics of the segmented neutrophils content was slightly different from that of stab neutrophils. Before treatment, the content of segmented neutrophils was elevated in 42.8% of patients. The mean content of segmented neutrophils in patients with CW was 4.2 ± 1.14 g/l with almost twice lower RN – 2.62 ± 0.06 g/l ($P > 0.05$).

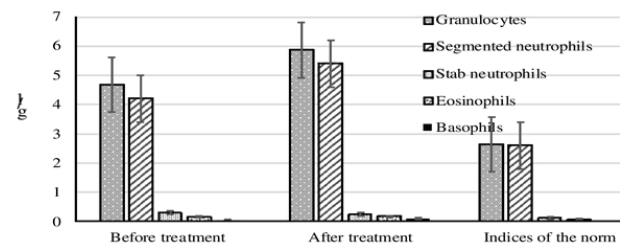


Fig. 2. The content of stab neutrophils, segmented neutrophils, eosinophils and basophils in patients with CW before and after treatment

After treatment, an increase in the segmented neutrophils content was registered in 71.4% of patients. Their content increased even more and amounted to 5.4 ± 0.65 g/l. Significant differences in this index, compared to the original data, were not registered, but it was reliably higher than the RN ($P < 0.05$). The ratio of stab neutrophilocytes to segmented neutrophils before treatment was 1:14 and decreased after treatment as 1: 21.6 at a regional rate of 1:21. It was noteworthy that this index changed in this way in 100% of patients with high efficacy and did not change or increased in patients with unsatisfactory efficacy of treatment. That is, this factor was indicative for monitoring of patients with CW.

Before treatment, 28.6% of patients with CW had values of eosinophils that exceeded the RN. After treatment, the number of patients with CW who had elevated eosinophils decreased to 14.2%, i. e. reduced almost by half. The content of eosinophils before treatment was 0.17 ± 0.04 g/l and was significantly, but not reliably higher than the RN – 0.08 ± 0.01 g/l ($P > 0.05$). After therapy, the content of eosinophils did not change and was 0.16 ± 0.05 g/l.

Basophils, which are not frequently registered in the peripheral blood, were detected in small numbers in 28.6% of patients with CW before treatment. Their mean content was 0.01 ± 0.006 g/l. After treatment, basophils were detected in 71.4% of patients, and their content significantly and reliably increased to 0.06 ± 0.02 g/l, compared to the baseline ($P < 0.05$). Although the increase in basophil content usually indicates the activation of allergic processes, but in this case, given the process of CW healing, they rather play a role in regulating the permeability of the vascular wall and therefore increase in their content can be regarded as a positive predictor of treatment efficacy. But, unfortunately, these elements of nonspecific resistance are not detected constantly.

The content of leukogram elements associated with the system of immunocompetent cells cooperation underwent changes that permitted to identify them as selectable monitoring and efficacy predictors of CW treatment.

Fig. 3 presents the study results data on the content of monocytes, lymphocytes and natural killers (NK-cells) in the peripheral blood of patients with CW.

Before treatment, patients with CW had a significant tendency to increase the content of monocytes, which was 0.42 ± 0.31 g/l and was significantly, but not reliably, greater than the RN indices – 0.11 ± 0.01 g/l ($P > 0.05$). The content of monocytes increased in all examined patients, but exceeded the norm only

in 14.2%. Against the background of recovery, the percentage of persons with monocyte content that exceeded the norm increased to 42.9%. The mean content of monocytes after treatment increased significantly compared to the baseline and was 0.55 ± 0.1 g/l, but had no significant differences from the baseline. The content of monocytes after treatment was significantly and reliably higher than the RN. Unfortunately, monocytes, like basophils, are not a constant element of the leukogram, particularly in the study by means of level I immunological methods, although an increase in their content can be regarded as an indicative predictor of recovery in CW.

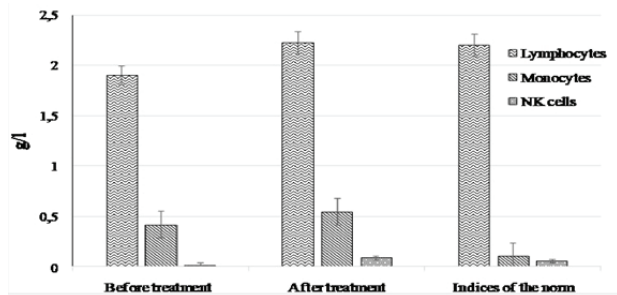


Fig. 3. Content of monocytes, lymphocytes, natural killers (NK) in patients with CW before and after treatment

Changes in the immune system were manifested by a tendency to decrease the content of lymphocytes in patients with CW. The mean content of lymphocytes in CW before treatment was 1.9 ± 0.13 g/l and was reliably lower than the RN indices – 2.2 ± 0.08 g/l ($P < 0.05$). A decrease in the content of lymphocytes compared to the lower limits of RN was registered in 28.6% in patients with CW.

Before treatment, taking into account the sum of young and dysfunctional cells in the pool of lymphocytes, latent immunocompromise was found in 85.7% of patients with CW. After treatment, 71.4% of patients had an increase in lymphocytes, in 42.8% this increase exceeded the RN, which indicated the activation of the immune system and was confirmed by the activation of monocytes that are part of the immunocompetent cells cooperation system. The mean content of lymphocytes amounted 2.23 ± 0.25 g/l, i. e. almost equalled to the RN indices. However, 57.14% of patients continued to have a latent immunocompromise, which requires further study and selection of adequate methods for correction of the immune system in these individuals. That is, indices such as lymphocyte content and latent immunocompromise respond more subtly and to changes in homeostasis and more clearly than other indices reflect the overall state of the immune system, which plays an important role in the pathogenesis of CW, and therefore they can be selected as predictors of monitoring the patients' condition and the efficacy of treatment in this pathology.

Before starting treatment, in 42.8% of patients natural killers (NK) were registered. Their content was insignificant and made 0.02 ± 0.009 g/l. These cells are not necessarily present in the peripheral blood, their mean content was reliably lower than the mean RN indices 0.06 ± 0.01 g/l. ($P < 0.05$). After treatment, NK were also detected in 42% of patients. Only 14.2% of those, in whom NKs were detected in the peripheral blood before treatment, they were registered after treatment. But the mean content of NK after therapy increased more than by 4 times and was 0.09 ± 0.009 g/l and reliably exceeded the baseline and the RN values ($P < 0.05$).

Changes in NK content fit perfectly to the picture of positive changes in activating the immune system and restoring control of the body's genetic homeostasis, but, unfortunately, these cells can not always be registered in immunological testing by level I methods and therefore their occurrence and increase in the process of monitoring can only be considered as indicative predictors of the positive dynamics in the CW patient's condition.

Conclusion. Thus, the studies performed have shown no sense in using of such elements of the hemogram as red blood cells as predictors of monitoring and treatment efficacy. As a result of the analysis on the features of changes in the content of other blood cells in patients with chronic wounds living in ecocrisis conditions during joint forces operations (JFO), the constant elements of the leukogram and their ratios were selected as predictors of monitoring and treatment efficacy.

Predictors of monitoring the status and efficacy of treatment in patients with chronic wounds can be the ratio of the stab and segmented neutrophils absolute content with increasing proportion of segmented neutrophils, and indicative predictors of monitoring and treatment efficacy in patients with CW – the occurrence and increase of basophilic granulocytes, monocytes and natural killers. The obtained results indicate the need to continue the search for predictors of monitoring the condition and efficacy of treatment in patients with chronic wounds at a more subtle level of cytomorphological studies of the peripheral blood leukogram elements.

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SUMMARY

SEARCH FOR NEW CRITERIA AMONG THE BLOOD HEMOGRAM INDICES TO ASSESS THE CONDITION OF PATIENTS WITH CHRONIC WOUNDS AND EFFICACY OF THEIR TREATMENT

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In order to identify the predictors for improving the monitoring and efficacy of treating patients with chronic wounds, a study was performed in 75 patients aged 21 to 92 years with chronic wounds of various etiology and living in an ecocrisis region during joint forces operations (JFO) in the dynamics of treatment. Studies have shown that predictors of monitoring the status and efficacy of treatment in patients with chronic wounds can be the ratio of the absolute content of stab and segmented neutrophils, lymphocytes and latent immunocompromise, and

as indicative indices of recovery and treatment efficacy the content of basophilic granulocytes, monocytes and natural killers was selected.

The obtained results indicate the need to continue the search for predictors of monitoring the condition and efficacy of treatment in patients with chronic wounds at a more subtle level of cytomorphological studies of the peripheral blood leukogram elements.

Keywords: chronic wounds, immunity, immunological parameters, predictors, treatment efficacy.

РЕЗЮМЕ

ПОИСК НОВЫХ КРИТЕРИЕВ ДЛЯ ОЦЕНКИ СОСТОЯНИЯ И ЭФФЕКТИВНОСТИ ЛЕЧЕНИЯ ПАЦИЕНТОВ С ХРОНИЧЕСКИМИ РАНАМИ ПО ПОКАЗАТЕЛЯМ ГЕМОГРАММЫ КРОВИ

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С целью выбора предикторов для улучшения мониторинга состояния и эффективности лечения пациентов с хроническими ранами различной этиологии проведено исследование 75 пациентов в возрасте от 21 до 92 лет, проживающих в зоне экокризисного района.

Результаты проведенных исследований показали, что предикторами мониторинга состояния и эффективности лечения больных с хроническими ранами являются соотношение абсолютного содержания палочкоядерных и сегментоядерных нейтрофилов, содержание лимфоцитов и скрытая недостаточность системы иммунитета, а в качестве ориентировочных показателей выздоровления и эффективности лечения - содержание базофильных гранулоцитов, моноцитов и естественных киллеров.

Полученные результаты указывают на необходимость продолжения поиска предикторов мониторинга состояния и эффективности лечения больных с хроническими ранами на более тонком уровне цитоморфологических исследований элементов лейкограммы периферической крови.

რეზიუმე

ქრონიკული ჭრილობებით დაავადებულთა მკურნალობის მდგომარეობისა და ეფექტურობის შეფასების ახალი კრიტერიუმების ძიება სისხლის ჰემოგრამის მაჩვენებლების მიხედვით

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სხვადასხვა ეტიოლოგიის ქრონიკული ჭრილობებით დაავადებულთა მდგომარეობის მონიტორინგისა და მკურნალობის ეფექტურობის პროგნოზირების

ასარჩევად ჩატარდა ეკოკრიზისულ ზონაში მცხოვრებთა და ერთობლივი ძალების ოპერაციის ჩატარების დროს (დონეცკის ოლქის ოკუპაცია, რუსეთის მიერ) 21-დან 92 წლამდე ასაკის 75 პაციენტის კვლევა მკურნალობის დინამიკაში.

კვლევის შედეგებმა აჩვენა, რომ ქრონიკული ჭრილობებით დაავადებულთა მდგომარეობისა და მკურნალობის ეფექტურობის მონიტორინგის პრედიქტორებს წარმოადგენენ სეგმენტბირთვიანი ნეიტროფილებისა და ჩხირბირთვიანი ნეიტროფილების აბსოლუტური შემცველობის თანაფარდობა, ლიმფო-

ციტების შემცველობა და იმუნური სისტემის ლატენტური უკმარისობა, ხოლო ადვანსისა და მკურნალობის ეფექტურობის ინდიკატორებს - ბაზოფილური გრანულოციტების, მონოციტებისა და ბუნებრივი კილელების უჯრედების შემცველობა. მიღებული შედეგები მიუთითებს ქრონიკული ჭრილობებით დაავადებულთა მდგომარეობის და მკურნალობის ეფექტურობის მონიტორინგის პროგნოზირების ძიების აუცილებლობაზე პერიფერიული სისხლის ლეიკოგრამის ელემენტების ციტომორფოლოგიური კვლევების უფრო დახვეწილ დონეზე.

ПОДХОДЫ К ЛЕЧЕНИЮ БОЛЕВЫХ СИНДРОМОВ, ВЫЗВАННЫХ ДЕГЕНЕРАТИВНО-ДИСТРОФИЧЕСКИМ ПОРАЖЕНИЕМ ПОЗВОНОЧНИКА (ОБЗОР)

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В арсенале современной медицины нет достаточно эффективных, универсальных и безопасных методов лечения дегенеративно-дистрофических заболеваний позвоночника. Полного выздоровления не гарантирует ни один из существующих методов консервативного или оперативного лечения [1-3]. Нет ни универсального терапевтического лечения, ни универсального хирургического вмешательства, которое могло бы обеспечить стойкое нивелирование симптомов неспецифической боли в спине [1,2,4]. Отсутствуют единый клинический подход и определенная последовательность применения медикаментозных и немедикаментозных методов лечения дегенеративно-дистрофических заболеваний позвоночника. Основная проблема адекватного лечения как острой, так и хронической боли в нижней части спины и корешкового синдрома состоит в противоречивой информации относительно клинических преимуществ различных медицинских препаратов и методик, а также разного рода оперативных вмешательств, нет общей концепции лечения таких пациентов, и отсутствует преемственность в работе врачей разных специальностей. Лечение боли в спине занимаются терапевты, семейные врачи, нейрохирурги, неврологи, ревматологи, ортопеды, реабилитологи, физиотерапевты [5]. Каждый из названных специалистов неизбежно отстаивает свой подход и свои лечебные принципы. Подходы к лечению боли в спине у представителей разных специальностей, разных научных школ часто отличаются, нередко существенно. Одни врачи основывают лечение на комплексной фармакотерапии и рекомендуют комбинацию анальгетиков, миорелаксантов, сосудистых препаратов и витаминов группы В. Другие специалисты делают акцент на диагностике, сразу направляя пациентов на рентгенографию, компьютерную томографию, магнитно-резонансную томографию, на консультацию к различным специалистам, надеясь получить информацию, «ключ» к выбору наилучшей терапии. Третьи убеждены, что таким пациентам поможет исключительно активное использование мануальной терапии, акупунктуры, физиотерапевтических процедур.

Что касается врачей хирургического профиля, они конечно, за различные оперативные вмешательства – от рутинных блокад до открытых оперативных вмешательств.

Для успешного лечения боли в спине необходимо определить ее патогенез, патоморфологические изменения, которые являются источником этой боли [6,7]. Только после определения источников боли и возможных механизмов ее развития, возможно адекватно помочь пациенту. Именно такие подходы определяют методы лечения, а не специальность врача, поскольку в наших условиях часто пациент, определившись с врачом, сам же и определяет метод своего лечения, так как при отсутствии комплексного, мультидисциплинарного подхода конкретный врач предлагает методики лечения, которыми он владеет.

Выделяем два общих вектора в лечении дегенеративно-дистрофических заболеваний позвоночника – консервативный и хирургический. Существенным недостатком консервативного метода является отсутствие прямого воздействия на патологический субстрат, что снижает эффективность такого лечения и способствует хроническому протеканию заболевания. Хирургические вмешательства компенсируют этот недостаток, однако несет в себе риск послеоперационных осложнений, рецидивов заболевания и необходимость повторных вмешательств, ухудшения течения заболевания и даже инвалидности [8-12]. Главное в выборе методики лечения находится в плоскости патогенеза развития конкретных клинических проявлений заболевания и в соотношении клинических проявлений с патоморфологическими изменениями в позвоночнике, этапности такого лечения.

В исследовании применялись методы: библиосемантический, сравнительный, системный анализ. Проведен анализ ранних и отдаленных результатов лечения разными методиками (от классического консервативного до хирургического) различными авторами, использован собственный опыт автора, как хирургического, так и консервативного лечения пациентов (более 1000) с дегенеративно-дистрофическим поражением позвоночника.