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COMBINATION OF ULTRAVIOLET RADIATION OF AUTOLOGOUS BLOOD, NEGATIVE PRESSURE WOUND THERAPY, AND ENDOLYMPHATIC ANTIBACTERIAL THERAPY IN THE TREATMENT OF POST-TRAUMATIC WOUND INFECTIONS

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The doctrine of the wound process is one of the current problems of surgery. It reflects the level of theoretical and practical medicine development. The purpose of this work was to study the improvement of treatment outcomes in patients with post-traumatic wound infections. A set of tools was used to treat patients: endolymphatic antibacterial therapy, ultraviolet irradiation of autologous blood and topical application of vacuum therapy. At the present stage, the best topical treatment method in bulky infected and purulent wounds is vacuum therapy using special technical equipment. The proposed complex of treatment reduces the severity of the disease and accelerates the debridement and regeneration of wounds. As a result, it allowed reducing the course of antibiotic administration by 1.8 times and the duration of inpatient treatment by 3.5 days compared to the traditional treatment methods.

Keywords: intoxication index, negative pressure wound therapy, endolymphatic administration of drugs, blood irradiation.

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КОМБІНАЦІЯ УЛЬТРАФІОЛЕТОВОГО ОПРОМІНЕННЯ АУТОКРОВІ, ВАКУУМНОЇ ТЕРАПІЇ ТА ЕНДОЛІМФАТИЧНОЇ АНТИБАКТЕРІАЛЬНОЇ ТЕРАПІЇ У ЛІКУВАННІ ПІСЛЯТРАВМАТИЧНОЇ ІНФІКОВАНІ РАНИ

Вчення про рановий процес відноситься до числа актуальних проблем хірургії та відображає рівень розвитку теоретичної і практичної медицини. Метою даної роботи було вивчення покращення результатів лікування хворих на післятравматичні інфіковані рани. При лікуванні хворих був застосований комплекс засобів: ендолімфатична антибактеріальна терапія, ультрафіолетове опромінення аутокрові та місцеве застосування вакуумної терапії. На сучасному етапі кращим методом місцевого лікування при наявності об'ємних інфікованих та гнійних ран є вакуумна терапія з використанням спеціального технічного оснащення. Запропонований комплекс лікування зменшує тяжкість перебігу захворювання, прискорює процеси очищення та регенерації ран. І в результаті, дозволив скоротити курсову дозу антибіотика у 1,8 рази та термін стаціонарного лікування на 3,5 діб в порівнянні з традиційними методами лікування.

Ключові слова: індекс інтоксикації, ВАК-терапія, ендолімфатичне ведення препаратів, опромінення крові.

The study is a fragment of the research project "Improvement of diagnosis and treatment tactics in purulent-inflammatory soft tissue diseases, acute and chronic surgical pathology of the abdominal cavity. Prediction of complications and their prevention, prediction of the course of wound healing in patients with allergic reactions to antibiotics", state registration No. 0118U006953.

The doctrine of the wound process is one of the current problems of surgery. It reflects the level of theoretical and practical medicine development [6]. Among the various areas of modern clinical surgery, the problem of treating patients with purulent, including wound infection, attracts special attention and is intensively studied in Ukraine and abroad [4, 9].

In recent years, the concept of wound healing has undergone significant changes under the influence of the following circumstances. Advances in pathophysiology, histochemistry and electron microscopy have significantly deepened the understanding of the wound process. In particular, they showed the significant role of various hitherto unknown biochemical substances in wound necrosis and healing processes.

The discovery of new antibacterial drugs and their widespread use has dramatically expanded the possibility of preventing and treating wound infection. Still, the biological properties of microbial factors have undergone significant changes. Extensive use of antibacterial drugs has led to significant changes in species and cultural characteristics of the wound microflora. The number of antibiotic-resistant, opportunistic and saprophytic microorganisms has increased.

The urbanisation processes, the widespread use of household chemicals and nuclear energy sources lead to changes in reactivity, reduced immunoresistance, and increased allergies in the population. All these factors affected the severity of the purulent surgical infection and increased the risk and severity of its manifestations. Currently, 35–40 % of surgical patients have purulent-inflammatory diseases. Postoperative purulent complications develop in an average of 30 % of patients. In the general structure of mortality, those related to infectious complications are 42–60 %. The increase in the number of purulent diseases, postoperative purulent complications, increasing the incidence of generalised infections, unsatisfactory results of treatment of patients with this pathology indicate the unresolved problem, which acquires a broad socio-economic significance both in Ukraine and abroad [2, 3].

Surgical treatment of post-traumatic purulent-inflammatory processes does not always ensure the recovery of patients due to disease progression, the development of systemic inflammatory response and septic conditions, and requires repeated surgical interventions and in vitro detoxification [14, 15].

An in-depth analysis of tissue changes revealed that significant microcirculation disorders occur in tissues due to inflammation, which does not allow therapeutic concentrations of antibiotics in purulent wounds when administered systemically. In addition, purulent-inflammatory processes are usually caused by antibiotic-resistant strains that are not sensitive to most antimicrobial drugs and are prescribed empirically. Topical treatment is not quite adequate due to unidirectional medications [1, 11].

The cause of purulent-inflammatory complications due to traumatic injuries is a significant local destabilisation of homeostasis due to the antigenic presence of microbial or debris nature. It exceeds the protective capabilities of local immune factors. It causes the involvement of additional immune factors in the locus morbi (development of local inflammatory response and acute phase response at the body level). In this case, the inflammatory focus functions as a temporary but full-fledged immune organ and regulates the body's response to the negative factor [5].

The statement that the antibiotic is needed only at the localisation site of pathogenic infection became the basis of the developed method of endolymphatic antimicrobial therapy.

Undoubtedly, complex therapy of this pathology should include systemic antimicrobial therapy and new technologies of adequate topical treatment.

The purpose of the work was to improve the results of treatment of patients with infected traumatic wounds by using the developed set of treatments: endolymphatic antibiotic therapy, ultraviolet irradiation of autologous blood and topical treatment with the use of vacuum therapy with a special standard AB-Thera kit.

Material and methods. We reviewed and analysed the treatment results of 12 patients of the main group (MG) and 10 patients of the control group (CG) who were hospitalised in the surgical department of Poltava Central District Hospital. The study was performed in accordance with ethical principles, and the written informed consent of patients was obtained.

The main group included: 3 patients with gunshot wounds and septicemic condition, 4 patients with chronic osteomyelitis after open fractures of the lower limbs, 2 patients with purulent wounds of post-traumatic amputation stumps, 2 patients with purulent large cut wounds of the torso and extremities, 1– patient with infected thermal burns of degree II-III for more than 15 %.

Clinical research methods were used: complaints, medical history, examination, heart rate, pulse, blood pressure, symptoms of intoxication. Local manifestations of purulent-necrotic processes were studied: local pain, skin hyperemia, infiltration, size of the purulent wound, amount of exudate, manifestations of necrosis, nature of granulation tissue and intensity of epithelialisation.

To assess the prevalence of the process, cytological examination of the wound by the “wound imprint” method on Days 1, 3, 5 and 7, microbiological examination of microflora and sensitivity to antibiotics were used.

All patients underwent clinical and biochemical blood tests. An effective method of determining endogenous intoxication was the determination of the modified leukocyte intoxication index (MLII).

MLII = (myelocytes + juvenile neutrophils + band neutrophils + segmented neutrophils + monocytes)/lymphocytes.

During cytological studies, attention was paid to determining the regenerative-degenerative index (RDI). RDI= (band neutrophils+segmented neutrophils)/degenerative neutrophils.

The studied and proposed treatment complex consists of many stages:

1. Primary surgical treatment of a purulent wound.

2. Ultraviolet irradiation of autologous blood (UIAB) on day 1 of treatment, followed by application every other day. The course of treatment was from 4 to 6 sessions using the Isolde-MD 73M device (Russian Federation) with a wavelength of 250 nm, the irradiation rate of 12–18 mL/min based on the volume of irradiated blood 2 mL/kg body weight.

3. Endolymphatic antibiotic therapy was used, taking into account the sensitivity of the wound flora. Endolymphatic administration of the antibiotic was performed in the regional lymph node using a syringe microdoser with a perfusion rate of 10–40 mL/h once a day (on days free from UIAB). The introduction and fixation of the catheter into the lymph node was performed according to the original method, "Method of antegrade lymphatic nodular therapy" (Shumeiko VM, 1995). Depending on the microflora sensitivity, different types of antibiotics were used: Ceftriaxone (PJSC Kyivmedpreparat, Ukraine) 2–4 g per day, Gentamicin sulfate (PJSC Pharmaceutical company Darnitsa, Ukraine) 160 mg per day, Kanamycin (PJSC Kyivmedpreparat, Ukraine) 2 g per day, Metronidazole (Eurolife Healthcare Pvt. Ltd., India) 50–80 mL per day. The course of treatment lasted for 3–5 days [3, 6].

4. The standard AB-There kit (4L Health Co., Ltd., China) was used for negative pressure wound therapy (NPWT). The course of treatment lasted for 3-4 days. The aspirator produced and maintained a negative pressure gradient in the wound, ranging 50–200 mm Hg.

Patients in the control group were treated by traditional methods: primary surgical treatment of a purulent wound with systemic antibiotics and detoxification therapy. Such antibiotics were used: Levomac (DP "Pharmatrade", India) in a daily dose of 500 mg, 2 times a day for 5–7 days, as well as Leflocin ("Yuria-Pharm" LLC, Ukraine) 250–500 mg 1–2 times a day for 7–10 days, depending on the severity of patients.

Mathematical processing was performed using standard methods of variation statistics: calculation of mean values (M), error of mean values (m), Student's criterion (t). Differences at p=0.05 were considered significant.

Results of the study and their discussion. According to the literature data, there are many indicators of endogenous intoxication and methods and formulas for their calculation and evaluation. For example, to determine the degree of reactivity of patients, there is a large number of integrated immunohematological coefficients: lymphocyte/granulocyte ratio, leukocyte Index (LI), neutrophil left shift (NLS), neutrophil right shift (NRS), resistance index (RI), general index (GI), nucleus intoxication index (NII), neutrophil to lymphocyte ratio (NLR), neutrophil to lymphocyte ratio (NLR) and others [7, 12,13].

In our calculations, we took as a basis the classic leukocyte intoxication index (LII) proposed by Ya. Kalf-Kalif (1941), determined by the formula: LII=(4M+3J+2B+S)x(PC.+1)/(L+Mo)x(E+1), where M – myelocytes; J – juvenile neutrophils; B – band neutrophils; PC – plasma cells; S – segmented neutrophils; L – lymphocytes; Mo – monocytes; E – eosinophils. We support the idea of including granulocytes and their juvenile forms in the numerator because neutrophilia and the shift of the leukocyte formula due to juvenile forms interpret the degree of intoxication. But we modified this ratio by removing plasma cells, which are derived from lymphocytes, from the numerator. And we refused to take into account the number of eosinophilic white blood cells in the denominator since they are representatives of granulocytes. Although monocytes are agranular leukocytes, we take into account the number of cells in the numerator. A high phagocytic activity characterizes them because they have a common origin with granulocytes. According to our statements, the modified leukocyte intoxication index should have the following formula:

MLII = (myelocytes + juvenile neutrophils + band neutrophils + segmented neutrophils + monocytes)/lymphocytes.

Counting MLII, based on the results of a clinical blood test of patients of the control and main (experimental) groups, is an effective method for determining endogenous intoxication. Usually, the MLII is 2.64±0.20, and with purulent-inflammatory processes, it increases to 3.0 and above.

RDI (regenerative-degenerative index) is a predictor of cytological changes in the wound process. RDI= (band neutrophils+segmented neutrophils)/degenerative neutrophils.

If RDI<1, then the wound process was characterized by significant inflammatory responses, and vice versa, if RDI>1, the inflammatory process passed into the regeneration phase. Counting cells on wound impression preparations was performed by D.M. Steinberg (1948). The "+" sign was used to indicate the group of cells. At the same time, the number of "+" characters depended on the number of cells per field of vision and directly on the type of cells. The 10–15 neutrophil granulocytes per the field of vision corresponded to "+", with an increase in the number of cells to 25 – "++", with an increase to 50 – "+++" and with an increase of more than 50 per the field of vision – "++++". The number of inflammatory macrophages from 2 to 4 per the field of vision corresponded to «+», for the number from 4 to 6 per the field of vision – "++", for the number up to 10 per the field of vision – "+++" and for the number from 14 to 16 – "++++". The number of macrophages from 2 to 3 per the field of vision corresponded to «+», for the number from 4 to 5, the result was interpreted as "++", for the number up to 8 – "+++", and for the number from 8 to 12 – "++++". The number of fibroblasts from 2 to 4 per the field of vision corresponded to "+", 6–8 per the field of vision – "++", for the number up to 10 per the field of vision – "+++" and for the number from 12 to 13 – "++++". The number of epithelial cells assessed epithelialization. The number of epithelial cells from 1 to 2 per the field of vision corresponded to "+", for 4–5 per the field of vision – "++", for the number from 8 to 10 per the field of vision – "+++" and for the number from 10 to 12 – "++++".

On the 1st day of surgical treatment of patients of both groups, purulent wounds were cytologically characterised by the presence of cocci bacteria, a significant number of neutrophilic leukocytes (++++) with signs of degeneration. The regenerative-degenerative index was in the range of 0.4–0.7. On the 3rd day, a small number of polyblasts and macrophages, single lymphocytes, and phagocytic neutrophils appeared in the main group. On the 5th day of complex treatment, a significant part of the specimen was occupied by fibroblasts. The RDI was in the range of 2.5–3.2. A significant number of degenerative leukocytes (+++) was detected in patients of the control group on the 5th day. Phagocytic neutrophils (+) and fibroblasts were not isolated.

In the wound exudate of studied patients of both groups, Staphylococcus monoculture was isolated in 51.7 % of cases, associated with Escherichia coli – 17.7 %. In 20.3 % of cases, gram-negative microflora was isolated. During the study of sensitivity to antibiotics, microflora resistance to the penicillin series was revealed. The highest sensitivity was found to Ceftriaxone – 95.3 %, to Levomac – 80 %, less one was found to Kanamycin – 60 %.

The severity of the condition was determined considering the size of the lesion, the localization of the process, the presence of the disease, and MLII and RDI ratio, cytological and microbiological studies.

The use of endolymphatic antibiotic therapy for local purulent-inflammatory pathology showed stable and positive results. These included: rapid cleansing of wounds from pus and necrotic masses, regression of signs of inflammation, a significant reduction in the duration of treatment by 3.5 days and reducing the course dose of antibacterial drugs by 1.8 times.

Significant effectiveness of NPWT was observed in patients with festering wounds after gunshot lesions. The dynamics were visually determined in two patients with insufficient wound cleansing according to wound smears and RDI. Long-term use of NPWT systems for more than 4 days under conditions of wound cleansing and reducing the amount of wound exudate is impractical.

The dynamics of topical changes evaluated the results of the effectiveness of the proposed treatment complex: clinical picture of the wound process, the dynamics of cytological studies, MLII and RDI ratio, as well as the general condition of patients – the presence of symptoms of intoxication, body temperature, heart rate, pulse, blood pressure. In 91 % of patients of the main group (experimental group), the clinical effect of the proposed treatment complex was manifested in the reduction of intoxication symptoms. After the first two sessions, the body temperature decreased to 37.5 %, adynamia disappeared, and peripheral blood parameters normalised faster. There was a 2.5-fold increase in haemoglobin compared to baseline by 4.5 %, which plays a vital role in the conditions of tissue hypoxia occurring in this group of patients. This indicates a significant detoxifying effect of the treatment.

On the 3rd day after the treatment complex, there was again a significant improvement in general condition, decrease and normalisation of body temperature, heart rate and pulse. In patients of the main group, RDI>1 was observed on the 5th day of complex treatment, while in the control group RDI>1 was determined only on the 7th day. This indicates a positive effect of this combination of therapeutic methods on the course and manifestations of pathological changes occurring in the focus of inflammation. These

cytological changes of locus morbi are also confirmed by the positive dynamics of immunohematological parameters expressed by MLII.

Dynamic changes in the MLII of the main and control groups are presented in table 1.

□□bl□1

Dynamic changes in MLII during treatment

Group	Day of treatment (after surgery)	MLII index
Main group	Day 1	3.72±0.21
	Day 3	3.11±0.22
	Day 5	2.64±0.17
	Day 7	2.60±0.20
Control group	Day 1	3.69±0.22
	Day 3	3.42±0.20
	Day 5	3.01±0.18
	Day 7	2.82±0.21

In patients of the main group with the proposed treatment method, a significant decrease in MLII=3.11±0.22 on day 3 and its normalisation on day 5 MLII=2.64±0.17 were observed. In contrast, in the control group, a decrease in MLII occurred only on days 5 and 7. On Day 5, MLII=3.01±0.18, and on day 7, MLII=2.82±0.21, which indicates the continuation of the purulent-inflammatory process in patients of this group. Dynamic changes of MLII are presented in fig. 1.

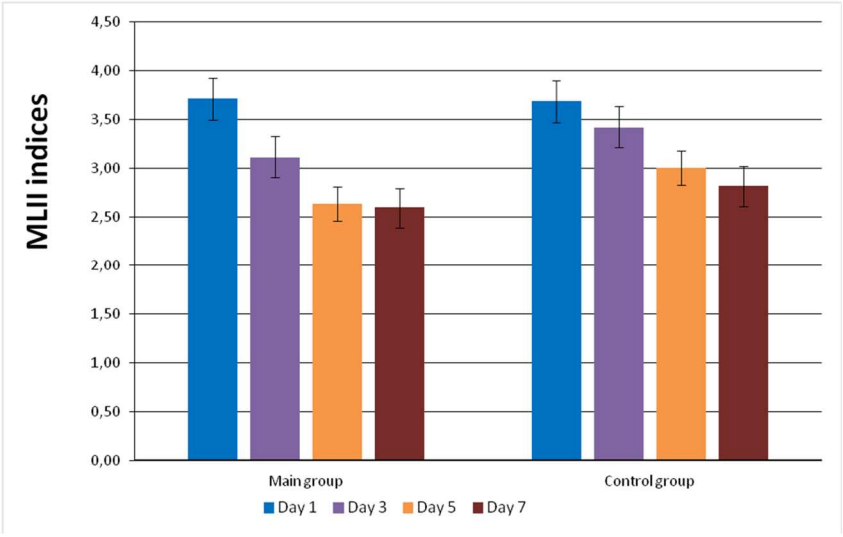

Fig. 1 Dynamic changes of MLII in the process of combined treatment

MLII studies prove the effectiveness of the proposed treatment complex, which is quite effective in intoxication.

The proposed complex of treatment is effective in patients who have previously received antibacterial therapy by traditional administration methods and desensitising, and immunotherapy did not give positive results. UIAB contributed to the improvement of impaired rheological properties of blood, normalisation of microcirculation, an increase in blood oxygen capacity, an increase in the content of immunocompetent cells and their functional activity, which leads to an increase in the synthesis of immunoglobulins and an increase in the bactericidal activity of blood [10].

Endolymphatic therapy, in comparison with other methods of antibiotic treatment, first of all, allows the formation of therapeutic concentrations of antibiotics in the lymphatic system and the use of the drug in smaller doses. This reduces the general toxic effect on the body and activates the barrier function of the lymphatic system. The developed method of endolymphatic therapy allowed to create and maintain a high and effective concentration of the antibiotic in the tissues of the purulent-inflammatory focus. This, in turn, provided high treatment efficiency, and UIAB increased the resistance of the body's natural forces [14, 15]. The results of clinical observations showed that NPWT provided positive dynamics of wound healing: contributed to a decrease in wound exudation, the removal of a significant amount of pathogenic microflora, improved microcirculation at the site of the inflammation, and led to cell proliferation and connective tissue synthesis [8, 10].

Conclusion

Existing methods and complexes of treatment of patients with post-traumatic infected and purulent wounds, accompanied by the development of endogenous intoxication, did not fully meet modern requirements. Therefore, the proposed treatment using a combination of UIAB, endolymphatic antibiotic

therapy and topical use of NPWT in patients with post-traumatic infected and purulent wounds is relevant and innovative.

The proposed complex of treatment reduces the severity of the disease, accelerates the processes of debridement and regeneration of wounds. As a result, it allowed reducing the course of antibiotic administration by 1.8 times and the duration of inpatient treatment by 3.5 days compared to the traditional treatment methods.

The proposed MLII is a simple and informative predictor of endogenous intoxication and can be used to monitor the severity of patients' conditions.

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