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Extremely High-frequency Therapy in the Complex Treatment of Pneumonia in Patients with Burn and Inhalation Trauma

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BACKGROUND The improvement of treatment tactics for nosocomial pneumonia in patients with burn and inhalation trauma is a relevant issue due to the frequency of this complication, which develops at any stage of treatment and aggravates the course of the underlying disease.

AIM OF STUDY To evaluate the effectiveness of extremely high frequency therapy (EHFT) in the complex treatment of pneumonia in patients with burn and inhalation injury.

MATERIAL AND METHODS The results of extremely high-frequency therapy (EHFT) was compared, studying 23 burn patients with complex EHFT and 30 patients without EHFT.

RESULTS EHFT reduces the signs of endogenous toxemia, as evidenced by a statistically significant decrease in elevated concentrations of dead leukocytes in venous blood from $147 \cdot 10^6$/L (98; $363 \cdot 10^6$/L) to $81.8 \cdot 10^6$/L (72; $150 \cdot 10^6$/L) (p=0.041, Wilcoxon test) on day 6–8 (after 5–6 procedures), whereas in the comparison group, on the contrary, an increase in the dead cells from $121 \cdot 10^6$/L (66; $210 \cdot 10^6$/L) up to $137.4 \cdot 10^6$/L (116; $207 \cdot 10^6$/L) was observed. When comparing this indicator in two groups on day 6–8 from the onset of pneumonia, a statistically significant difference was found (p=0.021, Mann–Whitney). The term of managing pneumonia in patients receiving EHFT was significantly shorter than in the comparison group, 18 (13; 23) versus 21 (18; 27) days (p=0.020, Mann–Whitney).

CONCLUSION EHFT reduced intensity of endogenous toxicosis and inflammation, approaching pneumonia relief for 3 days.

Keywords: nosocomial pneumonia, burns, inhalation injury, extremely high frequency therapy

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EA – early apoptosis
EHFT – extremely high frequency therapy
LA – late apoptosis

INTRODUCTION

The most frequent infectious complication in patients with a burn and inhalation injury is nosocomial pneumonia, which development contributes to a high percentage of skin burns (area and depth of tissue damage), inhalation injury of the 3rd degree, the elderly age of victims (over 75) and the male gender [1-3]. Many authors attach importance to inhalation injury in the development of pneumonia, where the frequency of nosocomial pneumonia is 2 times higher than without it [4-7]. Using only medical methods of treatment is not always effective, and often leads to undesirable side effects (allergy, toxic reaction of the blood, etc.). Therefore, the inclusion of physical factors into the complex of therapeutic measures is relevant. At present, electromagnetic radiation of extremely high frequency (30-300 GHz) is one of the most effective methods of physiotherapy in various inflammatory processes [8, 9]. When exposed to humans, extremely high-frequency radiation is almost completely absorbed by the skin at a depth of less than 1 mm The primary radiation acceptors are the structural elements of the skin located at this depth (receptors, nerve endings, mast cells, the microvasculature of the circulatory system). The cells of the immune system are most sensitive to this effect, in particular the skin depot of *T*-lymphocytes, blood cells and baroreceptors. The response to the impact forms like skin-visceral reflexes and the general reaction of the

body, aimed at the development of the adaptation syndrome [10].

Clinical and experimental studies have shown that EHF-radiation increases the functional activity of phagocytic blood cells, improves rheological indices, reduces the functional activity of platelets and coagulation potential, and also increases the blood fibrinolytic activity [10-13].

The positive effects of EHFT on the antioxidant system and the antiprotease activity of blood serum, the improvement of microcirculation and acceleration of tissue regeneration were revealed. At the same time, manifestations of the systemic inflammatory response are significantly reduced [14, 15].

Currently, there are various variants of EHF: the impact of a wideband EHF signal, the effect of discrete "resonant" frequencies (fixed wavelengths of 7.1; 5.6 and 4.9 mm) and others. Clinical studies have shown that the use of EHFT in patients with nonspecific pneumonia helps to accelerate the resorption of inflammatory infiltrate, and in pulmonary tuberculosis, abacillation and closing the decay cavities [16, 17]. It is of interest to work on the treatment of patients with sarcoidosis of the respiratory organs using EHFT. Resorption of interstitional parenchymal infiltration, reduction in symptoms of alveolitis and size reduction of intrathoracic lymph nodes were noted in 81% of patients receiving EHFT, accompanied by activation of the phagocytic function of macrophages in granulomatous lesions zone and in remote areas of the lung [18]. One of the advantages of EHF over other therapeutic physical factors is the limitation of contraindications. Relative contraindications are decompensated cardiovascular, respiratory, renal-hepatic failure, bleeding of various origins, blood diseases, as well as individual intolerance to procedures and pregnancy. The ability to influence various pathogenesis and restriction of contraindications led to our choice of EHF in the complex treatment of pneumonia in patients with burn and inhalation injury. An important advantage of EHFT is its availability, low cost devices and no need for consumables.

The aim of study: to evaluate the effectiveness of EHFT in the complex treatment of pneumonia in patients with burn and inhalation trauma.

MATERIAL AND METHODS

We treated and examined 53 patients with skin burns and inhalation trauma where the course of the underlying disease was complicated by the development of pneumonia. Two groups of patients were identified. The main group consisted of 23 victims (11 men and 12 women), who underwent EHFT in the complex of medical measures during the development of pneumonia. The comparison group included 30 patients (17 men, 13 women) who did not receive EHF. The age of patients in the main group was 74 (56; 78) years and it was statistically significantly higher than the age of patients in the comparison group - 56 (37; 68) years (p=0.017, *M-W*). Selected groups were comparable by the type of the injury, as evidenced by the data of Table 1.

Table 1

The distribution of patients in the compared groups according to the type of trauma

Type	Main group (n=23)	Comparison group (n=30)	p
Skin burns, n	17	13	0.787*
Inhale trauma of I / II / III degree, n	0 / 4 / 2	2 / 9 /6	0.651**

Notes: * – Fisher's test; ** – χ^2 test

The data of Table 2 indicates the absence of a statistically significant difference in the two groups in terms of the area and depth of skin lesions.

Table 2

The distribution of patients in the compared groups by the area and depth of skin lesions

Area and depth of skin lesion	Main group (n=17)	Comparison group (n=13)	p, Mann-Whitney U test
Total area (%)	25.0 (1.0; 50.0)	18.0 (10.0; 40.0)	p=0.675
Deep burns (%)	7.0 (2.0; 25.0)	7.5 (0.5; 25.0)	p=0.950

The comparability of groups was also noted in the location of inflammatory infiltration (Table 3).

Table 3

The distribution of patients in the compared groups by the location of inflammatory infiltration in the lungs

Location of inflammatory infiltration	Main group (n=23) abs./%	Comparison group (n=30) abs./%	P, Fisher's test
Right lower lobe pneumonia	9 / 39.1	11 / 36.7	p=0.920
Bilateral lower lobe pneumonia	14 / 60.9	19 / 63.3	p=0.913

The overwhelming number of patients in the main group of 74% (17 of 23) and 57% (17 of 30) in the comparison group had severe comorbidities: atherosclerosis, hypertension, coronary heart disease, atrial fibrillation, postinfarction cardiosclerosis, cerebrovascular disease, chronic obstructive pulmonary disease, duodenal ulcer, obesity and diabetes.

It should be noted that nosocomial pneumonia in the burn patients developed against the background of a burn disease, which pathogenesis is based on a systemic inflammatory response with all the classic signs of inflammation, which made clinical diagnosis difficult. In addition, the location of burns and dressings in the chest area prevented auscultation. The diagnosis of pneumonia was made on the basis of clinical and radiological data. X-ray examination of all the victims was carried out in the rear plane view using the mobile *SIEMENS* X-ray unit. Each patient underwent from 2 to 6 studies.

The severity of inhalation injury was assessed on the basis of the data of fibrobronchoscopy according to the standard method: I degree — soot, edema and hyperemia of the bronchial mucosa (catarrhal form), II degree — erosion (erosive), III degree — ulcer (ulcer), IV degree —necrosis of the mucous membrane (necrotic) [19].

All patients received complex pathogenetic treatment of burn disease, including infusion-transfusion therapy, antibiotic therapy, anticoagulants and symptomatic treatment. With the stabilization of the condition, the patients performed the complexes of special therapeutic exercises under the supervision of a doctor or an exercise therapy instructor (physiotherapy exercises).

EHFT was performed using the domestic apparatus "EHF-ND". The wavelength was 5.6 mm, the radiation energy exposure was 4–12 mW/cm^2, the mode was constant. The procedures started on day 2–8 from the moment of diagnosing pneumonia. Four patients were treated in the intensive care unit, 19 patients were treated in the hospital. The contact area of the epigastric region was stable, in the presence of a burn wound in this area or dressings, the effect was carried out on the region of the sternum in the III – IV intercostal space or on the area of the neurovascular bundle projection that was free of dressings (most often in the neck). The exposure duration was 10 minutes. The EHFT course included from 9 to 12 procedures performed daily with a break in the weekend.

The effectiveness of EHFT was evaluated on the basis of the clinical picture, radiological data and laboratory parameters over time.

The study of peripheral blood leukocytes and indicators of lymphocyte apoptosis was conducted in 19 patients of the main group and in 11 patients of the comparison group with the development of pneumonia (before EHFT) and during treatment, 6–8 days after 5–6 procedures of EHF. A repeated study of these indicators was carried out in 17 patients of the main group and in 10 patients of the comparison group 12–14 days after the course of EHF.

The study of lymphocyte apoptosis and counting of dead blood leukocytes was performed by flow cytometry. The concentration of lymphocytes in the blood was assessed at early (*AnnexinV* + / 7*AAD* -, early apoptosis – EA) (normal 3.2 (1.9; 4.2)%) and late (*AnnexinV* + / 7*AAD* +, late apoptosis – LA) (norm 0.10 (0.05; 0.15)%) stages of apoptosis. The reagents used were *AnnexinV-FITC* / 7 *AADKit* (*Beckman Coulter*). The severity of endogenous intoxication was assessed by the viability of leukocytes. The count of dead cells was performed by flow cytometry using the vital DNA-specific dye 0.005% solution of 7 amino-actinomycin *D* (7*AAD)* and pan-leukocyte marker *CD* 45+. The concentration of dead cells in venous blood normally varies from 20 to 100x10^6/l. The range from 101 to 400x10^6/l corresponds to moderate severity, from 401 to 800x10^6/l — severe and over 800x10^6/l — extremely severe degree of endogenous intoxication.

The statistical analysis of the data was performed using the *Statistica* 10 software package (*StatSoft*, *Inc.*, USA). The descriptive statistics of quantitative features are represented by medians and quartiles in the Me format (LQ; UQ). Independent groups were compared using the Mann–Whitney test, and Wilcoxon's test was used when comparing indicators within the group. The level of statistical significance was $p \leqslant 0.05$.

RESULTS AND DISCUSSION

In the course of EHF procedures, victims noted a decrease in pain in the area of burn wounds (3 patients out of 23), a slight warmth in the area of impact (4 patients out of 23). No discomfort in patients during and after the procedures was registered.

The dynamics of the studied laboratory parameters in the treatment process in patients of the two groups is presented in the Figure and Table 4.

Table 4

The dynamics of studied laboratory parameters in venous blood of patients of the compared groups

Studied parameters	Normal value	Terms					
		Primary examination		Day 6-8		Day 12-14	
		Main group (n=19)	Comparison group (n=11)	Main group (n=19)	Comparison group (n=11)	Main group (n=17)	Comparison group (n=10)
Leukocytes (10^9/L)	6.4 (5.1; 7.1)	11.7(8.5;14.8)	9.2(6.7;16.3)	9.1(6.4;12.7)	10.9(7.8;16.2)	6.2 (5.3; 9.4)	8.9(4.1;12.0)
Dead leukocytes (10^6/L)	43.1 (28.2; 67.3)	147(98;363)	121(66; 210)	81.8(72; 150) *,**	137(116; 207)	53(36; 135)	80(49; 148)
Early apoptosis,%	3.2(1.9;4.2)	10.7(6.7; 13.5)	10.3(7.4; 13.0)	12.8(10.2;16.0)	7.2 (5.4;12.1)	7.6(5.4;9.6)	5.6(5.5; 7.0)
Late apoptosis,%	0.10 (0.05; 0.15)	0.12 (0.05; 0.23)	0.18(0.13; 0.25)	0.14 (0.10; 0.19)	0.11 (0.09;0.27)	0.13(0.09;0.20)	0.11(0.09;0.20)

Notes: * — the difference from the initial value in the group, p<0.05 (Wilcoxon test); ** difference from control group, p<0.05 (Mann – Whitney test)

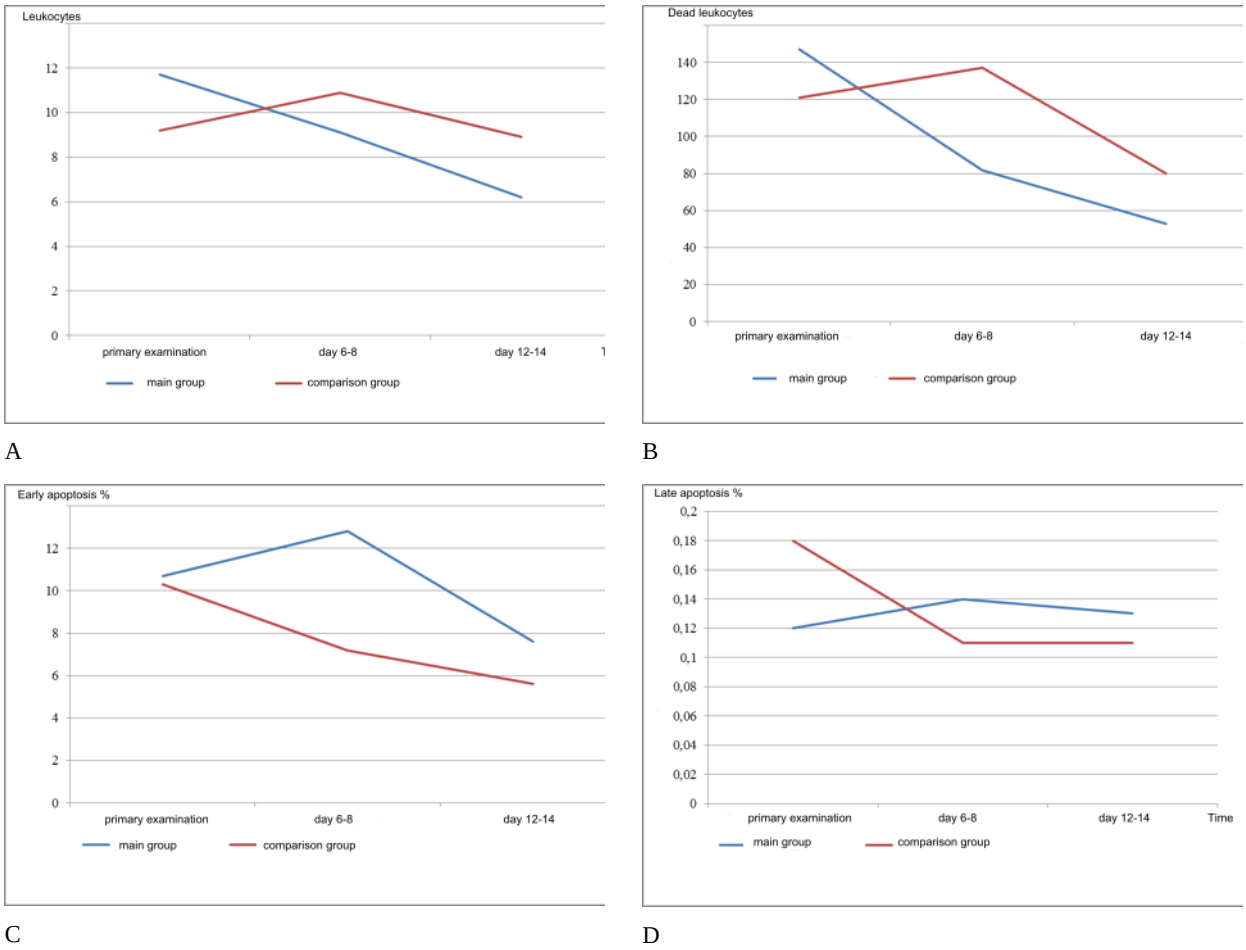

Figure. The dynamics of studied laboratory parameters in the venous blood of patients of the main and comparison group in the treatment process. A — the dynamics of the leukocytes concentration in venous blood; B — the dynamics of the dead leukocytes concentration in venous blood; C — indicators of early apoptosis; D — indicators of late apoptosis

Primary (up to EHFT) laboratory studies of venous blood in patients of the main group revealed signs of endogenous intoxication, such as leukocytosis and an increase in the concentration of dead leukocytes. The concentration of leukocytes was 11.7x10^9/l (8.5; 14.8x10^9/l), and the content of dead cells was 147x10^6/l (98; 363x10^6/l), which corresponded to moderate severity of endotoxemia. In the comparison group during this period, the concentration of leukocytes was 9.2x10^9/l (6.7; 16.3x10^9/l), and the dead cells 121x10^6/l (66; 210x10^6/l), which also corresponded to the moderate severity of endogenous intoxication. Despite the absence of a statistically significant difference between the studied parameters in the two groups (p= 0.923 and p=0.549, respectively, *M-U*) it

is worth noting that in the main group they were slightly higher (Table 4).

After 5-6 procedures of EHFT in patients of the main group, the concentration of leukocytes tended to decrease and amounted to 9.1x10^9/l (6.4; 12.7x10^9/l) (p=0.550, Wilcoxon test). At the same time, the concentration of dead leukocytes statistically significantly reduced to 81.8x10^6/l (72; 150x10^6/l) (p=0.041, Wilcoxon test). In contrast, the affected comparison groups showed a tendency to an increase in the concentration of leukocytes in venous blood to 10.9 · 10 ^{9} / l (7.8; 16.2x10^9/l) (p=0.865, Wilcoxon test) and dead cells to 137.4x10^6/l (116; 207x10^6/l) (p=0.176, Wilcoxon test) (Table 4). The analysis of the studied parameters revealed a statistically significant difference in the concentration of dead cells in venous blood in patients of the compared groups (p=0.021, *M-W*).

After the course of EHFT in patients of the main group, the trend towards normalization of the studied parameters preserved: the leukocyte count in venous blood was 6.2x10^9/l (5.3; 9.4x10^9/l), and the dead cells count was 53x10^6/l (36; 135x10^6/l). In the comparison group, at this time, a decrease in the level of leukocyte count to 8.9x10^9/l (4.1; 12.0x10^9/l) and the concentration of dead cells to 80x0^6/l (49; 148x10^6/l). When processing the data, no statistically significant difference of the studied parameters in the two groups was revealed: p=0.827, *M-W*; p=0.727, *M-W,* respectively. It should be noted that in 14 out of 17 patients of the main group (82%) during this period the concentration of leukocytes reached normal values, whereas in the comparison group only in 4 out of 10 (40%) (p=0.034, Fisher's test). In 6 patients of the comparison group, the content of leukocytes in venous blood raised to 12.0x10^9/l.

As can be seen from the Table 4, during the primary study of venous blood after the detection of pneumonia, an increase in the concentration of cells in EA and LA was observed (compared with the norm) in patients of both groups. In the main group, the EA indicator was 10.7 (6.7; 13.5)%, LA — 0.12 (0.05; 0.23)%; in the comparison group —10.3 (7.4; 13.0)% and 0.18 (0.13; 0.25)%, respectively; there were no significant differences between the groups. During the treatment, after 6–8 per day (after 5–6 EHFT procedures) in the main group and the comparison group, the percentage of lymphocytes in EA and LA was not statistically significantly changed. After the course of CVT, the concentration of lymphocytes in the early and late stages of apoptosis in patients of the main group tended to normalize and was recorded at the level of 7.6 (5.4, 9.6)% and 0.13 (0.09; 0.20)% respectively. A similar picture during this period was also observed in the comparison group: the EA indicator was 5.6 (5.5; 7.0)%, and LA — 0.11 (0.09; 0.20)%. During statistical processing of data, no significant differences were found between the groups.

Analyzing laboratory data, we can say that the use of EHFT in the complex treatment of pneumonia in patients with burn and inhalation injury contributes to a more rapid decrease in the degree of endogenous intoxication, as evidenced by the normalization of leukocyte levels and the concentration of dead peripheral blood cells in patients in the main group at an earlier date (after 5–6 EHFT procedures) than in the comparison group. After a course of EHFT, normalization of leukocyte levels in venous blood was observed in 82% of patients in the main group, which indicates both relief of the inflammatory process in the lungs and a decrease in the level of endotoxicosis. In the comparison group, in this period, despite a significant decrease in the level of dead cells, leukocytosis was preserved in 60% of patients, which could indicate a continuing inflammatory process. The values of the studied parameters of apoptosis after a course of EHFT were not statistically significantly changed.

Radiographic studies of the lungs over time showed a gradual decrease in the intensity of the inflammatory infiltrate and its length in all 23 patients receiving EHFT. The recovery period for pneumonia in them was 18 (13; 23) days. In the comparison group, a gradual decrease in the intensity of inflammatory infiltrate and its length was noted in 25 of 30 patients. In 5 patients, negative prevalence of inflammatory infiltration was noted. After 5 days, 4 patients showed bilateral lower lobe pneumonia instead of previously identified unilateral process. The spread of inflammatory infiltration in both lungs was associated with the phenomena of significant hypoventilation against the background of hypodynamia and reduced immunity. In the 5th patient with severe inhalation injury of the III degree, bilateral lower lobe pneumonia turned into bilateral polysegmental pneumonia. The resolution period for pneumonia in patients in the comparison group was 3 days longer than in the main group and amounted to 21 (18; 27) days. The analysis of the obtained data revealed a statistically significant difference in the duration of pneumonia in patients of the compared groups (p=0.020, *M-W*).

FINDINGS

1. Extremely high-frequency therapy in the complex treatment of pneumonia in patients with burn and inhalation trauma leads to reduction in the time of resolution of pneumonia for 3 days .

2. Data from laboratory studies indicate a decrease in the level of endotoxemia and the severity of inflammation in EHFT, which is reflected in accelerated normalization of leukocyte count and the concentration of dead cells in venous blood. At the end of the course of EHFT, the recovery of leukocyte concentration in venous blood was observed in 82% of patients in the main group and only in 40% of patients in the comparison group.

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