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Changes in immunological parameters of polytrauma patients with use of terahertz electromagnetic waves in complex treatment

Changes in immunological parameters of polytrauma patients with use of terahertz electromagnetic waves in complex treatment

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Abstract

Introduction Improving the results of treatment and rehabilitation is essential for polytrauma patients. **The aim of the study** was to prove the effectiveness of terahertz electromagnetic waves (TEW) in polytrauma patients early after traumatic event to improve immune parameters. **Material and methods** The study included 20 polytrauma patients who were divided into two groups. Patients of the treatment group (n = 10) received TEW early after traumatic event in addition to standard treatment using the damage control approach. Control patients (n = 10) received no TEW therapy in the complex of therapeutic measures. Immunological studies were performed during treatment. The effectiveness of rehabilitation was assessed at a long term using an evaluation scale. **Results** The mean rehabilitation score was significantly higher in the treatment group compared to the controls. The treatment group showed significantly higher production of TNFα and IL-2, spontaneous production of IFNγ by lymphocytes, phagocyte activity (NBT-test) and absorption activity of monocytes after the use of TEW in comparison with controls. An increased level of IgG and IgM was also noted in patients of the treatment group. **Discussion** The findings showed that the use of TEW in polytrauma patients early after traumatic event resulted in the increase in cytotoxic activity of lymphocytes and phagocytic cells. The immunostimulating effect of TEW was also achieved through boosting humoral immunity. **Conclusion** The TEW used early after traumatic event in polytrauma patients resulted in strengthening of the immune system which contributed to more effective rehabilitation.

Keywords: polytrauma, electromagnetic waves, terahertz range, immunity

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INTRODUCTION

The treatment of polytrauma patients is a special and difficult problem due to traumatic shock, a high risk of various complications including fat embolism, thromboembolism, pneumonia, bone nonunion, etc.), a high rate of disability and mortality (up to 80 %) [1-3]. An impaired immune system has an impact on body functions in polytrauma patients [4-8] who can develop signs of inhibited cellular and humoral immune reactions early post trauma [9]. It follows from the literature that the use of EHF-therapy in patients with polytrauma in its complex treatment prevents the development of immune pathology [10-13]. The method has advantages in terms of minimally invasiveness, availability of complex treatment for this group of patients. The experience of EHF-therapy is not significant in practical traumatology[14-17], and we have not encountered publications reporting its use in polytrauma. The objective was to identify the effectiveness of electromagnetic waves in the terahertz (THz) frequency range used for polytrauma patients early post trauma improving the immune system.

MATERIAL AND METHODS

The use of THz was reviewed in 20 polytrauma patients. Inclusion criteria included 1) the presence of more than one injury with one or combined trauma posing a threat to the patient's life causing the traumatic disease; 2) bone fractures; 3) the ISS scored 26-40; 4) patients aged 18-35 years. The exclusion criteria included decompensated function of internal body organs and systems, acute phase of chronic disease. The patients were divided into two groups. The treatment group (n = 10) included patients who were treated according to damage control principles and with the use of THz sessions that were not administered for control

patients (n = 10). The *Orbita* physiotherapy device (reg. no. FSR 2009/05497 dated 14.08.2009, indefinite validity period) was used for radiation with the amplitude of the modulating signal at 150 ± 0.75 GHz. The THz was applied daily to the xiphoid process of the sternum for 30 minutes (Fig. 1). Physiotherapy started at three days of injury. There were 10 sessions performed.

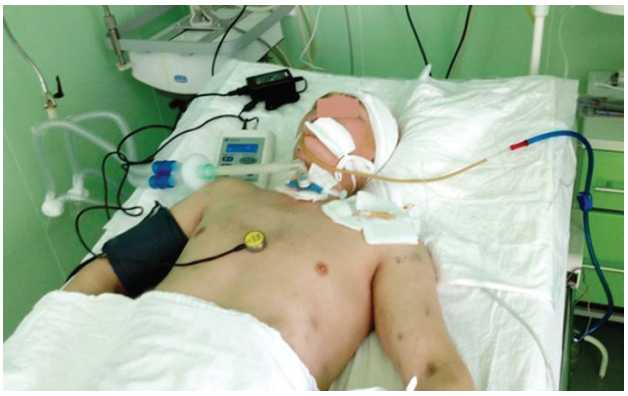

Fig. 1 Photo of a patient during a physiotherapy session

Clinical assessment. Integral evaluation of the results was performed. The measurements produced to calculate the rehabilitation index (M) included: 1) the mean value of the outcome scoring from 0 to 200 (O_m); 2) the mean quality of life index scoring from 0 to 80-100, according to the formula $L_m = B / n$, where B is the total score of the patients (if the fractures were combined in two limbs, the mean value of the total score was calculated for the upper (K1) and lower (K2) limbs: K = (K1 + K2) / 2), *n* being the number of observations; 3) overall disability rate from 0 to 100 (D) in each group of patients. The initial formula for calculating the rehabilitation index in each group of patients was as follows: $M = O_m + L_m + D$. A score of 0 points meant a good level of rehabilitation measures and 400 points indicated a poor quality of rehabilitation (Table 1).

Table 1

Matrix of integral assessment of rehabilitation in polytrauma patients

Description	Rehabilitation scored		
	good	fair	poor
Anatomic and functional result (O_m)	0-50	51-140	141-200
Mean quality of life index (L_m)	0-20	21-45	46-100
Disability	0-10	11-25	26-100
Rehabilitation index (M)	**0-80**	**81-210**	**211-400**

Immunological examination. An immunological study was performed on admission at 2 to 12 hours of injury. Blood test was performed before THz radiation (the third day after the injury) and after ten sessions of THz exposure. A hematology analyzer Cobas Micros 60 OT (ABX, France) was used for examination. Mononuclear cells were isolated from heparinized blood using a concentration gradient of 5.64 % and intracellular cytokine staining (ICS) was performed (Lympholyte®-H, Cedarlane Laboratories Ltd, the Netherlands). MICs washed in RPMI-1640 medium supplemented with 10 % inactivated fetal calf serum were resuspended at a concentration of 2×10^6/ml.

Monoclonal antibodies used for immunophenotyping of lymphocytes included: BD Multitest (CD3-FITC/CD16+CD56-PE/CD45-PerCP/CD19-APC; CD3-FITC/CD8-PE/CD45-PerCP/CD4-APC) (BD BioSciences, USA); CD3-FITC/HLA-DR+ (IO Test, Immunotech, France). Anti-IFN-γ-PE; anti-IL-4-PE; anti-IL-2-PE; anti-TNF-α-PE (IO Test, Immunotech, France) weres used to detect intracellular cytokines. Immunophenotyping of major subpopulations of lymphocytes was performed according to Protocol Direct Immunofluorescence Staining of Whole Blood, 2002 (BDIS, USA).

Intracellular cytokine production was analyzed using recommendations of the *Intracellular staining procedure*, 1996. Lymphocyte activation was performed for 4 hours at a temperature of 37 °C 25 ng/ml using Phorbol 12-myristate 13-acetate (PMA) with ionomycin (1 μg/ml) in the presence of brefeldin A (10 μg/ml) in 12 × 75 mm polystyrene tubes. Fluorochrome-conjugated isotype control was performed to rule out nonspecific binding of monoclonal antibodies. Activation efficiency was monitored by incubating one aliquot of ICSs with PMA and ionomycin without addition of brefeldin A. Activated ICSs were fixed for 10 minutes using 1× Facs Lysing Solution. Permeabilization was performed for 10 minutes using 1× Facs Permeabilizing Solution at room temperature in the dark. Monoclonal antibodies were stained for 30 minutes simultaneously for surface and intracellular markers. CD69PE/CD3-PerCP (BD BioSciences, USA) was added for activation control. Two-color analysis was performed using a FacsCanto II flow cytometer (BD BioSciences, USA). Data interpretation was performed using FacsDiva Version 6.1.3 (collecting at least 3000 leukocytes per sample). The bactericidal activity of leukocytes, monocytes and the absorption activity of neutrophils were analyzed as recommended by D.V. Mazurov et al. [18, 19]. Concentration of serum immunoglobulins IgM, IgG and IgA was measured using Mancini technique of radial immunodiffusion. Circulating immune complexes (CIC) were determined by immunoprecipitation in 4 % PEG-6000 followed by photometry using SF-2000 spectrophotometer. Laboratory studies were performed at the clinical diagnostic laboratory of the Clinical Diagnostic Center, Ekaterinburg. The laboratory parameters of patients measured at stages of treatment were compared with those of ten healthy individuals aged 20-35 years (reference group). The results are presented in tables

as arithmetic mean (X_i) and standard deviation (SD). The normality of samples was determined using the Shapiro-Wilk test. The significant differences in the parameters of the groups were assessed using Student's parametric t-test for independent samples. The minimum significance level (p) was taken at 0.05.

RESULTS

Integrated assessment of rehabilitation measures in polytrauma patients are presented in Table 2. The mean score measured with the matrix of the integrated assessment of rehabilitation in polytrauma patients with bone fractures that were not treated with physiotherapy corresponded to a satisfactory outcome in controls. The patients of the treatment group demonstrated the average score of a satisfactory result with rehabilitation index being significantly lower than that in the controls. A decrease in the absolute content of immunocompetent cells was revealed in patients of both groups post trauma (Table 3). There were no significant differences in the measurements of the treatment group relative to the comparison group. However, significant differences in the functional activity of immunocompetent cells were recorded (Table 4). A statistically significant increase in the activity of phagocytes (NBT-test), the production of IFNγ lymphocytes stimulated by the production of TNFα and IL-2, and the absorption activity of monocytes was observed with the use of EMWTHR in the patients of the treatment group as compared to controls. Patients of the main group showed differences in measurements of humoral immunity (Table 5) and increased IgG and IgM levels relative to the control and reference groups at the end of exposure to EMWTHR.

There were no adverse events in clinical manifestations, immunological status associated with the use of EMWTHR indicating the acceptable safe use in the treatment of polytrauma patients.

Table 2

Integrated assessment of rehabilitation in polytrauma patients ($X_i \pm SD$)

Description	Treatment group	Control group
Anatomic and functional result (O_m)	28.8 ± 4.5*	49.3 ± 6.3
Mean quality of life index (L_m)	46.1 ± 6.8	53.5 ± 7.4
Disability	15.2 ± 3.9*	35.9 ± 8.4
Rehabilitation index (M)	90.1 ± 9.8*	138.7 ± 10.5

Note: *statistically significant differences from the control group at a significance level $p < 0.05$.

Table 3

Cellular immunity measured in patients during the observation period ($X_i \pm SD$)

Parameters	Group	Reference group	Post trauma	Prior to EHF therapy	Following EHF therapy
T-lymphocytes CD3+, 10^9/l	T	1.331 ± 0.18	0.781 ± 0.28*	0.993 ± 0.25*	1.181 ± 0.33
	C		0.903 ± 0.12*	1.013 ± 0.15*	1.171 ± 0.17
B- lymphocytes CD19+, 10^9/l	T	0.253 ± 0.05	0.141 ± 0.06*	0.133 ± 0.08*	0.183 ± 0.09
	C		0.171 ± 0.03*	0.130 ± 0.08*	0.174 ± 0.05
T-helpers CD3+CD4+, 10^9/l	T	0.984 ± 0.03	0.463 ± 0.25*	0.634 ± 0.30*	0.843 ± 0.11*
	C		0.514 ± 0.14*	0.583 ± 0.13*	0.813 ± 0.08*
T-killers CD3+8+, 10^9/l	T	0.414 ± 0.08	0.243 ± 0.14*	0.302 ± 0.08*	0.444 ± 0.08
	C		0.314 ± 0.04*	0.312 ± 0.07*	0.384 ± 0.08
NK-cells CD3-16+56+, 10^9/l	T	0.381 ± 0.07	0.071 ± 0.04*	0.172 ± 0.11*	0.334 ± 0.03
	C		0.102 ± 0.04*	0.141 ± 0.06*	0.333 ± 0.06
TNK-cells CD3+16+56+, 10^9/l	T	0.0851 ± 0.016	0.0752 ± 0.016	0.084 ± 0.030	0.113 ± 0.048
	C		0.080 ± 0.023	0.074 ± 0.029	0.122 ± 0.060
Activated lymphocytes CD3+HLA-DR+, 10^9/l	T	0.102 ± 0.02	0.042 ± 0.02*	0.032 ± 0.01*	0.090 ± 0.03
	C		0.051 ± 0.02*	0.033 ± 0.02*	0.10 ± 0.04

Note: T, treatment group; C, controls; * statistically significant differences from the reference group at a significance level $p < 0.05$.

Table 4

Parameters of the functional activity of immunocompetent cells in patients during the observation period ($X_i \pm SD$)

Parameters	Group	Reference group	Post trauma	Prior to EHF therapy	Following EHF therapy
CD3 + IFNγ + stim., 10^9/l	T	0.281 ± 0.052	0.193 ± 0.104	0.246 ± 0.052	0.362 ± 0.164
	C		0.253 ± 0.072	0.237 ± 0.077	0.254 ± 0.080
CD3 + IFNγ + spont., 10^9/l	T	0.006 ± 0.001	0.005 ± 0.002	0.004 ± 0.005	$0.012 \pm 0.003^{0.05*}$
	C		0.006 ± 0.003	0.006 ± 0.001	0.006 ± 0.001
CD3 + TNFα + stim., 10^9/l	T	0.681 ± 0.078	0.346 ± 0.093*	0.379 ± 0.080*	$0.738 \pm 0.233^{0.04}$
	C		0.426 ± 0.079*	0.318 ± 0.100*	0.405 ± 0.140*
CD3 + TNFα + spont., 10^9/l	T	0.005 ± 0.001	0.004 ± 0.002	0.004 ± 0.003	0.006 ± 0.004
	C		0.004 ± 0.002	0.006 ± 0.001	0.005 ± 0.001
CD3 + IL2 + stim., 10^9/l	T	0.504 ± 0.118	0.222 ± 0.131*	0.323 ± 0.140*	$0.666 \pm 0.239^{0.04}$
	C		0.294 ± 0.100*	0.332 ± 0.088*	0.393 ± 0.067*
CD3 + IL2 + spont., 10^9/l	T	0.004 ± 0.001	0.003 ± 0.001	0.004 ± 0.003	0.004 ± 0.003
	C		0.004 ± 0.002	0.005 ± 0.002	0.005 ± 0.003
CD3 + IL4 + stim., 10^9/l	T	0.014 ± 0.005	0.007 ± 0.006	0.014 ± 0.010	0.018 ± 0.013
	C		0.008 ± 0.007	0.014 ± 0.009	0.017 ± 0.009
CD3 + IL4 + spont., 10^9/l	T	0.004 ± 0.002	0.003 ± 0.001	0.003 ± 0.002	0.005 ± 0.003
	C		0.004 ± 0.003	0.004 ± 0.002	0.004 ± 0.002
CD3-IFNγ+stim ., 10^9/l	T	0.031 ± 0.010	0.016 ± 0.005*	0.025 ± 0.020	0.053 ± 0.026
	C		0.016 ± 0.010*	0.022 ± 0.014	0.052 ± 0.009*
CD3-IFNγ+spont., 10^9/l	T	0.004 ± 0.002	0.003 ± 0.002	0.003 ± 0.002	0.006 ± 0.003
	C		0.003 ± 0.002	0.004 ± 0.002	0.005 ± 0.002
HCT-test spont., %	T	8 ± 2	9 ± 7	4 ± 2*	$5 \pm 1^{0.04*}$
	C		8 ± 5	4 ± 2*	2 ± 1*
HCT-test stim., %	T	52 ± 17	18 ± 7*	15 ± 8*	18 ± 8*
	C		17 ± 2*	15 ± 2*	17 ± 3*
Germicidal activity of leukocytes, %	T	33.2 ± 5.1	59.6 ± 15.5*	57.4 ± 14.3*	57.8 ± 17.5*
	C		59.2 ± 8.9*	41.8 ± 16.8	48.0 ± 14.2
Absorption capacity of neutrophils, %	T	90.4 ± 5.1	88.8 ± 8.7	87.7 ± 8.6	89.8 ± 3.3
	C		94.0 ± 7.7	88.4 ± 3.9	87.0 ± 8.0
Absorption capacity of monocytes, %	T	81.2 ± 6.3	83.2 ± 13.3	80.0 ± 9.0	$87.5 \pm 5.1^{0.04*}$
	C		77.5 ± 6.2	80.4 ± 8.1	79.4 ± 4.1

Note: T, treatment group; C, controls; *statistically significant differences from the reference group at a significance level $p < 0.05$; ^{superindex}, p value relative to control group.

Table 5

Humoral immunity measured in patients at follow-up periods ($X_i \pm SD$)

Parameters	Group	Reference group	Post trauma	Prior to EHF therapy	Following EHF therapy
IgA, g/l	T	2.85 ± 0.46	1.47 ± 0.43*	2.66 ± 0.66	3.44 ± 0.43*
	C		1.52 ± 0.32*	2.58 ± 0.52	3.46 ± 0.74*
IgG, g/l	T	13.5 ± 1.8	9.1 ± 2.2*	10.1 ± 2.5*	$17.5 \pm 2.7^{0.02*}$
	C		7.6 ± 0.7*	9.2 ± 1.2*	12.5 ± 0.7
IgM, g/l	T	1.25 ± 0.12	1.00 ± 0.18*	1.44 ± 0.31	$2.14 \pm 0.35^{0.04*}$
	C		0.90 ± 0.08*	1.34 ± 0.18	1.35 ± 0.44
CIC, units.	T	57 ± 14	49 ± 22	56 ± 20	70 ± 21
	C		43 ± 8	65 ± 17	77 ± 22

Note: T, treatment group; C, controls; * statistically significant differences from the reference group at a significance level $p < 0.05$; ^{superindex}, p value relative to control group.

DISCUSSION

Our series suggested that EMWTHR used in polytrauma patients early post trauma facilitated activation of the cytotoxic activity of lymphocytes and phagocytic cells. The immunostimulatory effect

of exposure to EHF radiation was also achieved by increasing the level of humoral immunity factors. The combination of the signs presented, including integrated scores indicated the effectiveness of EMWTHR therapy in the treatment of polytrauma patients. Comparative assessment of the findings we obtained was a difficult experience with no use of EMWTHR therapy reported for polytrauma patients. However, the available papers on the use of therapy in traumatology practice suggest that the EHF-therapy can promote fracture healing [13, 20] improving functional outcome and reducing complication rate post trauma [14, 21, 22]. The technology is also widely used in the complex treatment of osteoarthritis [23-25]. Indications to the technology are expanding to be employed for other conditions [26-28]. In general, the overall impression is that the use of EHF-therapy sessions in clinical practice is associated with a positive experience [29, 30].

The results reported with EMWTHR used in polytrauma patients may have limitations due to the small samples. It means that the effectiveness of EMWTHR used in polytrauma patients needs to be explored with greater populations. However, the experience presented confirms the hypothesis about the effectiveness of this physiotherapy in the complex treatment of the cohort of patients.

CONCLUSION

Exposure to electromagnetic waves of the terahertz range on the xiphoid process of the sternum used for 15-30 minutes in polytrauma patients early post trauma contributes to the activation of the cytotoxic activity of lymphocytes and phagocytic cells. The immunostimulating effect of EMWTHR is also achieved by increased level of humoral immunity factors. EMWTHR employed for polytrauma patients early post trauma in complex treatment improves the quality of rehabilitation and can be advocated to improve the immune system.

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Ethical expertise *The study received a favourable opinion from the local research ethics committee NMIRC TO (Abstract of minutes No. 3 (63) of 04/11/2019.*

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