Immune monitoring of magnetostimulation in complex treatment of burn injury

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SUMMARY

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The article presents the case of a female patient with an extensive 70% TBSA burn treated with a combination of routine operative surgery, general management and administration of expositions to low-frequency magnetic field (LFMF) generated by Viofor JPS Classic and Professional System emitters. The program P2M1 used for clinical purposes in a series of 10 daily expositions, 10 minutes each with the increasing intensity, results in the obtained value of magnetic induction of 10 μT in average, with the maximal value at the peak of impulse of 112 μT. These parameters of magnetostimulation were positively checked in preliminary investigations and then administered in the initiated clinical trial.

The beneficial effect of treatment of the analyzed case suggests that a therapeutic application of magnetostimulation should be introduced into the routine treatment of extensive burns and investigated in a larger clinical trial under the control of multidirectional clinical and immunological tests. It can be expected that enrichment of the routine therapy of burns with modern immunotherapeutic methods, including magnetostimulation and application of immunomodulating drugs, will contribute considerably to the improvement of therapeutic results.

Key words: *magnetostimulation, Viofor JPS System, burns, pro-regeneration, immunocorrection*

STRESZCZENIE

Monitorowanie immunologiczne magnetostytmulacji w kompleksowym leczeniu oparzeń

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Artykuł przedstawia przypadek pacjentki z rozległym oparzeniem 70% powierzchni ciała, leczonego kompleksowo poprzez rutynowe zabiegi chirurgiczne, leczenie ogólne i stosowanie ekspozycji ran na pola magnetyczne niskiej częstotliwości (WPM-wolnozmienne pola magnetyczne) generowane przez aparaty systemu Viofor JPS w wersji klasycznej i profesjonalnej. Program P2M1 używany w celach klinicznych w serii ekspozycji 10 dniowych, po 10 minut z wzrastającą intensywnością, powodował uzyskanie wartości indukcji magnetycznej średnio około 10μT, z maksymalna wartością na szczycie impulsu 112 μT. Parametry magnetostymulacji były sprawdzone w badaniach wstępnych i wtedy zastosowane w rozpoczętym badaniu klinicznym.

Korzystny wpływ leczenia w omawianym przypadku wskazuje, że zastosowanie terapeutyczne magnetostymulacji powinno być wprowadzone do rutynowego leczenia rozległych oparzeń i powinno być przedmiotem szerszych badan klinicznych pod kontrolą wielokierunkowych testów klinicznych i immunologicznych. Należy się spodziewać, że wzbogacenie klasycznego leczenia oparzeń w nowoczesne metody immunoterapeutyczne, w tym magnetostymulację i stosowanie leków immunomodulujacych, znacznie poprawi wyniki leczenia.

Słowa kluczowe: *magnetostymulacja, system Viofor JPS, oparzenia, pro-regeneracja, immunokorekcja*

Low intensity low frequency magnetic fields generated by the Viofor JPS System for magnetic stimulation purposes are well documented to have analgesic, anti-inflammatory, anti-spastic, pro-regenerating as well as blood circulation promoting action.

The effective co-operation of the neural, endocrine and immune systems in the integrative neuro-endocrine-immune network maintains the homeostatic balance of the organisms. The immune system contributes to the network with the efficient defensive, tolerogenic and pro-regenerative functions [1].

In the cases of extensive burns numerous pathogenic elements (tissue necrosis, local and general metabolic disturbances, electrolyte loss and haemodynamic dysfunction, shock, stress and massive infection) may disrupt the homeostatic balance to the life-threatening condition. The therapeutic success depends therefore, on the introduction of multidirectional procedures aiming to maintain the essential homeostatic functions of the organism. Among these different procedures, in addition to the anti-shock, anti-infective, improving the haemodynamics and anaesthetic therapy, the immunocorrective treatment seems to be no less important for the maintenance of defensive, tolerogenic and pro-regenerative functions of the immune system. Pharmacology (thymomimetic drugs, immunostimulants, cytokines and immunoglobulins) is not the only method to modulate the activity of the immune system. The exposition to electromagnetic fields (EMF) represents the other way of immunomodulation. In *in vitro* experiments *Dąbrowski* et al. [2] observed increase of human monocyte immunogenic activity and monokine production under the influence of pulse-modulated 1300 MHz EMF.

Moreover, preliminary investigations showed that a low frequency magnetic field generated by a Viofor JPS device, administered *in vivo* in a series of expositions, supports the renovation of thymus-dependent immunoregulatory functions of the immune system [3]. As the therapeutic effects of performed magnetostimulation also comprised analgesic, anti-inflammatory and pro-regenerative effects [4], one can expect that magnetostimulation, due to its multidirectional activities, introduced to the routine treatment of extensive burns, may contribute to improvement of both the immediate as well as prospective therapeutic effects. The low frequency magnetic field emitted by Viofor JPS affects biological organisms with the magnetomechanic and electrodynamic mechanisms and with the cyclothronic ionic resonance. Depending on the chosen program and kind of the applicator, both the homogenic or heterogenic magnetic field can be obtained with a basic impulse frequency in the range from 180 to 195 Hz in the collections serially emitted with the frequency of 12.5 – 29 Hz, 2.8 – 7.6 Hz and 0.08 – 0.3 Hz. The values of magnetic induction are at the level of several to several hundreds μT. The program P2M1 used for clinical purposes in a series of 10 daily expositions, 10 minutes each with the increasing intensity, results in the obtained value of magnetic induction of 10 μT in average, with the maximal value at the peak of impulse of 112 μT. These parameters of magnetostimulation were positively checked in the preliminary investigations and then administered in the initiated clinical trial.

MATERIAL AND METHODS

All patients admitted into the program of evaluation of clinical effects of magnetostimulation are tested for the following immunological parameters:

1. in the PBMC population
   a) quantitative estimation of different cellular phenotypes CD3, CD4, CD8, CD16/56, CD19 and CD3HLA-DR+ in the flow cytometry,
   b) functional evaluation of T lymphocyte and monocyte activity in the microculture system (response to PHA and to Con A, saturation of IL-2 receptors, T-cellsuppressive activity – SAT index, immunogenic activity of monocytes – LM index),
   c) determination (by the ELISA method) of the cytokine concentrations (IL-1β, TNFα, IL-1ra, IL-4, IL-10 i TGFβ) in the microculture supernatants;
2. blood serum determination of the concentration of immunoglobulins (IgA, IgG, IgM)) and chosen cytokines (the same like in the culture supernatants).

This combination of immunological tests characterizes in complex the functional efficiency of the immune system, comprising the estimations of immunoregulatory abilities (T-cell immune competence, regulatory cytokines), immunogenic activities (monocyte function and monokine production) [9] and humoral immunity (serum immunoglobulins).

Fig. 1. The equipment of Viofor JPS Systems (Classic and Professional) used in treatment of the described case at the clinical stand

The immunological monitoring of patients with severe burns, performed in this way, provides a sensitive and accurate measure controlling the effects of

administered treatment, including magnetostimulation. Patients with extensive burns, without symptoms of systemic illnesses and generalized infection, and with body temperature no higher than 38°C, were admitted into the trial and then treated routinely, including surgical procedures of necrotic tissue excision or supportive demarcation of eschar. Some of them, randomly chosen, were additionally treated with magnetostimulation.

Case Report

Initially we applied the LMF in a case of a critically burned patient without possibility of performing the early burn wound excision.

Patient T.D., woman, 52 years old, was admitted to the burn unit at 5th day after an extensive flame burn which occurred in her house. A 70% TBSA (50% III degree) burn wound estimated using Lund and Browder method was diagnosed. The burn wound involved the face and the neck, arms, thorax, abdomen and legs. The inhalation injury diagnosis was established, so the patient general state was extremely hard due to prolonged burn shock, circulatory instability, respiratory system insufficiency and evidences of deep haemostatic and other general homeostatic disturbances. The risk of death according to Bull and Fisher table was 100%, BUS Watson – Sachs – 210 points.

Surgical aid:

Day 13th – supportive demarcation of eschar (legs and underbelly), allografts

Day 21st – supportive demarcation (legs), allografts

Day 29th – demarcation of eschar, skin mesh grafts to the leg left, advanced technology dressings

Day 35th – removed eschar from the underbelly, dorsal surfaces of thighs and legs replaced with the skin transplants harvested from forearms

Day 95th – the remnant granulating wounds in inguinal and gluteal region were closed with the skin grafts

At day 37th pneumonia and respiratory insufficiency occurred, orotracheal intubation, respiratory control were done. At day 39th circulatory insufficiency, blood pressure 75/50, ventricular fibrillation, pulse 180/min, coagulation disorders (APTT 62.7 sec): the patient transferred to the Intensive Care Unit. The next day she improved, self-breathing, supported with the oxygen, circulatory stabilization. At day 65th the patient returned to the Clinic of Plastic Surgery. Later this day the circulatory and respiratory insufficiency returned and the patient once again was transferred to the Intensive Care Unit. After intensive cardiologic and antiinfective (antibiotics) treatment, blood transfusion and parenteral nutrition the patient regained circulatory, respiratory and metabolic balance. At day 81st the patient returned again to the Clinic of Plastic Reconstructive Surgery and Treatment of Burns. After initial rehabilitation the patient, in good health status, was transferred to the Rehabilitation Clinic. The patient was discharged being in satisfactory condition.

Magnetostimulation was administered to the patient in one time daily expositions (P2M1 program) for 60 days from the first day of her presence in the Clinic, except the periods of septic hyperthermia. The Viofor JPS Classic System double large applicator mats were used and finally the Professional one was applied at the end of cure.

Fig. 2. The patient during the LMF procedure. Viofor JPS System Classic (two control units and double – top and bottom large applicator mats)

RESULTS

The results of investigations of the presented case are shown in Table 1 and Table 2.

Table 1. Quantitative estimation (%) of different cellular phenotypes in PBMC population

Day after burn	Tested parameter						
	CD3	CD4	CD8	CD19	CD3/ HLA-DR	NK	Ratio CD4/CD8
5	82	33	55	11	55	7	0.60
19	73	53	30	18	24	20	1.77
66	84	36	58	7	47	9	0.62

Table 2. Response to mitogens and suppressive activity of T cells (SAT index), immunogenic activity of monocytes (LM index) in microcultures of PBMC

Day after burn	Tested parameter			
	Response to PHA dpm x 10³/cult.	Response to Con A dpm x 10³/cult.	SAT index	LM index
5	36.6	31.1	0	8.1
19	93.2	78.6	12.5	20.3
66	72.0	34.2	32.1	11.5

DISCUSSION

Burn injury is the source of strong immunotropic stimuli affecting different levels of structural organization of the immune system. At the central level the stressogenic agents of the shock (pain, catecholamines, adrenal steroids) inhibit the endocrine activity of the thymus [5, 6, 7]. The resulting impairment of the process of T lymphocyte maturation diminishes the cellular replenishments of the peripheral immune system, reducing its recognitive and immunoregulatory functions [8]. The concomitant massive tissue destruction joined with infection represents a significant charge for the effectory immune mechanisms. The increased presentation of numerous antigens and enriched production of pro-inflammatory monokines (IL-1, TNF) in the circumstances of insufficient immunocompetent cellular and humoral response, result in development and protraction of the inflammation [9-14]. The secondary decreased defensive, tolerogenic and pro-regenerative capacity of the immune system contributes to development of clinical complications (susceptibility to infections, appearance of autoagressive and/or allergic reactions, retarded healing of wounds). In the light of the fact that immune disturbances belong to the main elements participating in the pathogenesis of burns, the immune tests which determine the immune status of the patient, performed soon after the burn, may bring important information for the choice of the optimal way of treatment and for the better prognosis. The same tests repeated during and after the operational treatment may serve as a tool of a current control of the therapeutic effects.

Preliminary clinical and immunological observations (case of T.D. patient) clearly indicate that introduction of magnetostimulation with the low frequency magnetic field into the routine treatment of extensive and severe burns considerably improves the therapeutic results. The process of wound healing was accelerated and the surfaces covered with the skin transplants were cleared and well prepared for the grafts revascularization without bacterial lysis.

The fluctuations of the results of immunological monitoring (Table 1 and 2) precisely reflected the changes of clinical status of the patient, including the alternate improvements and deterioration.

The above described case was the first impulse to check the idea of immune system impairment in burns and to investigate the new methods of stimulation of the pro-regenerative and anti-suppressive therapy of burn disease. To date we have a group of 25 severely burned patients being exactly and systematically monitored and we are convinced that we have saved the life of some of them by early detection and proper curative reaction to immunological problems due to burn injury, especially in T cells and monocytes activity and response to burn trauma and burn wound. Our four years' clinical experience with application of the Viofor JPS System in treatment of burns indicates the unquestionable pro-regenerative, anti-inflammatory and anti-septic value of magnetostimulation procedures.

CONCLUSION

We have concluded that a special clinical trial, conducted in a large group of burned patients systematically monitored for their immune status during the treatment, should be performed to achieve the necessary data for introduction of magnetostimulation into the routine treatment of severe and extensive burns. It can be expected that enrichment of the routine therapy of burns with modern immunotherapeutic methods, including magnetostimulation and application of immunomodulating drugs, will contribute considerably to the improvement of therapeutic results.

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