Faculty of Engineering, Rijeka, Croatia
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Poznan University of Technology, Faculty of Electrical Engineering

XXII Symposium

ELECTROMAGNETIC PHENOMENA IN NONLINEAR CIRCUITS

June 26 - June 29, 2012, Pula, CROATIA

PROCEEDINGS

EPNC 2012

University of Rijeka, Faculty of Engineering, CROATIA, 2012
PTETiS Publishers, Poznań, POLAND 2012

APPLICATION OF VARIABLE MAGNETIC FIELDS IN THE TREATMENT OF DRUG-RESISTANT DEPRESSION

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***Abstract* - The therapeutic efficacy of microTesla variable magnetic field applied as magnetostimulation, in the treatment of patients with drug-resistant depression was analyzed. As a result of long-term daily exposures to variable magnetic field with induction of 15 μT, a significant regression of depression symptoms estimated with use of Beck's questionnaire, as well as Montgomery-Asberg's and Hamilton's scales was obtained, as compared to control patients subjected to sham-exposure. The results of this trial indicate that addition of three-week lasting magnetostimulation to routine pharmacotherapy intensifies the regression of depression symptoms but further prolongation of the cycle does not enhance the obtained clinical improvement.**

I. INTRODUCTION

Depressions resistant for routine pharmacotherapy make up about 30% of all depression syndromes, while in further 20-30% of patients with depression the application of different pharmacological and non-drug based methods (including invasive electroconvulsive therapy - ECT and transcranial magnetic field stimulation - TMS, using often strong, static magnetic field with induction values of 0.5-2 T) is unsatisfactory [1]. The results of numerous experimental studies proved that variable magnetic field with value of induction below 100 μT basing on ion cyclotron resonance mechanism, used in form of so called magnetostimulation, modifies the activity of central nervous system and behavior of experimental animals [2]. Moreover several clinical trials confirmed a potential therapeutic efficacy of this method in the treatment of depression syndromes [3], also in the course of some neurological diseases as sclerosis multiplex, Parkinson's disease, Alzheimer's disease and neurosis, mainly due to its positive influence on brain function [2], [4].

The aim of the study was to estimate if addition of magnetostimulation with use of microTesla variable magnetic fields to routine pharmacotherapy could intensify the regression of depression symptoms in patients with drug-resistant depression.

II. MATERIAL AND METHODS

A. Patients

38 patients from Psychiatric Department and Clinic of Internal Diseases, Angiology and Physical Medicine of Medical University of Silesia with confirmed drug-resistant depression (defined as two unsuccessful courses of anti-depressive therapy with use at least two anti-depressive drugs from different therapeutic groups administered for at least six weeks in relatively high doses) were prospectively enrolled into the trial.

The criteria of inclusion to the trial were as follows: fulfillment of diagnostic criteria for recurrent major depressive disorder without psychotic symptoms, the score of at least 18 points in 21-point Hamilton's Depression Scale (moderate depression) and age between 18 and 65 years.

The criteria of exclusion included typical contraindications for magnetostimulation as: cancer, pregnancy, active pulmonary tuberculosis or severe infections, gastrointestinal bleeding, not compensated diabetes, hyperthyroidism and implanted electronic devices such as a pacemaker.

During whole period of the trial all patients received a basic anti-depressive drug in individual dose.

The patients that fulfilled the above criteria were randomly into three study groups.

The patients from the first group (11 persons – 9 women and 2 men) were subjected to a cycle of magnetostimulation procedures with use of flat applicator, carried out in the active mode.

The patients from second group (13 persons – 11 women and 2 men) were subjected to a cycle of magnetostimulation procedures with use of flat applicator, carried out in the placebo mode.

The patients from third group (14 persons – 8 women and 6 men) were subjected to a prolonged cycle of magnetostimulation procedures with use of cylindrical applicator, carried out in the active mode.

B. Procedure of magnetostimulation

Magnetostimulation was carried out using the VIOFOR JPS device (Med&Life, Poland) consisting of generator with adjustable magnetic field parameters and option of sham exposure (placebo mode), and 2 different applicators.

The patients from the first group were subjected to magnetostimulation in the active mode, in form of 15 exposures to variable magnetic field with the saw tooth-like shape of basic impulses, frequency of basic impulses in range 180-195 Hz, that of overlapped clustered impulses in range 12.5-29 Hz, 2.8-7.6 Hz and 0.08-0.3 Hz, and effective induction of the magnetic field of 15 μT.

The 12 minute lasting exposures were performed once daily, 5 days a week with 2 day weekend break, over a period of three weeks. During exposure patients were lying down directly on applicator in form of flat mat.

The patients from the second group were subjected in the same time regimen to sham exposure (using placebo mode of the device), with no magnetic field generated by the device and no voltage applied to the clamps of the applicator.

The patients from the third group were subjected to magnetostimulation in the active mode, in form of 20

exposures to variable magnetic field with the same physical parameters as in the first group.

The 12 minute lasting exposures were performed twice daily, 5 days a week with 2 day weekend break, over a period of four weeks. During exposure patient's head was placed inside of cylindrical applicator.

C. Procedure of estimation of depression intensity

In patients from first and second group patients the intensity of depression symptoms was analyzed before the beginning of exposure cycle (day 0), and then on 7th and 21st days of exposure cycle, by means of patient's self-estimation with use the Beck's Depression Inventory (BDI) questionnaire, as well as with use of objective Montgomery-Asberg's Depression Scale (MADS) and 21-point Hamilton's Depression Scale (HDS). In patients from third group only self-estimation with use the Beck's Depression Inventory (BDI) questionnaire was carried out, before the beginning of exposure cycle and then on the last 28th day of exposure cycle.

III. RESULTS

The comparison of the intensity of depression symptoms in particular groups of patients and days of exposure cycle estimated by different tests are presented in tables I-IV.

Before the beginning of therapeutic cycle no significant differences in the intensity of depression symptoms between the magnetic field-exposed group and the group of patients subjected to sham exposure were noticed in applied tests.

On 7th day of exposure cycle, the depression symptoms in the magnetic field-exposed group were less pronounced than in the group of patients subjected to sham exposure in all applied testes, but the observed differences were not significant.

TABLE I
COMPARISON OF SELF-ESTIMATION OF DEPRESSION INTENSITY ACCORDING TO BECK'S DEPRESSION INVENTORY QUESTIONNAIRE IN GROUPS OF PATIENTS SUBJECTED TO ACTIVE AND SHAM EXPOSURE IN PARTICULAR DAYS OF EXPOSURE CYCLE WITH STATISTICAL EVALUATION

Day of exposure cycle	Self-estimation of depression according to Beck's questionnaire		Statistical significance
	Active exposure x ± SD	Sham exposure x ± SD	
Day 0	33.9 ± 6.8	39.8 ± 6.4	P = 0.109
Day 7	27.0 ± 7.2	32.3 ± 10.0	P = 0.146
Day 21	22.1 ± 6.9	34.5 ± 7.7	P < 0.001

TABLE II
COMPARISON OF DEPRESSION INTENSITY IN MONTGOMERY-ASBERGS'S SCALE IN GROUPS OF PATIENTS SUBJECTED TO ACTIVE AND SHAM EXPOSURE IN PARTICULAR DAYS OF EXPOSURE CYCLE WITH STATISTICAL EVALUATION

Day of exposure cycle	Depression intensity in Montgomery-Asberg's scale		Statistical significance
	Active exposure x ± SD	Sham exposure x ± SD	
Day 0	28.1 ± 8.2	31.1 ± 6.4	P = 0.246
Day 7	21.6 ± 7.8	26.5 ± 6.9	P = 0.137
Day 21	14.9 ± 6.9	27.5 ± 5.8	P < 0.001

TABLE III
COMPARISON OF DEPRESSION INTENSITY IN HAMILTON'S SCALE IN GROUPS OF PATIENTS SUBJECTED TO ACTIVE AND SHAM EXPOSURE IN PARTICULAR DAYS OF EXPOSURE CYCLE WITH STATISTICAL EVALUATION

Day of exposure cycle	Depression intensity in Hamilton's scale		Statistical significance
	Active exposure x ± SD	Sham exposure x ± SD	
Day 0	24.6 ± 5.4	25.5 ± 5.0	P = 0.560
Day 7	18.6 ± 5.2	21.5 ± 6.0	P = 0.211
Day 21	12.9 ± 4.8	22.0 ± 4.9	P < 0.001

On 21st day of exposure cycle, the analysis with use of all applied tests confirmed highly significant regression of depression symptoms in magnetic field-exposed group as compared to the group of patients subjected to sham exposure.

In turn in the group of patients subjected to more intense and prolonged exposure to variable magnetic field, on 28th of exposure cycle the results of self-estimation with use of Beck's Depression Inventory questionnaire confirmed in both sexes highly significant regression of intensity of depression symptoms, absolutely comparable to those obtained in the first group of magnetic field-exposed patients.

TABLE IV
SELF-ESTIMATION OF DEPRESSION INTENSITY ACCORDING TO BECK'S DEPRESSION INVENTORY QUESTIONNAIRE IN PATIENTS SUBJECTED TO PROLONGED ACTIVE EXPOSURE, BEFORE AND AFTER THE END OF EXPOSURE CYCLE WITH REGARD TO SEX AND STATISTICAL EVALUATION

Group of patients	Self-estimation of depression according to Beck's questionnaire		Statistical significance
	Before exposure cycle x ± SD	After exposure cycle x ± SD	
Women	33.6 ± 6.6	22.4 ± 4.8	P < 0.001
Men	31.2 ± 7.3	17.7 ± 7.4	P < 0.001
Total	32.7 ± 7.6	20.7 ± 6.0	P < 0.001

IV. CONCLUSIONS

The addition of magnetostimulation procedures to routine pharmacological treatment intensifies the regression of depression symptoms in patients with drug-resistant depression syndromes. During first three weeks of magnetostimulation procedures the therapeutic efficacy increases with the duration of exposure cycle, but further prolongation of exposure cycle does not enhance the obtained clinical improvement.

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