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"S.M. KIROV MILITARY MEDICAL ACADEMY"

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«25» января 2019

STUDY REPORT

on medical device "Transcutaneous electrostimulator for blood pressure correction "ABP-051" per TU 9444-005-12342964-2015" by "Inferum" LLC

Agreement № 19/13/8 dated 03.09.2019.

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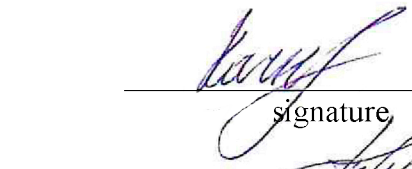

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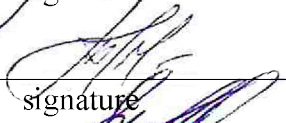

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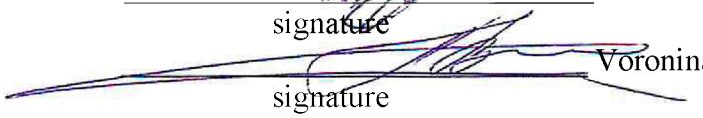

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ABBREVIATIONS

AH – arterial hypertension

BP – blood pressure

MMedA – S.M. Kirov Military-Medical Academy

DBP – diastolic blood pressure

PM – program and method

PSV – psychological strain value

SBP – systolic blood pressure

ABPM – 24-hour ambulatory blood pressure monitoring

STUDY RATIONALE

Order of the head of the Chief military medical administration of the Ministry of Defense of the Russian Federation № 161/6/8386 dated 08.08.2019.

BRIEF CHARACTERISTICS OF THE DEVICE

Electrostimulator “ABP-051” is intended for therapeutic non-invasive exposure (without skin damage) course exposure on wrist exposure using the method of transcutaneous electric neurostimulation for blood pressure correction combined with drug therapy. Electrostimulator “ABP-051” acts mainly on vascular tone. It is the most effective and safe method of exposure to blood pressure. The device does not almost influence cardiac output and heart rate. The stimulation is performed as series of impulses, the number of series of impulses corresponds to the set of frequencies for blood pressure correction. The efficiency of exposure depends on subject condition prior to the exposure and the area used.

The electrostimulator is a mobile, simple and compact device which allows to perform procedures in any convenient time, in any place.

Therapeutic indications:

- Resistant high systemic BP in patients with arterial hypertension– as an adjunct to complex drug treatment.
- Episodes of blood pressure increase in stress situations, weather changes, change of time zones, etc. in persons with labile arterial hypertension.
- Low blood pressure in hypotonic patients – as an adjunct to complex drug therapy.

Contraindications:

Absolute:

1. presence of an implanted pacemaker;
2. individual intolerability of the electric current;
3. atrial fibrillation;
4. general contraindications to physiotherapy.

Relative:

1. skin damage on the left distal forearm (macerations, wounds, burns, exanthema, etc.);
2. neoplasms (tumors) of any etiology or location;
3. acute fevers of unknown origin;
4. acute psychotic, alcohol or drug-induced excitation;

5. pregnancy.

Marketing authorization № RZN № 2016/3776 dated 31.03.2016 г.

The device appearance is presented in figure 1.

Fig.1. Type of medical device Electrostimulator “ABP-051”

STUDY BACKGROUND

Despite the efforts of scientists, physicians and healthcare management authorities, arterial hypertension in the Russian Federation remains one of the most significant medical-social problems. It is related both to wide incidence of the disease (about 40% of adult population of the Russian Federation has the increased blood pressure) and the fact that arterial hypertension is the most important risk factor of the principal cardiovascular diseases – myocardial infarction and cerebral stroke which determine primarily high mortality in our country.

According to the materials of the examination performed as part of target Federal program “Prevention and treatment of arterial hypertension in the Russian Federation, the incidence of arterial hypertension among the population has not almost changed for the last 10 years and amounts to 40.8% (in men 36.6%, in women 42.9%). The disease awareness of AH patients is 83.9–87.1%. 69.5% of AH patients take anti-hypertensive drug, among them, 27.3% are treated effectively, and only 23.2% of patients control BP on the target level. According to the forecasts, to 2025, about 60 % people globally will suffer from arterial hypertension.

Due to that, the search of new effective drugs and devices for control of blood pressure is rather challenging.

The study of transcutaneous electrostimulator “ABP-051” for evaluation of its effect on blood pressure level in patients with essential hypertension and hypertonic neurocirculatory asthenia is challenging.

STUDY AIM AND GOALS

Study aim – to evaluate the effect of trascutaneous electrostimulator “ABP-051” on blood pressure values in patients with essential hypertension. To evaluate the quality and utility of the medical device in the interests of the medical service of the Ministry of Defense of the Russian Federation.

Goals:

- to evaluate the blood pressure dynamics in office measurement and ambulatory measurement by a patient himself using device “ABP-051” or the placebo device simulating visually device “ABP-051” (hereinafter, placebo-“ABP-051”) in patients with essential hypertension receiving stable antihypertensive therapy;

– to evaluate the blood pressure dynamics according to 24-hour ambulatory blood pressure monitoring in when device “ABP-051” and placebo-“ABP-051” is used in outpatient settings in patients with essential hypertension receiving stable antihypertensive therapy;

– to investigate the effect of device “ABP-051” and placebo “ABP-051” on circadian blood pressure values: daytime and nocturnal mean systolic and diastolic blood pressure variability of daytime and nocturnal systolic and diastolic blood pressure, time index of daytime and nocturnal systolic and diastolic blood pressure, mean pulse blood pressure, nocturnal drop of systolic and diastolic blood pressure, Kario morning surge in blood pressure;

– to compare the effect of daily procedures by working devices “ABP-051” on circadian profile and BP level compared to the placebo-devices;

– to evaluate the safety and compliance of patients to therapy with transcutaneous electrostimulator “ABP-051”;

– to evaluate the quality of life of patients using transcutaneous electrostimulator “ABP-051” with questionnaire EQ-5D;

– to evaluate integral psychological strain and psychological stress level using questionnaire PSM.

Efficacy was evaluated by several parameters:

– measurement values of out-of-office blood pressure;

– measurement values of office blood pressure;

– ambulatory blood pressure monitoring values at baseline and values in 14 days of the use of transcutaneous electrostimulator “ABP-051” or placebo-device visually simulating device “ABP-051”;

– results of questionnaire EQ-5D;

– results of questionnaire PSM at baseline and 14 days of the use of transcutaneous electrostimulator “ABP-051” or placebo-device visually simulating device “ABP-051

SAFETY EVALUATION

Safety evaluation: it was confirmed by marketing authorization № RZN № 2016/3776 dated 31.03.2016. The device quality – declaration of conformity № ROSS RU.AI16.d 11301 dated 24.04.2016. Certificate of conformity № 1942/MDD dated 01.09.2017.

STUDY EXECUTOR

The study was carried out in the S.P. Botkin Hospital at the in the Federal State Budgetary Military Educational Institution of Higher Education ”S.M. Kirov Military Medical Academy” of the Ministry of Defense of the Russian Federation.

STUDY SITE AND PERIOD, STUDY POPULATION

The study was carried out from September 3, 2017 to December 20, 2019 at the S.P. Botkin Hospital of the Federal State Budgetary Military Educational Institution of Higher Education ”S.M. Kirov Military Medical Academy” of the Ministry of Defense of the Russian Federation. 81 subjects aged 19 to 70 years undergoing outpatient examination and treatment in the hospital of military-naval therapy for essential hypertension and hypertonic neurocirculatory asthenia were enrolled to the study.

INTRODUCTION

Cardiovascular diseases still remain the leading cause of mortality in many countries worldwide. Globally, about 17 mln. of people die annually due to cardiovascular diseases. In the Russian Federation, cardiovascular diseases consistently take the first position in the structure of the main causes of the population mortality. In 2018, the mortality coefficient (number of persons died/100 000 of population) for cardiovascular diseases in the Russian Federation was 565, meanwhile the coefficient in other European countries was lower in 3–4 times. Moreover, cardiovascular diseases are related to high mortality of active-age persons which leads to considerable economic losses.

In 2015, the number of patients with arterial hypertension worldwide was 1.13 bln, and over 150 mln. live in the Central and Eastern Europe. The incidence of arterial hypertension among adult population achieves 30-45% [2]. Arterial hypertension occurs more often in the elderly, and its incidence in persons above 60 years is >60%. As population ageing processes are observed, the high incidence of inactive life style and increase of body weight, the prevalence of arterial hypertension will continue growing worldwide, and up to 2025, the number of patients with essential hypertension, according to the estimates, will increase by 15-20% achieving about 1.5 bln. [2]. Essential hypertension contributes considerably to mortality and disability structure due to cardiovascular diseases. The increased blood pressure in 2015 was the main risk factor for premature death and led to almost 10 mln. of deaths and over 200 mln. of disability cases. SBP level ≥140 mm Hg is associated with mortality and disability in ~70% of cases, and the greatest SBP-related deaths occur within a year due to ischemic heart disease (4.9 mln), hemorrhagic (2.0 mln) and ischemic strokes (1.5 mln) [1,4,9].

Both office and out-of-office blood pressure values are independently and consistently correlated to frequency of some cardiovascular events (hemorrhagic stroke, ischemic stroke, myocardial infarction, sudden death, heart failure and peripheral arterial diseases), as well as, terminal stage renal failure. More and more data indicates the close relationship between arterial hypertension and the increased incidence of artrial fibrillation, and the data confirming that the increase of blood pressure is associated with cognitive dysfunction and dementia increases [3,5,7].

The pathogenesis of formation and maintenance of essential hypertension is related to close interaction between hemodynamic, neurohumoral, metabolic, genetic and psychological factors [8,12]. The complexity of differentiation of the leading mechanism in the disease development gives rationale for further comprehensive studies in this area. The discovery of new correlations in the pathogenesis of essential hypertension makes the treatment more effective

and, consequently, leads to temporary incapacity and disability which, in its turn, contributes to the decrease of economic losses.

The discussion in modern literature shows that the psychoemotional strain affecting autonomous nervous system plays an important role in the multi-factor pathogenesis of essential hypertension. One of the causes of blood pressure dysregulation is the change of a subject's psychoemotional status represented by development of anxiety disorders and depression. In addition, it should be noted that not only a subject's hormonal profile but also an emotional change depending also on the nature of his emotions is crucial for development of essential hypertension. The studies show that the change of sympathoadrenal and serotonin systems plays an important role in formation and maintenance of psychoemotional dysfunction, and essential hypertension.

Nowadays, the whole range of antihypertensive drugs are available and actively used, however, due to low patients' compliance, drug inefficacy, often the absence of necessary titration of drug dosage, the absence of proper correction of existing risk factors and whole range of other reasons, a large number of patients do not achieve target blood pressure values [6].

Due to the current situation in the prevalence of arterial hypertension and absence of control over blood pressure figures in most patients in real clinical practice, the development of new drugs and devices with mechanisms of action on blood pressure level is rather challenging [6,10.11].

1. STUDY OBJECTS, MATERIALS AND METHODS

1. 1. Study object

The study object was "Trascutaneous electrostimulator for blood pressure correction "ABP" per TU 9444-005-12342964-2015", model: "ABP-051" by "Inferum" LLC.

1. 2. Material -technical supplies

1 Device for blood pressure measurements – "Little Doctor", industrial number 65316, Marketing authorization FSZ 2012/11653.

2. 24-hour blood pressure monitor – software-hardware complex for 24-hour BP monitoring "BIPILAB", manufacturing plant "Pyotr Telegin" LLC, industrial number H13120288, H13120289, H13120290. H13120291, H13120292. Approval certificate of measurement instruments RU.C.39.026.A № 48309. Marketing authorization FSR 2011/10717.

3. Questionnaire EQ-5D (quality of life)

4. Questionnaire PMS (psychological strain and psychological stress level)

2. STUDY METHOD

2.1 General provisions

the program and method (PM) of the device study in the S.P. Botkin hospital of departmental therapy.

Prior the study and after obtaining of the voluntary informed consent, each subject had blood pressure measurements at rest, 24-hour ambulatory blood pressure monitoring was performed, the study subjects completed quality of life questionnaire EQ-5D (annex 1) and questionnaire for measurement of psychological strain and stress level PSM (annex 2).

After that, a patient was given a trascutaneous electrostimulator “ABP-051” (active or placebo device in ratio 1:1) which he used for 14 days in accordance with the device instruction (annex 3).

After 14 days of the use, each subject had recurrent measurements of office blood pressure at rest, 24-hour ambulatory blood pressure monitoring was performed, the patient completed the quality of life questionnaire EQ-5D (annex 1) and the questionnaire for measurement of psychological strain and stress level PSM (annex 2).

2.2. Processing, analysis and evaluation of the study results

Program MS Excel 2016 was used for generation of the database. The following programs were used for statistical processing of the results: Statistica for Windows, SPSS. The mean random values of quantitative parameters were presented as M±m, where M – mean arithmetic, and m – standard deviation.

For statistical data processing, the parametric and non-parametric statistical methods were used, their selection was provided by the nature of the distribution of the test parameters:

− for quantitative parameters – Student’s test;

− for qualitative and ordinal parameters – Mann-Whitney test and Chi-square.

2.3. Study inclusion and exclusion criteria

Inclusion criteria:

–I-III grade essential hypertension, hypertonic neurocirculatory asthenia;

– absence of contraindications to the proposed studies;

– presence of a subject’s informed consent.

Exclusion criteria:

– voluntary refusal of subjects from the study participation

– presence of an implanted pacemaker;

– atrial fibrillation;

– individual intolerability of the electric current;

–skin injury of the left wrist;

– acute fevers of unknown origin;

– acute psychotic, alcohol or drug-induced excitation.

3. STUDY RESULTS

A total of 81 patients were enrolled to the clinical study, they were randomly divided to 2 groups. Group 1 consisted of 40 patients using transcutaneous electrostimulator “ABP-051”. Group 2 consisted of 41 patients using placebo “ABP-051”.

At baseline, the groups were comparable by age, gender and structure of nosologic forms. The group characteristics at the study enrollment are given in table 1.

Table 1

Group characteristics at the study enrollment, p>0.05

Parameter	Group 1 (n=40)	Group 2 (n=41)
Men	48.3±15.2	48±13.9
Women	80% (n=32)	78% (n=32)
Neurocirculatory asthenia	20% (n=8)	22% (n=9)
Grade I essential hypertension	15% (n=6)	12.2% (n=5)
Grade II essential hypertension	5% (n=2)	2.5% (n=1)
Grade III essential hypertension	72.5% (n=29)	80.5% (n=33)

As table 1 showed, the mean age of the study patients was 48.3±15.2 and 48±13.9 years in group 1 and 2, correspondingly, males were predominant. In the structure of nosologic forms, grade II essential hypertension prevailed. Grade I and III essential hypertension was observed in a total of 5 patients of group 1 and 3 patients of group 2. The patients with essential hypertension received stable antihypertensive therapy throughout the study. In addition, 6 patients were enrolled to group 1, and 5 patients with hypertonic neurocirculatory asthenia – to group 2.

Both groups of patients with essential hypertension receiving antihypertensive therapy and untreated patients with hypertonic neurocirculatory asthenia had 24-hour ambulatory blood pressure monitoring (ABPM) with determination of circadian profile of blood pressure at baseline and in 14 days of the “ABP-051” use. ABPM data of group 1 is given in table 2.

Table 2

24-hour ambulatory blood pressure monitoring data in group 1 at baseline and in 14 days of the use of transcutaneous electrostimulator "ABP-051"

Parameter	Baseline	In 2 weeks of the device use	P=
Mean daytime SBP, mm Hg	142.8±15.3	141.6±13.7	0.53
Mean daytime DBP, mm Hg	88.9±8.6	85.6±11.4	0.09
Mean nocturnal SBP, mm Hg	130.7±15.1	124.8±17.3	0.06
Mean nocturnal DBP, mm Hg	77.3±8.9	72.5±12.1	**0.04**
Daytime SBP variability, mm HG	14.5±4.6	14.7±5.6	0.8
Daytime DBP variability, mm HG	10.5±3.0	10.6±3.5	0.9
Nocturnal SBP variability, mm HG	11.0±3.4	12.5±6.7	0.32
Nocturnal DBP variability, mm HG	8.4±3.4	10.5±4.9	0.06
Daytime SBP time index, %	51.8±31.2	49.7±32.4	0.64
Daytime DBP time index, %	45.2±31.2	34.6±24.2	0.07
Nocturnal SBP time index, %	60.8±33.5	46.4±32.3	**0.04**
Nocturnal DBP time index, %	59.3±34.2	40.5±35.3	**0.02**
Mean pulse BP, mm Hg	53.4±10.2	55.1±8.7	0.34
Degree of nocturnal SBP decrease	13.3±7.4	12.8±11.3	0.9
Degree of nocturnal DBP decrease	15.3±8.1	13.8±12.5	0.67
Kario morning BP surge	24.2±11.1	27.2±17.5	0.56

At baseline, mean daytime BP values in patients of group 1 receiving standard antihypertensive therapy were 142.8±15.3/88.9±8.6 mm Hg, nocturnal values 130.7±15.1/77.3±8.9 mm Hg. In 14 days when transcutaneous electrostimulator "ABP-051" was used, BP decrease up to 141.6±13.7/85.6±11.4 mm Hg in daytime and 124.8±17.3/72.5±12.1 mm during the night was observed. However, significant differences were shown only in mean nocturnal BP value (p=0.04). The values of mean nocturnal and daytime DBP did not significantly differ (p=0.06 and p=0.09) which could be related to a small sample size, meanwhile, the values were decreased up to 124.8±17.3 mm Hg and 85.6±11.4 mm Hg.

Daytime SBP and DBP variability values did not almost change. Meanwhile the values of nocturnal SBP and DBP variability were increased from 11.0±3.4 to 12.5±6.7 mm Hg and from 8.4±3.4 to 10.5±4.9 mm Hg, correspondingly (p=0.32 and p=0.06).

Daytime SBP time index did not almost change, meanwhile DBP time index tended to decrease from 45.2±31.2 to 34.6±24.2% (p=0.07), and nocturnal SBP and DBP time index was significantly decreased from 60.8±33.5 to 46.4±32.3% (p=0.04) and from 59.3±34.2 to 40.5±35.3% (p=0.02).

There were no significant differences between the mean pulse BP, degree of nocturnal SBP and DBP decrease, Kario morning surge during therapy with trascutaneous electrostimulator "ABP-051".

As well, prior to the study and in 14 days of "ABP-051" use, patients of both groups

completed quality of life questionnaire EQ-5D (annex 1) which provided 5 questions aimed to evaluate health condition. The data of questionnaire EQ-5D in group 1 is given in table 3.

Table 3

Data of questionnaire EQ-5D in group 1 at baseline and in 14 days of the use of trascutaneous electrostimulator "ABP-051"

Question	Response	Baseline, n	In 2 weeks of the device use, n	P= (χ2)
Locomotions	I do not have locomotion problems	35	36	0.72 (0.13)
	I have some locomotion problems	5	4	0.72 (0.13)
	I am confined to bed	0	0	
Self-care	I do not have self-care problems	36	38	0.39 0.72
	I have some washing or dressing problems	4	2	0.39 0.72
	I cannot wash or dress myself	0	0	
Everyday activity	I do not have problems in everyday activities (work, studies, home routine, family responsibilities, leisure time)	35	39	0.09 (2,88)
	I have some problems with everyday activities	5	1	0.09 (2,88)
	I cannot perform everyday activity	0	0	
Pain and discomfort	I do not feel pain and discomfort	27	31	0.32 (1.0)
	I feel now mild pain or discomfort	13	9	0.32 (1.0)
	I am tormented with pain or discomfort	0	0	
Anxiety and depression	I do not feel anxiety and depression	20	31	**0.01 (6.54)**
	I have now a mild anxiety or depression	15	9	0.14 (2.14)
	I have a marked anxiety or depression	5	0	**0.02 (5.33)**

The baseline analysis of questionnaire EQ-5D in group 1 showed 5 subjects who had some locomotor limitations, 4 subjects – washing or dressing limitations, 5 subjects had some problems with everyday activities, 13 subjects – a mild pain and discomfort, 15 subjects – a mild anxiety or depression, and 5 subjects – profound anxiety or depression. During the therapy with transcutaneous electrostimulator "ABP-051", some positive dynamics by such criteria as locomotions, self-care, pains and discomfort, and everyday activity was observed, however, the parameters were not significant. However such criterion as everyday activity was the most

significant (p=0.09). Meanwhile, such criterion as anxiety and depression were significant: during the use of transcutaneous electrostimulator “ABP-051”. Thus, the number of subjects not having anxiety and depression was significantly increased, and the number of subjects with a profound anxiety or depression was decreased (p=0.01 and p=0.02, correspondingly).

To evaluate psychological strain and stress level as baseline and in 14 days of the use of “ABP-051”, both groups used questionnaire PSM. The data of questionnaire PSM in group 1 are presented in table 4.

Table 4

Data of questionnaire PSM in group 1 at baseline and in 14 days of the use of transcutaneous electrostimulator “ABP-051”

Parameter		At baseline	In 2 weeks of the device use	P= (χ^2)
Stress level	High	n=2	n=0	0.15 (2,05)
	Moderate	n=17	n=11	0.15 (1.98)
	Low	n=21	n=29	0.06 (3.41)
Scores		98.6±32.6	86.5±28.7	0.00001

The analysis of the questionnaire for measurement of psychological strain and stress PSM showed the following changes in group 1. Thus, at baseline, 2 subjects with high stress level, 17 – with moderate stress level, and 21 with low stress level were found. The mean questionnaire score prior to the therapy with transcutaneous electrostimulator “ABP-051” was 98.6±32.6. In 14 days of the use of transcutaneous electrostimulator “ABP-051”, no patients with high stress level were shown. Meanwhile, the number of examined subjects with a moderate stress level was decreased from 17 to 11, and the number of subjects with a low stress level was increased, correspondingly, and the significance level was 0.06. The mean questionnaire scores was decreased up to 86.5±28.7 (p=0.00001).

In group 2, at baseline and in 14 days when the device visually simulating device “ABP-051”was used in patients with essential hypertension and hypertonic neurocirculatory asthenia, ABPM was also performed with determination of circadian blood pressure values. ABPM data in group 2 is given in table 5.

Table 5

24-hour ambulatory blood pressure monitoring data in group 2 at baseline and in 14 days of the use of placebo device visually simulating transcutaneous electrostimulator "ABP-051"

Parameter	Baseline	In 2 weeks of the device use	P=
Mean daytime SBP, mm Hg	144.1±10.4	143.7±11.5	0.64
Mean daytime DBP, mm Hg	89.1±11.4	89.3±11.5	0.84
Mean nocturnal SBP, mm Hg	131.2±11.7	131.0±12.3	0.79
Mean nocturnal DBP, mm Hg	79.0±11.5	80.1±12.9	0.3
Daytime SBP variability, mm HG	15.7±7.9	14.0±5.9	0.08
Daytime DBP variability, mm HG	14.8±16.2	11.4±3.5	0.2
Nocturnal SBP variability, mm HG	13.9±13.4	11.8±4.4	0.32
Nocturnal DBP variability, mm HG	11.6±13.1	9.9±4.3	0.39
Daytime SBP time index, %	55.8±28.6	57.2±30.5	0.44
Daytime DBP time index, %	44.4±34.2	50.0±34.4	0.08
Nocturnal SBP time index, %	63.5±30.8	63.3±32.9	0.94
Nocturnal DBP time index, %	59.3±39.5	59.7±40.1	0.91
Mean pulse BP, mm Hg	54.3±8.4	53.6±8.5	0.36
Degree of nocturnal SBP decrease	8.8±6.2	9.1±6.2	0.38
Degree of nocturnal DBP decrease	11.3±8.0	11.3±7.9	0.97
Kario morning BP surge	26.9±13.5	25.6±13.7	0.16

In group 2 using the placebo device visually simulating device "ABP-051" for 14 days, significant differences in mean daytime and nocturnal SBP and DPB levels were not shown. As well, no significant differences in daytime and nocturnal SBP and DBP variability and time index, mean pulse BP, nocturnal decrease in SBP and DBP, Kario morning surge.

Likewise, prior to the study and in 14 days of the use of placebo device visually simulating device "ABP-051", the patients of group 2 completed quality of life questionnaire EQ-5D (annex 1). The data of questionnaire EQ-5D in group 2 are given in table 6.

Table 6

Data of questionnaire EQ-5D in group 2 at baseline and in 14 days of the use of placebo device visually simulating "ABP-051"

Question	Response	Baseline, n	In 2 weeks of the device use, n	P= (χ2)
Locomotions	I do not have locomotion problems	37	37	1 (0)
	I have some locomotion problems	4	4	1 (0)
	I am confined to bed	0	0	0
Self-care	I do not have self-care problems	37	37	1 (0)
	I have some washing or dressing problems	4	4	1 (0)

	I cannot wash or dress myself	0	0	0
Everyday activity	I do not have problems in everyday activities (work, studies, home routine, family responsibilities, leisure time)	36	37	0.72 (0.12)
	I have some problems with everyday activities	5	4	0.72 (0.12)
	I cannot perform everyday activity	0	0	0
Pain and discomfort	I do not feel pain and discomfort	27	28	0.81 (0.06)
	I feel now mild pain or discomfort	14	13	0.81 (0.06)
	I am tormented with pain or discomfort	0	0	0
Anxiety and depression	I do not feel anxiety and depression	23	26	0.5 (0.46)
	I have now a mild anxiety or depression	14	12	0.64 (0.23)
	I have a marked anxiety or depression	4	3	0.69 (0.16)

The analysis of questionnaire EQ-5D data at baseline in group 2 showed 4 subjects having some locomotion limitations, 4 subjects – washing or dressing limitations, 5 subjects have some problems with everyday activities, 14 subjects had a mild pain and discomfort, 14 subjects had a mild anxiety or depression, and 4 subjects – a marked anxiety or depression. During the therapy with the placebo device visually simulating device “ABP-051”, no significant dynamics was shown in either of the parameters.

Likewise, for measuring psychological strain and stress level at baseline and 14 days of the use of placebo device visually simulating device “ABP-051”, group 2 completed questionnaire PSM. The data of questionnaire PSM in group 2 are given in table 7.

Table 7

Data of questionnaire PSM in group 2 at baseline and in 14 days of the use of the placebo device visually simulating device “ABP-051”

Parameter		At baseline	In 2 weeks of the device use	P= (χ^2)
Stress level	High	n=1	N=0	0.3 (1,01)
	Moderate	n=17	N=18	0.82 (0.05)
	Low	n=23	N=23	1.0 (0)
Scores		97.9±25.4	97.6±24.7	0.27

The analysis of the questionnaire data for measuring psychological strain and stress level during the use of the placebo device visually simulating device “ABP-051” in group 2 did not show significant changes. Thus, at baseline, 1 subject had a high stress level, 17 – moderate, and 23 subjects had a low stress level. In 14 days when placebo device was used, no patients with a high stress level were observed. Meanwhile, the number of examined subjects with a moderate stress level was increased from 17 to 18, and the number of subjects with a low stress level did not change and amounted to 23 persons.

The tolerability of both transcutaneous electrostimulator “ABP-051” and the placebo device visually simulating device “ABP-051” was rather good. 2 subjects from group 1 felt a slight skin tingling in sites of application of transcutaneous electrostimulator “ABP-051” during stimulation, however, the fact did not interfere with further use of the device.

CONVENIENT HANDLING OF THE DEVICE, DEVICE INTERFACE AND DESIGN, FAILURES AND MALFUNCTIONS

The device is rather convenient, well-tolerated and is not accompanied with adverse effects.

However, 2 subjects from group 1 felt a slight skin “tingling” in the site of application of transcutaneous electrostimulator “ABP-051”, however, the fact did not interfere with further use of the device.

No device failures and malfunctions were reported.

The device use has shown that it is energy-consuming, and one set of AAA batteries is sufficient for long-term use, but the posterior lid of the battery compartment is inconvenient for opening.

DEVICE ELABORATION

The location of control keys on the upper part of the device periodically led to their incidental pressing, due to that, it is appropriate to translocate them to the lateral device surface or change a pressure force.

It is appropriate to consider whether to increase the size of the color indicator for convenient use of the device.

PRACTICAL RECOMMENDATIONS

1. It is appropriate to use transcutaneous electrostimulator “ABP-051” in complex therapy of I-III grade essential hypertension and hypertensive neurocirculatory asthenia as an adjunct to standard antihypertensive therapy.

2. When transcutaneous electrostimulator “ABP-051” is applied in patients with patients with essential hypertension and hypertensive neurocirculatory asthenia, it is appropriate to use questionnaire PSM for evaluation of psychoemotional condition of patients.

CONCLUSIONS

1. During the study, positive results of the use of transcutaneous electrostimulator “ABP-051” in patients with essential hypertension and hypertensive neurocirculatory asthenia as an adjunct to standard combined antihypertensive therapy.

2. It is found that when transcutaneous electrostimulator “ABP-051” is used as an adjunct to standard combined antihypertensive therapy, some parameters tend to decrease according to the 24-hour ambulatory blood pressure monitoring. The absence of the significant dynamics of some blood pressure values can be related to both a small sample of patents and a relatively short period of observation of such patients.

3. The decreased anxiety and depression was observed in the patients using transcutaneous electrostimulator “ABP-051”, as well, stress level was reduced which was not observed in the group using the placebo device.

4. The improvement of psychoemotional condition of subjects which has been found during the clinical study of transcutaneous electrostimulator “ABP-051”, on our opinion, plays a key role in the change of circadian profile of blood pressure influencing the neurovegetative pathogenesis chain of essential hypertension and hypertensive neurocirculatory asthenia.

CONCLUSION

By its technical characteristics, functional possibilities and safety level, transcutaneous electrostimulator “ABP-051” fully meets the data declared by the manufacturer. As a result of the study, the device can be used in complex therapy of essential hypertension and hypertensive neurocirculatory asthenia as an adjunct to standard antihypertensive therapy.

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Annex 1

Questionnaire EQ-5D

Please evaluate your current health condition

Below are given 5 questions aimed to evaluate your health condition. Answering each question, check in the left box which of the variants describes your current health condition the best (mark only one item).

Locomotions

- I do not have locomotion problems
- I have some locomotion problems
- I am confined to bed

Self-care

- I do not have self-care problems
- I have some washing or dressing problems
- I cannot wash or dress myself

Everyday activity

- I do not have problems in everyday activities (work, studies, home routine, family responsibilities, leisure time)
- I have some problems with everyday activities
- I cannot perform everyday activity

Pain and discomfort

- I do not feel pain and discomfort
- I feel now mild pain or discomfort
- I am tormented with pain or discomfort

Anxiety and depression

- I do not feel anxiety and depression
- I have now a mild anxiety or depression
- I have a marked anxiety or depression

Annex 2

Questionnaire for measuring psychological strain and stress level (PSM)

The questionnaire provides the list of statements characterizing psychological condition. Please evaluate your condition during the last week using the 8-score scale. For that, check the number 1 to 8 near each statement at the blank form of the questionnaire which defines your psychological condition most accurately. Number 1 to 8 denote frequency of emotions: 1- "not at all"; 2- "not really"; 3 – "very little"; 4 – "a bit"; 5 – "somewhat"; 6 – "quite a bit"; 7 – "very much"; 8 – "much extremely (daily)".

1	I feel strained and overexcited (overnervous)	1 2 3 4 5 6 7 8
2	I have lump in my throat and/or dry mouth	1 2 3 4 5 6 7 8
3	I feel rushed; I do not seem to have enough time.	1 2 3 4 5 6 7 8
4	I swallow food in a rush or forget to eat	1 2 3 4 5 6 7 8
5	After work, I cannot switch off my thoughts on completed activities, plans, I am "stuck" feeling stressed about working situations and unsolved matters, think over my ideas again and again	1 2 3 4 5 6 7 8
6	I feel lonely and misunderstood	1 2 3 4 5 6 7 8
7	I feel malaise, I am dizzy, I have headaches, feel strained and have discomfort in cervical region, back aches, stomach aches.	1 2 3 4 5 6 7 8
8	I feel preoccupied, tormented, or worried.	1 2 3 4 5 6 7 8
9	I feel suddenly hot and cold	1 2 3 4 5 6 7 8
10	I forget about meetings or tasks to be made or solved	1 2 3 4 5 6 7 8
11	My mood spoils often, I can easily cry due to insult or become aggressive, furious	1 2 3 4 5 6 7 8
12	I feel tired	1 2 3 4 5 6 7 8
13	In difficult situations, I clench my teeth (or my fists)	1 2 3 4 5 6 7 8
14	*I feel calm and peaceful	1 2 3 4 5 6 7 8
15	It is difficult to breath, or I am suddenly out of breath	1 2 3 4 5 6 7 8
16	I have gastrointestinal problems (pains, colics, diarrhea, constipation)	1 2 3 4 5 6 7 8
17	I am worried, disturbed, excited	1 2 3 4 5 6 7 8
18	I am easily confused, noise or rustle make me shudder	1 2 3 4 5 6 7 8
19	I need more than half an hour to get asleep	1 2 3 4 5 6 7 8
20	I feel confused; my thoughts are muddled; I lack concentration; I cannot focus	1 2 3 4 5 6 7 8
21	I look tired, I have pouches or dark circles under the eyes	1 2 3 4 5 6 7 8
22	I feel a great weight on my shoulders.	1 2 3 4 5 6 7 8
23	I am worried, need to move constantly, I cannot stand or sit in one spot	1 2 3 4 5 6 7 8
24	I have difficulty controlling my reactions, emotions, moods or gestures.	1 2 3 4 5 6 7 8
25	I feel strained	1 2 3 4 5 6 7 8

Remark * Reverse question

Processing and interpretation of the results

The sum of all results is calculated – integral psychological strain value (PSV)/

Question 14 is evaluated in the reverse order. The more is PSV, the higher is the psychological stress value

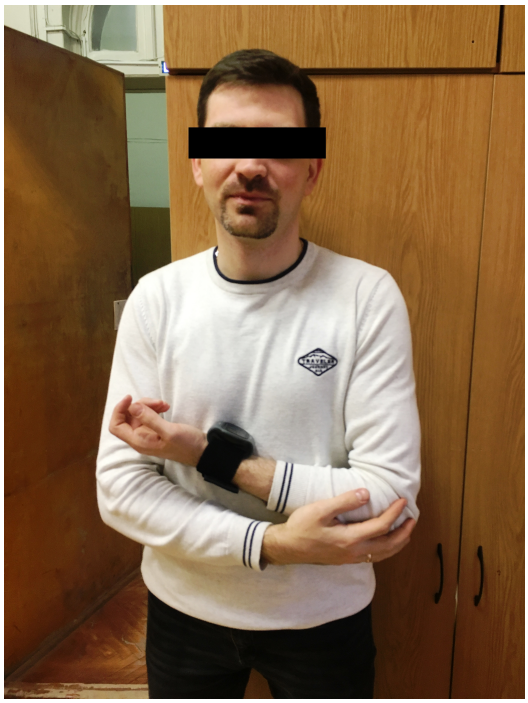
PSV > 155 scores –high stress level, shows disadaptation and psychological discomfort

PSV in the range of 154-100 scores – moderate stress level

Low stress level, PSV < 100 scores, shows psychological adaptation to work loads.

Annex 3

Active device –transcutaneous electrostimulator “ABP-051”



Placebo device –transcutaneous electrostimulator “ABP-051