ROSTOV STATE MEDICAL UNIVERSITY
Rostov
2019

ABP 051

Зарегистрирован
в качестве **медицинского изделия в РФ и ЕС**

Регистрационное удостоверение
РЗН 2016/3776 от 31.03.2016.
EC Certificate № 1942/MDD от 01.09.2017.

CLINICAL STUDY PROTOCOL

Name of the study device: "Trascutaneous electrostimulator for blood pressure correction "ABP-051" per TU-9444-005-12342964-2015" (hereinafter referred to as Electrostimulator "ABP-051"). Model: ABP-051.

Marketing Authorization issued by the Federal Service for Surveillance in Healthcare, № RZN 2016/3776 dated 31 March, 2016.

EU Certificate for Conformity under Directive 93/42/EEC dated 01.09.2017.

Producer: Limited Liability Company "Inferum", 620026, Russia, Sverdlovsk Region, Yekaterinburg, Belinsky Str., 86-487

Manufacturing site: 623417, Russia, Sverdlovsk Region, v. Kamensk-Uralsky, Mechanizatorov Str., 74.

Division of the medical organization carrying out the medical study of the medical device:

Federal State Budgetary Educational Institution of Higher Education "Rostov State Medical University" of the Ministry of Health of the Russian Federation, chair of internal diseases 1, Russia, 344015, Rostov-on-Don, Blagodatnaya Str., 170.

The study was carried out in outpatient settings on the base of State Budgetary Institution "Rostov Regional Clinical Hospital" in accordance with the agreed and approved study protocol.

Principal Investigator: Candidate of Medical Sciences, Associate Professor M.Z. Gasanov.

Study period: 20.02 - 10.09.2019.

Relevance of the problem

The problem of increased blood pressure (BP) is of much concern for global medical society. It is related with the fact that arterial hypertension is the leading cause of death and disability in 70% of cases if cardiovascular complications develop.

Low BP is also considered as a negative cardiovascular factor increasing the risk of hypotonic encephalopathy, atherosclerosis, coronary artery disease and other cardiovascular diseases influencing quality of life and working capacity of humans, often in young age.

Arterial hypotension (AHT) is understood as the decrease of blood pressure for over 20% from baseline/common values, or in absolute figures – below 90 mm Hg of systolic blood pressure (SBP) and 60 mm Hg of diastolic blood pressure (DBP). BP is considered low on level < 100/60 mm Hg in men and < 95/60 mm Hg in women. AHT can be considered as physiological in healthy persons, sportsmen and inhabitants of high lands.

AHT is considered pathological in those cases when it is accompanied with clinical symptoms and decrease of quality of life and professional activity. In accordance with ICD-10, the following is specified: idiopathic (195.0), orthostatic (195.1), drug-induced (195.2) and other types of hypotension (195.8). Blood pressure decrease can be acute and chronic.

Among all chronic forms, there is idiopathic AHT (IAHT) which incidence in the population is about 12-15%. However, due to non-specificity of complaints, absence of precise diagnostic criteria, as well low referral of patients for medical care even in clinically manifested BP lowering, actual AHT incidence is presented above.

Most patients – young women that complain often on headaches, dizziness, faintness, weakness, tearfulness, liability for depression, memory problems, weather sensitivity in low blood pressure, and their first symptoms can manifest already in pediatric age. About 70% of women aged 18-35 years complain on rapid fatigue in physical exercise - 38%), cold hypersensitivity (cold wet palms, feet) - 42%, calf and foot edemas to the evening - 13%) related to impaired peripheral blood circulation. All mentioned symptoms in 80% of cases often manifest somatoform dysfunction of the vegetative nervous system (ICD - F 45.3) known as neurocirculatory dystonia or vegetovascular dystonia requiring timely non-drug and drug correction.

To confirm the diagnosis of idiopathic arterial hypotension, causes of low BP should be ruled out which dictates the necessity of consultations by physicians of various specialties depending on a clinical picture and complaints. Complex laboratory-instrumental examination including cardiovascular, endocrine and nervous system tests, should be performed (triple BP measurements with interval of 3-5 min, ABMP, ECG (at rest/with load tests), EchoCG, EEG, determination of glucose level in blood, electrolytes, etc.

Patient's IAHT requires selection of pathogenetic and symptomatic therapy. Non-drug approaches include modification of life style (optimization of sleep/wake regime, balanced nutrition, refusal from social habits), psychotherapy, high intake of common salt and sufficient amount of fluid, massage of cervical collar zone, acupuncture, physiotherapy (general body conditioning, balneotherapy, hydromassage, neck electrophoresis), physical exercises, wearing of compression stockings as indicated, etc.

If the abovementioned measures are insufficient, drug treatment is initiated: herbal drugs (magnolia vine, aralia, ginseng, eleutherococcus), midodrine-based drugs, cerebroprotective drugs, nootropic agents, antioxidants, vitamin complexes, antidepressants, ets.

Meanwhile, high AHT incidence, absence of diagnostic algorithms and clinical recommendation of management of patients of the discussed group dictate the necessity of search of new additional methods for correction of low blood pressure.

In period February to September 2019, we investigated a new physiotherapeutic device for transcutaneous electroneurostimulation "ABP-051".

Study design "Correction of low blood pressure in young women using device "ABP-051""		
	30 patients with low blood pressure	ABMP
	Device ABP-051	
	25	5 sham control
	The device administration twice a day, BP measurement prior and after the procedure, in 20 minutes	14 days
	BP measurement twice a day	14 days
	ABMP control	

Figure 1. Study design.

30 young women with AHT and symptoms of low BP inducing discomfort were enrolled to the study with sham control (fig. 1).

Statistical data processing:

Statistical data analysis was made using applied software package "Statistica 10,0" ("StatSoft", USA). The methods of descriptive statistics were applied, statistical significance of differences in two mean values was determined using the Student's test in normal distribution of the sample, if differed from normal – Mann-Whitney test. The relationship between quantitative variables in normal distribution was assessed with Peason coefficient, abnormal – Spearman coefficient. Differences were considered statistically significant at $p<0.5$.

Study aim: to assess effect of electrostimulation course with device ABP-051 on BP circadian profile values in young women with arterial hypotension and typical symptoms.

Study object: 30 women were enrolled to the study: 25 of them comprised the first treatment group (mean age was 22.5±1.5 years), 5 of them comprised the second group – control with sham device (mean age was 22.4±3.7 years). Mean age of all responders was 22.5±0.4 years.

Obtained results: mean duration of clinical history of arterial hypotension was 9.8±0.8 years, family history of arterial hypotension was complicated in 50±0.1%.

The proportion of patients responding on course electrostimulation with device ABP-051 with BP increase in the treatment group was 60±0.5%, in the control group - 20±0.5% (2 out of 5 patients).

The proportion of patients responding on course electrostimulation with device ABP-051 with less frequent symptoms of BP lowering in the treatment group was 72±0.5%, in the control group - 40±0.5% (2 out of 5 patients).

On average, frequency of BP lowering symptoms among all responders causing discomfort was 3.7±2.6 times a week. In the **treatment group,** prior course electrostimulation, they occurred significantly more often, 3.8±2.7 versus 2.5±1.7 times a week after course electrostimulation, and in the control group, the discussed parameters did

not significantly differ and were 2.4±2.1, and 2.8±2.5 times a week, respectively.

To manage symptoms of low BP, the responders used strong tea most often – 33.3±0.5%, coffee - 60±0.5% and other methods - 10±0.3%, 16.7±0.4% of the study subjects failed to eliminate discomfort symptoms associated with low BP.

SBP and DBP in the treatment group after course device electrostimulation **in the morning** were significantly higher than those prior the device electrostimulation and were 102.3±7.6/68.7±8.8 mm Hg versus 99.8±8.1/66.7±8.9 mm Hg, respectively ($p<0.01$). However, statistically significant difference of the discussed values was not shown in the control group: 103.2±8/66.6±9.7 mm Hg versus 102.2±8.6/66.6±9.4 mm Hg ($p<0.02$).

SBP and DBP in the treatment group after course device electrostimulation **in the evening** were significantly higher than those prior electrostimulation and were 103.5±8.5/68.6±8.4 mm Hg versus 100.8±8.1/67.9±8.9 mm Hg, respectively ($p<0,01$). However, statistically significant difference of the discussed values was not also shown in the control group: 104.9±9.2/67.4±9.2 mm Hg versus 104.4±8.2/66.7±8 mm Hg ($p<0.05$).

The comparative SBP and DBP analysis prior the study and in 2 weeks after the study completion in the treatment and control group did not show any significant difference in values, despite high significance. BP tended to recover to baseline figures shown by the study subjects prior the study.

Despite the absence of a profound growth of BP figures in responders after course administration of device ABP-051, all of them had the statistically significant BP increase in the treatment group ($p<0.01$). Frequency of AHT symptoms causing discomfort in 2 weeks after course electrostimulation with device ABP-051 was maintained on the level corresponding to the level after the study completion.

Due to the fact that treatment compliance in the study was indirectly assessed based on the results obtained in a small control group (n=5), its true contribution to endpoints is unlikely to be determined. The detailed analysis of BP self-control diaries of the study subjects did not allow to rule out impact of low treatment compliance of responders likely related to the age of the study participants, low motivation, presence of medical knowledge and other factors which should be considered in further studies.

It should be noted that 40% of responders in the treatment group had a more profound effect of course device electrostimulation. Thus, *prior* the study, their mean SBP1 *in the morning* was 97.9±5.2 mm Hg, DBP1 was 66.8±5.6 mm Hg, and *after* the study, mean SBP2 was 102.3±5.2 mm Hg, DBP was 70.4±5.6. Mean SBP1 *in the evening* was 101.6±4.9 mm Hg, DBP1 was 69.1 ±6.6 mm Hg *prior* course device electrostimulation, and SBP2 was 104.4±4.9 mm Hg, DBP2 70.3±4.9 mm Hg *after* electrostimulation with device ABP-051.

Conclusion

Young people with arterial hypotension – a specific group of patients with increased cardiovascular risk. Their early detection will allow to optimize diagnostics and treatment approaches and influence quality of life and prognosis.

The absence of precise recommendations on management of patients with chronic (idiopathic) AHT requires the search of additional methods of BP correction, especially in clinically manifested forms. In this context, course electrostimulation with device ABP-051 can be recommended for correction of low BP and symptoms of low BP in young women

with idiopathic arterial hypotension.

It should be noted that 40% of responders in the treatment group had more profound effect of electrostimulation with device ABP-051 shown not only as more significant BP increase but also minimization of frequency of clinical manifestations related to low BP.

It is evident that appearance of device ABP-051 shows new opportunities for non-drug correction of idiopathic arterial hypotension, and electostimulation used in combined therapy can have additional positive impact on health condition and quality of life of subjects with arterial hypotension and potentiate clinical therapeutic effect in general.

Cumulative effect of course device electrostimulation, as well as assessment of the effect duration after course treatment should be further investigated. Efficacy study of course ABP-051 administration in adult women (in perimenopause?) with arterial hypotension and qualitative assessment of treatment compliance deems to be prospective.

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