MINISTRY OF HEALTH
OF THE SVERDLOVSK REGION

FEDERAL SERVICE FOR SURVEILLANCE
ON CONSUMER RIGHT PROTECTION
AND HUMAN WELLBEING
FEDERAL BUDGETARY
SCIENTIFIC INSTITUTION
“EKATERINBURG MEDICAL RESEARCH
CENTER FOR PREVENTION AND HEALTH
PROMOTION OF INDUSTRIAL WORKERS”
(FBSI EMRC PHPIW of Rospotrebnadzor)

FEDERAL STATE BUDGETARY
EDUCATIONAL INSTITUTION OF THE
HIGHER PROFESSIONAL EDUCATION
“URALS STATE MEDICAL UNIVERSITY”
OF THE MINISTRY OF HEALTH OF THE
RUSSIAN FEDERATION
(FSBEI HPO of the Russian MoH)

USE OF TRANSCUTANEOUS ELECTROSTIMULATOR ABP-051 FOR CORRECTION OF SYSTEMIC BLOOD PRESSURE IN CLINICAL PRACTICE

METHODICAL GUIDELINES

Ekaterinburg
2018

SVERDLOVSK REGION MINISTRY OF HEALTH

FEDERAL SERVICE FOR SURVEILLANCE
ON CONSUMER RIGHT PROTECTION AND HUMAN WELLBEING
FEDERAL RESEARCH INSTUTUTE
"EKATERINBURG MEDICAL RESEARCH CENTER FOR MEDICAL PREVENTION
AND OCCUPATIONAL HEALTH"

FEDERAL HIGH EDUCATION INSTITUTE
"URALS STATE MEDICAL UNIVERSITY"
OF THE MINISTRY OF HEALTH OF THE RUSSIAN FEDERATION

APPROVED:
Deputy Minister of Health
of the Sverdlovsk region:

/Cand. of Med. Sc., Top-level physician
S.B. Turkov/
May 18, 2018

APPROVED:
Chief Cardiologist of the Sverdlovsk region:

/Doctor of Medicine, Prof., honored physician, Head of the Cardiology Department of FSBEI of HE USMU, full member of RAMS, Vice-President of VNOK (Society of Cardiology of the Russian Federation)
Ja.L. Gabinski/
May 18, 2018

USE OF TRANSCUTANEOUS ELECTROSTIMULATOR ABP-051 FOR CORRECTION OF SYSTEMIC BLOOD PRESSURE IN CLINICAL PRACTICE

METHODICAL GUIDELINES

Ekaterinburg
2018

UDC 615.8
ISBN 978-5-907080-14-0
The Guidelines are recommended or publication by the Academic Board of the Faculty of the Advanced Training and Vocational Education at: Federal State Budgetary Educational Institution of the Higher Education "Urals State Medical University" of the Russian Ministry of Health (Minutes No 6 dated March 30, 2018)

Authors:

- **Malakhov V.V.**, Doctor of Medicine, Professor, Medical Advisor the Inferum group;
- **Fedorov A.A.,** Doctor of Medicine, Professor, Officer in Charge of the Chair of Physical therapy, Exercise Therapy and Sports Medicine at: Federal State Budgetary Educational Institution of the Higher Education "Urals State Medical University"; Officer in Charge of the Research and Production Association for Restorative Treatment, Physiotherapy and Spa Medicine at: Federal Budgetary Research Institution "Ekaterinburg Medical Research Center for Prevention and Health promotion of Industrial Workers";
- **Guliaev V.Y.,** Doctor of Medicine, Professor, Chair of Physiotherapy, Exercise Therapy and Sports Medicine at: Federal State Budgetary Educational Institution of the Higher Education "Urals State Medical University";
- **Ryzhkin V.M.,** Chief External Expert in Physiotherapy at: Sverdlovsk Regional Ministry of Health; Officer in Charge of Physiotherapy Department at: Sverdlovsk Regional Clinical Hospital No 1;
- **Ozhgikhin I.V.,** Deputy General Director for Development of Sales, Marketing and Service Support Systems at Shvabe JSC;
- **Ivanov V.V.,** Candidate of Engineering, Chairman of the Board of Directors, the Inferum group
- **Gurov A.A.,** Senior Research Associate of Inferum Group.

Reviewers:

- **A.M. Vasilenko,** Doctor of Medicine, Professor, Senior Research Associate of the Federal State Budgetary Institution "National Medical Research Center for Rehabilitation and Spa Medicine" of the Russian Ministry of Health, Moscow;
- **A.V. Yashkov,** Doctor of Medicine, Professor, Officer in Charge of the Chair of Medical Rehabilitation, Sports Medicine, Physiotherapy and Spa Medicine at: Federal State Budgetary Educational Institution of the Higher Education "Samara State Medical University" of the Russian Ministry of Health, Samara.

In the methodical guidelines, the physiotherapeutic correction of systemic blood pressure is presented as transcutaneous electric neurostimulation of specific areas using device ABP-051. The device has a high therapeutic efficacy and significantly reduces treatment terms both in patients with arterial hypertension and arterial hypotension.

These Guidelines present the mechanism of action, particularities of the use, technique and methods for procedures of transdermal correction of systemic blood pressure. The treatment may be provided in outpatient settings predominantly as monotherapy and in inpatient facilities of various profile in combination with other treatment methods.

The methodical guidelines are intended for physicians - physiotherapists, reflexotherapists, neurologists, cardiologists, general practitioners and pediatricians and may be followed in treatment and prevention facilities including sanatoria and health resorts. The impaired systemic blood pressure can be corrected using ABP-051 device by the mid-level medical personnel of PTD and PTR, and a patient himself/herself in home settings.

ISBN 978-5-907080-14-0

TABLE OF CONTENTS

ABBREVIATIONS

AH	arterial hypertension (hypertensive disease)
BP	blood pressure
ASFC	artificial stable functional connection
VMC	vasomotor center
VNS	vegetative (autonomous) nervous system
VVD	vegetovascular dystonia
DBP	diastolic blood pressure
DENS	dynamic electric neurostimulation
ICD	international classification of diseases
NCD	neurocirculatory dystonia
PD	pathological determinant
PNS	peripheral nervous system
UAR	useful (positive) adaptive result
PFS	pathological functional system
SBP	systolic blood pressure
SDVNS	somatoform dysfunction of the vegetative nervous system
CVS	cardiovascular system
PTR	physiotherapy room
PTD	physical therapy department
PFS	physiological functional system
CAH	chronic arterial hypotension (hypotensive disease)
CNS	central nervous system
TENS	transcutaneous electric neurostimulation

INTRODUCTION

The principal reason for the impaired regulation of systemic blood pressure (BP) lies in acute or chronic stress situations involving social determinants, such as globalization, urbanization, income level, education and housing conditions [1].

The initial signs of functional disorders in the circulatory system shown as **«maladaptation syndrome»** (decreased physical tolerance, increased anxiety and transient vegetative disorders) become evident as early as in the school age. Therefore the preventive examinations show that 58.3-74.6% of school children, without any health complaints present transient BP fluctuations which ranges are wider than the statistically normal range [2], and, if medical advice is sought, neurocirculatory dystonia (NCD), neurocirculatory asthenia [3, 4], vegetovascular dystonia (VVD) [5] or somatoform dysfunction of the vegetative nervous system (SDVNS, IDC-10 code: F 45.3) [6] is diagnosed. There is no generally accepted SDVNS classification [7].

The following clinical signs and symptoms of SDVNS are known: pain syndrome (cephalgias, cardialgias, abdomenalgias, etc.); signs of vagotony; signs of sympatheticotony, systemic BP disorders.

In the structure of cardiovascular (CV) diseases, **SDVNS** occurs three times more frequently than the organic pathology and is of great social and economic importance as it may limit the choice of profession and be an insuperable obstacle to military service [8]. The 10-year prospective study provided the conclusive evidence that SDVNS can be considered as the borderline condition preceding one or other form of arterial hypertension in 30% of the monitored children [9].

According to the modern concepts [6, 10] SDVNS is a stress-induced phychovegetative cardiovascular disorder, its treatment is based on elimination of all stress-provoking factors, selective use of mild sedative or tonic agents depending on the VNS imbalance (such as valerian, motherwort, glycine or eleuterococcus, ginseng, Chinese magnolia vine), nootropics, tranquilizers and neuroleptics. With the profound predominance of one of the VNS segments, either beta-adrenoblockers (to suppress sympathetic nervous system activity), or beladonna drugs (to reduce vagus nerve activity) are administered. Physical therapy (massage, electrically-induced sleep therapy or exercise therapy) and balneotherapy are used.

Arterial hypertension (AH, increased blood pressure or hypertension, hypertensive or hypertonic disease – ICD-10 code: I10-I15) is one of the key risk factors for CV diseases. Hypertension is a silent and invisible killer that induces evident symptoms rarely [1]. Globally, there are more than a billion of people suffering from hypertension or 20% of the global population. Hypertension causes myocardial infractions and cerebral strokes. Increased blood pressure kills nine million people every year [11].

The algorithms for AH diagnostics and drug therapy are known, help physicians to solve the challenging task of AH patient treatment and to develop more effective schemes for BP drug therapy [12]. However according to the study results carried out within the targeted program "Prevention and Treatment of Arterial Hypertension in the Russian Federation", AH incidence rate is 39.5% of the examined subjects, AH awareness – 77.9%, with 59.4% of the population treated, and the treatment efficacy only 21.5% [13]. In 2003 – 2013, AH incidence in Russian men was increased on 20% [14]. In the USA, 68% of people with high BP values were aware of their disease; of them, 53.6% were treated. However, only 27.4% of the treated people had the adequate BP control (below 140/90 mm Hg) [15].

Therefore the relevance of seeking methods for correction of VNS balance in AH both in the population and in each individual clinical case is still high.

Chronic arterial hypotension (CAH, primary arterial hypotension, essential arterial hypotension, chronic hypotension, hypotonic disease – ICD-10 code: I95.0) is diagnosed in 33% of women and 4% of men [16, 17], achieving about 12-15% in the population, being only inferior to SDVNS in incidence rates. However due to the long-term compensated condition and low rates of medical referrals of the population, low awareness of physicians in the diagnostic criteria and absence of perfect treatment methods, actual incidence rates of CAH are largely higher than the values stated above [18]. Meanwhile, CAH is a risk factor for vascular (hypotensive) encephalopathy, atherosclerosis, resistant arterial hypertension, ischemic heart disease and other cardiovascular diseases, and it worsens quality of life and working capacity as early as in the young age [19]. In CAH exposed to stress factors both transient cerebrovascular disorders and severe cerebral disorders [20], the body is actively ageing [14, 16].

The principal CAH syndrome is decreased BP combined with the decreased total peripheral resistance and specific clinical symptoms. The first symptoms such as complaints on headaches, vertigos, syncopes, weakness, tearfulness, liability to depression, weather sensitivity, etc., allowing to suspect hypotensive VVD, reveal CAH most often as early as at the age of 8-9 years [21].

In ongoing emotional and age-specific stresses (extension periods, psycho-neuroendocrine changes, pregnancy, etc.), clinical symptoms are gradually aggravating [22]. However such condition remains compensated for a long time, subjects consider themselves to be relatively healthy managing their health problems on their own using folk treatment methods (coffee, tinctures of hawthorn, schizandra, eleuterococcus, ginseng, etc.).

Only the presentation of symptoms (syncope crises and severe symptoms of psycho-vegetative dysregulation) makes them refer to physicians [23].

The recommendations available in the literature for drug therapy of CAH-related disorders are divided into two types: pathogenetical (aimed to increase BP) and symptomatic treatment [24-26].

The recommendations on CAH treatment are extensive but not sufficiently systematized due to unpredictable multiple symptoms and absence of reasonability in drug selection, moreover, most drugs used have serious limitations and adverse effects if taken for a long time.

Among physiotherapy procedures in CAH, general body conditioning, dosed physical exercise, balneotherapy, photo- and electrotherapy, acupuncture and massage [27, 28] are recommended.

Moreover, recently as the close relationship between CAH and chronic fatigue syndrome [29-31] was established, the search for new effective and reliable methods for BP management has acquired a special importance. The ultimate goal for such efforts is the development of methods for timely, safe and individualized management of adaptive body capabilities in decreased BP.

Therefore the disorders of the systemic BP regulation are widely spread in all age groups of the global population. However, despite the available range of drug products, it is not always possible to achieve long-lasting stable target effect. On the other hand, long-term drug therapy may result to addiction to one or another drug, withdrawal ("rebound") syndrome, resistance and adverse effects.

Considering information expansion of the modern society, etiology and pathogenesis of systemic BP dysregulation, the necessity of the search for new and improvement of the known methods of non-drug BP therapy is evident, among which physical therapy has the leading role as the most natural trend for recovery of impaired functions [32-36].

Almost for 10 years, the dynamic electric neurostimulation (DENS) has been successfully used for systemic BP management, both in polyzonal technique and within any single exposure area [37-39]. However the accumulated experience of the use shows some disadvantages such

as: inconvenience in emergency care in under extreme situations, use only for AH and moderate temperature [40, 41].

The fundamentally new physical therapy device for transcutaneous electric neurostimulation (TENS) ABP-051 has been designed. Used in systemic BP disorders, it shows high efficacy both in hypertension and hypotension, with the increase in the cohort (proportion) of treatment responders.

1. ABP-051

1.1. Indication

Transcutaneous electrostimulator ABP-051 intended for normalization of blood pressure manufactured by Inferum LLC (Ekaterinburg, Russia) is an autonomous physical therapy device for non-invasive exposure to the low-frequency electric current impulses in distal dermatometer areas located in the left forearm.

It is intended for general regulating exposure to human physiological functional systems (PHFS) in treatment and prevention facilities, home and field settings to provide treatment and secondary preventive care in systemic BP disorders and concomitant symptoms in persons above 14 years.

Procedure course promotes:

- Management and stabilization of the impaired BP;
- Elimination of pain syndrome and other symptoms accompanying BP increase or decrease;
- Improvement of the overall health condition;
- Improvement of the emotional condition;
- Improvement of the working capacity;
- Decrease of weather sensitivity and time dependence;
- Improvement of patient' quality of life.

Device ABP-051 is approved for medical use by the Federal Service for Surveillance in Healthcare and introduced to the Registry of the Medical Devices (Marketing authorization № RZN 2016/3776 dated March 31, 2016; EC Certificate № 1942/MDD dated September 1, 2017) and conforms with TU 9444-005-12342964-2015.

1.2. Program and exposure parameters

The Program of the device exposure is the further development of TENS and DENS. The hallmark of device ABP-051 is formation of hormetic [42-46] electric current parameters for dual functional signaling by the Monte Carlo method [47] to restore intermittent activity of the functioning structures [48].

Two automatic software programs are used in ABP-051. Program No 1 is intended for management of increased BP and systemic AH, while Program No 2 is used for management of decreased BP and CAH. Each such program consists of consequent series of electric impulses (Fig. 1) differing in frequency, stimulation time intervals and exposure amplitude (Fig. 2) which makes the electrostimulator effective and prevents body adaptation to it.

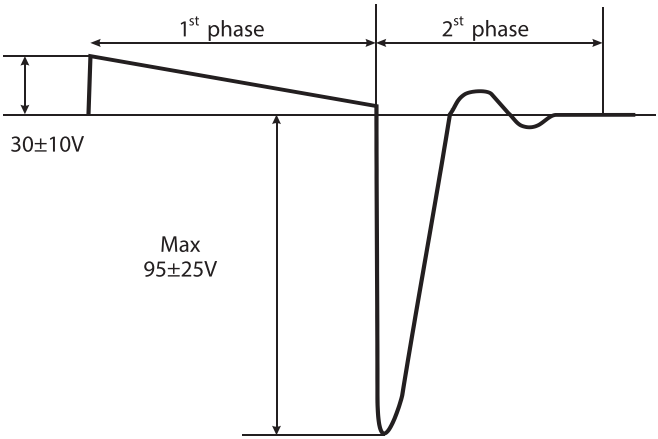

Fig. 1. Shape and parameters of one impulse

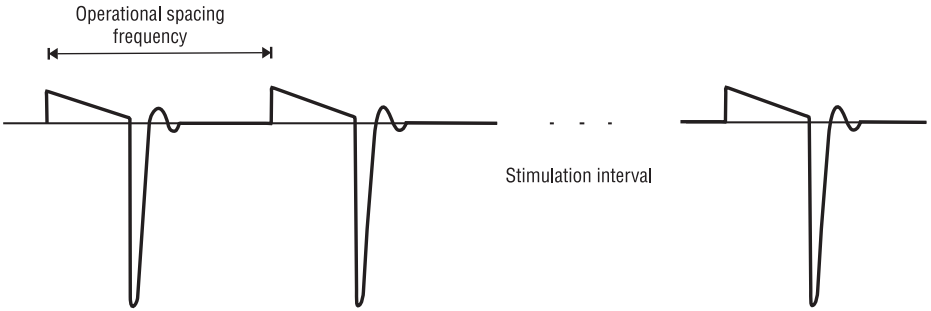

Fig. 2. Working repetition rate and stimulation interval

1.3. Main technical characteristics

Main technical device characteristics are shown in Table 1.

Table 1

Major technical characteristics of ABP-051

Description		Value and purpose
Program No 1	Exposure purpose:	Arterial hypertension
	Working impulse rates, Hz	9,2 and 77
	Total operation time, min.	5
Program No 2	Exposure purpose:	Arterial hypotension
	Working pulse rates, Hz	77 and 140, amplitude modulation with frequency: 4
	Total operation time, min.	6
Electric pulse amplitude (load-free)	Phase 1, V	30±10V
	Phase 2, V	95±25
Dimensions (without the cuff), not more than, mm		75x75x40
Electrostimulator weight (with the cuff and built-in electrodes (without power supply cells)), not more than, kg		0,1
Power consumption, not more than mA		200
Supply voltage, V		3±0,6
Electric power supply source		Galvanic batteries, Type AAA (R03), 2 pcs.
Degree of the device body protection		IP41 pcs.
Degree of protection of the working units from electric current damage		Class BF

1.4. Appearance and design

Appearance and design of the device are shown in Fig. 3.

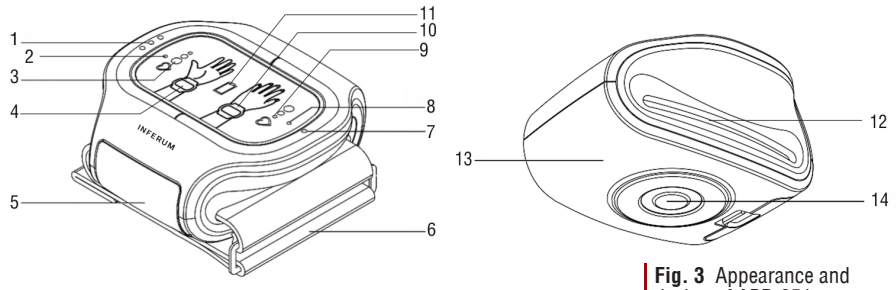

Fig. 3 Appearance and design of ABP-051

External side of the device contains screen and control keys as follows:

1 – ON/OFF button, Program No 1 (contains three relief points on its surface)

2 – LED indicator, Program No 1. After the LED starts flashing white, a sound signal occurs to state that Program No 1 operation is over

3 – Program No Symbol for management of increased BP (orange)

4 – Symbol of the correct device installation on the forearm for Program No 1 for management of increased BP (orange)

5 – Battery compartment lid

6 – Cuff for fixing the device upon the wrist

7 – ON/OFF key, Program No 2 (contains one relief point on its surface)

8 – Light emitting diode, Program No 2. After the light emitting diode starts flashing white, a sound signal occurs to state that Program No 2 operation is over

9 – Program No 2 symbol for management of decreased BP (blue)

10 – Symbol of the correct installation of the device on the forearm for Program No 2 for management of decreased BP (blue)

11 – Low battery indicator

Internal side of the device contains:

12 - Cuff holder

13 – Operational surface of the device body

14 – Electrodes for electric stimulation

2. INDICATIONS FOR THE USE,CONTRAINDICATIONS AND POTENTIAL ADVERSE EFFECTS OF ABP-051

2.1. Indications for the use

- NCD of hypo- or hypertensive type (CV dysfunction in VVD syndrome, SDVNS) as a supplement to drug therapy or as an individual treatment method;
- Episodes of BP increase in stress situations, weather changes, change of time zones, etc. in persons with labile AH form;
- Steady high systemic BP in patients with AH – as a supplement to complex drug treatment;
- Low BP in CAH patients – as a supplement to complex drug treatment;
- The device is indicated for the use in persons above 14 years.

2.2. Contraindications for the use

Absolute contraindications:

- Individual intolerability of the electric current;
- Presence of an implanted pacemaker;
- Atrial fibrillation;
- General contraindications to physical therapy.

Relative contraindications:

- Open skin wounds or injuries in the distal third of the left forearm (macerations, wounds, burns, exanthema, etc.);
- Neoplasms (tumors) of any etiology or location;
- Acute fevers of unclear etiology;
- Acute psychotic, alcohol or drug-induced excitation;
- Pregnancy.

2.3. Potential adverse effects

Any known adverse effects of ABP-051 use are not shown.

3. MECHANISM OF ACTION OF ABP-051

3.1. Mechanism formula for systemic BP management

Systemic BP is managed as a result of reconstruction of the body sanological functional system [48, 49, 50] per the type of artificial stabile functional connection (ASFC) [51], as the original exposure of ABP-051 signals to nervous-vascular receptors in the distal segments in left forearm dermatometers which have segmentary and suprasegmentary connection with cardiovascular and vasomotor centers.

3.2. Pathogenesis of systemic BP disorders and their general treatment approach

Modern biomedical science considers SDVNS, AH and CAH as stress-induced psycho-vegetative cardiovascular disorders [5, 10, 15, 17, 20, 52].

More than 100 years ago, W.B. Cannon was the first to describe somatic changes in negative emotions [53] and introduced later the term “stress” to physiological and psychological practice [54]. Later H. Selye described the general adaptation syndrome [55] and two specific stress types: positive stress and negative stress.

In positive stress - eustress (ancient Greek εὖ – “good, genuine” and stress) –physiological functional system (PHFS, Fig. 4) formed by the body under external exposure provides restoration of normal human homeostasis; the stress ends with a positive adaptive result (UAR); and PHFS as no longer needed, is dissociated preserving the “functional system with the advanced UAR prediction” in the memory [56, 57].

In negative stress case – distress, the body is unable to achieve UAR [58] and to stabilize homeostasis. In such cases, a focus of continuous nervous excitement arises in CNS – unsatisfied, pathological dominant (PD) which causes dysregulative pathology of the vasomotor center (VMC) and clinical picture of SDVNS [50, 52, 59].

If PD is not eliminated timely, it leads, sooner or later, to formation and consolidation of the pathological functional system (PFS) – a never-ending, vicious circle, a rigid cyclical program – chronic dysregulative disorder [60]. Each type of the systemic BP disorder and the clinical syndrome has its own PFS. The stressor impairing the general homeostasis ceased exciting nerve receptors, and PFS activity continues, and energy resources (biophysical) and material (biochemical) body resources are wasted strenuously in vain (Fig. 5).

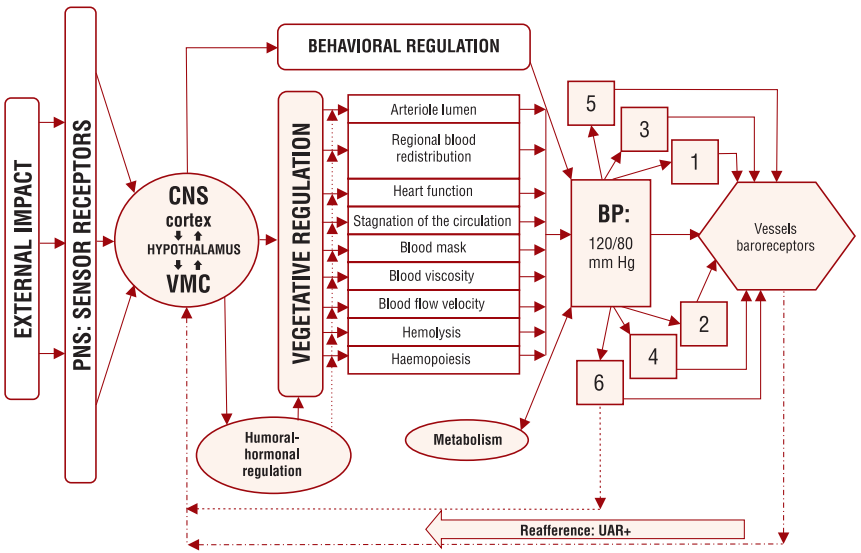

Fig. 4. Scheme of the physiological functional system that provides a metabolically optimal rate for systemic blood pressure (Sudakov K.V., 2006; modification). Digital symbols used show the number of attempts to achieve UAR (support).

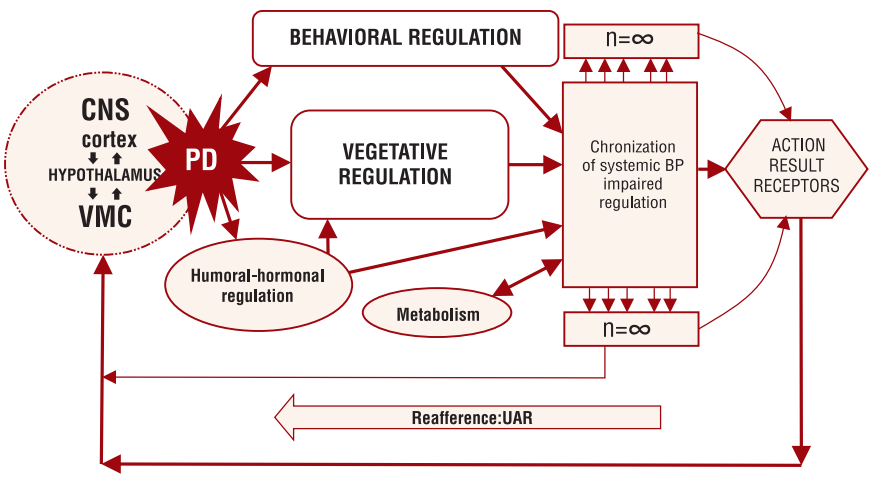

Fig. 5. General scheme of the pathological functional system that excites systemic BP continuously: a vicious circle. The number of attempts to achieve UAR in the situation has no limit (n=∞).

PFS is a permanent generator of irritations maintaining persistent imbalance in VNS and the hypothalamus-pituitary gland-adrenal gland system. This, in its own turn, leads to the impaired tone and geometry of resistant peripheral vessels (initially functional; afterwards, morphological re-modulation of arterioles, terminal arterioles, capillaries and venules); increase or decrease of peripheral blood flow resistance with the impaired microcirculation, lower perfusion rates and metabolic disorders in target organ tissues; centralized or decentralized blood circulation; and arterial hypertension or hypotension in the systemic circulation. AH or CAH form so up to drug-resistant and complicated disease forms [18, 36, 61-65].

In such settings, the use of ABP-051 is pathogenetically justified and associated with the universal biological categories and principles. Systemic BP is corrected with the introduction of ABP-051 device into external behavioral chain of the body self-regulation (Fig. 6). This provides PFS elimination, activation of the sanological system and restoration of the general integrative cerebral control [50, 57, 60, 66] forming ASFC as result of which the brain restores its original capabilities to control the systemic BP homeostatic balance [51].

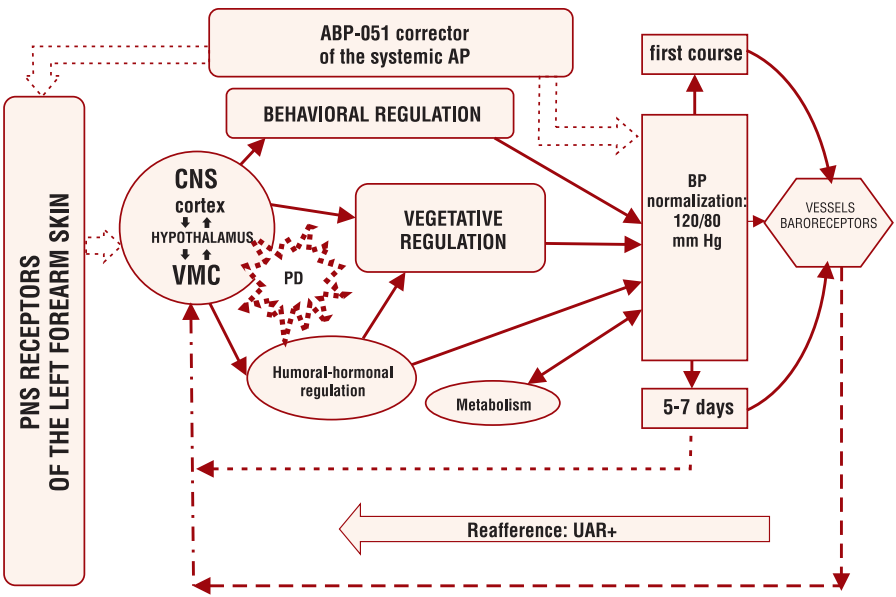

Fig. 6. Scheme of the artificial sanogenetical system for systemic BP management using ABP-051

Such cerebral phenomenon was first discovered by V.N. Smirnov and Y.S. Borodkin [67] as they were using tagged-in electrodes to restore normal CNS balance (excitement-inhibition). The ASFC phenomenon shows mainly the rehabilitation of the previously existing but later impaired cerebral connections which provides opportunity for more comprehensive use of cerebral reserves and their control.

It is explained by the fundamental physiological principles: dual functional signaling and antagonistic regulation (any such event involves both activating and inhibiting structures), intermittent activity of the functioning structures and latent adaptation reserve (any activity is maintained by intermittent functioning of individual groups within the homogeneous structure) and the principle of long-term matrix memory (by which the first principles are maintained). The further studies showed that stimulation frequency and certain treatment exposure time are important to obtain the consistent reaction as the short-term exposure may end with the rapid ASFC fading [49, 50, 51, 52, 56, 57, 59, 60].

3.3. Selection of exposure area

To provide effective formation of ASFC and obtain the expected body reactions in response to ABP-051 exposure in patients with systemic BP disorder, two exposure areas were selected (Fig.7). The areas were selected in accordance with the universal biogenetical metamerism principle, peculiarity of segmentary distribution of somato-visceral innervations and somato-vegetative integrations, and also availability of emergency care procedures with regards to exposure individualization and standardization.

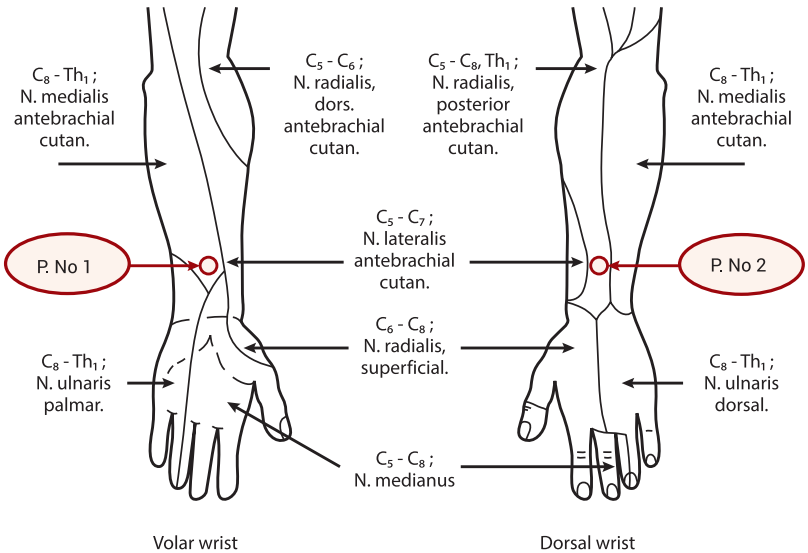

Fig. 7. Left forearm and hand. Segmentary innervation and skin sensitivity distribution in accordance with the peripheral nerves [68, 69]. ABP-051 electrode positions required for the treatment procedures with the use of: Program No 1 (P. No 1) and Program No 2 (P. No 2)

The evolution-mediated particularities of the metameric structure of human upper extremities are known [70-74]. They are presented as the common vegetative-segmentary innervation available for internal organs and for certain metameres: one and the same spinal segments contribute to innervation (although dissimilar in its nature) of dermatometers of the arm and cardiovascular organs [75, 76]. For instance, forearm skin is somatically innervated from segments of C_5-C_8, Th_1; sympathetical arm innervation from Th_4-Th_7; vegetative heart innervation from C_3-C_5, C_8, Th_1-Th_3; and aorta – from Th_1-Th_3 [70, 72, 73, 77].

The cardiovascular center and vasomotor center are represented by network-connected, dynamic community of CNS structures, and they include sympathetic nervous system centers and pre-ganglion spinal neurons C_6, Th_1-Th_3; parasympathetic nervous system centers represented by pre-ganglion neurons of the vagus nerve, by the higher VNS centers and individual nuclei of the hypothalamus, limbic system and cerebral cortex [77-81].

The spinal intimal dynamic contacts make the concept of impulse switch from the somatic segment to the vegetative segment and vice versa and also on suprasegmentary-integrative levels. The cervix-thorax ganglion plays an important role in differentiation of exposure areas and communicative topology (C_6-C_8; n. vagus; n. vertebralis; n. cardiacus cervicalis inferior).

4. TECHOLOGY OF ABP-051 USE

4.1. Procedure conditions and preparation

Treatment procedures with the use of ABP-051 do not require any specific conditions. It is desirable that the room in which the device exposure occurs, is clean, dry and light.

Before the device is used, its operator should:

- Review and always bear in mind the precautions stated in the operation manual of ABP-051 electrostimulator.
- Decide on of indications and contraindications to the device use (Sections 2.1 and 2.2). It should be considered that if there are any relative contraindications, the device may be used only after a consultation with an experienced physician.

Before the device is used, the patient should be warned:

- It is not allowed to discontinue the drug treatment on his own in the period of BP treatment using device ABP-051: after a steady therapeutic effect is obtained, drug doses may be changed only by the attending physician.
- The use of ABP-051 should be promptly discontinued if any allergic or any other unexpected reactions occur as the result of a skin contact with the device or working electrodes; in such a case, the patient should promptly consult the specialist.

Before the treatment, each patient should review the device and possible nature of sensations occurring during the session of the device exposure, the intended treatment purpose should be explained to him/her; he/she should take off all items from the left arm/hand (wrist watch, rings, chains, etc.) and free the distal third of his/her left forearm from the clothes.

For a treatment session using device ABP-051, a patient should take any body position comfortable for him/her (either a sitting or supine position). The procedure is not made while the patient stays in a vertical position.

During the procedure, the patient should never read, sleep, touch the device body or change the device position on his/her arm on his own.

After the treatment procedure, it is recommended to have rest for 20-30 min.

After each treatment procedure, the device electrodes should be wiped with a soft absorbent cloth slightly impregnated in the disinfectant solution (such as 3% aqueous hydrogen peroxide solution). Take precautions to avoid any liquid getting into the device.

Store the device with its electrodes dry.

4.2. Procedure technique for management of the increased BP and systemic arterial hypertension (Program No 1)

4.2.1. Take off all objects from the left forearm and free from the clothes.

4.2.2. Select the exposure area. The exposure area zone for patients with high BP is on anterior surface of the distal third of the left forearm.

4.2.3. Treat the device electrodes and the patient's skin in the exposure area, with a moist napkin or tampon slightly moistened with water or saline solution (0.9% aqueous sodium chloride solution) to ensure better contact.

4.2.4. Put the patient's left hand into the device cuff so that.

4.2.5. Shift it upon the forearm.

4.2.6. To ensure proper treatment efficacy, place the device to the lower third of the forearm so that right rim of the device body is parallel to the radiocarpal fold (Fig. 8).

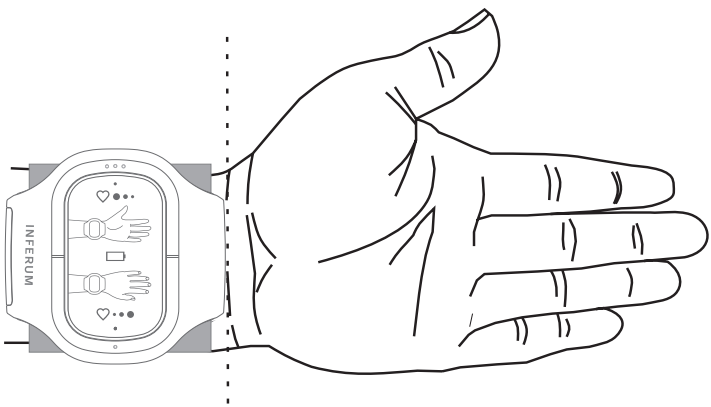

Fig. 8. The proper working position of the device on left forearm for management of the increased BP

4.2.7. Tighten and fix the cuff so that that close contact is maintained between the device electrodes and the skin; while avoiding any empty areas between the cuff and the forearm surface but so that the forearm is not strapped over-tightly. The patient should never feel any discomfort.

4.2.8. Turn the device on pressing ON/OFF key, Program No 1 (Fig. 3, Position 1). The appropriate light emitting diode signal will appear on the screen (Fig. 3, Position 2), and automatic Program for high BP management will be activated, to operate for 5 min.

4.2.9. After the treatment session, the appropriate sound signal will be heard, the device will be turned off automatically, and the LED signal will fade away.

4.2.10. To turn off the device forcefully, press and hold ON/OFF key, Program No 1 (Fig. 3, Position 1), pressed for more than 1 second; the device will emit the appropriate sound signal and be turned off, and the LED signal will fade away.

4.2.11. After the device is turned off, relax the cuff fixture and take ABP-051 from the patient's arm.

4.2.12. After the treatment session, it is recommended that the patient should rest for 20-30 min.

4.3. Procedure technique for the management of low BP and chronic arterial hypotension (Program No 2).

4.3.1. Take off a wrist watch or bracelets from the distal third of the left forearm and free from the clothes.

4.3.2. Select the exposure area. The exposure area for patients with low BP is the posterior surface of the distal third of the left forearm (Fig. 9)

4.3.3. Treat the device electrodes and the patient's skin in the exposure area, with a moist napkin or tampon slightly moistened with water or saline solution (0.9% aqueous sodium chloride solution) to ensure better contact

4.3.4. Put the patient's left hand into the device cuff so that.

4.3.5. Shift it upon the forearm.

4.3.6. To ensure proper treatment efficacy, place the device in the lower third of the forearm, so that right rim of the device body is parallel to the radiocarpal fold (Fig. 9).

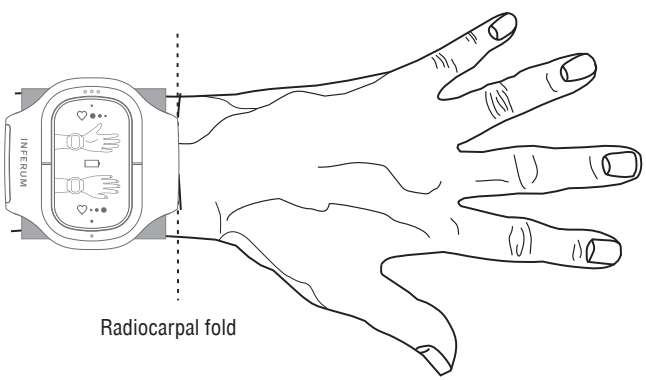

Fig. 9. The proper working position of the device on the left forearm for management of low BP

4.3.7. Tighten and fix the cuff so that that a close contact is maintained between device electrodes and the skin; while avoiding any empty areas between the cuff and the forearm surface but so that the forearm is not strapped over-tightly. The patient should never feel any discomfort.

4.3.8. Turn the device on pressing ON/OFF key, Program No 2 (Fig. 3, Position 8). The appropriate light emitting diode signal will appear on the screen (Fig. 3, Position 7 and 8), and automatic program for low BP management will be activated, to operate for 6 min.

4.3.9. After the treatment session, the appropriate sound signal will be heard, the device will be turned off automatically, and the light emitting diode signal will fade away.

4.3.10. To turn the device off forcefully, press and hold ON/OFF key, Program No 2 (Fig. 3, Position 7 and 8), pressed for more than 1 second; the device will emit the appropriate sound signal and be turned off, and the light emitting diode signal will fade away.

4.3.11. After the device is turned off, relax the cuff fixture and take ABP-051 from the patient's arm.

4.3.12. After the treatment session, the patient should rest for 20-30 min.

4.4. General treatment recommendations

Usually, the treatment procedures are made 1-3 times daily, within a 14-day treatment course, preferably in one and the same time of the day; after the targeted BP value is achieved regardless of BP level before the treatment procedure. The device exposure has the cumulative effect – that is, BP becomes steadily stable to the end of the treatment course.

In the event of occasional (but recurrent) BP increase or decrease a treatment course of not less than 14 days, 1-3 procedures a day, is required. In the beginning of the treatment, a temporary BP destabilization can occur followed by the steady BP decrease in hypertension or steady BP growth in hypotension).

With the diagnosis of labile AH (a rare occasional and insignificant BP increase up to not more than 150 mm Hg), ABP-051 device may be used as monotherapy. Such approach suppresses and prevents the disease transfer from aggravating into persistent AH form.

AH patients (hypertensive disease) need recurrent regular treatment courses at least once in a month (for instance: since 1st through 14th day of each month).

AH or CAH patients aged above than 70 years need a more sparing rates of BP decrease. For that, one exposure session using ABP-051 once a day is recommended. In such cases, the recommended duration of each treatment course should be not more than 7-8 days. After 10-15 day break, it is appropriate to repeat the same treatment. During the first treatment courses, BP may slightly fluctuate.

In patients with resistant, non-controlled AH (persistently high SBP – more than 180 mm Hg despite the drug therapy), the number of procedures using ABP-051 per day, and duration of the treatment course should be determined after consultation with the attending physician.

5. EFFICACY OF ABP-051

Study design: multi-center prospective randomized, placebo-controlled study

Clinical study sites: State Budgetary Healthcare Institution of the Sverdlovsk Region "Sverdlovsk Region Clinical Hospital No 1" (Ekaterinburg) [82]; Budgetary Healthcare Institution of the Udmurt Republic "Republican Clinical-Diagnostic Center" of the Ministry of Health of Republic of Udmurtia (Izhevsk) [83].

Study aim: to assess efficacy of new physiotherapy device "Transcutaneous electrostimulator for blood pressure management ABP-051" in AH and CAH patients.

Inclusion and exclusion criteria: in accordance with the indications and contraindications for the use of ABP-051 (Sections 2.1 and 2.2).

Clinical study control specifications:

- study protocol "Efficacy and Safety of ABP-051 device for BP Management";
- Package insert;
- Patient's voluntary informed consent for the study and for processing of his/her personal data;
- Patient's study log;
- Patient's questionnaire;
- Patient monitoring card, 2 forms;
- Adverse reaction records sheet;
- Reporting form for any adverse event induced by the medical device (event/event risk).

Study patients: 153 patients of both sexes (of them: 57 male and 96 female) aged 20-80 years, (average age: 62.5±11.6 years) suffering from AH (initial BP value: 140/90 mm Hg or more) or CAH (initial BP value: less than 100/60 mm Hg). Average disease duration was 20.3±1.8 years.

The patients' diagnoses were verified in accordance with the recommendations of the Russian Medical Society for AH, namely: "Clinical Recommendations: AH in Adults" and "National Guidelines: Cardiology" prepared under the aegis of the Russian Society of Cardiology and the Association of Medical Societies for Quality.

Examination methods: general clinical tests (complete blood count and urine analysis, ECG, fluorography; gynecological examination for female patients); office BP measurement (OMRON Compact semi-automatic tonometers, Japan-Russia); daily BP monitoring (BPLab equipment for daily BP monitoring, Russia).

Patient groups and treatment methods:

Group 1: Group 1: 38 AH patients treated with ABP-051 under Program No 1, during the conventional standard drug treatment and/or hypotensive therapy.

Group 2: 39 AH patients having placebo procedures during the conventional hypotensive treatment; device ABP-051 was used in mock-operation mode. Such mode fully simulated the operation mode: the light emitting diode signal was flashing; the operational sound worked while the electrodes were disconnected from the circuit.

Group 3: 38 CAH patients treated with ABP-051 and Program No 2.

Group 4: 38 CAH patients receiving similar placebo procedures.

Mathematical methods

Statistical significance of the differences was determined with the Student's t-test or Pearson's chi-squared test depending on the distribution parameters. The accepted significance level of the differences was $p<0.05$. Data were processed using standard package of applied software "SPSS 13.0 Mathematica 5.1".

Considering the uniform study design, patient examination methods and treatment outcome assessment, it is possible to develop the uniform database for the two independent studies and to analyze it. The study design is shown on Figure 10.

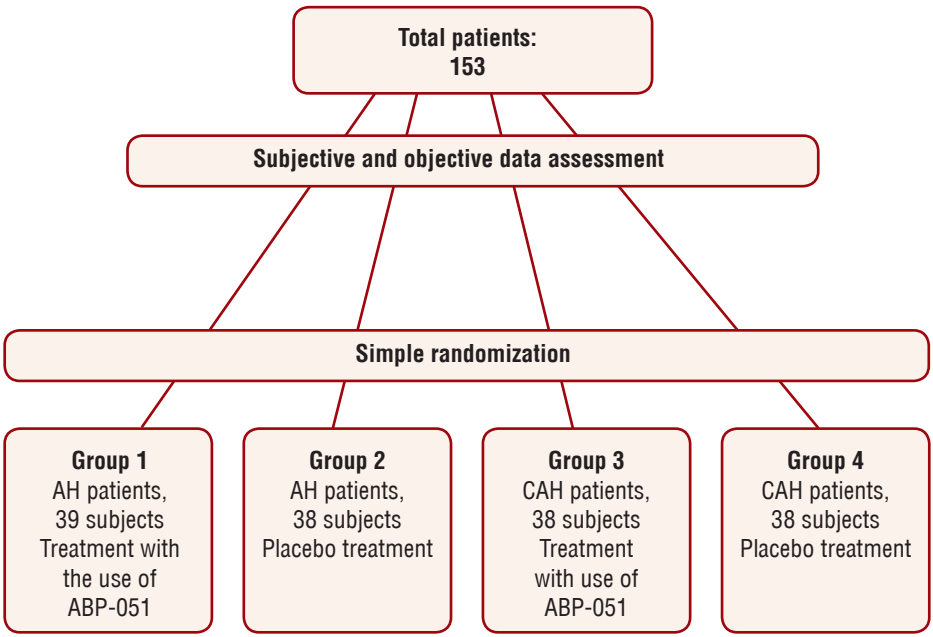

Fig.10 Group distribution of the patients

Study results

All patients tolerated the treatment procedures well. There were no adverse effects or balneoreactions.

AH patients total of 77 patients (of them: 24 men and 53 women) took part in the study, average age: 51.2 ± 2.5 years. The AH patients were divided into the treatment group and control group (placebo group) (Group 1 and 2, respectively). In its turn, each of the groups was divided into Sub-Groups 1.1 (19 patients) and 2.1 (19 patients) in which the patients had SDVNS (NCD, VVD) and/or AH of Stage 1; and also into Sub-Groups 1.2 (20 patients) and 2.2 (19 patients) in which they had AH of Stage 2 and 3.

When ABP-051 was used for 9 days, with Program 1 and standard drug treatment, patients of Group 1.1 had the significant SBP decrease, from 149.3±7.2 to 130.2±5.3 mm Hg (p<0,05). DBP reported in patients of such sub-group decreased also evidently, but the statistical significance of differences was not achieved (Table 2).

Table 2

BP values in Sub-Group 1.1 patients with SDVNS and AH of Stage 1 prior to and after the treatment course

BP (mm Hg)	Prior to the treatment	After the treatment	Efficacy Δ
SBP	145.3±11.2	130.2±9.2*	15.1±3.2
DBP	82.3±2.4	76.3±1.8	6.0±0.7

Note: * means significant differences (p<0.05).

The use of ABP-051 and Program No 1 for 9 days and in combination with conventional hypotensive treatment in patients of Sub-Group 1.2. also showed the significant SBP decrease from 175.3±13.2 to 160.2±9.8 mm Hg (p<0.05). DBP in patients of such sub-group tended to decrease evidently (Table 3).

Table 3

BP values in Sub-Group 1.2 patients with AH of Stage 2 and 3, prior to and after the treatment course

BP (mm Hg)	Prior to the treatment	After the treatment	Efficacy Δ
SBP	175.3±13.2	160.2±9.8*	15.1±3.6
DBP	92.7±2.4	86.3±1.8	6.4±0.8

Note: * means significant differences (p<0.05)

Likewise, in both AH patient groups, there was next-to-identical difference in SBP and DBP decreases (efficacy Δ) over the time.

As the analysis of BP values in patients receiving the treatment with Program No 1 showed, there were gender-dependent, but clearly positive unidirectional changes over the time, both in male and female patients (Fig. 11).

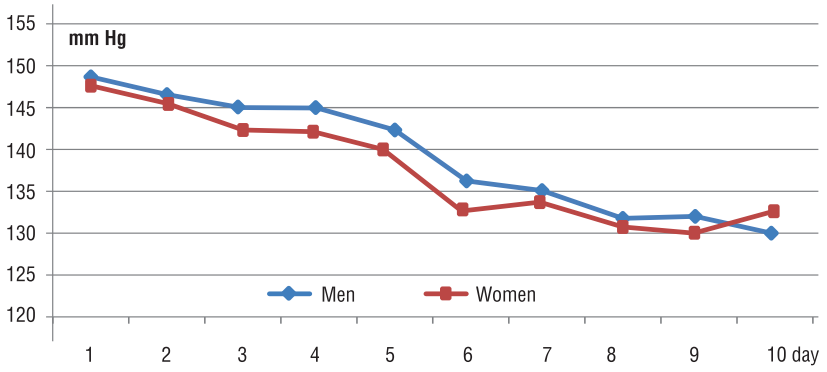

Fig.11. Gender-dependent SBP changes in AH patients over the time

It is noteworthy that SBP values both in male and female patients became normal evidently from treatment day 6-7.

Placebo treatment in AH patients of Sub-Groups 2.1 and 2.2 (control group) showed no therapeutic effects: there were SBP and DBP decreases – only on 1…2 mm Hg.

The individualized analysis of hypotensive effects of the treatment course using ABP-051 showed an overwhelmingly larger number of AH Stage 1 patients, who achieved the targeted BP values (33 out of 39 patients; 84.6%) as compared to patients of the group who received placebo treatment combined with their hypotensive treatment and did not have any significant therapeutic effects.

CAH patients. There were 76 young CAH patients enrolled to the study (of them: 51 female and 25 male): 20-40 years (average age: 32.4±5.1 years).

The use of ABP-051 and Program No 2 for 7 days in CAH patients (Group 3) showed a statistically significant SBP increase from 97.1±3.8 up to 114.9±4.1 mm Hg ($p<0,001$) on treatment day 5. DBP values in patients of the same group were also increased, although without any statistical significance (Table 4).

In the control group of CAH patients (Group 4), the placebo treatment did not provide any therapeutic effects: after the treatment course, SBP and DBP were increased on not more than 1…2 mm Hg.

Table 4

BP values in CAH patients of Group 2, prior to and after the treatment course

BP (mm Hg)	Prior to the treatment	After the treatment	Efficacy Δ
SBP	97.1±3.8	114.9±4.1*	17.8±0.3
DBP	64.3±3.1	71.5±3.8	7.2±0.7

Note: * means significant differences ($p<0.05$).

The segregated analysis of BP values in patients receiving the treatment with the use of Program No 2, showed that the positive health changes over the time did not have any significant gender-dependent difference (Fig. 12).

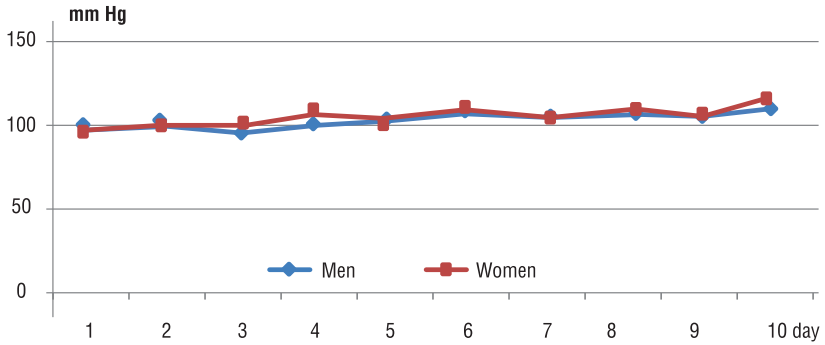

Fig.12. Gender-dependent SBP changes in CAH patients over the time

The individualized analysis of therapeutic effects of the treatment course with the use of ABP-051 and Program No 2 showed significantly more CAH patients of Group 2 who achieved steady normalization of their BP values (31 out of 38 patients; 81.6%) than those of the control group in which placebo was administered and in which no such effects were achieved.

Summary and recommendations

Therefore the clinical study showed that:

- Transcutaneous electrostimulator for blood pressure management ABP-051 (Marketing authorization No RZN 2016/3776 dated March 31, 2016) conforms with the manufacturer's regulatory, technical and operational documents;
- The use of the electrostimulator is proven to be effective in treatment of patients with the increased BP and AH, and decreased BP and CAH;
- The treatment courses using ABP-051 provides steady and statistically significant SBP improvement and evident tendency to normalization of DBP values by treatment day 5-7;
- Mediatory effects by ABP-051 used to manage increased systemic BP are equal to those in management of SDVNS (NCD, VVD) and AH of Stage 1, 2 and 3;
- The use of ABP-051 for BP management allows to reduce drug doses and can be recommended as a supplement to hypotensive drug treatment or as an individual treatment method (SDVNS and AH of Stage 1);
- To achieve steady therapeutic effects in patients with AH of Stage 2 and 3, it is recommended to have a course of BP management with the device for at least 14 days;
- Control placebo groups of AH and CAH did not have any therapeutic effects;

- The use of ABP-051 for BP management in such patient categories can be considered as safe; no adverse effects or balneoreactions were reported;
- ABP-051 can be recommended for the wide use in clinical practice of treatment and prevention facilities, or by a patient in home settings provided that the patient consults his/her physician in advance.

REFERENCES

1. A global brief on hypertension. Silent killer, global public health crisis. WHO. – World Health Day. – 2013. – 40 p. http://www.who.int/cardiovascular_diseases/publications/global_brief_hypertension/ru/ (access date: 04.11.2017).
2. Anikin V.V., Kurochkin A.A. Modern concept of terminology and classification of neurocirculatory dystonia in children and adolescents // Clinical medicine. – 2001. – N 7. – P. 69-72.
3. Makolkin V.I., Abbakumov S.A., Sapozhnikova A.A. // Neurocirculatory dystonia. – Cheboxary: Nauka. – 1995. – 250 p.
4. Geoge J. Cararasos. Neurocirculatory Asthenia.// Stress and Heart. – New York, 1981. – P. 219-244.
5. Vein A.M., Solovieva A.D., Kolosova O.A. Vegetovascular dystonia. – M., 1981.
6. IDC-10. F-45.3. Somatoform dysfunction of the vegetative nervous system. http://mkb-10.com/index.php?pid=4274 (access date: 04.11.2017).
7. Atsel E.A., Gazizov R.M. Somatoform dysfunction of the vegetative nervous system in adolescents: particularities of diagnostics and treatment. // Practical medicine. – No 4 (28) August 2008. – p. 65-67
8. Dvoretsky L.I. // RMJ. – 2002. – V.10. – P. 1-11.
9. Beliaeva L.M., Rostovtsev V.N., Kuptsevich N.V., Korol S.M., Khrustaleva E.K. Structural for primary arterial hypertension prognosis. // "Medical panorama". – No 1, February 2003. http://www.plaintest.com/pediatrics/model-prognosis (access date: 04.11.2017).
10. Bova A.A. Neurocirculatory dystonia or somatoform vegetative dysfunction? // "Medical news". – Archive. – No 7, 2006. http://www.mednovosti.by/journal.aspx?article=607 (access date: 04.11.2017).
11. Cardiovascular diseases (CVDs). – WHO. – Fact sheet Updated May 2017. http://www.who.int/mediacentre/factsheets/fs317/en/ (access date: 04.11.2017).
12. Diagnostics and treatment of arterial hypertension. Russian recommendations (fourth revision). – Moscow, 2010. – 34 p.
13. Shalnova S.A., Balanova Y.A., Konstantinov V.V., et al. Arterial hypertension: occurrence, awareness, antihypertensive drugs and treatment efficacy in population of the Russian Federation. // Russian Cardiol. Journal. – 2006. – No 4. – P.45-50.
14. Shalnova S.A., Deev A.D., Balanova Y.A., Kapustina A.V., Imaeva A.E., Muromtseva G.A., Kiseleva N.V., Boitsov S.A. Twenty-year trends in obesity and arterial hypertension and their associations in Russia.// Cardiovascular therapy and disease prevention, 2017. – No 4. – P.4-10.
15. Kaplan N.M. Systemic Hypertension: Mechanisms and Diagnosis, Therapy.// in Heart Disease, ed. Braunwald E. – Harcourt International Edition. – 2001. – P.941-994.
16. Samochulova T.B. Arterial hypotension, its occurrence, primary and secondary prevention: Doctor of Medicine thesis. – Vladivostok, 1998.
17. Shapiro M.F., Korda H., Robbins J. Diagnosis and treatment of low blood pressure in the Canada community. // Can. Med. Assoc. J. – 1982. – 126. – P. 918-920.

18. Letunovskaya N.A. Assessment of the role of professional factors in development of primary arterial hypotension // Actual problems of professional and environmental pathology. – Kursk, 1994. – P.238 - 239.
19. Vein A.M., Yakovlev N.A., Karimov T.K., Sliusar T.A. Treatment of vegetative dystonia. Traditional and non-traditional approach. Brief manual for physicians. – M., 1993. – 237 p.
20. Glaurov A.G. Transient cerebral circulation disorders in primary arterial hypotension // All-Russian Convention of Neuropathologists and Psychiatrists: Report theses. – M., 1976. – V.2. – P.253-255.
21. Owens P., OrBrian E. Hypotension: a forgotten illness // Blood Pressure Monitoring, 1996. – No 2. – P. 3-14.
22. Studenikin M.Y., Abdullaev A.R. Hypertensive and hypotensive conditions in children and adolescents. M.: Meditsina, 1973. – 208 p.
23. Chefranova Z.Y., Laskov V.B. Age-related changes of clinical - paraclinical characteristics over the time and adaptation in case of chronic essential arterial hypotension. Collected research works // Actual problems of medicine and pharmacy: Papers of 63th Final Scientific Session in Kursk State Medical University (May 20-21, 1998). – Kursk. – 1998. – P. 69-70.
24. Lapin V.V. Medical practice in case of essential hypotension: Collected research works. – L., 1991. – P. 216-221.
25. Mikhailov A.A. Chronic arterial hypotension: the potential of drug management // Russian Medical Journal. 2004. No 7. P. 468-471
26. Robbins J., Korda H., Shapiro M. Treatment for a nondisease: the case of low blood pressure // Soc. Sci. Med. – 1982. –16 – P.27-33.
27. Gusev E.V., Anufrienko A.A., Kolesnik I.G. Acupuncture as a non-traditional method of treatment of hypotensive vegetovascular dystonia // Report thes.: Sanatorium and health resort care of patients with diseases of cardiovascular system. – M., 1989. – 145 p.
28. Temkin I.B. Exercise therapy in primary arterial hypertension. – M.: Meditsina, 1971. – 180 p.
29. Samochulova T.B. Arterial hypotension, its occurrence, primary and secondary prevention: Doctor of Medicine thesis. – Vladivostok, 1998.
30. Rowe P.C., Bou-Holaigah I, Kan J.S., Calkins H. Is neurally mediated hypotension an unrecognised cause of chronic fatigue? // Lancet. – 1995. – 345. – P. 623-624.
31. Bou-Holaigah I, Rowe PC, Kan JS, Calkins H. Relationship between neurally mediated hypotension and the chronic fatigue syndrome. // JAMA. – 1995; 274:961-7.
32. Vein A.M., Yakovlev N.A., Karimov T.K., et al. Treatment of vegetative dystonia. Brief manual for physicians. – M. – 1993.
33. Chernyshev V.V., Malakhov V.V., Vlasov A.A., et al. Manual for dynamic electric neurostimulative therapy with use of DENAS devices. – Ekaterinburg. – 2002. – 248 p.
34. Guliaev V.Y., Shchekoldin P.I., Chernyshev V.V., et al. Electric pulse therapy (review). // "DENS Department" archive of research and practical works: Theoretical, fundamental and methodological aspects of dynamic electric neurostimulation, Volume I. Malakhov V.V., Editor in charge. – Ekaterinburg, 2004. – p. 49-58.
35. Umnikova M.V., Kieeva N.V., Tabashnikova S.V., et al. Clinical efficacy of dynamic electric neurostimulation in comprehensive treatment of hypertensive disease. // Papers of International Symposium dedicated to 10th Anniversary of DENAS MS Corp. – Ekaterinburg. – 2008. – p. 58-60.
36. Physiotherapy: a national manual/G.N.Ponomarenko, ed – M.:GEOTAR-Media.– 2009. – 864 p.
37. Malakhov V.V., Chernyshev V.V., Riavkin A.Y., Ivanov V.I., et al. Dynamic electric neurostimulation (DENS). Sources. Notion. Effects. // Reflexotherapy. – 2005. – No 1(12). – p. 14-24.
38. Chernyshev V.V., Riavkin A.Y., Malakhov V.V., Meizerov E.V., Koroleva M.V., Chernysh I.M.,

Gurov A.A. Dynamic electric neurostimulation. Methodological recommendations for physicians. – M.: 2005. – 32 p.
39. Dynamic electric neurostimulation method. Federal Service for Surveillance in Healthcare and Social Development. Registration Certificate No ФС-2005/004 dated March 04, 2005.
40. Batdieva V.A., Nagapetyan V.K, Rusenko N.I. Dynamic electric neurostimulation with use of DiaDENS-Cardio device in treatment of hypertensive patients: physician's manual. – Ekaterinburg. – 2007. – 16 p.
41. Svintsova G.A. The potential of dynamic electric neurostimulation for improvement of control over resistant arterial hypertension. // Author's abstract of Candidate of Science thesis. – Moscow. – 2010. – P. 17.
42. Rattan S.I. Principles and practice of hermetic treatment of aging and age-related diseases. // Hum. Exp. Toxicol. – 2008. – No 27(2). – P. 151-154.
43. Mattson M.P. Hormesis and diseases resistance: activation of cellular stress response pathway. // Hum Exp Toxicol. – 2008. – No 27. – P. 155-162.
44. Calabrese E.J. Hormesis: a fundamental concept in biology // Microb Cell. – 2014. – May 5; 1(5): 145–149.
45. Garkavi L.H., Kvakina E.B., Kuzmenko T.S. Anti-stress reactions and activation therapy. Activation reaction as a road to health through self-organization processes. – M.: Imedis. – 1998. – 656 p.
46. Malakhov V.V., Vasilenko A.M. Dialectics of sano- and pathogenetical reactions is an important component of restorative medicine methodology.// Russian Journal of Restorative Medicine. – 2013. – No 2 – P. 36-43. Access model: http://rjrm.ru/Documents/3%20%D0%BD%D0%BE%D0%BC%D0%B5%D1%80.pdf, access date: March-April 2016.
47. Malakhov V.V., Khorozov S.V., Spitsyna R.R. Informational Model of the organism's systemic reaction to excitations. // Reflexotherapy. – 2005. – No 1(12). – P. 6-11.
48. Anokhin P.K. Physiology and cybernetics. – Voprosy filosofii. – 1957. – No 4. – 142 p.
49. Nikolis G., Prigogine I. Self-organization in non-equilibrium systems: From dissipative structures to order through fluctuations. – M.: Mir, 1979. – 512 p.
50. Kryzhanovsky G.N. Fundamentals of general pathophysiology. – M.: Medical Information Agency, LLC, - 2011. – 256 p.
51. Bekhtereva N.P. Healthy and diseased human brain. – M.: AST, 2010. – 400 p.
52. Kryzhanovsky G.N. Systemic disintegration and disinhibition of functional structures as universal pathological patterns. – Path. physiol. and exper. Ter. – 1977. – No 5. – P. 33.
53. Cannon W. B. Bodily changes in pain, hunger, fear and rage: An account of recent researches into the function of emotional excitement. – New York and London: D. Appleton and Co. – 1915. – 334 P.
54. Cannon W. B., The wisdom of the body. – New York: W. W. Norton, 1932. – P.52.
55. Selye H., A syndrome produced by diverse nocuous agents.// Nature. – vol. 138, July 4 (1936). – p. 32.
56. Anokhin P.K. Outlines of functional system physiology. – M.: Meditsina. – 1975. – 448 p.
57. Sudakov K.V. Dominant motivation. – M.: RAMS Publishers. – 2004. – 236 p.
58. Selye H. The stress of life. – New York, Toronto, London. – McGraw-Hill Book Co, Inc. – 1956. – P. 12.
59. Dysregulative pathology of nervous system / E.I. Gusev, G.N. Kryzhanovsky, eds. – M.: Medical Informational Agency, LLC, 2009. – 512 p.
60. Dysregulative pathology / G.N. Kryzhanovsky, ed. – M.: Meditsina, 2002. – 632 p.
61. Impaired endothelial function in hypertensive patients with target organ damage / J. Z. Xu [et al.] // J. H. Hypertens. – 2009. – No 23(11). – P. 751-757.

62. Possible role of the vascular rennin-angiotensin system in hypertension and vascular hypertrophy / R. Morishita [et al.] // Hypertension. – 1992. – No 19. Suppl. II – P. 66-67.
63. Struicer-Boudier H.A.J. Microcirculacion in hypertension // European Heart J. Supplements. – 1999. – Vol. 1, Suppl. L. – P. 32-37.
64. Gibbons G.H., Dzau V.J. The emerging concept of vascular remodeling // New Engl. J. Med. – 1994. – No 20. – P. 1431-1438.
65. Golikov B.M. Systemic and cerebral circulation in patients with primary arterial hypotension // Klin.med. – 1988. – No 2. – P.30-33.
66. Sudakov K.V., Kuzichev I.A., Nikolaev A.B., et al. Evolution of terminology and schemes of functional systems in P.K. Anokhin scientific school. – M.: European Polygraphic Systems, 2010. – 238 p.
67. Smirnov V.M., Borodkin Y.S. Artificial stabile functional connections. – L.: Meditsina, 1979. – 192 p.
68. Gray H. Anatomy, descriptive and surgical. – Philadelphia: Blanchard and Lea, 1859. – 752 p. https://collections.nlm.nih.gov/bookviewer?PID=nlm:nlmuid-06220300R-bk
69. Cunningham D.J. Text-book of anatomy. – Edinburgh; Pentland, 1902. – 1309 p.
70. Corning H.K. Lehrbuch der topographischen Anatomie. – Myenchen,Bergmann,1923. – 817p. https://www.zvab.com/servlet/SearchResults?an=Corning&tn=Lehrbuch+der+topographischen&cm_sp=mbc-_-SRP-_-all
71. Vorobiev V.P. Human anatomy. V. 1. – M.: State Medical Publishers. – 1932. – P. 94.
72. Kiss F., Szentagothai J. Atlas of human anatomy. – Verlag der Ungarischen Akademie der Wissenschaften Editions de l'Academie Hongroise des sciences. – 1962. – 894 p.
73. Sinelnikov R.D. Atlas of human anatomy. Volume III. – M.: Meditsina. – 1974. – p. 190.
74. Prives M.G., Lysenkov N.K., Bushkovich V.I. Human anatomy. 9th edition, translated and extended. – M.: Meditsina. – 1985. – 672 p.
75. Head H. Sensibilitatsstorungen der Haut bei Vis-ceralerkrankungen, B., 1898.
76. Zakharyin G.I. Clinical lectures and selected articles. – 2nd edition, extended. – M.: Pechatnia A.I. Snegirevoi, 1910. — 557 p.
77. Bing R. Manual for topical diagnosing of cerebral and spinal diseases. Translated from German. – M-L, 1929; 192-201.
78. Duus P. Topical diagnosis in neurology. Anatomy. Physiology. Clinics. Translated from German. – Georg Thieme Verlag, Stuttgart, NY. – M.: IPC "Vazar-Ferro". – 1996. – 400 p.
79. Primary research reports: Studies on electromyography, sympathetic nervous system, reflex, and related topics (1947-1978) / The Collected Papers of Irvin M. Korr Vol. I. – 1997. – P. 18-77.
80. Primary research reports: Studies on electromyography, sympathetic nervous system, reflex, and related topics (1947-1978) / The Collected Papers of Irvin M. Korr Vol. I. – 1997. – P. 18-77.
81. Fundamental and clinical physiology / A.G. Kamkin and A.A. Kamensky, eds. – M.: Academia Publishing Center, 2004. – 1072 p.
82. State Budgetary Healthcare Institution of the Sverdlovsk Region "Sverdlovsk Regional Clinical Hospital No 1": ABP-051 electrostimulator for blood pressure management. Assessment Report of the Clinical Test Results on the medical device No 07082017-01 dated August 07, 2017 (manuscript) – Ekaterinburg. – 7 p.
83. Budgetary Healthcare Institution in the Republic of Udmurtia " Rebublican Clinical Diagnostic Center" under the Ministry of Health, the Republic of Udmurtia: ABP-051 transcutaneous electrostimulator for blood pressure management. Medical Test Protocol No 15122017-02 dated December 15, 2017 (manuscript) – Izhevsk. – 12 p.

METHODICAL GUIDELINES

USE OF TRANSCUTANEOUS ELECTROSTIMULATOR ABP-051 FOR CORRECTION OF SYSTEMIC BLOOD PRESSURE IN CLINICAL PRACTICE

Подписано в печать 31.08.2018
Формат бумаги 60x84 1/16. Гарнитура AGLettericaCondensed.
Бумага офсетная. Печать плоская.
Усл. печ. л. 1,86. Тираж: 3000 экз. Заказ №1359

Отпечатано в Издательско-Полиграфический Комплекс «Лазурь»
623750, Свердловская область, г. Реж, ул. П. Морозова, 61
Тел.: +7(343) 227-23-23
www.lazurprint.ru

CG “INFERUM”
Legal address:
86, Belinskogo st., apt. 487
Ekaterinburg, Russia, 620026
Postal address of the central office:
12 bld. 1, Sibirsky Tract, of. 206
Ekaterinburg, Russia, 620100

Tel.: +7 (343) 247-84-51
E-mail: info@inferum.ru
www.inferum.ru

INFE 05.01-08.08-01