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МЕТОД УСИЛЕННОЙ НАРУЖНОЙ КОНТРПУЛЬСАЦИИ В КЛИНИЧЕСКОЙ ПРАКТИКЕ

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The Method of Enhanced External Counterpulsation in Clinical Practice

Резюме

Хронические неинфекционные заболевания представляют важную медико-социальную проблему для системы здравоохранения. Оптимальная фармакотерапия не всегда оказывается достаточно эффективной, а применение хирургических методов лечения возможно не у всех больных. Кроме того, важным звеном комплексного ведения таких пациентов является дозированная физическая активность, однако у большинства из них низкая толерантность к нагрузкам не позволяет их осуществлять, запуская порочный круг, приводящий к снижению функционального резерва организма. В данном случае полезным может быть использование немедикаментозных методов лечения, например, усиленной наружной контрпульсации. Настоящий обзор посвящен анализу литературных данных о возможностях использования данного метода, что имеет существенное значение в клинической практике.

Ключевые слова: *хронические неинфекционные заболевания, усиленная наружная контрпульсация, немедикаментозные методы лечения*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract

Chronic non- infectious diseases represent an important medical and social problem for the healthcare system. Optimal pharmacotherapy is not always effective enough, and the use of surgical treatment methods is not possible in all patients. In addition, an important link in the comprehensive management of such patients is dosed physical activity, however, in most of them, low exercise tolerance does not allow them to exercise, starting a vicious circle that leads to a decrease in the functional reserve of the body. In this case, the use of non-pharmacological treatment methods, for example, enhanced external counterpulsation, may be useful. This review is devoted to the analysis of literature data on the possibilities of using this method, which is important in clinical practice.

Key words: *chronic non- infectious diseases, enhanced external counterpulsation, non-pharmacological treatment methods*

Conflict of interests

The authors declare no conflict of interests

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IHD — ischaemic heart disease, CPST — cardiopulmonary stress test, ECP — external counterpulsation, DM — diabetes mellitus, CVD — cardiovascular diseases, EECP — enhanced external counterpulsation, LV EF — left ventricle ejection fraction, CNCD — chronic non-communicable diseases, COPD — chronic obstructive pulmonary disease, CRD — chronic respiratory diseases, CCI — chronic cardiac insufficiency, 6MWT — 6-minute walk test

Introduction

Chronic non-communicable diseases (CNID) are one of the global problems all over the world due to their high incidence, poor prognosis (incapacitation and death) and negative impact on the quality of patients' lives [1]. Almost a half of the world population have at least one chronic condition [2]. According to the Russian Society for the Prevention of Noncommunicable Diseases [3], the most common CNCD are cardiovascular diseases (CVD), malignancies, chronic respiratory diseases (CRD), and diabetes mellitus (DM). These conditions deplete the functional reserves of the human body and reduce the intensity of compensatory and regenerative responses.

Currently, pharmacological and surgical treatment strategies have been actively developing, and they can improve the well-being of such patients. However, it is worth mentioning that even the optimal drug therapy in such patients is not always efficient enough, and surgery is possible not in all patients. Besides, in recent decades, physical exercises have been widely used for the management of patients with CNCDs. A systematic overview [4], comprising results from 85 meta analyses on 22 various chronic conditions, demonstrated that graduated exercises are a safe way to boost physical and functional capabilities in patients with CNCDs. It means aerobic training, strength training, combined exercises with weight, as well as a majority of other training protocols, typical for a specific condition of the body. Still, not all patients can do exercises due to poor tolerance and long-lasting hospitalisations, thus bringing about a vicious circle of muscle dysfunction resulting in body de-training and depletion of its functional reserves. Such cases require additional non-drug therapies, one of which is enhanced external counterpulsation (EECP), which allows patients not only to boost their motor performance, but can also be used together with physical exercises.

Background of the method

The external counterpulsation (ECP) method has been used in the clinical practice since recently. The term "counterpulsation" appeared just in the second half of the 20th century. It was used in 1962 for the first time to describe a mechanism of fast reverse movement of the blood in the aorta. Then the new method was tested in an experiment in dogs. Cuffs were placed on the lower extremities of animals, then air was pumped to increase the diastolic pressure in the aorta. Some time later, these experiments were used to create the first device for ECP in humans as an alternative to intra-aortic balloon counterpulsation, which is an invasive and technically sophisticated method. First ECP devices used only two cuffs; later, the addition of a buttock cuff enhanced the haemodynamic efficacy of the method, hence the name of the method.

A modern EECP device comprises an electronic control unit, compressor, air hoses, couches, fitted cuffs for patient's shanks, hips and buttocks, electrodes to synchronise the device with the patient's ECG and finger photoplethysmograph (Fig. 1).

EECP mechanism of action

During the diastolic phase, the air is quickly and consistently pumped from the cuff from the bottom up (from shanks to buttocks), which compresses arterial vessels. The resulting reverse arterial blood flow and increased diastolic pressure in the aorta facilitate an increase in perfusion pressure in arterial vessels and better organ perfusion. Before systole, cuffs are deflated; therefore, blood from the heart is pumped to partially empty vessels with lower resistance, reducing the afterload [5].

The EECP mechanism of action includes haemodynamic, neurohumoral and tissue effects (Table 1).

Haemodynamic effects are associated with increased diastolic coronary blood flow, increased venous return

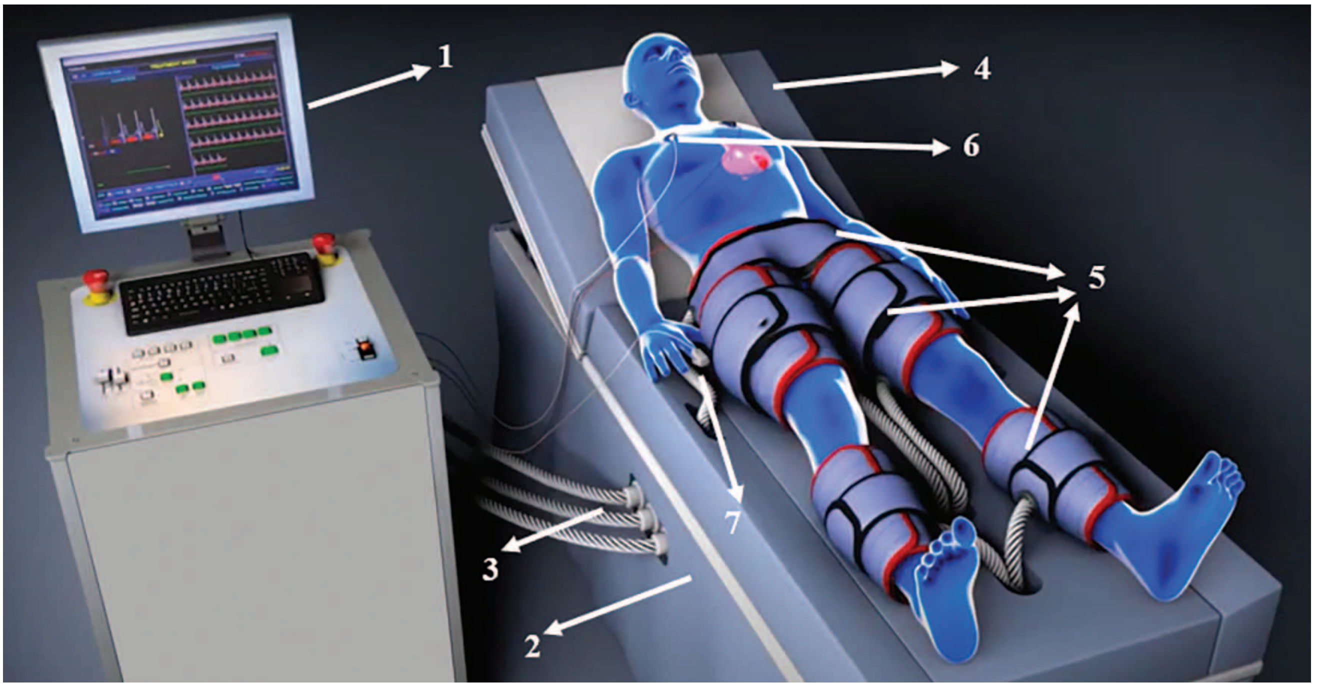

Figure 1. *Device for enhanced external counterpulsation*
Note: 1 — electronic control unit; 2 — compressor; 3 — air hoses; 4 — couch; 5 — cuffs; 6 — electrodes; 7 — finger photoplethysmography

Table 1. *Effects of enhanced external counterpulsation*

Hemodynamic	Vascular	Tissue
- Increased diastolic coronary blood flow; - Improvement of systemic microcirculation; - Reduction of postload on the heart; - Increased venous return;	- Improvement of the elastic properties of blood vessels (reduction of stiffness); - Improvement of endothelial function; - Formation of collaterals (angiogenesis); - Slowing down the progression of atherosclerosis;	- Improvement of metabolic activity in tissues; - Increased tissue resistance to ischemia; - Increased insulin sensitivity;

to the heart, better system microcirculation, as well as reduced afterload to the heart. The haemodynamic effect of EECP is based on an increase in perfusion pressure in coronary arteries during the diastole and lower resistance to the cardiac output during left ventricle systole [6].

Vascular effects are due to better elastic properties of vessels and endothelial function, formation of collaterals and slowing down of atherosclerosis progression. It has been found out that EECP improves athrombogenic activity of the vascular wall, increases antitrombin III and plasminogen levels, and reduces antioxidant tissue-type plasminogen activator inhibitor levels [7]. Also, EECP causes an increase in nitrogen oxide levels and reduction in endothelin 1 levels [8], as well as contributes to neoangiogenesis activation. This effect is possible due to shear stress in vessel endothelial cells, resulting from friction between a blood layer and vessel wall. Faster blood flow in arteries during compression of lower limbs increases this value and stimulates release of various vasoactive substances (α-actin, von Willebrand factor, basic fibroblast growth factor, hepatocyte growth factor, vascular endothelial growth factor, and nitrogen oxide) [9-11].

Tissue effects are associated with better metabolic activity in tissues, better tissue resistance to ischaemia and insulin sensitivity.

This review presents results of an analysis of the literature data for 1998–2024 from PubMed, RSCI (Russian Science Citation Index), Scopus on the use of EECP in clinical settings. The following keywords were used: external counterpulsation, non-drug treatment, rehabilitation. These scientific researches describe the capabilities of this method in various conditions, as well as discuss possible mechanisms of positive effect from EECP, which is of importance in clinical practice and further studies.

Use of the method in clinical practice

In clinical settings, EECP was used for the first time in patients with chronic cardiac insufficiency (CCI) [12] and ischaemic heart disease (IHD) [13]. In the Russian clinical recommendations on stable IHD, EECP is recommended for the management of refractory (both to drug therapy and surgery) angina (grade of recommendation A, level of evidence 2) [13]. In the European clinical recommendations, EECP is suggested for the management of symptoms in patients with severe angina, which is refractory to optimal drug therapy and revascularisation (grade of recommendation IIb, level of evidence B) [14]. Currently, EECP is included in the standards of management of patients with stable IHD [15] and CCI [16].

The method is unique since it is cost-effective and can be used in outpatient settings, therefore, it is available for a majority of patients. Also, EECP does not require a high level of body training, that is why the method can be used to treat patients who are not able to do exercises. In Russia, EECP has been included into territorial programs of compulsory health insurance for patients with IHD. At the same time, poor awareness of this method among healthcare providers and patients and inadequate availability of required equipment at the hospitals are still a problem.

Indications for EECP

Stable IHD (refractory angina) is the main indication for the use of this method, including cases where surgical revascularisation is not possible.

Also, EECP has proven to be effective in the management of patients with other conditions (including CCI, acute ischaemic cerebrovascular event, cognitive disorders, central retinal artery occlusion, inner ear diseases, ischaemic erectile dysfunction, obliterating diseases of lower limb arteries, chronic obstructive pulmonary disease), so the use of this method in these conditions is justified [17].

Contraindications to EECP

Despite the efficiency and safety, EECP has a number of contraindications [18, 19]:

- a history of thrombophlebitis and/or phlebitis;
- stage 2–3 pulmonary hypertension;
- decompensated cardiac insufficiency;
- myocardial infarction within the last three months;
- instable angina;
- uncontrolled arterial hypertension;
- haemorrhagic conditions (blood-clotting disorder with the international normalised ratio of > 2.0 or prothrombin time > 15 s);
- severe cardiac valve pathology;
- critical ischaemia of lower extremity arteries;
- abdominal and/or thoracic aortic aneurysm;
- irregular and tachysystolic atrial fibrillation, frequent ventricular extrasystoles, heart rate of > 135 or < 35 bpm);
- cardiac catheterisation within the last two weeks;
- surgery within the last six weeks;
- pregnancy.

Use of EECP in cardiology

As mentioned earlier, the capabilities of EECP are widely used in CVD management, and the effects of this procedure are studied most in this group of patients. The first large-scale study was MUST-EECP [20], which demonstrated the positive effect of a course of EECP in reduction of the number of angina episodes, thus in reduction in the need for nitroglycerine products, as well as longer physical exercise tolerance and the time to segment depression of ≥ 1 mm during the stress test. According to V. Singh et al. (2018) [21], 163 patients participating in the study also experienced reduction in clinical signs of IHD. According to R. Subramanian et al. (2005) [22], patients with CCI have elevated left ventricle ejection fraction (LV EF) after a course of EECP: from 46.40 ± 15.88 % to 50.05 ± 13.20 % ($p < 0.001$). Similar results were described in a study by A. Sardari et al. (2016) [23]: after a course of EECP, LV EF increased from 42.65 ± 11.82 % to 44.26 ± 11.86 % ($p < 0.001$). In addition to increased LV EF, EECP improves exercise tolerance. It was demonstrated in a study by E. Wu et al. (2013) [24], where exercise tolerance was evaluated using the 6-minute walk test (6MWT). Following EECP, the distance walked by patients increased by 7 %, from 410 m to 439 m ($p < 0.001$). The long-term effects of EECP on the structural and functional parameters of heart and vessel condition, exercise tolerance, and quality of life of patients with stable IHD with CCI, were studied in the Russian EXCEL study [25]. 120 patients were randomly divided into three groups of 40 subjects; two groups were treated with an optimal drug therapy plus EEPC once every six or 12 months, while the third group had placebo counterpulsation. During a 12-month follow-up period, groups 1 and 2 demonstrated better cardiac performance (LV EF increased from 40.6 ± 7.5 to 47.5 ± 10.2 % and from 41.3 ± 6.8 to 43.9 ± 10.3 %, respectively), as well as better exercise tolerance during 6MWT (distance walked increased by 44.5 % and 24.9 %, respectively) and improved quality of life, as evidenced by specialised questionnaires. These positive changes lasted for the entire study, i.e. 36 months [26].

Also, patients with IHD often have peripteral artery conditions, which are a relative contraindication to EECP. However, a study by B. Thakkar et al. (2010) [27] demonstrated safety of the method in such patients, provided they do not have signs of critical ischaemia of lower extremities. In another study [28], a course of therapy (35 EECP sessions) in patients with obliterating atherosclerosis of lower limb arteries resulted in significant reduction in leg pain, calf muscles myotonia and chills in feet. Also, this category of patients demonstrated a significant increase in the rheographic index of shanks and feet (by 23.9 % and 23.2 %, respectively), longer distance of pain-free walking (in controls, an increase in distance was 64.5 ± 25.1 m ($p < 0.05$), while in the EECP group the distance increased by 250 ± 31.2 m ($p < 0.05$)), and a higher ankle-brachial index in the anterior and posterior tibial artery (by 31.4 and 35.2 %, respectively ($p < 0.05$). In this case, the positive effect of EECP was a result of endothelial effects.

Often, patients with IHD have arterial hypertension, when endothelial cells are damaged. A study by J. Liang et al. (2021) [29] demonstrated positive effects of EECP: reduction in systolic (133.2 ± 4.9 mm Hg vs. 139.3 ± 6.4 mm Hg, $p < 0.05$) and diastolic (83.4 ± 4.5 mm Hg vs 89.5 ± 7.6 mm Hg, $p < 0.05$) blood pressure and better reparative capability of endothelial cells.

Use of EECP in pulmonology

As far as the use of EECP in patients with CRDs is concerned, the studies are scarce and mechanisms of positive effects are understudied. The largest study is the study by M. Zhao et al. (2020) [30] to evaluate the effects of EECP on exercise tolerance of healthy volunteers and patients with chronic obstructive pulmonary disease (COPD). This randomised clinical trial enrolled 72 subjects aged 27 to 82 years of age who were randomly assigned to two groups: EECP group and non-EECP group. Depending on the highest oxygen consumption, groups with normal exercise tolerance, low exercise tolerance and COPD (symptoms, risk factors and the ratio of 1 second forced expiratory volume to forced vital capacity of < 70 %) were assigned as well. To evaluate the efficiency of a 15-session EECP, cardiopulmonary stress test (CPST) results obtained before and after the course were used. The study showed a considerable improvement in the anaerobic threshold of oxygen consumption, highest oxygen consumption, aerobic pulse threshold, anaerobic threshold of training load, metabolic equivalent of the anaerobic threshold, and highest metabolic equivalent in all subgroups of the EECP group vs. non-EECP group ($p < 0.05$). It has been demonstrated that EECP improves exercise tolerance, which is very important for patients with COPD. Although this study did not evaluate the pulmonary function, a small sampling study showed positive changes in the pulmonary function of patients with COPD who underwent a course of EECP. Another US clinical study conducted in 2021 [31] evaluated the efficiency of EECP in the management of long COVID-19. The study enrolled 16 patients with confirmed long COVID. Of note, in addition to

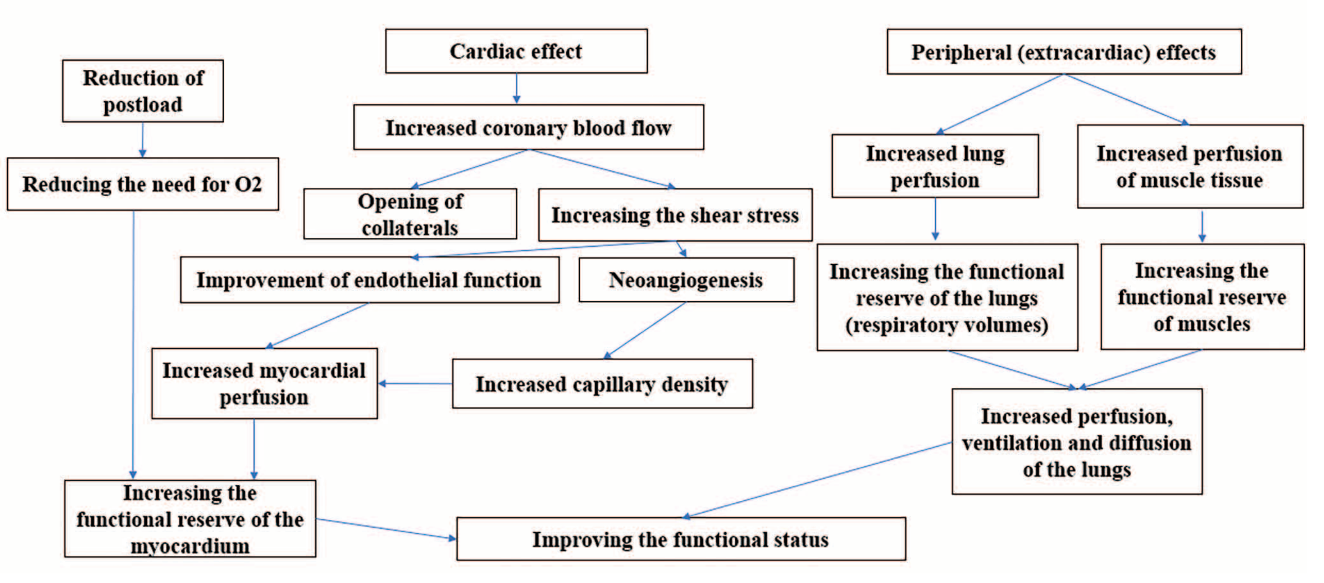

Figure 2. *Mechanism of action of enhanced external counterpulsation in chronic respiratory diseases*

long COVID, these patients had comorbidities, such as IHD and/or arterial hypertension. All patients had 15 to 35 EECP sessions. After a course of therapy, exercise tolerance (6MWT) was significantly better (the distance increased by 200.00 ± 180.14 m, $p = 0.002$) vs. baseline. Also, 44 % of study subjects noted improvement in their dyspnoea (Rose scale), 63 % of subjects had better angina functional status (Canadian Cardiovascular Society classification). A recent pilot study conducted at the Sechenov University [32] also showed the efficiency of EECP in patients with CRDs. The study enrolled 30 subjects aged 35 to 74 years of age with severe and moderate ventilation disorders without comorbidities. All patients had a 20-session course of EECP. Unlike other studies, in addition to CPST and 6MWT, EECP efficiency was for the first time evaluated using body plethysmography and a study of diffusing lung capacity. A course of therapy resulted in significant positive changes in lung capacity: 18 % increase in the total lung capacity, mostly due to the lung capacity, which grew by 24 % ($p < 0.001$). It is worth noting that there were no significant changes in diffusing lung capacity. CPST showed a significantly higher anaerobic threshold, ventilation reserve and exercise tolerance ($p < 0.001$). There is also a description of EECP use in post-COVID syndrome management [33]. In October 2020, a 38-year-old otherwise healthy woman had COVID-19 infection without pneumonia. Once a majority of symptoms had resolved, she was still complaining of dyspnoea during exercises, weakness and headache. The symptoms persisted for three months, then the patient had one-hour long EECP sessions three times per week. After 10 days of the therapy, the patient noted improvement in her dyspnoea; five weeks later, she reported that she had the pre-disease physical performance.

The primary points of EECP application in patients with CRDs can be: impaired lung perfusion and diffusing capability, reduced muscular strength and endurance, increased muscular fatigue, and impaired diaphragmatic mobility. Respiratory muscle dysfunction, together with limb muscle dysfunction, is a significant problem in patients with CRDs; it contributes to the development and persistence of respiratory insufficiency [34]. Thus, the mechanism of EECP action in CRDs (Fig. 2) is likely to be a result of better perfusion of the lung tissue (improperly ventilated alveolar and bronchiolar areas), diaphragm and other respiratory muscles. M. Melin et al. (2018) [35] demonstrated that EECP can induce a response by skeletal muscle cells and increase expression of their growth factors, thus increasing muscle metabolism and ability to oxygenate muscles. These mechanisms facilitate better functional reserve of the body, which decreases in this group of diseases.

Use of EECP in endocrinology

According to study results, EECP has positive effect on glycaemic control in patients with DM2. Studies by P. Sardina et al. (2016) [36, 37] confirm that in two weeks after a course of 35 sessions, fasting glycaemia, postprandial glycaemia and glycated haemoglobin levels dropped by 12.0, 13.5, and 19.6 %, respectively. The positive change in insulin resistance index HOMA-IR after a course of EECP was −31.1 %. Also, a significant reduction in pro-inflammatory cytokine levels and advanced glycation end product lasted up to 6 months after a course of therapy. Besides, a number of studies [38, 39, 40] demonstrated positive effect of EECP on DM complications, such as diabetic retinopathy and diabetic nephropathy.

Use of EECP in neurology

Studies demonstrate improvement in cerebral blood flow and artery collateralisation in the ischaemic area after a stroke following EECP [41], so that this method can be used for the management of neurological patients. Better cerebral perfusion contributes to better metabolism of neurons and glial cells, as well as remyelination, and can affect motor function recovery in patients with upper limb palsy [42]. According to G. Kozdağ et al. (2013) [43], EECP facilitates improvements in all cognitive areas, except for verbal and visual memory tests. Q. Zhou et al. (2004) [44] were the first to notice that, among 33 patients with Parkinson's disease treated with EECP, 87.9 % demonstrated improvement in symptoms, probably due to better cerebral blood flow, which, in turn, improved performance of various neurotransmitters and receptors in dopaminergic neurons in the substantia nigra of the brain stem. Also, EECP improved insomnia due to better cerebral blood flow and modulation of respective neurotransmitters [45].

Use of EECP in ophthalmology

A retrospective analysis by Chinese scientists [46] showed positive effects of EECP in combination with drug therapy in patients with ischaemic eye diseases and stenotic carotid artery. Another study [47] demonstrated that EECP increased the mean blood velocity, end diastolic and peak systolic blood flow in ophthalmic arteries and central retinal artery in patients with ischaemic neuropathy of the optic nerve, and improved vision and haemodynamic parameters.

Use of EECP in otorhinolaryngology

In a study by C. Offergeld et al. (2000) [48], EECP therapy in patients with acute persistent hearing loss and tinnitus resulted in better blood flow in carotid arteries (by 19 %) and better blood flow in spinal arteries (by 11 %). Besides, 47 % of patients reported tinnitus improvement, 28 % of patients noted better hearing, which lasted for a year after the therapy.

Use of EECP in urology

A study by S. Froschermaier et al. (1998) [49] reported for the first time about significantly increased peak systolic blood flow in cavernous artery and subsequent improvement in erectile function, which lasted for over 6 months. Another study by W. Lawson et al. (2007) [50] demonstrated EECP efficiency in ischaemic erectile dysfunction management in patients with refractory angina. Comparison of the values of the International Index of Erectile Function before and after EECP showed improved erectile function ($p = 0.003$), satisfaction with sexual intercourse ($p = 0.009$) and overall satisfaction ($p = 0.001$). Considering that currently erectile dysfunction is treated mostly with phosphodiesterase type 5 inhibitors, which are contraindicated in patients with IHD taking nitrates, this method can be a useful alternative.

The main characteristics of EECP studies are presented in Table 2.

Table 2. *Characteristics of the EECP research*

Research	Nosology	Research design, n	Endpoints	Results
MUST-EECP (1999) [20]	CHD	Randomized, blind, placebo-controlled; n=139; 8 weeks	The duration of physical activity and the time to ST segment depression ≥1 mm, the average daily number of angina attacks and the use of nitroglycerin	An increase in the time to ST segment depression ≥1 mm (p=0,01) compared to the baseline and placebo group. Episodes of angina pectoris were less frequent in the active EECP group compared with placebo (p <0.05)
Singh et al. (2018) [21]	CHD with or without diabetes mellitus type 2	Non-randomized, uncontrolled; n=163; 12 months.	Severity of angina pectoris according to the CCS classification, severity of dyspnea on the MRC scale, indicators of glycemic control (fasting glycemia and HbA1c)	A decrease in the severity of angina pectoris and the severity of shortness of breath, a decrease in fasting glycemia and HbA1c (p < 0.001)
Subramanian et al. (2005) [22]	CHD, CHF	Non-randomized, uncontrolled; n=72; 8 weeks	LVEF, CASP, AI	An increase in LVEF compared to the baseline level after the course of EECP (p <0.001). A decrease in CASP, AI with normal blood pressure, an increase in CASP, AI with low blood pressure and left ventricular dysfunction (p <0.05)
Sardari et al. 2018 [23]	CHD, CHF	Non-randomized, uncontrolled; n=34; 7 weeks	LVEF, duration of physical activity, workload	After the course of EECP, LVEF, maximum workload and duration of physical activity increased compared to the baseline level (p <0.001)
Wu et al. (2013) [24]	CHD	Non-randomized, uncontrolled; n=34; 6 months	Exercise tolerance (6MWT), quality of life (SF-36), severity of angina pectoris according to the CCS classification	After the course of EECP, exercise tolerance increased compared to the baseline level, quality of life improved and the severity of angina pectoris decreased (p <0.001)
EXCEL (2024) [25]	CHD, CHF	Randomized, placebo-controlled; n=120; 36 months	Exercise tolerance (6MWT), quality of life (MLHFQ and SF-36), functional parameters of the vascular bed (capillaroscopy) and heart (LVEF), adverse cardiovascular clinical outcomes	An increase in exercise tolerance, quality of life, functional parameters of the vascular bed and heart (p < 0.05) compared with the baseline and placebo group, as well as a decrease in the incidence of adverse outcomes

Table 2. Continued

Research	Nosology	Research design, n	Endpoints	Results
Badtieva et al. (2019) [28]	Obliterating athero-sclerosis of the vessels of the lower extremities	Non-randomized, controlled; n=68; 7 weeks	The frequency of characteristic complaints, the pain-free walking distance, the state of peripheral hemodynamics, the ankle-shoulder index	A decrease in the severity of symptoms in the EECP group, an increase in the pain-free walking distance, an improvement in peripheral hemodynamics and an increase in the ankle-shoulder index ($p < 0.05$)
Liang et al. (2021) [29]	Arterial hyperten-sion of the 1st degree	Randomized, controlled; n=40; 7 weeks	Blood pressure, FDV, EPC	A decrease in systolic and diastolic blood pressure, an increase in the value of FDV and an improvement in EPC function ($p < 0.05$)
Zhao et al. (2020) [30]	COPD	Randomized, controlled; n=72; 3 months	Physical endurance: anaerobic threshold oxygen uptake, maximum oxygen uptake, anaerobic threshold impulse, anaerobic threshold metabolic equivalent and maximum metabolic equivalent (CPST)	Compared with the baseline and the control group, indicators of physical endurance increased ($p < 0.05$)
Sathy-amoorthy et al. (2021) [31]	Long-Covid	Non-randomized, uncontrolled; n=16; 5 months	Exercise tolerance (6MWT), severity of shortness of breath on the Rose scale, DASI activity index, quality of life (SAQ and PHQ-9), fatigue (PROMIS), severity of angina pectoris according to the CCS classification	After the course of EECP, exercise tolerance increased compared to the baseline level ($p=0.002$), the severity of shortness of breath decreased, the indicators of the DASI activity index, quality of life improved and the severity of angina pectoris decreased ($p < 0.001$)
Nikolaeva et al. (2023) [32]	Chronic lung diseases with ventilation disorders	Non-randomized, uncontrolled; n=30; 4 weeks	Pulmonary volumes, lung diffusion capacity, exercise tolerance (CPST, 6MWT)	After the course of EECP, an increase in total lung capacity was observed, and exercise tolerance increased compared to the baseline level ($p < 0.001$). There was no significant dynamics in the diffusion capacity of the lungs
Sardina et al. (2016) [36, 37]	Diabetes mellitus type 2	Randomized, controlled; n=30; 3 and 6 months	Fasting plasma glucose, postprandial glycemia, HbA1c	A decrease in glycemic control indicators compared to the baseline level and the control group ($p < 0.05$)
Yang et al. (2013) [46]	Ischemic ophthal-mopathy	Non-randomized; controlled; n=65; 2 months	Visual acuity, visual fields and optical hemodynamics	Improvement of visual acuity, visual fields and optical hemodynamics compared to baseline and control group ($p < 0.05$)
Zhu et al. (2015) [47]	Front ischemic optic neuropathy	Non-randomized, uncontrolled; n=16; 2 weeks	The average blood flow rate, peak systolic velocity and final diastolic velocity in the ocular artery and central retinal artery, the value of intraocular pressure, visual fields and visual acuity	An increase in the blood flow rate in the ocular artery and central retinal artery, a decrease in intraocular pressure, an increase in visual fields and visual acuity ($p < 0.05$)

Table 2. *The end*

Research	Nosology	Research design, n	Endpoints	Results
Offergeld et al. (2000) [48]	Diseases of the inner ear	Non-randomized, uncontrolled; n=33; 12 months	The volume of blood flow in the internal carotid arteries and in the vertebral arteries, the intensity and/or appearance of noise and the audibility threshold (audiogram)	An increase in blood flow in the internal carotid arteries and in the vertebral arteries, a decrease in the intensity and/or appearance of tinnitus, an increase in the hearing threshold ($p < 0.05$)
Froschermaier et al. (1998) [49]	Erectile dysfunction	Non-randomized, uncontrolled; n=13; 3 weeks	Penile rigidity, peak systolic blood flow and erection quality	Increased penile rigidity, peak systolic blood flow and erection quality ($p < 0.05$)
Lawson et al. (2007) [50]	CHD, erectile dysfunction	Non-randomized, uncontrolled; n=120; 7 weeks	International Index of Erectile Function, DASI activity index	Improvement of erectile function ($p < 0.05$) and DASI activity index. There were no significant changes in orgasmic function and sexual desire

Note: EECP — enhanced external counterpulsation; CHD — coronary heart disease; CHF — chronic heart failure; CASP — central aortic systolic pressure; AI — augmentation index; FDV — flow-dependent vasodilation; EPC — endothelial progenitor cells; COPD — chronic obstructive pulmonary disease; LVEF — left ventricular ejection fraction; CPST — cardiopulmonary stress test; 6MWT — 6-minute walking test

Conclusion

EECP has been used as a support therapy for decades, and it has proven its efficiency and safety in management of various diseases. In recent years, great achievements have been made in understanding the physiological mechanisms of its effects for the body in some CNCDs, including IHD, CCI, DM2, COPD, etc. Nonetheless, a lot of aspects of this method in clinical settings are still unclear and require further studies in order to assess EECP capabilities and evaluate long-term effects. Also, a range of indications is growing. A promising area is the study of EECP efficiency in CNCDs, such as systemic connective tissue disorders and kidney diseases.

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